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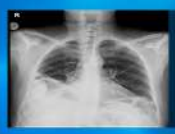

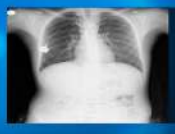

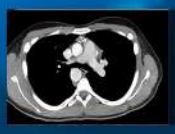

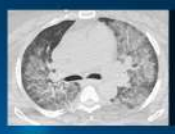

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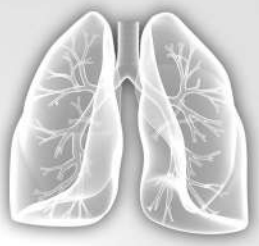

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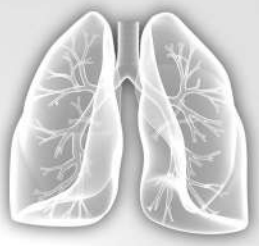

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RESPIRATORY CASE REPORTS

Tuberculous Empyema and *Candida tropicalis*: A Rare Co-infection of Two Different Pathogens

Tüberküloz Ampiyemi ve Candida tropicalis: İki Farklı Patojenin Nadir Bir Koenfeksiyonu

Esra Birekul[1], Atilla Can[1], Halil Şen[2], Burcu Yormaz[3], Hüseyin Yıldıran[1]

Abstract

In most cases, empyema develops pathophysiologically as a result of untreated and uncontrolled parapneumonic pleural effusion. Such cases may be treated with various interventional procedures depending on the amount of fluid, such as thoracentesis or chest tube drainage, supported by pathogen-targeted antibiotic therapy. The underlying infectious cause of empyema is often viral or bacterial, while fungal-related empyema is much rarer. The presented case is of particular interest due to the simultaneous occurrence of fungal and tuberculosis empyema.

Keywords: *Empyema, Pleural Effusion, Candida Tropicalis, Tuberculosis.*

Öz

Ampiyem, patofizyolojik olarak çoğunlukla tedavi almamış ve kontrol edilememiş parapnömonik pleral efüzyon sonucu gelişir. Etkene yönelik antibiyoterapi ile birlikte sıvı miktarına bağlı olarak sıvının torasentez ile boşatılması, göğüs tüpü ile drenajı gibi farklı girişimsel işlemler gerekebilir. Altta yatan enfeksiyöz neden çoğunlukla viral ya da bakteriyal olmakla birlikte mantara bağlı ampiyem oldukça nadirdir. Sunulan olgu eş zamanlı mantar ve tüberküloz ampiyemi görülmesi nedeniyle ilginçtir.

Anahtar Kelimeler: *Ampiyem, Plevral Efüzyon, Candida Tropicalis, Tüberküloz.*

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Empyema is the term given to accumulations of infected fluid in the pleural space, occurring due to such pulmonary infections as pneumonia and lung abscesses, or conditions such as bronchiectasis, previous thoracic surgery, septic pulmonary embolism, trauma, mediastinitis, malignancy, esophageal perforation, spontaneous pneumothorax and sepsis (1). The most common causative agents of empyema are *Streptococcus pneumoniae*, anaerobes and *Staphylococcus aureus* (2), while tuberculosis is one of the most frequent causes of pleural effusion in developing countries (3). In rare cases, fungal pathogens, as opportunistic infections, can lead to empyema. The most common predisposing factors to candida-induced empyema are a history of thoracic or abdominal surgery and esophageal perforation (4), although it may also develop secondary to bronchopulmonary infections (5). Various treatments can be proposed following a diagnosis empyema depending on factors such as the patient's clinical condition and the amount of fluid involved, although medical therapy combined with fluid drainage is the standard approach (6).

CASE

A 58-year-old male patient presented to the emergency department with complaints of dyspnea and right-sided chest pain. A physical examination revealed the patient to be in good general condition, conscious, oriented and cooperative. Peripheral oxygen saturation was 87%, blood pressure was 120/75 mmHg and heart rate was 89 beats per minute. The patient had been diagnosed with laryngeal squamous cell carcinoma two years prior and had been treated with chemotherapy and radiotherapy, and a tracheostomy had been performed 1 year later. He was not on any regular medication. Rales were present in the right hemithorax on auscultation, and an arterial blood gas analysis revealed pH: 7.47, pCO_2: 24 mmHg and pO_2: 59 mmHg. Hematologic tests showed WBC: 20.21 K/uL and HGB: 9.7 g/dL. Posteroanterior (PA) chest X-ray showed increased consolidation and pleural effusion in the lower zone of the right hemithorax (Figure 1). A thoracic computed tomography (CT) scan revealed an area of consolidation with air bronchogram in the right lower lobe as well as pleural effusion (Figures 2, 3, and 4). Diagnostic thoracentesis was performed, and an analysis of the aspirated purulent fluid revealed LDH: 32,768 U/L, albumin: 0.8 g/dL and total protein: 2.7 g/dL. Simultaneous serum results were LDH: 196 U/L, albumin: 3.4 g/dL, and total protein: 6.9 g/dL. Tube thoracostomy was performed to address the right-sided empyema (Figure 5), and 1200 cc of purulent fluid was drained. The patient underwent fiberoptic bronchoscopy, and bronchoalveolar lavage (BAL) was obtained.

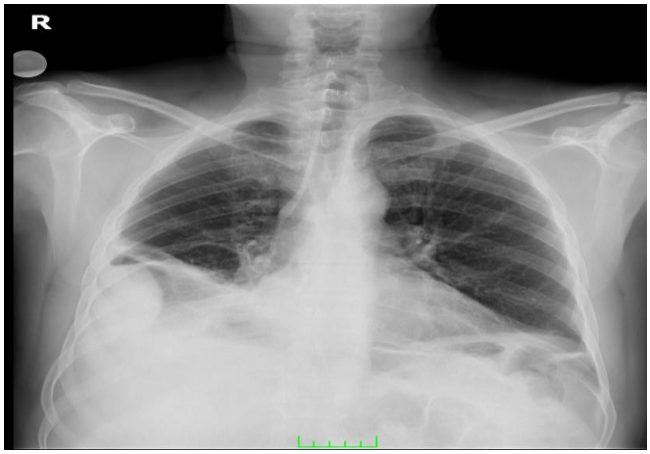

Figure 1: *Pleural effusion in the right hemithorax*

No bacterial growth was detected in the BAL culture; however, the galactomannan antigen was reported as positive. *Candida tropicalis* growth was detected in the culture of the thoracentesis sample. To rule out the possibility of contamination, a repeat sample from the pleural fluid was sent, again revealing *Candida tropicalis*, and so the appropriate antifungal therapy was initiated. Subsequent tuberculosis tests of the pleural fluid revealed the growth of *Mycobacterium spp*. on Löwenstein-Jensen medium. A sputum sample was collected for acid-fast bacilli (AFB) staining and was found to be AFB $^{++}$.

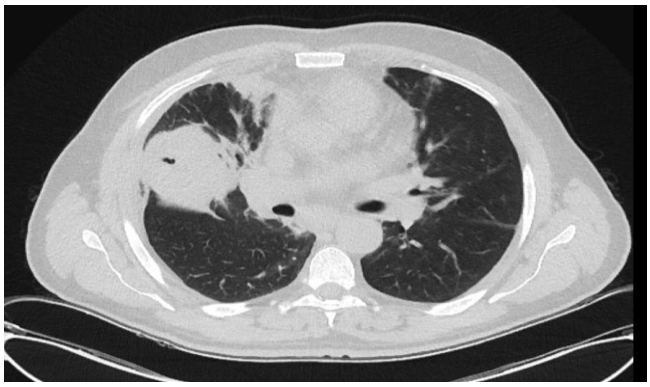

Figure 2: *Increased consolidation in the right lower lobe of the lung (Lung window)*

The samples were subsequently sent to the National Tuberculosis Reference Laboratory of the General Directorate of Public Health (HSGM). PCR analysis detected *M. tuberculosis* complex DNA. The patient's treatment regimen included Pyrazinamide 500 mg 4 times/day, Rifampicin 300 mg 2 times/day, Ethambutol 500 mg 3 times/day and Isoniazid 300 mg once/day. Following the completion of empyema treatment, the chest tube was removed (Figure 6) and the patient was discharged 16 days after admission. He is continuing with antituberculosis treatment and followed up by the Chest Diseases and Tuberculosis Dispensary.

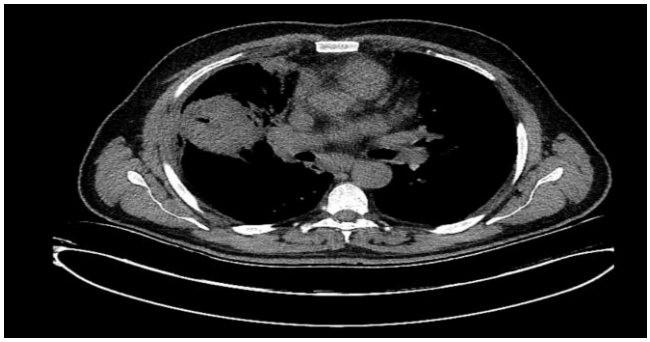

Figure 3: Increased consolidation in the right lower lobe of the lung (Mediastinal window)

DISCUSSION

Although the etiology of empyema is multifactorial, the majority of cases arise from bacterial pneumonia and the associated parapneumonic effusion. Of the approximately 1 million patients hospitalized annually for pneumonia, an estimated 20–40% develop parapneumonic effusion and 5–10% develop empyema, revealing the significance of empyema as a health issue (7). Although there are no specific symptoms of empyema, shortness of breath, pleuritic chest pain and cough are common symptoms. Physical examination can reveal a decrease in breath sounds in the hemithorax affected by empyema, and subsequent radiological investigations, including chest X-ray and thoracic CT, will be required. Chest X-ray will reveal bluntness in the sinuses and increased consolidations in the empyema-affected hemithorax (6). Thoracentesis plays a crucial role in the diagnosis of empyema, while fluid samples sent for analysis are important for pathogen identification. Studies have shown the most common cause of empyema to be parapneumonic effusion resulting from bacterial or viral pneumonia, while effusions caused by opportunistic microorganisms and leading to empyema are less common.

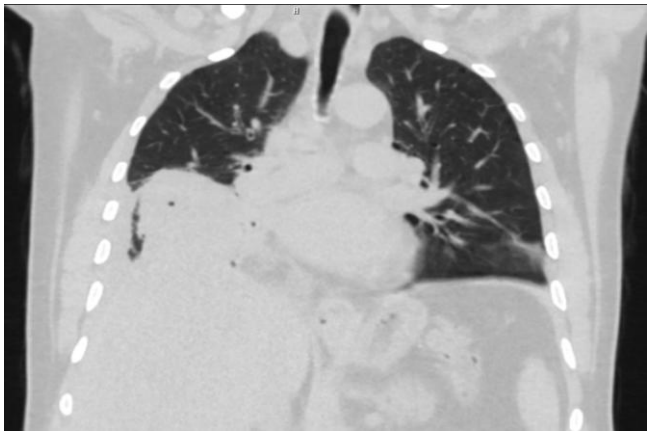

Figure 4: Increased consolidation and pleural effusion in the right lower lobe of the lung

Pleural tuberculosis can be acute or subacute, with symptoms including cough, chest pain, fever, loss of appetite, weight loss, night sweats and variable degrees of shortness of breath. Tuberculosis-related pleural effusions are usually unilateral (8). Candida species are common microorganisms in the environment and are part of the normal flora of the human body. However, under certain conditions, they can become opportunistic pathogens and cause infections (9). *Aspergillus fumigatus* is the most common pathogen responsible for fungal pleural empyema, although other emerging forms, such as *Histoplasmosis, Coccidioidomycosis, Blastomycosis, Paracoccidioidomycosis, Cryptococcosis, Mucormycosis and Monosporiosis, as well as Fusarium, Pseudoallescheria boydii, Paecilomyces, Scopulariopsis, Penicillium marneffei, Pneumocystis carinii, Actinomyces and Nocardia*, have also been identified as pulmonary pathogens (10). The increasing number of immunocompromised patients, the rise in intensive care unit admissions and the over-reliance on broad-spectrum antibiotics have led to an increase in fungal empyema cases (5). Candida infections are also common causes of fungal empyema, and while *Candida albicans* is the most frequent pathogen (11), *Candida tropicalis* has emerged as another fungal empyema pathogen, although cases are rare. Candida infections have been linked to the increased use of invasive devices and the changes in gastrointestinal flora resulting from the use of broad-spectrum antibiotics (5).

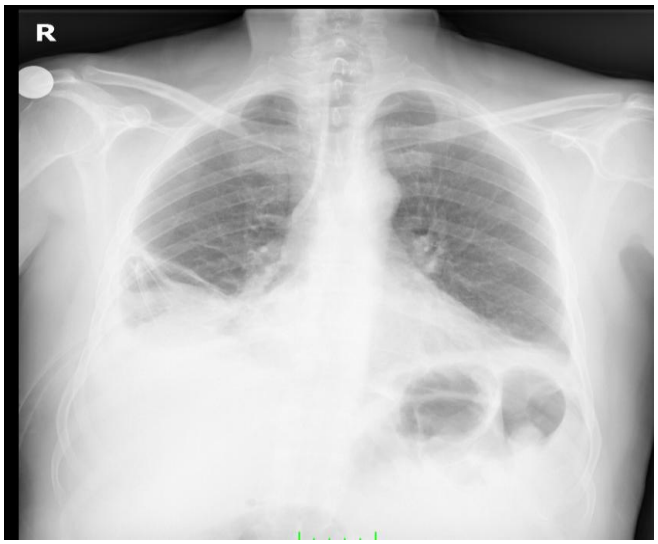

Figure 5: Post-procedure image of the patient's right tube thoracostomy

In a case reported by Sahu et al. (12) in 2020, pleural effusion samples obtained for the investigation of empyema showed growth of *Candida albicans, Candida tropicalis, Candida glabrata and Candida krusei*. In our case, *Candida tropicalis*, a rare pathogen, was isolated from the purulent fluid sample obtained via diagnostic thoracentesis, and *Mycobacterium spp*. on Löwenstein-Jensen medium was identified in the pleural fluid sent for tuberculosis culture. The clinical course of the patient was thought to have developed as a *Candida tropicalis* infection on a tuberculosis background. Pleural empyema caused by Candida species is extremely rare, particularly cases involving non-albicans Candida species such as *Candida tropi-*

calis, with only a limited number of reports in the literature to date. Such cases usually arise in patients with underlying immunodeficiency, prolonged antibiotic use, malignancy or long-term intensive care unit stays.

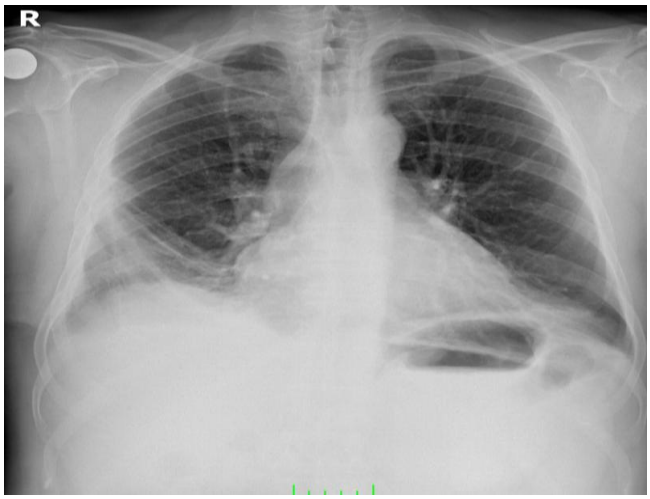

Figure 6: Control chest X-ray after chest tube removal

CONCLUSION

Although rare, the potential of *Candida tropicalis* in the etiology of pleural empyema in cases with tuberculosis-induced immunosuppression serves as an important reminder that fungal pathogens should not be overlooked, particularly when complicated pulmonary infections are encountered. Further case presentations of rare infections such as *Candida tropicalis*-induced pleural empyema are needed, given the limited number of cases reported in the literature to date, as this will help improve our understanding of the epidemiology and treatment of this rare condition and expand the knowledge base in this field.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - E.B., A.C., H.Ş., B.Y., H.Y.; Planning and Design - E.B., A.C., H.Ş., B.Y., H.Y.; Supervision - E.B., A.C., H.Ş., B.Y., H.Y.; Funding - ZE.B., A.C., H.Ş., B.Y., H.Y.; Materials - E.B., A.C., H.Ş., B.Y., H.Y.; Data Collection and/or Processing - E.B., A.C., H.Ş., B.Y., H.Y.; Analysis and/or Interpretation - E.B., A.C., H.Ş., B.Y., H.Y.; Literature Review - E.B., A.C., H.Ş., B.Y., H.Y.; Writing - E.B., A.C., H.Ş., B.Y., H.Y.; Critical Review - E.B., A.C., H.Ş., B.Y., H.Y.

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Non-Thrombotic Pulmonary Embolism Due to Catheter Fracture in a Case of Hemophilia

Hemofili Olgusunda Kateter Kırığına Bağlı Trombotik Olmayan Pulmoner Emboli

Ersin Erdem Demirtaş[1], Selvi Aşkar[1], Müntecep Aşkar[2], Rasa Beyzaei Oskouei[3]

Abstract

Central venous catheter complications are rare in patients with hemophilia, but should not be ignored. A 19-year-old male with hemophilia who presented with hemoptysis was found to have a 7 cm catheter fragment lodged in his pulmonary artery. Despite the chronic presence of this foreign object, no pulmonary hypertension developed over a 3-year follow-up. The conservative management option was selected due to the risks associated with invasive procedures in hemophilia. This report highlights the significance of long-term monitoring and individualized care in patients with retained intravascular foreign bodies.

Keywords: *Hemophilia, Central Venous Catheter, Catheter Fracture, Pulmonary Embolism, Pulmonary Hypertension, Foreign Body.*

Öz

Santral venöz kateter komplikasyonları hemofili hastalarında nadir ancak önemli sorunlardır. Bu olgu sunumunda, hemoptizi şikâyeti ile başvuran ve pulmoner arterde 7 cm uzunluğunda kateter parçası saptanan 19 yaşında bir erkek hasta sunulmaktadır. Bu yabancı cismin kronik varlığına rağmen, üç yıllık takip süresince pulmoner hipertansiyon gelişmemiştir. Hemofili tanısı olan hastada invazif prosedürlerin riskleri nedeni ile konservatif tedavi tercih edilmiştir. Bu olgu, intravasküler yabancı cisim bulunan hastalarda uzun süreli takip ve kişiselleştirilmiş bakımın önemini vurgulamaktadır.

Anahtar Kelimeler: *Hemofili, Santral Venöz Kateter, Kateter Kırılması, Pulmoner Emboli, Pulmoner Hipertansiyon, Yabancı Cisim.*

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Hemophilia is a genetic disorder characterized by a defect in the normal blood clotting mechanism that increases the tendency for spontaneous or traumatic bleeding in patients. Central venous catheter (CVC) use is common in patients with hemophilia due to the need for frequent intravenous therapy. However, CVCs can cause complications such as infection, thrombosis, embolism and, in rare cases, catheter fracture (1). The present study reports on a patient with hemophilia who presented with hemoptysis and a foreign body lodged in the pulmonary artery resulting from a CVC fracture.

CASE

A 19-year-old male patient was admitted to the chest diseases outpatient clinic with a complaint of blood coming from the mouth (hemoptysis). Chest radiography revealed a 7 cm linear opacity with a smooth border in the central zone of the right lung (Figure 1). An analysis of the patient's previous imaging records revealed that the opacity had been present for approximately 4 years, before which, the catheter opacity was kinked but was seen as a whole (Figure 2). It was learned from the patient's history that he had been followed up with a diagnosis of hemophilia and had been carrying a CVC for approximately 12 years. When the removal of the CVC was planned, it was found that the catheter was detached and a piece of it remained in the intravascular system. A thoracic CT scan with and without contrast revealed a 7 cm long foreign body in the pulmonary artery that was thought to be a catheter fragment (Figure 3). The patient was duly evaluated for pulmonary hypertension and a transthoracic echocardiography was performed, the results of which were within normal limits. An angiographic intervention was planned for the removal of the catheter fragment, but was abandoned due to its organization, the risk of embolization and the patient's hemophilia. The patient was subsequently followed up clinically and radiologically. Low-dose antithrombotic therapy was administered initially, but was discontinued after 3 months. The patient has been followed up in the pulmonary hypertension outpatient clinic for approximately 3 years without any clinical deterioration or pulmonary hypertension development.

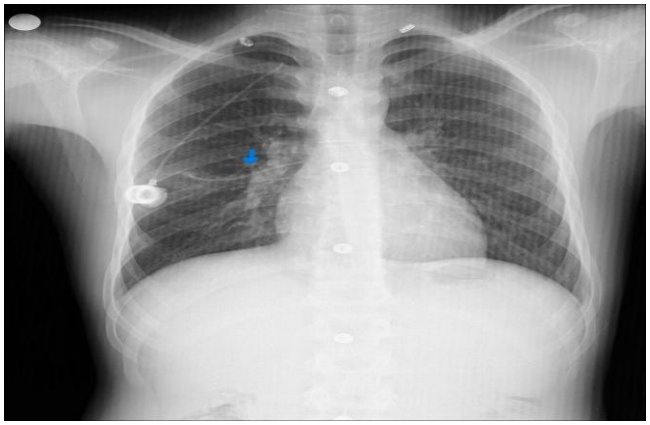

Figure 1: Chest radiography revealed a 7 cm linear opacity with a smooth border in the middle zone of the right lung

DISCUSSION

Central venous catheters are vital for patients with chronic intravenous therapy needs, such as those with hemophilia; however, risks such as mechanical complications, infection and thrombosis may occur with prolonged catheter use. Non-thrombotic pulmonary embolism associated with catheter fracture is a rare but potentially serious condition, and although surgical or endovascular intervention is usually recommended in such cases, follow-up was preferred in the presented case due to his coagulopathy. A foreign body in the pulmonary artery may organize over time, leading to chronic pulmonary embolism or pulmonary hypertension. Previous studies have reported an association between foreign body embolization and pulmonary hypertension, with inflammation, fibrosis and increased vascular resistance in the pulmonary vessel wall (2). El-Heis et al. (3) reported a remarkable case in which a fractured catheter fragment remained lodged in the pulmonary artery for 16 years before detection and clinical evaluation.

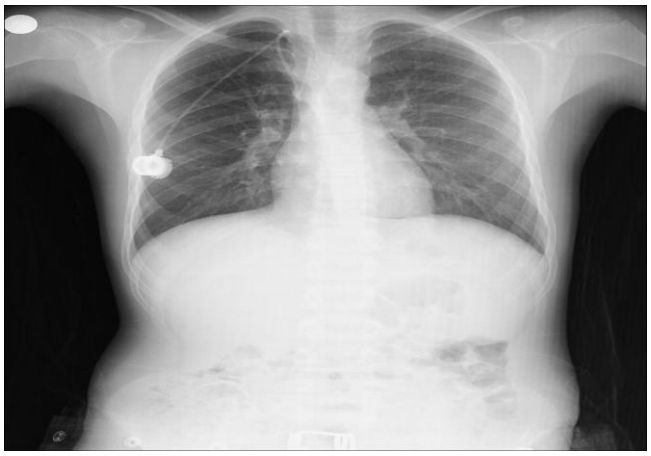

Figure 2: Four years earlier, the catheter opacity was kinked but could be seen as a whole

This highlights the potential for long-term retention of catheter fragments without immediate life-threatening complications, although such cases still carry significant risk of pulmonary hypertension, hemoptysis or embolic phenomena. Similar cases have been reported in the literature. Thanigaraj et al. (4) described a patient in whom a peripherally inserted central catheter (PICC) fragment embolized to the pulmonary artery and remained there for 11 years before successful retrieval. Likewise, Dell'Amore et al. (5) reported a case of peripheral venous catheter fracture with pulmonary artery embolization that was retrieved surgically. These reports highlight the diverse management strategies that may be employed when dealing with embolized catheter fragments. Shrestha et al. (6) successfully removed a catheter fragment from a pulmonary artery using an endovascular method. In our case, the organization of the catheter fragment led to a decision for conservative follow-up, given the high risk of invasive intervention in patients with hemophilia. In this respect, our case differs from other cases in terms of management preference, and emphasizes the importance of an individualized approach when dealing with patients with concomitant bleeding diatheses such as hemophilia.

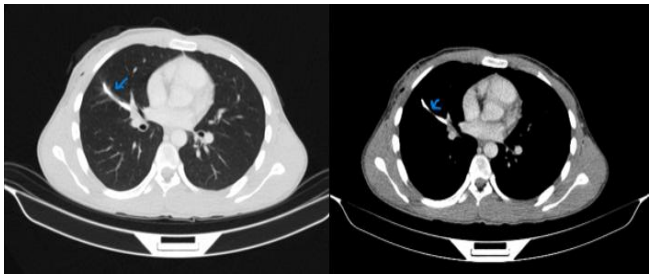

Figure 3: Thoracic CT scan without contrast showed a 7 cm long foreign body in the pulmonary artery, which was thought to be a catheter fragment

CONCLUSION

Foreign body embolization due to CVC fracture is a rare condition and can be difficult to manage in certain patient groups, such as those with hemophilia. While pulmonary hypertension and bleeding complications have been observed in similar cases reported in the literature, no such complications developed in our case, which may be attributable to patient-based variables and differences in the organization of the foreign body. The present case can be considered remarkable due to the non-thrombotic pulmonary embolism, and highlights the importance of long-term follow-up, the early detection of complications and individualized treatment approaches. Invasive intervention decisions in cases of foreign body embolization should be evaluated with a multidisciplinary approach, taking into account the patient's general condition, comorbidities and bleeding risk.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - E.E.D., S.A., M.A., R.B.O.; Planning and Design - E.E.D., S.A., M.A., R.B.O.; Supervision - E.E.D., S.A., M.A., R.B.O.; Funding - E.E.D., S.A., M.A., R.B.O.; Materials - E.E.D., S.A.; Data Collection and/or Processing - E.E.D., S.A., M.A.; Analysis and/or Interpretation - E.E.D., S.A., M.A.; Literature Review - E.E.D., S.A., M.A.; Writing - E.E.D., S.A., M.A.; Critical Review - E.E.D., S.A., M.A.

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Rare Vasculo-pathologies in a Case with Klinefelter Syndrome: Pulmonary Embolism, Right Aortic Arch and Aberrant Subclavian Artery

Klinefelter Sendromlu Bir Olguda Nadir Vasküler Patolojiler: Pulmoner Emboli, Sağ Aortik Ark ve Aberran Subklaviyen Arter

Alev Yıldırım[1], Coşkun Doğan[1], Zeynep Nihal Kazcı[2], Gönül Seven Yalçın[1]

Abstract

Klinefelter syndrome (KS) is a sex chromosome abnormality characterized by a 47, XXY karyotype. While the exact cause of the condition remains unknown, the incidence of pulmonary embolism (PE) is higher in KS patients. Several hypotheses have been put forward to explain this condition, including hypogonadism, which leads to hormonal imbalances due to low testosterone levels and an increased estrogen-to-testosterone ratio, as well as testosterone deficiency and the associated adverse effects on the vascular endothelium. A number of congenital cardiovascular anomalies have been reported in the literature in patients with KS. That said, no cases involving a right-sided aortic arch and aberrant subclavian artery have been reported to date. We present here the case of a patient who was admitted to our clinic with a PE after being diagnosed with KS, and with a right aortic arch and an aberrant subclavian artery anomaly.

Keywords: *Aberrant Subclavian Artery, Klinefelter Syndrome, Pulmonary Embolism, Right-Sided Aortic Arch.*

Öz

Klinefelter sendromu (KS), bir seks kromozomu anomalisi olup, çoğunlukla 47, XXY karyotipi ile karakterizedir. Her ne kadar kesin olarak sebebi bilinmese de Pulmoner Emboli (PE) insidansının KS'li olgularda arttığı bilinmektedir. KS'li olgularda hipogonadizm sonucu serum testosteron düzeyleri yetersiz seviyelerde seyretmesinin bir hormonal dengesizliğe yol açması, östrojen/testosteron oranı artması, testosteron eksikliğinin, damar endoteli üzerinde olumsuz etkilere yol açması gibi birden fazla hipotez ile durum açıklanmaya çalışılmaktadır. Yine KS'li olgularda şu ana kadar literatürde bildirilen çok sayıda konjenital kardiyovasküler anomali var iken Sağ Aortik Ark ve Aberran Subklavian Arter anomalisi bildirilmemiştir. Burada, KS tanısı aldıktan sonra PE teşhisi ile kliniğimize yatan ve bu sırada Sağ Aortik Ark ve Abberan Subklavian Arter anomalisi tespit edilen bir olgu paylaşılmıştır.

Anahtar Kelimeler: *Abberan Subklavian Arter, Klinefelter Sendromu, Pulmoner Emboli, Sağ Aortik Ark.*

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Klinefelter syndrome (KS) is the most common sex chromosome abnormality in males and is most frequently characterized by a 47, XXY karyotype. The most common clinical findings include reduced testicular volume, hypogonadism, infertility, gynecomastia and tall stature. During adolescence, many patients experience subnormal serum testosterone levels as a result of hypogonadism, which can lead to such symptoms as decreased muscle mass, low bone mineral density, fatigue, loss of libido and depression (1).

The most significant risk factors for PE include a history of venous thromboembolism, lower extremity fractures, hip or knee arthroplasty, major trauma, recent hospitalization within the past 3 months due to heart failure or atrial fibrillation, recent myocardial infarction and spinal cord injury (2). Although the exact cause is not known, KS patients have a predisposition to PE. The increased procoagulant PAI-1 (plasminogen activator inhibitor-1) levels in KS patients associated with their genetic structure and low testosterone levels significantly increase the risk of PE. The risk of venous thromboembolic events is approximately three to six times higher in KS patients than in the general population (3). We present here the case of a 27-year-old patient with Klinefelter syndrome (KS) who was newly diagnosed with pulmonary embolism (PE), along with pectus excavatum, a right-sided aortic arch and an aberrant subclavian artery. We introduce this case to the literature, given the rarity of the coexistence of PE alongside these vascular anomalies in association with KS.

CASE

A 27-year-old male patient who had undergone a right radical orchiectomy 1 month earlier and was diagnosed with KS was admitted to the emergency department following the sudden onset of right-sided chest pain, shortness of breath and palpitations. On inspection, his vital signs were within normal ranges, while a physical examination revealed the patient to have a tall and thin phenotype, measuring 185 centimeters in height and 70 kilograms in weight, with a calculated body mass index (BMI) of 20.45. The patient was also noted to have a pectus excavatum deformity (PED) (Figure 1). Auscultation revealed crackles at the base of the right lung, and a posteroanterior chest radiograph showed an oligemic appearance in the right hemithorax and a right-sided aortic arch (Figure 2). Thoracic computed tomography angiography (CTA) revealed a filling defect consistent with pulmonary embolism (PE) in a segmental branch of the right lung, as well as a ground-glass opacity in the right lower lobe that was consistent with infarction.

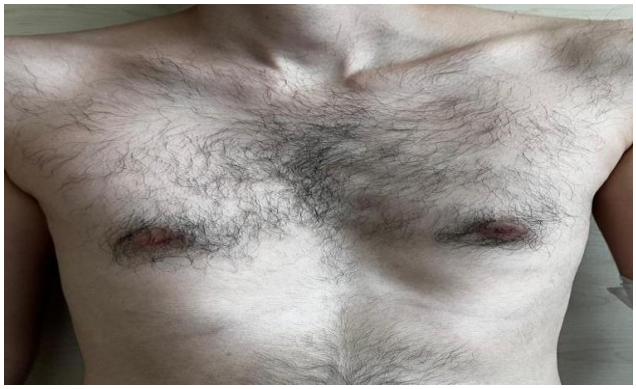

Figure 1: Pectus excavatum deformity observed phenotypically in the patient.

Aside from the pectus excavatum deformity (PED), the patient was also noted to have a right-sided aortic arch variation (RAAV) and an aberrant subclavian artery (ASA) (Figures 3 and 4). Laboratory tests (Table 1) revealed elevated serum C-reactive protein (CRP), D-dimer and mildly increased estradiol (E2) levels. No other abnormalities were detected (CRP: 37.4, D-Dimer: 0.87, E2: 43.9). Further anamnesis revealed that the patient had been diagnosed with Klinefelter syndrome (KS) following genetic testing conducted due to a decrease in testicular size and the presence of a palpable lesion in the testis 1 month prior (Figure 5). The histopathological report reported the orchiectomy specimen to be a "Benign Leydig cell tumor". Based on these findings (KS, PE, PED, AAV, ASA), the patient was admitted to the Chest Diseases Department for further evaluation and treatment. The PE severity index (PESI) score was 37, corresponding to class 1. The patient was started on low molecular weight heparin treatment at a therapeutic dose, a medical genetics consultation was requested and a thrombophilia panel was sent. Bilateral lower extremity venous Doppler ultrasonography was reported as normal, and echocardiography revealed no pathology other than mild mitral regurgitation. Cardiac enzymes (troponin and BNP) were normal. The patient was considered low-risk for PE and discharged with oral anticoagulation and coagulation profile follow-up. Informed consent for this report was obtained from the patient.

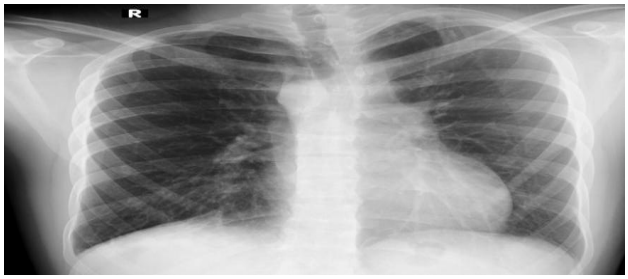

Figure 2: Posteroanterior chest radiograph taken at presentation showing increased aeration (oligemic appearance) in the right hemithorax and a right-sided aortic arch.

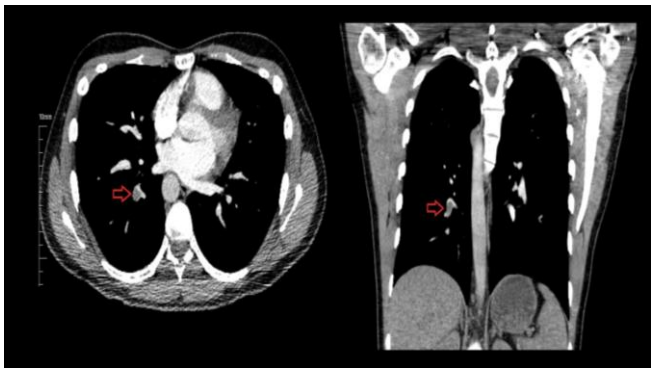

Figure 3: Thoracic computed tomography angiography (CTA) of the patient revealing a filling defect compatible with PE in a segmental branch of the right lung

DISCUSSION

Described here is the case of a 27-year-old male with Klinefelter syndrome (KS) who was diagnosed with pulmonary embolism (PE) in the absence of any known major risk factors. We present this case to the literature to highlight the increased predisposition to PE in individuals with KS, as well as the potential for accompanying anatomical anomalies. The numerous risk factors for pulmonary embolism (PE) that have been identified are generally categorized into three main groups, representing major, intermediate or minor risks (Table 2) (4). Major risk factors, such as significant trauma, prior PE and lower extremity fractures, are associated with up to a 10-fold increase in PE risk. Hormone replacement therapy, oral contraceptive use and chemotherapy, on the other hand, are classified as intermediate risk factors and have been reported to increase the risk 2–9-fold. It has long been known that estrogen increases the risk of venous thromboembolism, and consequently PE, by elevating procoagulant factors, suppressing the natural anticoagulant systems and reducing fibrinolytic activity (5). Patients with KS are more likely to develop pulmonary embolism (PE) than the general population, and most are under the age of 30 years. Studies have also reported an increased incidence of PE in individuals with KS, which is, in turn, considered a persistent risk factor for recurrent PE (6-8). Many hypotheses have been put forward to explain the predisposition to PE of patients with KS (high homocysteine levels, antithrombin III, protein C and S deficiency, vascular abnormalities, decreased muscle mass and decreased physical activity making venous return difficult, genetic variations on the X chromosome affecting the F8 and F9 genes and coagulation pathways, etc.). The most widely accepted hypothesis suggests that elevated PAI-1 promotes a prothrombotic state by inhibiting the tissue plasminogen activators, thereby reducing the conversion of plasminogen to plasmin and impairing fibrinolytic mechanisms (9). Studies have also shown that men with KS exhibit relative hyperestrogenism, with higher estradiol/testosterone ratios when compared to controls (10). This hyperestrogenic state may play a role in the development of thromboembolic disease in KS patients, as estrogen can alter the levels of procoagulant and anticoagulant proteins, particularly in the presence of inherited thrombophilia (9,11). It has been reported in the literature that testosterone replacement therapy can increase the risk of thrombosis, especially in young men (12). However, the fact that the presented case had never received testosterone therapy suggests that the pathogenesis of KS-related thrombosis is much more complex, and that the risk is higher in the early period. A review of previous studies of vascular anomalies in KS reveals reports of both anatomical anomalies (such as portal vein aneurysms and cerebellar arteriovenous malformations) and functional vascular abnormalities (including arterial narrowing and endothelial dysfunction). However, to the best of our knowledge, there have to date been no studies reporting an association between congenital anomalies such as pectus excavatum (PED), right-sided aortic arch (RAAV) or aberrant subclavian artery (ASA) and KS (13–16). A review article by Calogero et al. (17) listed a number of cardiovascular anomalies observed in patients with KS, including mitral valve prolapse, acute mitral regurgitation, bilateral internal carotid artery hypoplasia, bilateral vertebral artery dilatation, hypertrophic cardiomyopathy, atrial and ventricular septal defects, partial anomalous pulmonary venous return, pulmonary hypertension, tricuspid regurgitation and patent ductus arteriosus.

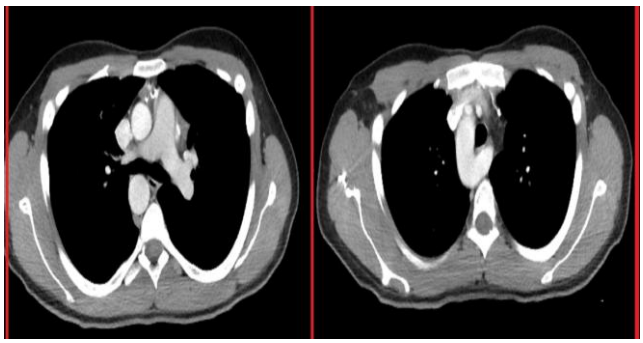

Figure 4: Thoracic computed tomography angiography (CTA) showing a right-sided aortic arch variation and an aberrant subclavian artery

Table 1: Laboratory values of the case

Parameter	Result	Reference	Parameter	Result	Reference
WBC (103uL)	7	4 -10	CRP (mg/L)	37.4	0 – 5
Hemoglobin (g/dL)	12.7	12-16	Procalcitonin (μg/L)	0.063	<0,5
Hematocrit (%)	38	36 – 47	D-dimer	0.87	<0,50
Urea (mg/dL)	16	16.6 - 48.5	Glucose (mg/dL)	110	74 – 106
Kreatinin (mg/dL)	0.85	0.5 - 0.9	Total Bilirubin (mg/dL)	0.95	0 - 1.2
ALT (U/L)	13	0 – 33	Sodium (mmol/L)	142	135-145
AST (U/L)	11	0 – 32	Potassium (mmol/L)	3.8	3,1 - 5,1
Estradiol E2 (ng/L)	43.9	11.3-43.2	Progesterone (ng/mL)	0.55	0.15-1.0

ALT: Alanin Amino Transferaz, AST: Aspartat Amino Transferaz, CRP: Serum Reaktif Protein, LDH: Laktat Dehidrogenaz, WBC: White Blood Cell

Gerretsen et al. (18) reported a case of KS with vascular anomalies similar to ours, but without involvement of a right-sided aortic arch (RAAV) or an aberrant subclavian artery (ASA). Their described a 14-month-old pediatric patient with Down syndrome (DS) and KS associated with a double aortic arch, which was considered a case of double aneuploidy. However, the authors did not explain the possible pathophysiological mechanisms of the double aortic arch, stating only that it may be incidental or associated with DS. It is unclear whether the presence of cardiovascular anomalies in cases with KS can influence the development of PE. We believe, however, that a detailed anatomical examination should be performed in patients with KS. Although an association between PE and KS was considered in our case, the history of surgery 1 month prior should not be ignored. The development of PE in postoperative patients is known to occur predominantly in those who do not receive prophylactic treatment for the condition, and typically within the first week following surgery. Additionally, postoperative PE is more common in patients with obesity, those who have undergone cancer-related surgery, and those with a history of cerebrovascular disease or prior thromboembolic events. In our case, the absence of these risk factors, the diagnosis of PE 1 month after surgery and the onset of symptoms (sudden chest pain, dyspnea, palpitations) on the day of diagnosis all reduce the likelihood of the PE being related to the surgery (19). In conclusion, this case report concurs with previous studies in the literature reporting an association between PE and KS, and suggests that this association may be present even at an early age and close to diagnosis. The importance of a comprehensive radiological evaluation for pulmonary vascular pathologies such as PE as well as rare accompanying anatomic vascular anomalies in KS should thus be emphasized.

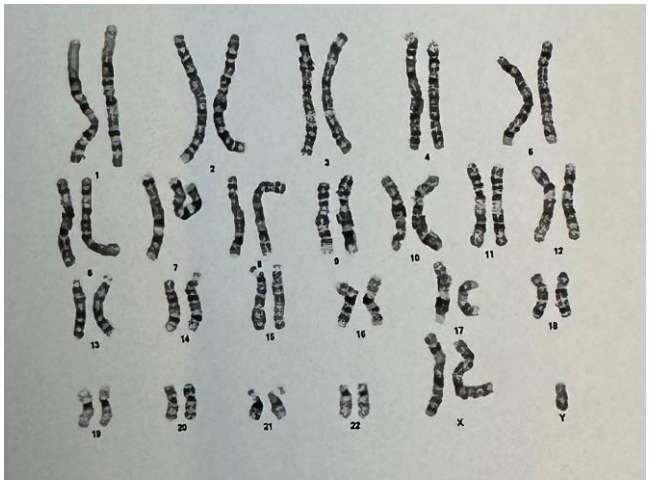

Figure 5: Genetic analysis result of the patient confirming the diagnosis of Klinefelter syndrome (47, XXY karyotype)

Table 2: Risk factors for Pulmonary Embolism (*)

Major risk factors	Moderate risk factors	Minor risk factors
-Fracture of the lower extremity -Hospitalization due to heart failure (HF), atrial fibrillation (AF), or flutter (within the last 3 months) -Hip or knee replacement surgery -Major trauma -Myocardial infarction (MI) within the last 3 months -History of venous thromboembolism (VTE) -Spinal cord injury	-Arthroscopic knee surgery -Autoimmune diseases -Blood transfusion -CVP and IV catheters -Chemotherapy -CHF or respiratory failure -Erythropoiesis-stimulating agents -Hormone replacement therapy -In vitro fertilization -Oral contraceptives, Postpartum treatment -Infections (Pneumonia, UTI, HIV) -Inflammatory bowel disease -Cancer diagnosis -Paralytic stroke -Superficial vein thrombosis -Thrombophilia	->3 days bed rest -DM -Arterial hypertension -İmmobilization -Advanced age -Laparoscopic surgery -Obesity -Pregnancy -Varicose veins -Venous catheters
(>10-fold risk)	**(2-9-fold risk)**	**(<2-fold risk)**

AF: atrial fibrillation , CVP: Central venous pressure catheters, DM: Diabetes mellitus, CHF: Congestive Heart Failure, KY: Kalp Yetmezliği, IV: İntravenous, UTI: Urinary Tract İnceftion, MI: Myocardial infarction, VTE: venous thromboembolism

(*) Adapted from reference number 4.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - A.Y., C.D., Z.N.K., G.S.Y.; Planning and Design - A.Y., C.D., Z.N.K., G.S.Y.; Supervision - A.Y., C.D., Z.N.K., G.S.Y.; Funding - Z.N.K.,C.D.; Materials - Z.N.K., G.S.Y.; Data Collection and/or Processing - A.Y., C.D.; Analysis and/or Interpretation - A.Y.,G.S.Y.; Literature Review - C.D.,G.S.Y.; Writing - A.Y., C.D.; Critical Review - A.Y., C.D.

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RESPIRATORY CASE REPORTS

Diffuse Alveolar Hemorrhage Due to Warfarin Use in a Patient with Chronic Kidney Failure

Kronik Böbrek Yetmezliği Hastasında Warfarin Kullanımına Bağlı Gelişen Yaygın Alveolar Hemoraji

Yalda Behjat[1], Faranak Rouzehkhah Azad[1], Tuğberk Türkoğlu[2], İlker Yılmam[1]

Abstract

Diffuse alveolar hemorrhage syndrome is characterized by diffuse alveolar bleeding caused by capillary damage, and delays in diagnosis and treatment can significantly increase the risk of mortality. Warfarin is an oral anticoagulant that is commonly used today for the prevention of arterial and venous thromboembolic events. As with other anticoagulants, the risk of hemorrhage increases with the use of warfarin, and while alveolar hemorrhage resulting from warfarin use is a very rare complication, it can progress rapidly to become life-threatening if not diagnosed and treated early. We present here the case of a patient with chronic kidney failure who developed diffuse alveolar hemorrhage following the prophylactic use of warfarin for atrial fibrillation.

Keywords: *Diffuse Alveolar Hemorrhage, Warfarin, Chronic Kidney Failure.*

Öz

Diffüz alveolar hemoraji sendromu, kapiller harabiyete bağlı diffüz alveoler kanama ile karakterize olup, tanı ve tedavideki gecikmeler hayatı tehdit edici boyuta ulaşabilmektedir. Warfarin günümüzde yaygın olarak kullanılan oral antikoagulanlardan biridir. Warfarin, arteriyel ve venöz tromboembolik olayların önlenmesinde yaygın olarak kullanılan oral antikoagülandır. Diğer antikoagülanlarda olduğu gibi, warfarin kullanımı ile birlikte hemoraji riski artmaktadır. Warfarin kullanımına bağlı alveoler hemoraji gelişimi oldukça nadir görülen bir komplikasyondur. Erken tanı konulup tedaviye başlanmadığı durumda, hızlı progresyon göstermekte ve hayatı tehdit etmektedir. Olgumuz, kronik böbrek yetmezliği hastasında atrial fibrilasyon nedeni ile profilaktik olarak kullanılan warfarine bağlı yaygın alveolar hemoraji komplikasyonu nedeni ile sunulmuştur.

Anahtar Kelimeler: *Yaygın Alveolar Hemoraji, Warfarin, Kronik Böbrek Yetmezliği.*

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Warfarin, an oral anticoagulant, is commonly used for the treatment of thromboembolic events, and for the prevention of pulmonary embolism, deep vein thrombosis, coagulation disorders and thromboembolism in atrial fibrillation. Warfarin works by inhibiting the carboxylation of vitamin K-dependent factors, producing an anticoagulant effect, and its most significant side effect is bleeding. Since warfarin's serum concentration is influenced by factors such as food intake and medications, no direct relationship can be established between the drug dosage and serum concentrations, although a significant relationship can be observed between the intensity of the anticoagulant effect and bleeding risk. Previous studies have reported that when the International Normalized Ratio (INR) value exceeds 3, the risk of bleeding increases five times (1). The bleeding risk from warfarin therapy is more severe in patients with compromised gastrointestinal mucosa integrity, hypertension, and renal and cerebrovascular diseases. Diffuse alveolar hemorrhage (DAH) is a rare complication of warfarin use that can become life-threatening if diagnosed early and if treatment is not started (2). Immune causes such as ANCA-associated vasculitis, isolated pulmonary capillarity, connective tissue diseases, anti-glomerular basement membrane disease, anti-phospholipid antibody syndrome and Behçet's disease are common in the etiology of DAH, while non-immune causes include heart disease, coagulation disorders and infections (3). We present here a case in which the patient, who had chronic renal failure, developed diffuse alveolar hemorrhage as a complication of warfarin use. The report highlights alveolar hemorrhage as a significant side effect of warfarin therapy, especially in patients with a high risk of bleeding, as seen in our case.

CASE

A 60-year-old female patient presented to the emergency department with complaints of coughing up blood, weakness, palpitations and shortness of breath for the past 3 days. She had a history of hypertension (HT), hyperlipidemia, chronic glomerulonephritis (a fistula for dialysis had been created 1 month earlier) and atrial fibrillation, for which she was using warfarin. Her general condition was moderate, and she was conscious and cooperative. Blood pressure: 120/80, pulse rate: 97 bpm, oxygen saturation: 95% on nasal O2 at 4 L/min. The patient's hemoglobin level at the time of admission was 6.3, and the other laboratory values are presented in detail in Table1. The patient was transfused with an erythrocyte suspension (ES) and fresh frozen plasma (FFP) to address her low hemoglobin, but despite the transfusion, here hemoglobin levels did not improve. It was learned that the patient was regularly using warfarin for atrial fibrillation, but had not been monitoring her INR levels regularly during treatment. The patient's chest X-ray revealed bilateral opacities in the hilar regions of both lungs (Figure 1).

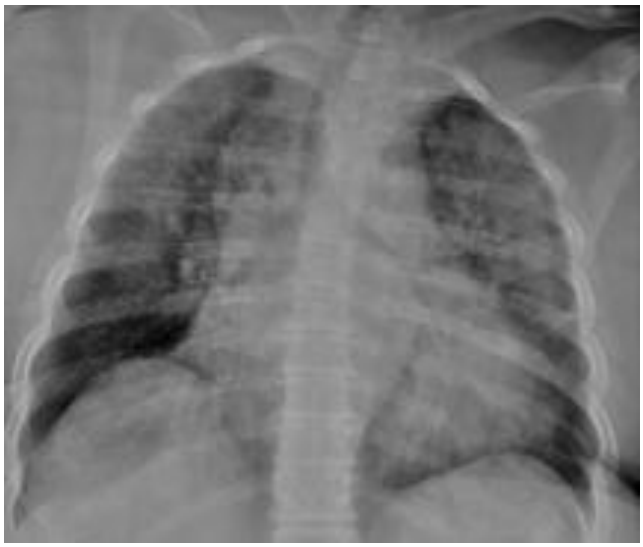

Figure 1: Chest X-ray at the time of admission

A chest CT scan revealed alveolar hemorrhage, pulmonary edema and diffuse pneumonia, as well as widespread ground-glass opacities and consolidation areas in the central part of both lungs (Figure 2). As the clinical and radiological findings suggested warfarin-related alveolar hemorrhage, the patient was treated with FFP and three units of erythrocyte suspension in the emergency department, and was then admitted to the chest diseases clinic with a provisional diagnosis of DAH associated with warfarin use. The patient had known stage 5 chronic kidney failure (CKF) and had previously been prepared for hemodialysis. At the time of admission, the patient's CKF was stable, and hemodialysis was not indicated, but hemodialysis became necessary, and the patient was started on hemodialysis twice a week.

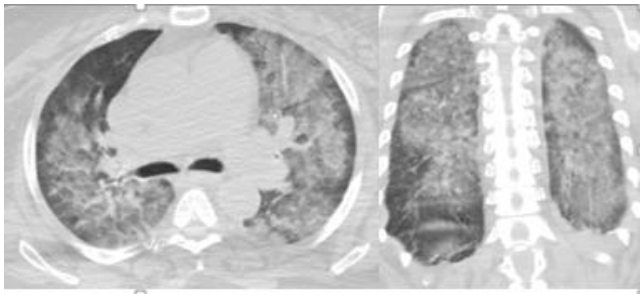

Figure 2: High-resolution computed tomography at the time of admission

As the patient's clinical and radiological findings were highly suggestive of alveolar hemorrhage, and he was reluctant to undergo bronchoscopy due to the bleeding risk, a rheumatologist was consulted for differential diagnosis, including systemic vasculitis. The patient's test results (ANA 4+, Anti Ro 52 +3, MPO-ANCA +, Anti-CCP negative, IGG, IGA, IGM, C3, C4 negative) ruled out

vasculitis, while rheumatology follow-up was recommended due to his MPO-ANCA positivity. The patient was started on moxifloxacin antibiotic therapy during his hospitalization, and oxygen support was halted 6 days later after becoming unnecessary. The patient improved clinically and radiologically, and was discharged on the 10th day of follow-up in good health (Figure 3).

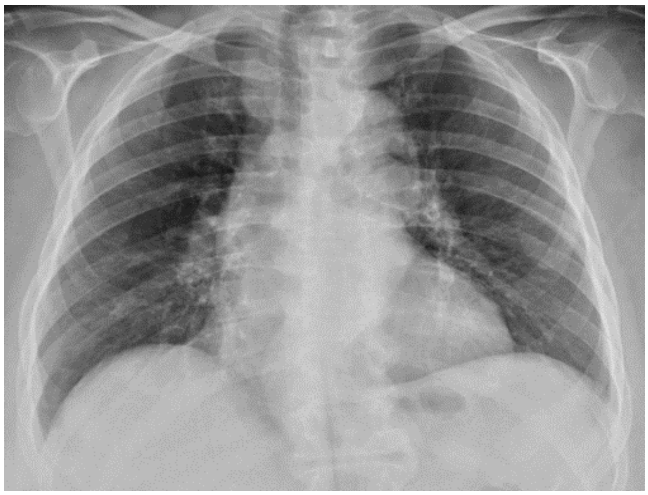

Figure 3: Chest X-ray after treatment

DISCUSSION

Diffuse alveolar hemorrhage (DAH) is a rare but life-threatening clinical and pathological condition, characterized by extensive intra-alveolar bleeding due to severe damage to the alveolar-capillary membrane. DAH can occur due to both congenital and acquired coagulation disorders, after inhalation of toxic substances or secondary to infection. The most common systemic diseases leading to DAH are small vessel vasculitides, such as microscopic polyangiitis and Wegener's granulomatosis, while Goodpasture's syndrome and systemic lupus erythematosus are less common causes (4,5). In the presented case, the alveolar hemorrhage was attributed to the prophylactic use of warfarin for the treatment of atrial fibrillation. DAH presents with an acute clinical picture in which alveolar infiltration is followed by hypoxemia. Clinical signs include shortness of breath, cough, hemoptysis, anemia, abnormal lung X-ray findings showing bilateral alveolar infiltrations, and hypoxia. Hemoptysis, anemia and diffuse alveolar consolidation on chest X-ray can be suggestive of alveolar hemorrhage, but are not always specific and may not always be associated with DAH. Not all patients with hemoptysis develop alveolar hemorrhage, and massive bleeding may not lead to hemoptysis in cases of alveolar hemorrhage if there is no free connection between the sinus hemorrhage and the proximal airways (5). Bleeding is the most significant complication in patients receiving anticoagulant therapy, occurring in 2–10% of cases. The most common bleeding sites are the soft tissues (21%), gastrointestinal system (15%), urinary system (15%), nose and pharynx (35%), intracranial space (4%), thorax (3%), eyes (2%), retroperitoneum (0.5%) and joints (1%) (6). The first case of DAH associated with warfarin intoxication was reported by Brown et al. (7) in 1965, and since then, there have been only a few reports described in the literature. Warfarin-induced DAH is usually severe and can be lethal, and the incidence of anticoagulant-induced DAH can be expected to increase in the future as the need for anticoagulation in the aging population increases for the treatment of such conditions as atrial fibrillation, cardiovascular disease and valvular heart disease. It should be noted that associations have also been drawn between DAH and the more potent anticoagulants that have recently entered the market, including abciximab and eptifibatide (8). Patients with alveolar hemorrhage are identified with bilateral alveolar consolidations that do not involve the apex of the lungs. If alveolar hemorrhage does not recur, infiltrations resolve within 3 days, leaving a reticular appearance that may eventually disappear, but may progress to fibrosis after recurrent bleeding (9,10). An accurate, rapid and non-invasive diagnosis of DAH can be achieved with high-resolution CT (HRCT), revealing alveolar infiltration in the acute phase, and patchy ground-glass areas and diffuse nodules in the subacute phase. Hemosiderin-laden macrophages and large amounts of erythrocytes identified in bronchoalveolar lavage (BAL) are the optimum diagnostic finding for DAH (10). In the presented case, the patient's chest CT scan was typical for DAH, but the patient refused to undergo bronchoscopy, so BAL could not be performed.

Table 1: The patient's laboratory values at the time of admission

CBC	Biochemistry	Blood Gas	Coagulation Parameters
HGB (g / DL): 6.3	Glucose (mg/dL): 119	pH : 7.34	Aptt: 32.3 (sn)
Htc (%): 20.2	Creat. (mg/dL): 7.2	pO2: 42.8	INR: 2.88
MCV (fL): 94.4	Ure (mg /dl): 91	pCO2: 57.3	PT: 32.6 (sn)
Leukocyte (mm3): 9.840	Na (mEq/L): 139	HCO3: 28.6	
Plt (mm3): 248.000	K (mEq/L): 5.1	SO2: 88.0 %	

In early-stage DAH associated with anticoagulant use, reversing the anticoagulant effect with vitamin K and FFP is considered life-saving. Corticosteroids are recommended in cases of alveolar hemorrhage, but may need to be avoided in the presence of infection. In such cases, broad-spectrum antibiotics should be administered until infection is ruled out (11).

In conclusion, Warfarin-associated DAH is rare, but respiratory complications may be fatal. In cases of warfarin overdose, early diagnosis and aggressive treatment are required to prevent complications, and INR and PT tests should be performed at least twice a month to avert bleeding complications. As can be understood from the presented case, close monitoring is necessary when there is a high probability of complications such as bleeding. DAH should be considered in the differential diagnosis in patients on warfarin who present with shortness of breath, hemoptysis, hypoxia and infiltrations on chest X-ray. Delays in the diagnosis of DAH can have life-threatening consequences, and early interventions with easily accessible treatments like vitamin K and FFP can be life-saving.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - Y.B., F.R.A., İ.Y., T.T.; Planning and Design - Y.B., F.R.A., İ.Y., T.T.; Supervision - Y.B., F.R.A., İ.Y., T.T.; Funding - Y.B., F.R.A., İ.Y., T.T.; Materials - Y.B., F.R.A., İ.Y., T.T.; Data Collection and/or Processing - Y.B., F.R.A., İ.Y., T.T.; Analysis and/or Interpretation - Y.B., F.R.A., İ.Y., T.T.; Literature Review - Y.B., F.R.A., İ.Y., T.T.; Writing - Y.B., F.R.A., İ.Y., T.T.; Critical Review - Y.B., F.R.A., İ.Y., T.T.

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Tension Pneumothorax in a Patient with Behçet's Disease: A Rare Condition Managed with Surgery

Behçet Hastalığı Olan Bir Hastada Tansiyon Pnömotoraks: Cerrahi Girişimle Yönetilen Nadir Bir Durum

Atilla Can[1], Hüseyin Yıldıran[1], Pınar Karabağlı[2]

Abstract

Behçet's disease is a chronic multisystemic condition characterized by systemic vasculitis in which pulmonary involvement is uncommon, and pneumothorax is a particularly rare complication. We describe here the case of a 53-year-old male with a known history of Behçet's disease who presented with acute chest pain and dyspnea. Chest X-ray revealed a left-sided tension pneumothorax. Thoracic CT revealed large apical bullae, and the patient subsequently underwent video-assisted thoracoscopic surgery (VATS) with wedge resection and partial pleural decortication. Histopathological evaluation was consistent with bullous emphysema and no evidence of vasculitis was observed. This case illustrates that tension pneumothorax can, in rare cases, develop in patients with Behçet's disease, even in the absence of pulmonary vasculitis. VATS may be considered as a safe and effective treatment option in appropriately selected cases.

Keywords: *Behçet's Disease, Pneumothorax, Tension Pneumothorax, VATS, Surgical Management.*

Öz

Behçet hastalığı, sistemik vaskülit ile karakterize ve birçok organ sistemini etkileyebilen kronik bir hastalıktır. Pulmoner tutulum nadir görülür; pnömotoraks ise son derece ender bir komplikasyondur. Burada, ani başlayan göğüs ağrısı ve nefes darlığı ile başvuran, akciğer grafisinde tansiyon pnömotoraks saptanan 53 yaşındaki Behçet hastalığı tanılı bir erkek olguyu sunmaktayız. Hastaya, acil tüp torakostomi uygulanmış, toraks BT'de dev büller saptanması üzerine video yardımlı torakoskopik cerrahi (VATS) ile wedge rezeksiyon ve parsiyel dekortikasyon yapılmıştır. Patoloji sonucu büllöz amfizem ile uyumlu idi ve vaskülit bulgusu saptanmadı. Olgumuz, Behçet hastalarında nadir görülen ancak hayatı tehdit edebilen tansiyon pnömotoraksın, parankimal vaskülit olmadan da gelişebileceğini göstermesi açısından özgündür. VATS, uygun seçilmiş olgularda güvenli ve etkili bir tedavi seçeneği olabilir.

Anahtar Kelimeler: *Behçet Hastalığı, Pnömotoraks, Tansiyon Pnömotoraks, VATS, Cerrahi Tedavi.*

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Although pulmonary involvement in Behçet's disease is rare, it ranks among the most severe and life-threatening complications. The most commonly encountered pulmonary manifestations include pulmonary artery aneurysms (PAAs), pulmonary artery thrombosis, pulmonary infarction, alveolar hemorrhage, pleural effusion, bronchiectasis and, more rarely, pneumothorax. Among these, PAAs can lead to massive hemoptysis and represent the most fatal complication of the disease, often determining the overall prognosis. For diagnosis, thoracic CT angiography and magnetic resonance imaging (MRI) are preferred due to their effectiveness in evaluating aneurysms, thrombosis and parenchymal involvement (1–3). In cases of massive hemoptysis or aneurysms refractory to medical treatment, endovascular embolization (e.g., coil or stent placement) or surgical interventions (lobectomy or segmentectomy) may be required; however, surgery carries high risk and is generally reserved as a last resort (4–6). Pneumothorax is a particularly rare manifestation in Behçet's disease and is typically associated with parenchymal destruction or cavitation. Cases of pneumothorax requiring surgical intervention have been reported in the literature, although most have involved lobectomy or procedures targeting cavitary lesions (4). We present here a case of tension pneumothorax requiring surgical management in a patient with Behçet's disease, and describe the clinical course and treatment approach.

CASE

A 53-year-old male patient presented to the emergency department with sudden-onset chest pain and dyspnea. On physical examination, the trachea was deviated to the right, breath sounds were diminished over the left hemithorax and percussion revealed hyperresonance. Blood pressure was 120/75 mmHg, and peripheral oxygen saturation was measured at 86%. Chest radiograph revealed a left-sided tension pneumothorax, prompting immediate tube thoracostomy (Figure 1 and 2). The patient was hospitalized and admitted to the thoracic surgery unit for further management. His medical history revealed a diagnosis of Behçet's disease, for which he had been taking oral prednisolone and colchicine for the past 10 years. Laboratory tests showed WBC: 12.84 K/uL, Hgb: 13.8 g/dL and Plt: 311 K/uL, while biochemistry and coagulation parameters were within normal limits. Thoracic CT revealed bullous structures measuring up to 5.5 cm in diameter in the left upper lobe (Figure 3).

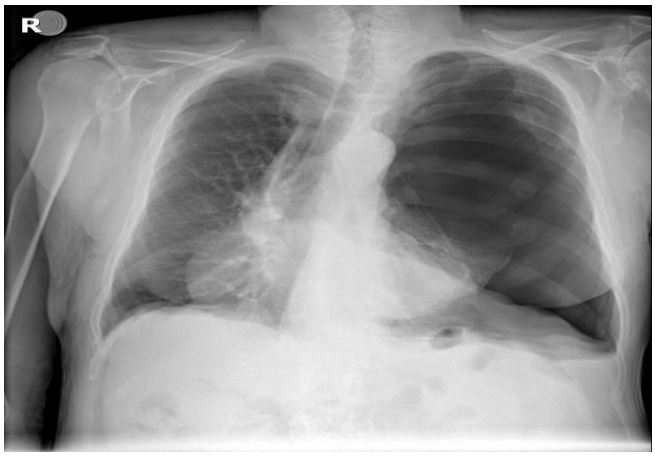

Figure 1: Left-sided tension pneumothorax on posteroanterior chest radiograph, with marked hyperlucency in the left hemithorax, consistent with a large volume of intrapleural air. The left lung is totally collapsed, and the mediastinal structures, including the trachea and cardiac silhouette, are shifted to the right, diagnostic of left-sided tension pneumothorax.

The patient had no history of smoking or occupational exposure that could predispose to bullous lung disease. Thoracic CT scans obtained 15 years earlier showed no evidence of bullous changes or emphysema, indicating the later development of the bullous formations. Following the placement of a chest tube for tension pneumothorax, a persistent and significant air leak continued for 4 consecutive days. Although 4 days may be considered a relatively short observation period, the severity of the air leak, coupled with the presence of giant bullae, prompted the decision for surgical intervention. In addition, the patient had been under chronic immunosuppressive therapy for Behçet's disease, increasing the risk of infection and impaired healing. Early surgical intervention was thus considered the safer and more appropriate approach.

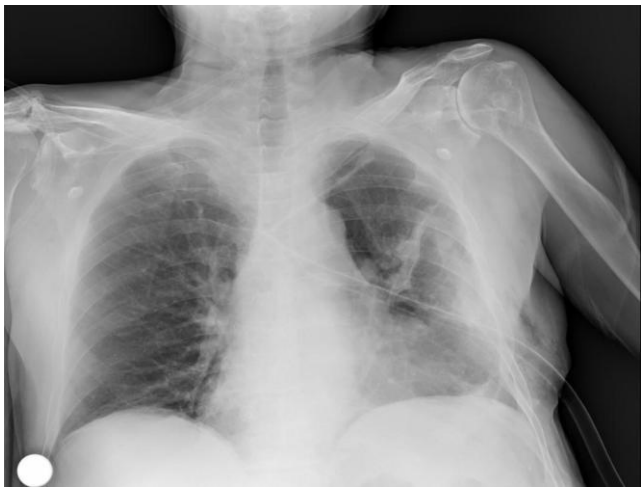

Figure 2: Anteroposterior chest radiograph following emergency tube thoracostomy. The partial re-expansion of the left lung following the insertion of a chest tube for tension pneumothorax can be seen in a comparison with Figure 1. The tube can be seen projecting into the left pleural cavity, as well as the partial return of the mediastinal structures toward the midline

The patient underwent video-assisted thoracoscopic surgery (VATS) for the excision of the bullous lesions in the left lung via wedge resection and partial parietal pleural decortication. The postoperative course was uneventful, and the patient was discharged on postoperative day 5. Histopathological analysis revealed bullous emphysema, with no evidence of vasculitis in the lung parenchyma. Although Behçet's disease may rarely contribute to parenchymal changes, in our case, no histopathological evidence of vasculitis was found. The bullous changes were thus considered idiopathic rather than directly attributable to Behçet's disease, although the coexistence of Behçet's disease may have contributed to disease complexity. Microbiological cultures obtained from both the pulmonary parenchyma and the parietal pleura revealed no growth of Mycobacterium tuberculosis. The patient remains asymptomatic in the 5th postoperative month, and continues to be followed without complications (Figure 4).

DISCUSSION

Spontaneous pneumothorax is an extremely rare complication in Behçet's disease, with available evidence limited to isolated case reports given the lack of definitive epidemiological data regarding its prevalence. In cases with Behçet's disease, spontaneous pneumothorax typically occurs in the later stages of the disease and is associated with severe pulmonary involvement or vascular complications. It is exceedingly uncommon in patients with milder disease or those with predominantly systemic manifestations (7). In our case, the absence of histopathological evidence of vasculitis in the lung parenchyma suggested that the pneumothorax developed outside the classical setting of pulmonary involvement, and indicated that pneumothorax may occur even in patients without overt pulmonary vasculitis. A review of the literature revealed no direct case reports describing tension pneumothorax specifically related to Behçet's disease. While spontaneous pneumothorax and pneumothorax secondary to large cavitary lesions have been reported in patients with Behçet's disease, no cases of tension pneumothorax have been explicitly documented in the literature (4). Recurrence rates after video-assisted thoracoscopic surgery (VATS) for spontaneous pneumothorax have been reported in the range of 2–25%, depending on the study. Recurrence risk is influenced by additional procedures performed (e.g., pleurodesis, pleurectomy), patient-specific factors and the experience of the surgeon. In a large meta-analysis of 23,531 patients, an average recurrence rate of 10% (range 8–12%) was reported, with increased risk in males, young people, those with low body mass index (BMI), and those with a history of contralateral pneumothorax (8). A large cohort study from Taiwan involving 6,654 patients reported a 1-year recurrence rate of 13.7%, with a total recurrence rate of 24.8% over a mean follow-up period (9).

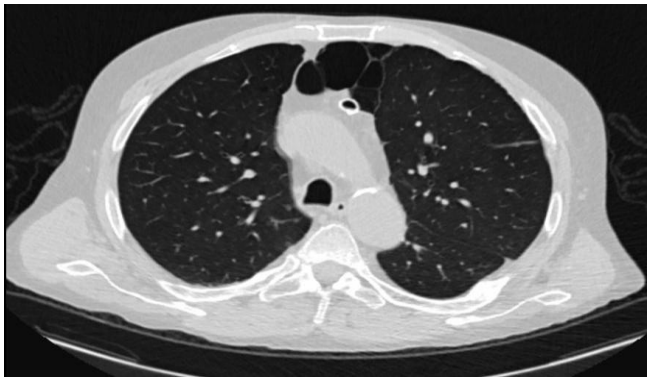

Figure 3: Axial chest CT image demonstrating apical bullous disease. The high-resolution computed tomography (HRCT) of the thorax shows multiple air-filled bullae in the apical segment of the left upper lobe, the largest of which measures 5.5 cm in diameter. The surrounding lung parenchyma appears otherwise preserved, with no radiological evidence of vascular involvement

Given that pneumothorax in Behçet's disease is often associated with significant pulmonary and vascular involvement, close and multidisciplinary follow-up is essential after surgery. During the first year in particular, regular clinical assessments, chest imaging, and symptom monitoring are recommended for the early detection of recurrence and complications. Follow-up imaging is also recommended for the evaluation of underlying conditions such as pulmonary artery aneurysms, cavitary lesions or pneumatoceles. Clinicians should remain vigilant for the potential development of recurrent pneumothorax, infection or bronchopleural fistula, and promptly re-evaluate the patient should such symptoms arise. In a case reported by Gülyüz et al. (10), a young male patient with Behçet's disease developed bilateral spontaneous pneumothorax that was managed conservatively. This case suggests that pneumothorax may represent a potential pulmonary manifestation of Behçet's disease, although most previously reported cases have involved either bilateral or non-tension forms. In contrast, our case involved a rare presentation of tension pneumothorax requiring surgical intervention. The absence of significant parenchymal lesions in the case reported by Gülyüz et al. (10) and the subsequent development of bilateral pneumothorax suggests that such complications may arise not only in advanced stages of the disease, but also in the absence of a clear vascular pathology. Similarly, no histopathological evidence of vasculitis was found in our case, indicating that spontaneous pneumothorax in Behçet's disease may also occur in its less active or atypical forms. While most reported cases in the literature were managed

conservatively, our patient required surgical intervention due to persistent air leakage and the presence of large bullae. The present case can thus be considered unique, and is presented to the literature due to both the clinical decision-making and therapeutic strategy employed. It demonstrates that spontaneous tension pneumothorax, although rare, may occur in patients with Behçet's disease even in the absence of histopathological vasculitis, and that VATS-based surgical intervention can be considered a safe and effective treatment option in appropriately selected cases.

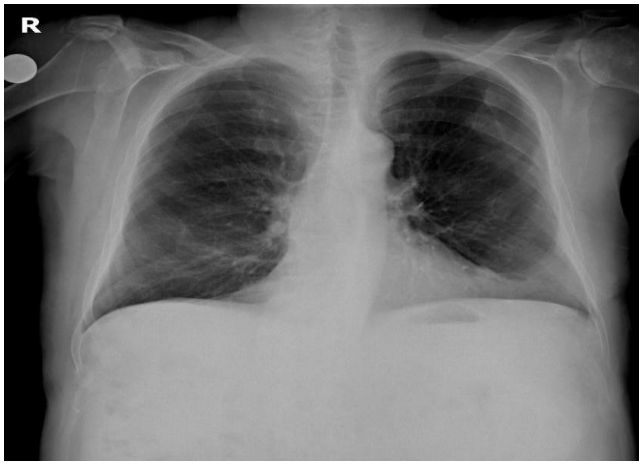

Figure 4: Postoperative posteroanterior chest radiograph. The complete re-expansion of the left lung following video-assisted thoracoscopic surgery (VATS) and wedge resection can be seen. Mediastinal structures are in normal alignment, with no evidence of residual pneumothorax or subcutaneous emphysema

CONCLUSION

Spontaneous pneumothorax is an exceptionally rare and serious complication of Behçet's disease, although only a limited number of cases have been reported in the literature to date. Most previously reported cases involved bilateral or non-tension forms, with surgical intervention typically indicated in the presence of parenchymal destruction or cavitary lesions. The present case contributes uniquely to the existing literature by documenting a spontaneous tension pneumothorax in a patient with Behçet's disease that was managed surgically via video-assisted thoracoscopic surgery (VATS), despite the absence of histopathological evidence of vasculitis. The broader clinical spectrum of pulmonary involvement in Behçet's disease is thus highlighted, supporting the role of surgery as a safe and effective therapeutic option in well-selected patients. In cases with life-threatening presentations such as tension pneumothorax, prompt diagnosis and appropriate management are critical for the reduction of morbidity and mortality. The presented case also underlines the need to consider surgical management in Behçet's patients who present with persistent air leak and bullous disease, even in the absence of classic vasculitic findings.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - A.C., H.Y., P.K.; Planning and Design - A.C., H.Y., P.K.; Supervision - A.C., H.Y., P.K.; Funding - A.C., H.Y., P.K.; Materials - A.C., H.Y., P.K.; Data Collection and/or Processing - A.C., H.Y., P.K.; Analysis and/or Interpretation - A.C., H.Y., P.K.; Literature Review - A.C., H.Y., P.K.; Writing - A.C., H.Y., P.K.; Critical Review - A.C., H.Y., P.K.

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A Case of Giant Mediastinal Teratoma Occupying the Anterior Mediastinum

Anterior Mediasteni Kaplayan Dev Mediastinal Teratom Olgusu

Tayfun Kermenli[1], Cebrail Azar[2], Tamer İmamoğlu[3]

Abstract

Mature cystic teratomas are rare tumors of the anterior mediastinum that may, in rare cases, contain pancreatic cells and can reach considerable sizes, depending on their structure. The currently preferred treat-ment for benign mediastinal tumors is video-assisted thoracoscopic surgery (VATS). We present here a case of a giant mediastinal mature cystic teratoma with a pathological finding of pancreatic islets that was success-fully treated with bilateral VATS. Our findings support the use of VATS in such cases, regardless of size.

Keywords: *Mature Cystic Teratomas, Mediastinal Tumors, Anterior Mediastinum.*

Öz

Matür kistik teratomlar, anterior mediastenin nadir tümörleridir. Nadiren pankreas hücreleri içerebilirler. Bazen, yapılarına bağlı olarak, dev boyutlara ulaşabilirler. Videotorakoskopi cerrahisi artık bu iyi huylu mediastinal tümörlerde yaygın olarak kullanılmaktadır. Olgu sunumumuzda, bilateral videotorakoskopik cerrahi ile tedavi edilen dev mediastinal olgun kistik teratom olgusunu sunduk. Hastanın patolojik sonucunun pankreas adacıkları içermesi olguyu daha da ilginç hale getiriyor. Videotorakoskopik cerrahinin bu tür olgularda boyuttan bağımsız olarak başarıyla uygulanabileceğine inanıyoruz.

Anahtar Kelimeler: *Matür Kistik Teratom, Mediastinal Tümörler, Ön Mediasten.*

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Mature cystic teratomas are rare mediastinal tu-mors that usually develop in the anterior mediasti-num, but may also occur in the posterior medias-tinum, and account for 3–12% of all mediastinal tumors (1). The most common extra-gonadal loca-tion of germ cell tumors is the anterior mediasti-num, accounting for 15% of all anterior mediasti-nal tumors in adults (2). Most tumors of this kind are benign and slow-growing, and so are most commonly found incidentally (3). Their low malig-nant potential makes surgical resection the treat-ment of choice, providing excellent long-term disease-free survival (3). We present here a case of a giant mature cystic teratoma that was treat-ed with VATS and was completely resected.

CASE

A 23-year-old male patient was referred to our unit after a two-view chest X-ray performed at another center to investigate a cough revealed a giant mediastinal mass (Figure 1). The patient underwent a contrast-enhanced thoracic CT scan, revealing a giant cystic mass with an axial length of approximately 19 cm in the anterior mediastinum (Figure 2). The patient's medical history and physical examination results were unremarkable. Surgical excision was proposed, and after giving written consent, the patient was prepared for video-thoracoscopic resection. Following left double lumen intubation, the patient was placed in the left lateral 45-degree position, and the thorax was entered via an incision between the right 6th and 8th intercostal spaces (ICS) along the anterior axillary line. The mass was visualized with a 30-degree optical aid (Figure 3). No invasion of the mediastinum by the mass was noted, and the cyst was subsequently released from the right mediastinal surface and perforated using an energy device.

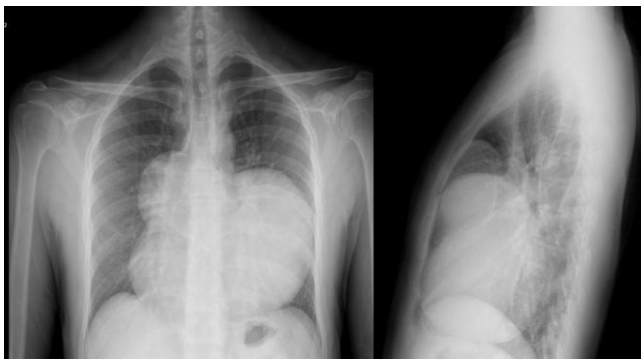

Figure 1: PA and lateral chest radiograph image of mature cystic teratoma

The cystic content was aspirated and the cyst volume was reduced. The patient was then placed in the right lateral 45-degree position, and incisions were made for the left hemithorax through the same intercostal spaces used for the right side. The mediastinal pleura was dissected, and the mass was explored and separated from the mediastinum. The incision was then widened and a cystic mass measuring approximately 19 cm was removed from the thoracic cavity with the help of a thoracoscopic specimen bag (Figure 4), after which, a hemovac drain was placed in the mediastinum. The procedure was completed without complications, and the patient was discharged on the 2nd postoperative day. The mass was identified as a mature cystic teratoma in a pathological examination, which also revealed pancreatic islets and cystic structures within the tumor tissue (Figure 5). No problems were reported at the 6th postoperative month follow-up.

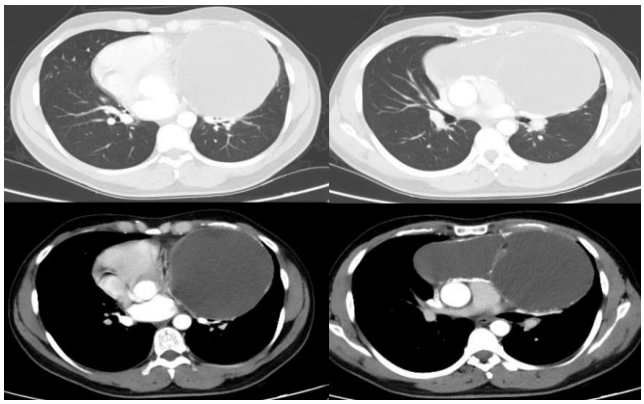

Figure 2: Thoracic CT image of mature cystic teratoma

DISCUSSION

Mature cystic teratoma is the most common type of mediastinal germ cell tumor, and is a benign tumor that does not spread through neoplastic metastasis. The etiology of mediastinal teratomas has yet to be fully explained, but two embryological theories have been proposed. The first refers to an abnormal differentiation of exocrine pancreatic tissue occurring as a result of the settlement of pluripotent epithelial cells from the ventral primary foregut and heteroplastic tissue in the mediastinum, while the second refers to the potential migration or localization of cells in the pancreas to different regions. A similar case to ours of mature cystic teratoma containing pancreatic islets was reported previously by Cansever et al. (4). Of particular significance in the presented case is the pathological identification of pancreatic islets within the giant 19 cm mediastinal mass removed from the patient, and the use of video-assisted thoracoscopic surgery (VATS) in its removal. VATS is used for many different surgical procedures, and is today frequently considered in cases of teratomas, cystic lesions of the mediastinum and other mediastinal lesions.

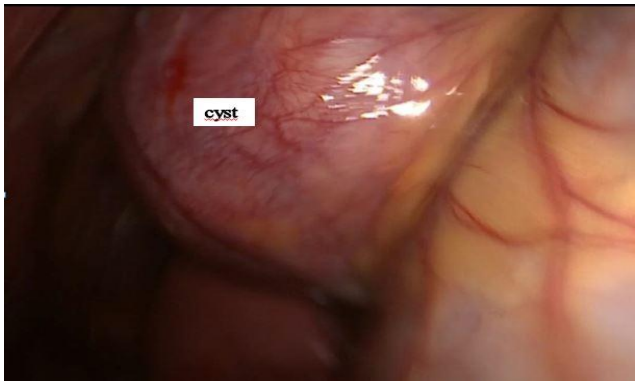

Figure 3: Perioperative view of the cyst

There have been several reports to date describing the use of VATS and RATS for the management of mediastinal masses (5,6). Ramcharran et al. (5) described the use of robot-assisted thoracoscopic surgery (RATS) in the successful excision of a mediastinal teratoma in a 43-year-old female patient. Tian et al. (7), on the other hand, reported that in a large case series of 108 mediastinal teratoma cases, 22 patients underwent surgery with VATS, while around 80 underwent thoracotomy. A simple neck collar incision was made in one case, while five cases underwent median thoracotomy combined with neck incision. Similar cases to ours involving giant mediastinal teratomas have also been presented in the literature (8).

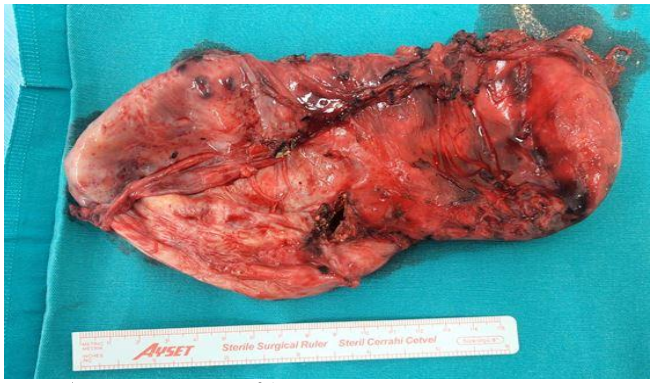

Figure 4: Postoperative view of the cyst

Zhang et al. (1) reported the successful excision of a giant mediastinal teratoma measuring 129 mm using the VATS method in a case with a ruptured teratoma resembling an encapsulated empyema. In another study, Zúñiga-Garza et al. (9) described a case in which VATS was used to excise a giant 15 cm mediastinal mature cystic teratoma that was found on gross pathological examination to have a wall structure composed of epidermis and dermis with some hair follicles. A subsequent microscopic examination of the mass revealed mucosecretory glands containing columnar epithelium, serous acini and ducts lined by columnar epithelium. Luo et al. (10), on the other hand, presented a case of a giant mediastinal teratoma located in the right middle and upper mediastinum that was compressing the deep section of the azygos vein arch and the superior vena cava. In this case, the tumor tissue was destroyed due to the presence of vascular adhesions that prevented its removal en bloc. In our case, there was no invasion of any vascular structure, allowing the tumor tissue to be removed en bloc from both the right and left pleural spaces using VATS. Carcinoids are rarely observed in pathological examinations of mediastinal mature cystic teratomas. Ohno et al. (11) reported a rare case in which a carcinoid tumor, identified as originating from a mature cystic teratoma of the mediastinum in a 30-year-old patient who presented with chest pain, was completely resected with VATS. A subsequent histological examination revealed a 3 mm carcinoid component in the capsule with no pathological necrosis, a MIB-1 index of 1%.

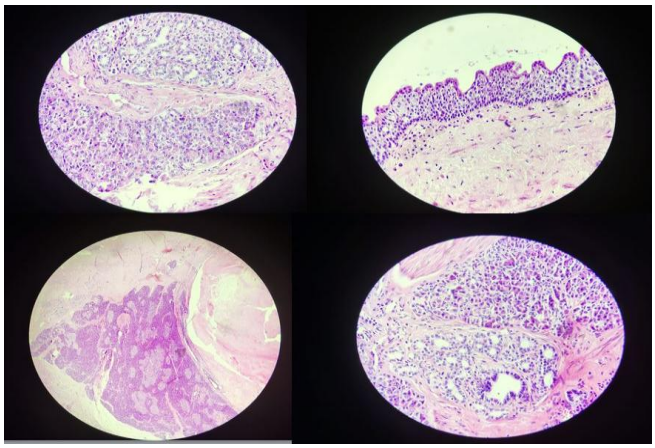

Figure 5: Postoperative pathological images of mature cystic teratoma (H&E X20)

CONCLUSION

We present this case in support of the use of VATS for the excision of giant mature cystic teratomas, regardless of the size of the mass. Of particular note in the presented case is the identification of tissues containing pancreatic islets. We believe that VATS should be considered a safe treatment option in cases of benign mediastinal masses.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - T.K., C.A.; Planning and Design - T.K.; Supervision - T.K., C.A., T.İ.; Funding - T.K., C.A., T.İ.; Materials - T.K., T.İ.; Data Collection and/or Processing - T.K., C.A.; Analysis and/or Interpretation - T.K., C.A., T.İ.; Literature Review - T.K.; Writing - T.K., C.A., T.İ.; Critical Review - T.K., C.A., T.İ.

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Negative Pressure Pulmonary Edema: Early Diagnosis ve Early Treatment

Negatif Basınçlı Akciğer Ödemi: Erken Tanı ve Erken Tedavi

Hüseyin Çetik, Gönül Ölmez Kavak, Zeynep Baysal Yıldırım, Mahir Kuyumcu

Abstract

Negative pressure pulmonary edema is a rare complication following general anesthesia, potentially requiring intensive care monitoring and mechanical ventilatory support. Prompt clinical suspicion and early diagnosis, along with appropriate management and respiratory support, can support rapid and complete recovery with favorable outcomes. Particular care should be taken in young, adult and male patients who develop laryngospasm during extubation, including close monitoring, and negative pressure pulmonary edema should be considered in the differential diagnosis if pulmonary edema develops. We present here the diagnostic, monitoring and therapeutic approach applied to a young male patient who developed negative pressure pulmonary edema following extubation after undergoing appendectomy.

Keywords: *Negative Pressure, Pulmonary Edema, Mechanical Ventilation, Laryngospasm, Appendectomyac.*

Öz

Negatif basınçlı akciğer ödemi, genel anestezi sonrasında görülebilen nadir bir komplikasyon olup, yoğun bakım izlemi ve mekanik ventilasyon desteğini gerektirebilen bir akciğer ödemi tablosudur. Klinik şüphe duyup erken teşhis edilmesi, doğru yönetim ve solunum desteği tedavisi, hızlı ve tam iyileşme sağlar ve sonuçlar yüz güldürücüdür. Özellikle ekstübasyon işlemi sırasında laringospazm gelişen genç, erişkin ve erkek hastalarda dikkatli olunmalı, yakın takip edilmeli ve akciğer ödemi bulguları gelişirse ayırıcı tanıda mutlaka negatif basınçlı akciğer ödemi tanısının akılda tutulması gerekmektedir. Bu olgumuzda apendektomi operasyonu geçiren genç, erkek hastada, ekstübasyon sonrası gelişen negatif basınçlı akciğer ödeminin tanı, takip ve tedavi yaklaşımları sunulmuştur.

Anahtar Kelimeler: *Negatif Basınç, Akciğer Ödemi, Mekanik Ventilasyon, Laringospazm, Apendektomi.*

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Negative pressure pulmonary edema (NPPE) is an uncommon complication of general anesthesia that can develop after extubation or in the postoperative period, and that may necessitate intensive care monitoring and mechanical ventilatory support. The reported incidence of NPPE in anesthesia practice ranges between 0.05% and 0.1%, although it has been suggested that the condition develops more frequently than documented (1). Although rare, its clinical manifestations are striking, and early recognition followed by immediate initiation of treatment can prevent significant morbidity and mortality associated with NPPE. Clinicians should thus be familiar with the condition, promptly recognize it and avoid delays in management (1,2). We present this case report to the literature to serve as guidance to colleagues in the management of this rare complication. For this purpose, the evaluation, monitoring and treatment course of a patient who developed NPPE are presented.

CASE

A 29-year-old male patient weighing 75 kg and 180 cm in height was scheduled for surgery in the general surgery department with a diagnosis of acute appendicitis. The patient had no known comorbidities or history of allergies, and laboratory results and chest radiography were within normal limits (Figure 1). The patient had no history of smoking or alcohol consumption and was classified as ASA Physical Status 1E before surgery. Standard ASA monitoring was conducted. After an 8-hour fasting period, anesthesia induction was performed with intravenous midazolam (0.05 mg/kg), propofol (2 mg/kg), lidocaine (1 mg/kg), fentanyl (2 μg/kg) and rocuronium (0.6 mg/kg).

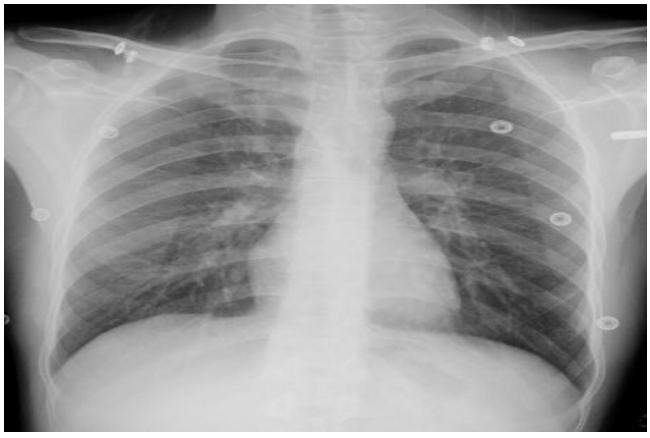

Figure 1: Preoperative chest radiograph of the case

Orotracheal intubation was achieved with a 7.5 mm cuffed endotracheal tube. Anesthesia was maintained with sevoflurane (1–2%) in a mixture of 50% air and 50% oxygen at a fresh gas flow rate of 2 L/min. The surgical procedure lasted approximately 100 minutes, during which no respiratory or hemodynamic instability occurred. The patient received 1000 mL of crystalloid fluid intraoperatively. At the conclusion of the surgery, the neuromuscular blockade was reversed with sugammadex (200 mg). Extubation was performed once spontaneous breathing and response to verbal stimuli were confirmed. Five minutes after being transferred to the postoperative recovery room, the patient developed inspiratory effort, agitation and laryngospasm. Abdominal breathing and intercostal retractions were observed, and oxygen saturation decreased to 60%. Airway maneuvers and mask ventilation with 100% oxygen were applied, improving saturation to 85%. Electrocardiography (ECG), arterial blood gas analysis and other laboratory investigations were obtained. The ECG showed only mild sinus tachycardia, while the arterial blood gas analysis revealed pH: 7.24, pO_2: 58.1 mmHg, pCO_2: 54.6 mmHg and SpO_2: 78.9%. Biochemistry, complete blood count, cardiac markers, D-dimer and pro-BNP were within normal limits. The patient produced several episodes of pink, frothy sputum, and bilateral diffuse rale was auscultated, and was administered intravenous methylprednisolone (80 mg), pantoprazole (40 mg) and furosemide (20 mg). Echocardiography showed normal cardiac function and chamber dimensions. The patient was subsequently transferred to the intensive care unit due to persistent dyspnea and tachypnea. In the ICU, noninvasive blood pressure was 118/65 mmHg, heart rate 106 bpm and oxygen saturation 87%. Chest radiography revealed bilateral infiltrates consistent with pulmonary edema, and chest computed tomography revealed diffuse consolidations, septal thickening and ground-glass opacities. Considering the development of respiratory distress after laryngospasm, the absence of pre-existing cardiac disease, bilateral crackles on auscultation, laboratory findings and the presence of pink, frothy sputum, the patient was diagnosed with NPPE and the appropriate treatment was initiated (Figures 2 and 3).

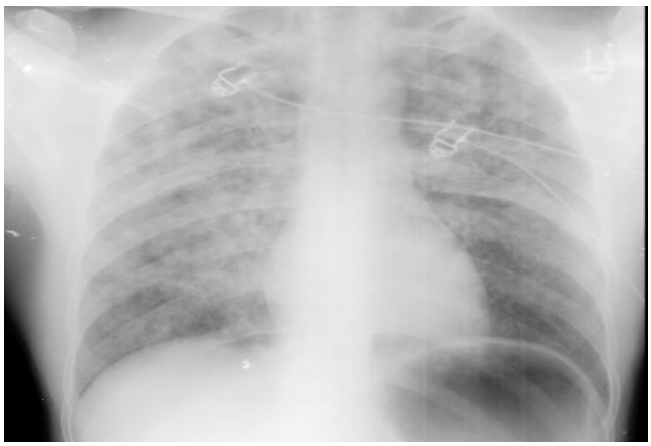

Figure 2: Postoperative chest radiograph showing infiltrative areas consistent with bilateral pulmonary edema

Fluid restriction was applied, and limited intravenous fluid administration, salbutamol and budesonide nebulization were provided. Noninvasive mechanical ventilation (NIMV) was started with an oronasal mask in CPAP mode, with PEEP 10 cm H_2O, pressure support 15 cm H_2O and FiO_2 60%, and after one hour of NIMV, clinical improvement and resolution of hypoxemia were observed, with SpO_2 rising to 95% on 6 L/min oxygen. The results of an arterial blood gas analysis at the fourth hour were pH: 7.27, pO_2: 92.8 mmHg, pCO_2: 49.1 mmHg and SpO_2: 93.9%. Oxygen therapy was continued via a nasal cannula. The tachypnea and dyspnea regressed, and a follow-up blood gas analysis at 12 hours showed pH: 7.39, pO_2: 181 mmHg, pCO_2: 40.5 mmHg and SpO_2: 99.4%. Chest radiography confirmed the resolution of the pulmonary edema findings (Figure 4). After 24 hours of monitoring and treatment, the patient no longer required supplemental oxygen and remained stable in room air. Chest radiography on postoperative day 2 revealed a marked regression of pulmonary edema (Figure 5). The patient, who had been monitored and treated in the ICU for one day, was transferred to the general surgery ward and discharged in good condition after an additional day of observation. The blood gas analyses and hemodynamic results recorded during the process are presented in Table 1.

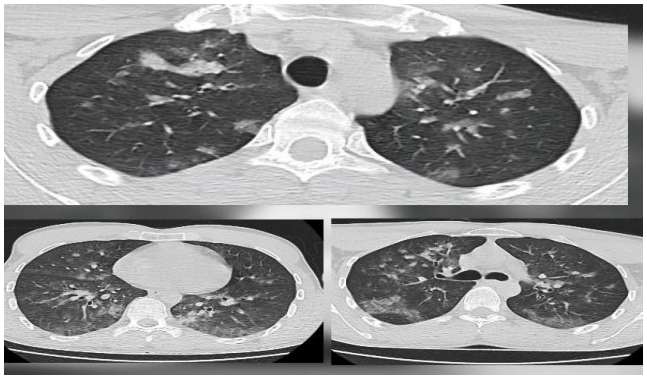

Figure 3: Thoracic computed tomography revealing ground-glass opacities and areas of consolidation

DISCUSSION

The incidence of NPPE is higher among male patients and those with ASA physical status I or II (3), which is likely attributable to the ability of otherwise healthy adults to generate markedly elevated intrathoracic negative pressures. Other risk factors for NPPE include procedures involving the upper airway, obesity, smoking, short neck anatomy, difficult intubation, upper respiratory tract infection and obstructive sleep apnea (4). In the presented case, it is thought that the healthy status and young age of the patient, and the development of laryngospasm following extubation contributed to the onset of NPPE. During forceful inspiration, the increase in negative intrathoracic pressure augments venous return to the right heart and elevates pulmonary venous pressure. This disrupts pulmonary microvascular circulation, and the resulting increase in pulmonary capillary permeability allows transudation of fluid from the pulmonary capillaries into the alveolar spaces, culminating in pulmonary edema. Pulmonary perfusion is further compromised by fluid accumulation, leading to hypoxemia. Hypoxemia and acidosis due to inadequate ventilation exacerbate pulmonary vascular resistance via alveolar-capillary membrane injury, which intensifies the hyperadrenergic response and may result in diffuse alveolar hemorrhage as well as cardiac complications (2,5). While the symptoms of NPPE typically manifest immediately after extubation, they may develop at any time during the postoperative period. Clinically, initial manifestations include oxygen desaturation, pink frothy sputum production and radiographic abnormalities consistent with pulmonary edema, all of which evolve in a characteristic sequence. The occurrence of laryngospasm during extubation, followed by respiratory distress and hypoxemia, strongly supports the diagnosis (6). Signs of laryngospasm include suprasternal retractions, stridor, use of accessory inspiratory muscles and agitation, and bilateral diffuse crackles and rhonchi may be present on lung auscultation. Radiologic findings are critical for both diagnosis and follow-up, while thoracic CT and chest radiography in NPPE patients may reveal bilateral pulmonary infiltrates and interstitial edema (1).

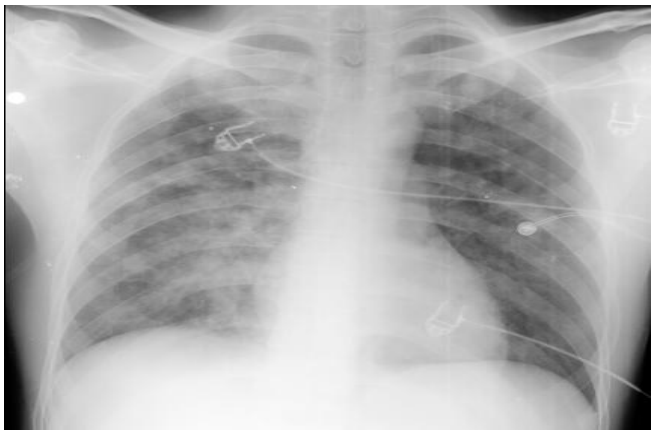

Figure 4: Chest radiograph taken approximately 12 hours after treatment showing regression in the infiltrative areas

In cases where clinical suspicion necessitates differentiation between cardiogenic and non-cardiogenic pulmonary edema, echocardiography (ECHO) may be employed for the assessment of right and left ventricular dimensions, left ventricular ejection fraction, valvular function and wall motion abnormalities (7). Differential diagnoses for NPPE include fluid overload, cardiogenic pulmonary edema, anaphylaxis and Mendelson's syndrome, and excluding these is crucial for management guidance (1,5). No evidence of anaphylaxis was

observed perioperatively in the presented case, and there was no known history of allergy. The use of a cuffed endotracheal tube, absence of vomiting during or after extubation, and lack of perioperative oxygen desaturation ruled out Mendelson's syndrome, and the absence of underlying cardiac disease, the normal postoperative ECG and echocardiography results, and the timing of pulmonary findings after laryngospasm argued against cardiogenic pulmonary edema. Furthermore, the administration of 1000 mL of isotonic solution during surgery was not considered sufficient to cause fluid overload. The primary goal in NPPE management is to ensure adequate oxygenation and airway patency, with early application of positive pressure ventilation when necessary. In mild cases, oxygen supplementation via a face mask may be sufficient (8). However, if there is no clinical or oxygenation improvement, non-invasive mechanical ventilation (NIMV) should be initiated. NIMV reduces venous return and pulmonary preload, thereby limiting the progression of pulmonary edema, and if alveolar fluid is already present, it facilitates its redistribution into the interstitial space. In most cases, NPPE resolves with NIMV without the need for invasive mechanical ventilation (3,7). Nonetheless, there are reports in the literature of cases requiring reintubation and invasive ventilation (3,4). In the presented case, oxygen supplementation via a face mask was insufficient, and the hypoxemia was dramatically corrected following NIMV. The available pharmacologic treatments include diuretics, although their use remains controversial (7). Even in the absence of fluid overload in the pathophysiology, diuretics may be administered to enhance alveolar fluid clearance with careful monitoring of urine output, electrolytes and hemodynamics, for which a few favorable results have been reported (9). While the use of steroids remains a subject of debate, Chuang et al. (10) reports that steroids may be beneficial in cases of alveolar injury, reducing respiratory distress and accelerating recovery. Beta-2 agonists have also been recommended, as bronchodilator therapy may alleviate pulmonary edema symptoms (7). The presented case was administered diuretics, steroids and beta-2 agonists, leading to clinical improvement. In conclusion, NPPE is a rare complication of general anesthesia, for which prompt clinical suspicion, appropriate management and timely respiratory support typically ensure rapid and complete recovery and favorable outcomes. Particular caution should be exercised in young, healthy male patients who develop laryngospasm during extubation as a higher risk group. Such patients should be closely monitored, and NPPE should be considered in the differential diagnosis when pulmonary edema findings emerge.

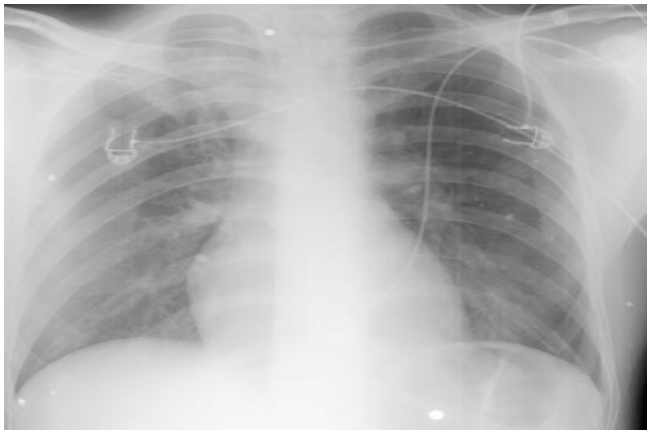

Figure 5: Chest radiograph prior to discharge

Table 1: Blood gas and hemodynamic values of the patient during the treatment period

Parameter	Before extubation	After extubation	After extubation 5th minute	Upon ICU admission	ICU 4th hour	ICU 12th hour
BP (mmHg)	124/65	126/70	133/76	118/65	124/69	121/67
HR (beats/min)	76	85	115	106	87	70
SpO_2 (%)	99	97	60	91	94	99
pH			7.24		7.27	7.39
pO2 (mmHg)			58.1		92.8	181
pCO2 (mmHg)			54.6		49.1	40.5
Lactate ($mmol \cdot L^{-1}$)			2.2		1.5	2
BG-SpO_2 (%)			78.9		93.9	99.4

BP: Blood pressure, HR: Heart rate, SpO_2: Peripheral oxygen saturation, pO_2: Partial pressure of oxygen, pCO_2: Partial pressure of carbon dioxide, BG-SpO_2: Blood gas oxygen saturation, ICU: Intensive Care Unit

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - H.Ç.; Planning and Design - H.Ç., Z.B.Y., G.Ö.K.; Supervision - H.Ç., Z.B.Y.; Funding - ; Materials - ; Data Collection and/or Processing - H.Ç., Z.B.Y., G.Ö.K.; Analysis and/or Interpretation - ; Literature Review - H.Ç., Z.B.Y., G.Ö.K.; Writing - H.Ç., Z.B.Y., G.Ö.K.; Critical Review - H.Ç., Z.B.Y., G.Ö.K.

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RESPIRATORY CASE REPORTS

A Rare Case of Birt–Hogg–Dubé Syndrome

Birt–Hogg–Dubé Sendromlu Nadir Bir Olgu

Selime Kahraman, Nur Simge Kökleş, Tamer Okay

Abstract

Birt-Hogg-Dubé syndrome (BHDS) is a systemic disease characterized by bilateral pulmonary bullae, hair follicle hamartomas and renal tumors. We present here the case of a 41-year-old male who presented with spontaneous pneumothorax with a history of surgery due to a renal tumor. The patient was referred for genetic testing based on clinical suspicion and a family history of pneumothorax, and was subsequently diagnosed with BHDS.

Keywords: *Hemophilia, Birt–Hogg–Dubé Syndrome, Bullous Lung, Rare Lung Diseases.*

Öz

Birt-Hogg-Dube' sendromu (BHDS), akciğerde bilateral büller, saç folikülü hamartomları, renal tümörler karakterize sistemik bir hastalıktır. Spontan pnömotoraks ile başvuran 41 yaşında erkek hastamızda renal tümör nedeniyle operasyon öyküsü mevcuttu. Ailesinde pnömotoraks öyküsü olduğu öğrenilmesi üzerine klinik şüphe ile hasta genetik incelemeye yönlendirildi ve sonuçta hastamıza BHDS tanısı konuldu.

Anahtar Kelimeler: *Birt–Hogg–Dubé Sendromu, Büllöz Akciğer, Nadir Akciğer Hastalıkları.*

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Birt-Hogg-Dubé syndrome (BHDS), first described by Birt et al. (1) in 1977, is an autosomal dominant disorder caused by mutations in the FLCN gene on chromosome 17p11.2. The disease is characterized by multiple pulmonary cysts, recurrent spontaneous pneumothoraxes, cutaneous fibrofolliculomas and kidney tumors of various histological types. It typically manifests in the third or fourth decade of life and does not show a gender predilection (2,3).

CASE

A 41-year-old male patient presented to the emergency department with complaints of chest pain and was admitted to the hospital after a minimal pneumothorax was observed on chest radiography. His medical history revealed no history of smoking, a diagnosis of leiomyosarcoma from a soft tissue biopsy of the right forearm two years earlier and a partial nephrectomy for renal cell carcinoma in the same year. The patient's medical history revealed pneumothoraxes in the patient's father, sister and brother. High-resolution computed tomography (HRCT) of the thorax revealed multiple bullae in the bilateral lung parenchyma (Figure 1) that were indicative of Birt-Hogg-Dubé syndrome, and so the patient was referred for genetic testing. The genetic analysis confirmed a mutation in the FLCN gene. The patient was subsequently monitored with 2 L/min of oxygen via nasal cannula for 3 days and was discharged following the resolution of the pneumothorax on chest radiography, but was warned of the risk of recurrence.

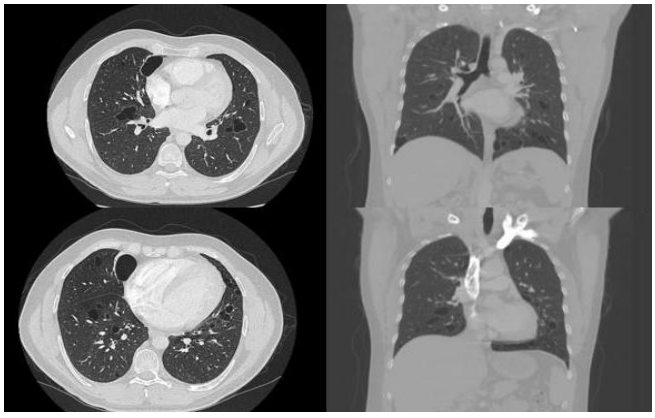

Figure 1: Transverse and sagittal sections from the thorax computed tomography, with widespread bullae seen in the lung parenchyma

DISCUSSION

Birt-Hogg-Dubé syndrome is diagnosed based on major and minor criteria (4), with one major criterion or two minor criteria considered sufficient for diagnosis. The major criteria include mutations in the FLCN gene and the presence of at least five histologically confirmed fibrofolliculomas or trichodiscomas of adult onset, while the minor criteria include bilateral basal lung cysts (with or without spontaneous pneumothorax), early onset (age <50), multifocal or bilateral renal cancer, or a first-degree relative with BHDS. Our patient had an FLCN gene mutation, renal cell cancer and bullae in bilateral basal lung fields, supporting the Birt-Hogg-Dubé syndrome diagnosis. The patient gave consent for the presentation of his case. Other lung diseases included in the differential diagnosis of BHDS are lymphangioleiomyomatosis, pulmonary Langerhans cell histiocytosis, lymphocytic interstitial pneumonia, cystic lung metastases, amyloidosis, and fungal and parasitic infections such as Pneumocystis jirovecii pneumonia, coccidioidomycosis, paragonimiasis and echinococcosis (5). The air cysts in the lungs in BHDS can range in size from a few millimeters to 2 cm and are most commonly found on computed tomography. Unlike other cystic lung diseases, the size and number of pulmonary cysts in BHD syndrome do not progress over time (6). A study of 96 patients revealed normal FEV1, FVC and FEV1/FVC ratios. In the same study, patients' residual volumes increased by 116%, while DLCO values decreased by 85%. BHDS rarely leads to respiratory failure, unlike other cystic lung diseases (7). Most cases of BHDS reported in the literature were diagnosed based on dermatological lesions and a history of pneumothorax (8–11), while the presented case was diagnosed based on the presence of renal cell carcinoma, in addition to pneumothorax and a family history of pneumothorax. The diagnostic methods applied in various earlier case reports are summarized in Table 1.

Table 1: Case reports reported in the literature and data from our study

Case Report	Date/Number of cases	Age / Gender	Presence of pneumothorax / Family history	Diagnosis
Akay BN (8)	2013/1	59/M	-/-	Fibrofolliculoma
Uçar HA (9)	2025/1	53/M	+/ Not included in the article	Trichodiscoma
Cimsit C (10)	2016/2	Not included in the article	+/+	Fibrofolliculoma
Aksoy S (11)	2021/1	58/M	+/+	Fibrofolliculoma
Our Case Report	2025/1	41/M	+/+	Renal Cell Carcinoma

The initial treatment of primary spontaneous pneumothorax includes observation, aspiration and tube thoracostomy. In cases with prolonged air leakage or disease recurrence, excision of the bullae via video-assisted thoracoscopic surgery (VATS) or pleurodesis may be required (12). In the presented case, lung re-expansion was achieved with nasal oxygen therapy, and there was no recurrence within a 1-year follow-up. Smoking, age and sex are not considered risk factors for recurrence in BHDS (13).

CONCLUSION

Birt-Hogg-Dubé syndrome is a rare condition characterized by bilateral pulmonary cysts associated with spontaneous and recurrent pneumothoraces. Unlike other cystic lung diseases, it is non-progressive and does not impair pulmonary function, and its recurrent pneumothoraces are unrelated to smoking. The disease is definitively diagnosed through the identification of FLCN gene mutations and is often associated with a family history of pneumothorax. Our case emphasizes the importance of recognizing this rare syndrome.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - S.K., N.S.K., T.O.; Planning and Design - S.K., N.S.K., T.O.; Supervision - S.K., N.S.K., T.O.; Funding - S.K., N.S.K.; Materials - N.S.K., T.O.; Data Collection and/or Processing - S.K., T.O.; Analysis and/or Interpretation - S.K., T.O.; Literature Review - S.K., N.S.K.; Writing - S.K., N.S.K.; Critical Review - S.K., T.O.

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RESPIRATORY CASE REPORTS

Hamartoma Mimicking Asthma in A Female Patient: A Case Report with Unusual Clinical, Radiological and Pathological Findings

Kadın Hastada Astımı Taklit Eden Hamartom: Sıradışı Klinik, Radyolojik ve Patolojik Bulguları ile Olgu Sunumu

Yadigar Dila Keş[1], Cigdem Ozdilekcan[1], Deniz Doğan[2], Hale Kivrak[3]

Derya Yenibertiz[1]

Abstract

Endobronchial hamartomas are rare, but may cause bronchial obstruction, leading to persistent respiratory symptoms and radiological abnormalities such as atelectasis. A 43-year-old female patient with a diagnosis of asthma who had never smoked presented with complaints of cough, sputum and pleuritic chest pain. The initial diagnosis was community-acquired pneumonia, for which antibiotic treatment was administered. Although the patient's complaints regressed, atelectasis was a persistent finding on chest X-ray and so computed tomography (CT) was performed. A hypodense lesion obstructing the left upper lobe bronchus was detected in the thorax CT. An excisional biopsy was obtained during rigid bronchoscopy, the pathology of which confirmed the hamartoma diagnosis. We present the case of a patient with an endobronchial hamartoma and persistent atelectasis, and with treatment-resistant respiratory symptoms mimicking asthma.

Keywords: *Endobronchial Hamartoma, Asthma, Bronchoscopy, Electrocoagulation.*

Öz

Endobronşiyal hamartomlar ise nadir görülür ve bronş obstrüksiyonuna neden olarak, persistan solunum semptomları ile atelektazi gibi radyolojik anormalliklere yol açabilir. Sigara kullanmamış, astım tanısı olan 43 yaşındaki kadın hasta; öksürük, balgam ve plevral göğüs ağrısı şikâyetleri ile başvurdu. İlk değerlendirmede toplum kökenli pnömoni ön tanısı ile antibiyotik tedavisi başlandı. Hastanın semptomlarında gerileme olmasına rağmen, akciğer grafisinde atelektazi bulgusu devam ettiğinden toraks bilgisayarlı tomografisi (BT) yapıldı. Toraks BT'de, sol üst lob bronşunu tıkayan hipodens bir lezyon saptandı. Rijit bronkoskopi eşliğinde eksizyonel biyopsi gerçekleştirildi ve patolojik inceleme sonucunda hamartom tanısı doğrulandı. Bu olgu sunumunda, kalıcı atelektazi ve persistan solunum semptomları ile astımı taklit eden endobronşiyal hamartom tanılı bir hastayı sunmaktayız.

Anahtar Kelimeler: *Endobronşial Hamartom, Astım, Bronkoskopi, Elektrokoagülasyon.*

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Pulmonary endobronchial hamartomas are rare, and typically benign tumors. They are mostly asymptomatic and are frequently detected incidentally, but can cause bronchial obstruction and present with symptoms such as chronic cough, sputum production, hemoptysis and dyspnea as they grow in size (1). Histologically, endobronchial hamartomas are composed of fibroelastic tissue, cartilage, fat tissue and epithelial components, and are usually unilateral. Endobronchial hamartomas mostly develop in people aged 50–60 years, and are more common in males. The most common radiologic presentation is a solitary lesion localized in the upper lobe of the left lung. Pulmonary hamartomas are the most common type of benign lung lesion, and endobronchial localization is rare, occurring in 1.4–10% of the reported cases (1,2). Lesions can develop with bronchial obstruction features, and with clinical and radiological findings that can be confused with malignancy. Endobronchial lesions, in particular, can present with such symptoms as persistent lung infections and fever due to airway obstruction. For this reason, endobronchial hamartomas should be kept in mind in the differential diagnosis of pulmonary diseases. Endobronchial hamartomas are diagnosed based on bronchoscopy and biopsy, while imaging methods such as CT and positron emission tomography (PET) can clarify the nature of the lesions and rule out malignancy through metabolic characterization. Early diagnosis is crucial for successful treatment management and appropriate follow-up. The treatment for endobronchial hamartomas is surgical excision, although treatments may vary depending on the size, location and symptoms of the patient. Bronchoscopic methods can be considered as a minimally invasive and effective treatment option, especially for small and accessible lesions. Our case with an endobronchial hamartoma presented with persistent respiratory symptoms mimicking asthma and atelectasis on chest X-ray. We present this less common case of a female patient to the literature, including the diagnostic and management approaches employed and the endobronchial treatment strategy applied. Aside from patient's unusual clinical and radiological presentation, the absence of cartilage, fat and bone tissue in the pathological findings was another notable feature. The patient provided written informed consent for the publication of this case report.

CASE

A 43-year-old non-smoker female patient presented to our outpatient clinic with complaints of cough, yellow sputum and pleuritic chest pain for the past 20 days, but no fever. She had been prescribed clarithromycin 500 mg at a family health center, which she had taken regularly and had completed the treatment, but her symptoms had not improved, prompting her to seek further evaluation at our pulmonology outpatient clinic.
Her medical history included asthma, hypertension and hypothyroidism, and she had been treated for asthma with salmeterol/fluticasone for 4 years without significant objective benefit. Regarding the chest pain and venous thromboembolism risk, she had no recent long travels, immobilization history or hormone therapy use. Her pain was localized to the left anterior chest. A physical examination revealed normal breath sounds, no abnormalities were identified on inspection and a cardiac evaluation was also normal. As can be seen from the flow-volume curve in Figure 1 and in spirometric values in Table 1, FVC (Forced Vital Capacity) increased from 3.14 L (PRE) to 3.51 L (POST) – a >12% improvement that suggested improved lung volume after medication.

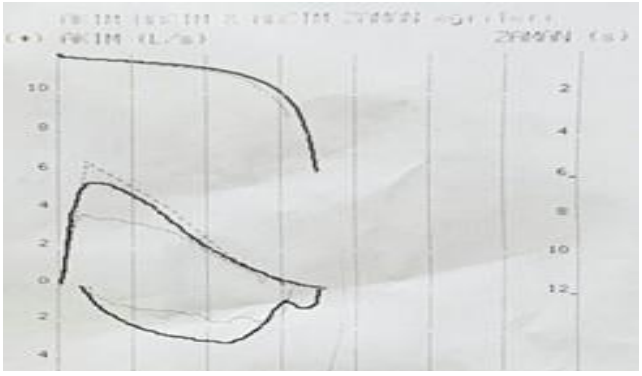

Figure 1: *Reversibility spirometry flow – volume curve*

FEV1 (Forced Expiratory Volume in 1 second) improved by +9% post-bronchodilator, which is considered negative reversibility as it does not meet the commonly applied threshold of ⩾12% and 200 mL for significant bronchodilator response. The FEV1/FVC ratio decreased slightly after bronchodilator use (from 78.3% to 76.0%), but remained close to the normal range (normal: typically >70%). Partial post-bronchodilator reversibil-

ity was also noted, especially in FVC. The overall spirometry pattern did not indicate a clear obstruction or restriction, though mild obstruction could not be ruled out depending on clinical context and full PFTs. Among the laboratory test results, C-reactive protein (CRP) was 148 mg/L, and community-acquired pneumonia was initially considered due to the elevated inflammatory markers. The patient, who had previously been taking clarithromycin, was started on a respiratory quinolone monotherapy. A follow-up examination 10 days later revealed a decrease in complaints and inflammatory marker response, while her CRP level had regressed to 5 mg/L. All other routine blood workups were within the normal range.

Table 1: *Spirometry values*

Parameter	Predicted	Pre (Before Meds)	Post (After Meds)	% Change (Δ)
FVC (L)	3.17	3.14	3.51	+12%
FEV1 (L)	2.72	2.46	2.67	+9%
FEV1/FVC (%)	80.0	78.3	76.0	−3%
PEF (L/s)	6.53	3.74	5.44	+45%
FEF25–75% (L/s)	3.35	2.33	2.82	+21%

A linear band formation was observed extending from the left hilum to the periphery, as well as an area of heterogeneous infiltration in the left apex associated with the atelectasis noted in the patient's postero-anterior chest X-ray (Figure 2). The atelectasis noted during the chest X-ray had persisted, and a Chest CT scan was planned for further evaluation (Figure 3). The CT scan revealed a hypodense 7 mm-diameter lesion within the left upper lobe bronchus (secretion, tumor, foreign body), and a distal nodular atelectasis area measuring approximately 77x37 mm with air-fluid bronchograms. The size of the described area was noted to have increased significantly in a comparison with the previous examination, prompting a bronchoscopic evaluation with a subsequent PET CT correlation, if necessary. A subsequent PET CT scan was requested by radiology for the metabolic characterization of the lung lesion, and fiberoptic bronchoscopy and PET/CT for further imaging were planned. The patient's PET/CT imaging revealed no distinguishable pathological FDG uptake in the millimetric densification area within the left upper lobe bronchus. Increased FDG uptake (SUVmax: 3.58) was observed in the area of atelectasis and consolidation, extending from the left lung apicoposterior segment to the suprahilar region, adjacent to the fissure and between the mediastinal pleura and costal pleura, where some areas were identified to contain air bronchograms.

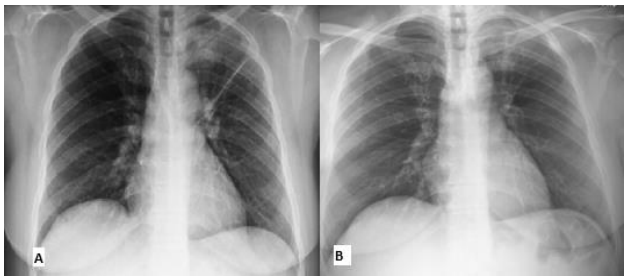

Figure 2: *Chest radiograph obtained prior to treatment revealing an area of atelectasis with a linear band formation (A). Post-treatment image showing the lack of complete radiological resolution (B)*

The left lung findings primarily suggested an inflammatory process; however, it was recommended that these findings be evaluated in conjunction with clinical data for differential diagnosis, along with close follow-up. The bronchoscope was passed through the right nasal cavity into the trachea. The trachea, carina and right airways were inspected up to the segmental bronchi, and were within normal limits. A bright, regular-surfaced, white-colored endobronchial lesion with lobulations was observed at the entrance to the left upper lobe, completely obliterating it, and so a punch biopsy was performed to obtain lavage from the area. The collected samples were sent for cytological and pathological examination. The endobronchial mass was observed to shrink during the punch biopsy procedure, and the obliterated bronchus was slightly opened. The patient tolerated the procedure well, with oxygen saturation remaining above 93% throughout the procedure. He was hemodynamically stable and experienced no complications (Figure 4). The pathological analysis of the punch biopsy revealed "findings of chronic inflammation, with blood, fibrin, and bronchial epithelial cells observed in a mucous substrate in the cell block".

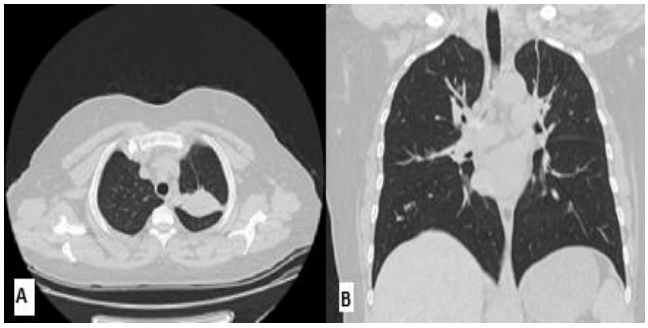

Figure 3: *Chest-lung window (A) and chest-mediastinal window (B) showing post-obstructive atelectasis secondary to endobronchial obstruction*

Due to the lack of diagnostic value of the biopsy obtained via flexible bronchoscopy, an excisional biopsy of the endobronchial lesion obliterating the bronchus was planned, for which the patient was referred to an interventional pulmonology center. The endobronchial lesion was excised via cryotherapy and was identified as a hamartoma in the pathology report. The biopsy specimen revealed a polypoid mass (A, X2) with spindle cells in the fibrotic and edematous stroma without a myxoid component, and the surface was lined with benign airway epithelium (B, X20). Immunohistochemically, the spindle cells expressed SMA (C, X10) and Desmin (D, X10). No necrosis or increased mitotic activities were observed; immunohistochemically S100, PanCK and STAT6 were negative, and no loss of expression was observed with Rb (Figure 5).

DISCUSSION

A comprehensive review of endobronchial hamartoma cases reported between 2010 and 2025 was made for the case report, the relevant details of which are presented in Table 2, with references provided in the first column (3–16). Hamartomas of the respiratory tract are rare benign lesions that are primarily composed of mature mesenchymal tissue such as cartilage, adipose tissue and smooth muscle. They are usually clinically silent and discovered incidentally (14). In a series assessed by Van den Bosch et al. (17), segmental atelectasis was the most frequently observed radiological finding, in alignment with the segmental atelectasis of the upper lobe that was predominant on computed tomography in the presented case. Pulmonary hamartoma were first described in 1904 by German pathologist Eugen Albrecht (15). They are generally composed of mature mesenchymal tissue commonly found in the lung, but without the preservation of the normal architecture (18). The histological makeup of these tumors usually includes a mix of mesenchymal tissue, such as adipose tissue, cartilage, bone or smooth muscle bundles, as well as fibromyxoid tissue, in varying proportions. They are noninvasive, slow-growing, nodular lesions that sometimes feature cleft-like spaces lined with respiratory epithelium (19). Unlike in previously reported cases, no cartilage, fat or bone tissue was observed in our case, while scattered smooth muscle cells without fascicular organization were observed in the vascularized fibrotic stroma. Small hamartomas typically do not require intervention but only follow-up for growth. When larger, however, they may obstruct the bronchial lumen, leading to symptoms such as cough, or pleuritic chest pain, as observed in our patient. Our case underlines the importance of differential diagnosis when evaluating endobronchial lesions, especially in patients with atypical presentations. This case report presents a rare case of endobronchial hamartoma with asthma-like symptoms to the literature, and discusses the diagnostic and therapeutic approaches followed. Our patient was 43 years old, which was not significantly different from the mean age reported in the cases summarized in Table 2. The fact that the patient was female is particularly noteworthy, given the predominance of males featured in earlier studies. Of the reported cases detailed in Table 2, eight were identified as non-smokers (4,5,7,8,11,13,14) and five were current or former smokers (1,9,10,15,16), while the smoking status of the remaining two cases was not reported (3,6). Consistent with the majority of these cases, our patient was a non-smoker, and her symptoms were strikingly similar to those usually associated with asthma, which led to a misdiagnosis and the initiation of asthma treatment.

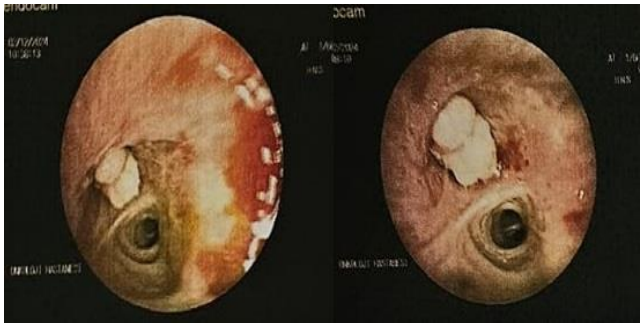

Figure 4: *Bright polypoid lesion obliterating the left main bronchus*

Previous studies have reported cases with symptoms such as cough and dyspnea, similar to our case; however, in the cases described by Habip et al. (15) and Minalyan et al. (9) in 2024, hemoptysis was also reported in addition to cough. Our evaluation of the bronchoscopic findings in the presented case revealed a lesion that was completely obliterating the left upper lobe. In the cases summarized in Table 2, the reported endobronchial hamartomas had various localizations, including the upper lobes in six cases (5,7,9,10,11,13), the lower lobes in two cases (7,15), the main bronchi in three cases (3,4,16), the intermediate bronchus in one case (12) and the trachea in one case (14). Our case had left upper lobe involvement, consistent with the most commonly reported sites. Histopathological evaluation is crucial for a definitive diagnosis. In our case, standard bronchoscopic procedures failed to yield sufficient histopathological data to support our preliminary differential diagnoses of lipoma, hamartoma, carcinoid tumor and malignancy, and so the patient underwent a rigid bronchoscopy for both diagnostic and therapeutic purposes. The endobronchial lesion was excised via rigid bronchoscopy, which allowed for both confirmation of the diagnosis and initiation of appropriate treatment. The histological appearance of such tumors is generally a mixture of mature mesenchymal tissue, including adipose tissue, cartilage, bone and smooth muscle bundles, and fibromyxoid tissue, in varying proportions. Atypically, no cartilage, fat or bone tissue was observed in our case; instead, scattered smooth muscle cells without fascicular organization in vascularized fibrotic stroma.

Our review of the literature revealed that similar diagnostic bronchoscopies were often followed by rigid bronchoscopies for differential diagnosis and treatment purposes, and then by cryotherapy, argon plasma coagulation, electrocautery and laser resection procedures. In most reported cases, definitive diagnosis was obtained following resection. In our case, the team applied electrocautery in combination with a snare probe for lesion removal, the patient underwent fiberoptic bronchoscopy (FOB). Among the preliminary differential diagnoses for the observed smooth-surfaced endobronchial lesion was carcinoid tumor, and so a bronchoscopic biopsy was performed with great caution, and after confirming the absence of bleeding with the first sample, the procedure continued safely. As our center lacked the necessary facilities for histopathological verification, the patient was referred to a specialized endobronchial treatment center for definitive diagnosis and treatment. Although rigid bronchoscopy may be considered preferable for lesions with a high risk of bleeding, our approach was guided by a clinical assessment and the available resources, and the procedure was completed without complications. The main differential diagnoses are other benign lesions, such as bronchial tuberculosis, bronchial lipoma, leiomyoma, fibroma, chondroma and neurogenic tumors, although malignant airway tumors such as a carcinoid tumor and bronchial metastasis, should also be kept in mind (12). This case highlights the importance deeper diagnostic evaluation in patients who do not exhibit objective or subjective improvement during treatment, as pulmonary endobronchial hamartomas can be clinically misdiagnosed as other conditions.

In the early stages, both benign and malignant endobronchial tumors may have similar signs and symptoms, which can be misdiagnosed as asthma, COPD or pulmonary infection. Most commonly, patients seek treatment for cough and hemoptysis, chest pain, dyspnea, localized wheezing, recurrent pneumonia or atelectasis due to bronchial obstruction. In the absence of airway obstruction, the patient may be asymptomatic. This case emphasizes the need of further investigation in patients who do not show objective or subjective benefit during treatment, as pulmonary endobronchial hamartomas may be confused with other pathologies. If the tumor is in the lumen of the trachea or bronchi, the patient's complaints may mimic respiratory diseases such as bronchial asthma, chronic obstructive pulmonary disease or recurrent pneumonia.

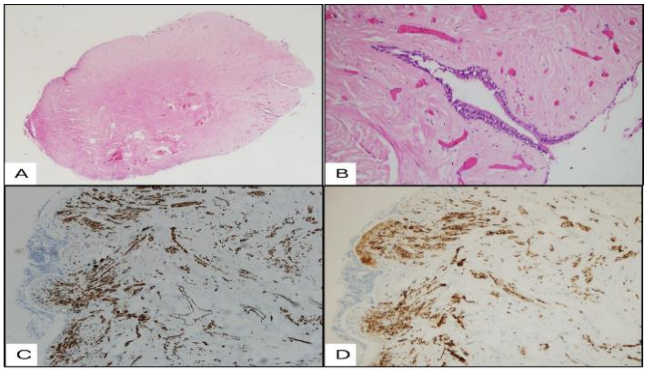

Figure 5: *Histopathological examination ((A) H&E, x2, (B) H&E, x20, (C) SMA, x10, (D) Desmin, x10))*

Our resected endobronchial lesion measured 12 × 11 mm in diameter, and lobulation was observed. As can be seen from the summary of earlier cases in the literature presented in Table 2, lesion sizes ranged from 10 × 7 × 5 mm (16) to 40 × 20 × 10 mm (11). Our lesion, therefore, can be considered of average size among the other reported cases. The larger reported lesions in the summary were generally managed with surgical resection. Endobronchial hamartomas are generally associated with a favorable prognosis; however, recurrence rates of approximately 10% following bronchoscopic resection have been documented (20). There is currently a lack of consensus on the optimal surveillance interval or follow-up duration. Notably, the malignant transformation of such lesions has rarely been observed on long-term follow-up. Our case remains asymptomatic and her clinical, radiological and spirometric follow-up is continuing, with no evidence of relapse observed to date. However, serial computed tomography (CT) imaging will be used for postoperative follow-up to monitor for possible recurrence annually. The patient's asthma-like symptoms resolved and radiological improvement was confirmed on CT imaging (Figure 6), indicating a marked regression in the atelectasis and obstruction findings; consequently, inhaler therapy was discontinued. The patient will continue to be monitored for potential future relapses. One limitation of this report is the relatively short follow-up period, which prevents the assessment of long-term recurrence. Furthermore, while the diagnosis of hamartoma was made based on a histopathological analysis, the absence of cartilage and adipose tissue may pose diagnostic challenges in similar cases in the future. Finally, a more comprehensive account of the patient's long-term functional and radiological outcomes would enhance the clinical significance of this case.

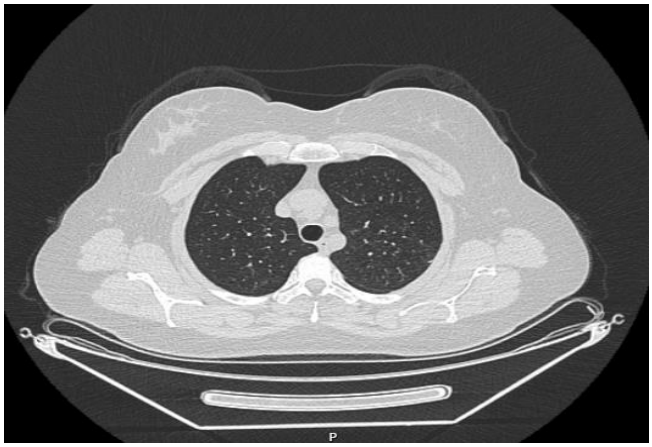

Figure 6: *CT image demonstrating marked regression of atelectasis following the removal of the lesion through electrocautery in combination with a snare probe*

Table 2: *The Review and The Summary of Cases between the Years 2010- 2025*

Year	Author	Age	Gender	Smoking	Symptoms	Diameters of Lesion	Location of Lesion	Treatment	Relapse
2010	Rai et al. (3)	40	Male	Unknown	Cough, Fever, Anorexia	Unknown	Left Main Bronchus	Diode Laser	No
2011	Mondello et al. (4)	65	Male	Non-Smoker	Asymptomatic	Unknown	Left Main Bronchus	Electrosurgical Snaring	No
2012	Guarino et al.(5)	35	Female	Non-Smoker	Dyspnea, Cough, Chest Pain	Unknown	Left Upper Obe	Fenestrated Crocodile Biopsy Forceps	No
2013	Gayathri et al.(6)	65	Male	Unknown	Cough	Unknown	Right Upper Lobe	Conservative Follow Up	No
2013	Seğmen et al. (7)	59	Male	Non-Smoker	Cough and Dyspnea	30 Mm	Left Lower Lobe	APC and Electrocautery	No
2015	Mertoğlu et al. (8)	45	Male	Non-Smoker	Cough, Fever	Unknown	Right Main Bronchus	APC and Electrocautery	No
2017	Ahmed et al. (1)	53	Male	Former Smoker	Cough, Dizziness	Unknown	Left Upper Lobe	Laser Resection	Yes
2019	Minalyan et al. (9)	49	Male	Former Smoker	Fever, Cough, Hemoptysis	14mm	Left Upper Lobe	Forceps Debulking and Cauterization	No
2022	Suzuki et al(10)	51	Male	5 Pack/Year	Asymptomatic	10 Mm	Right Main Bronchus	High-Frequency Electrocautery	No

Table 2: *Continued*

2023	Fernandez-Trujillo et al. (11)	44	Female	Non-Smoker	Cough, Expectoration	40x20x10mm	Right Main Bronchus	Cryotherapy	No
2024	Bouanani et al. (12)	57	Male	Former Smoker	Cough	Unknown	Right Intermediate Bronchus	Surgical Resection	No
2024	Takigawa et al. (13)	82	Male	Non-Smoker	Dyspnea	40x20 Mm	Left Upper Lobe	Cryotherapy	Unknown
2024	Kaziród et al. (14)	53	Male	Non-Smoker	Dyspnea,Wheezing	18 Mm	Trachea	Endoscopic Electroresection	No
2024	Habib et al. (15)	71	Male	20 Pack/Year	Cough, Hemoptysis	13x4 Mm	Right Middle Lobe Segmental Bronchus	Cryotherapy and APC	Unknown
2025	Daboussi et al. (16)	64	Male	Former Smoker	Cough	10x7x5mm	Left Main Bronchus	Segmentectomy	No

CONCLUSION

This case highlights the importance of deeper diagnostic evaluation in patients who do not exhibit objective or subjective improvement during treatment, as pulmonary endobronchial hamartomas can be clinically misdiagnosed as other conditions. Patients with undiagnosed dyspnea should be further evaluated using CT imaging and bronchoscopy. Endobronchial hamartomas can be treated effectively and safely using interventional bronchoscopic methods. After a complete resection, additional therapeutic options (such as cryotherapy) applied to the root of the lesions may help prevent recurrence. Successful results have been achieved with endobronchial resection approaches both in our case and in the cases reviewed in Table 2. All patients should be followed up for recurrent disease.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - Y.D.K., Ç.Ö, D.Y.; Planning and Design - Y.D.K., Ç.Ö.; Supervision - Y.D.K., Ç.Ö.; Funding - Y.D.K., Ç.Ö, D.D., H.K.; Materials - Y.D.K., Ç.Ö, D.D., H.K.; Data Collection and/or Processing - Y.D.K.; Analysis and/or Interpretation - Y.D.K., Ç.Ö.; Literature Review - Y.D.K., Ç.Ö.; Writing - Y.D.K.; Critical Review - Y.D.K., Ç.Ö.

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Respir Case Rep 2025;14(3):119-122 DOI: 10.5505/respircase.2025.29974

RESPIRATORY CASE REPORTS

Adult Presentation of Swyer–James–MacLeod Syndrome Masquerading as COPD and Pulmonary Embolism: A Diagnostic Challenge of an Overlooked Childhood Disease - A Case Report

Swyer-James-MacLeod Sendromunun Erişkin Yaşta KOAH ve Pulmoner Emboli ile Karışan Sunumu: Unutulmuş Bir Çocukluk Çağı Hastalığında Tanısal Bir Tuzak - Olgu Sunumu

Sibel Karakaya, Elif Torun Parmaksız, Eylem Tunçay, Metin Karakaya

Abstract

Swyer-James-MacLeod Syndrome (SJMS) is a rare broncho-pulmonary disorder that typically develops following an infection in the lungs during childhood, such as viral bronchiolitis or pneumonia. Radiologically, it is characterized by a unilateral hyperlucent lung, decreased pulmonary vascularity, and air trapping. Clinically, the syndrome can present with symptoms such as cough, sputum production and exertional dyspnea, although it may also remain asymptomatic and be discovered incidentally during imaging. SJMS can mimic various pulmonary conditions, including pulmonary thromboembolism. We present here a case from our outpatient clinic in which a patient was initially evaluated with a preliminary diagnosis of pulmonary thromboembolism, but was ultimately diagnosed with SJMS after thorough clinical and radiological assessment.

Keywords: *Swyer-James MacLeod Syndrome, Unilateral HyperlucentLlung, Air Trapping, Respiratory Bronchiolitis, Bronchiectasis.*

Öz

Swyer-James-MacLeod Sendromu (SJMS), genellikle çocukluk çağında viral bronşiolit veya pnömoni gibi enfeksiyöz bir süreci takiben gelişen nadir bir bronkopulmoner hastalıktır. Radyolojik olarak tek taraflı hiperlusent akciğer, azalmış pulmoner vaskülarite ve hava hapsi ile karakterizedir. Klinik olarak öksürük, balgam ve eforla artan dispne gibi semptomlarla prezente olabilir; ancak asemptomatik de seyrederek görüntüleme sırasında tesadüfen saptanabilir. SJMS, pulmoner tromboemboli (PTE) dahil olmak üzere çeşitli akciğer hastalıklarını taklit edebilir. Bu yazıda, polikliniğimizde PTE ön tanısı ile değerlendirilen, ancak detaylı klinik ve radyolojik değerlendirme sonrası SJMS tanısı konulan bir olgu sunulmaktadır.

Anahtar Kelimeler: *Swyer-James MacLeod Sendromu, Tek Taraflı Hiperlusent Akciğer, Hava Hapsi, Respiratuvar Bronşiolit, Bronşektazi.*

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Swyer-James-MacLeod Syndrome (SJMS) is a rare, acquired pulmonary disorder that usually develops after childhood viral bronchiolitis, and most commonly due to adenovirus infection (1,2). It is characterized by obliteration of the small airways, hypoplasia or absence of a pulmonary artery, or the underdevelopment of the peripheral pulmonary vasculature, resulting in a unilateral hyperlucent and hypoperfused lung (1,2). Clinical manifestations range from asymptomatic radiographic findings to chronic respiratory symptoms such as exertional dyspnea, pleuritic chest pain, chronic cough and recurrent lower respiratory tract infections (2,3). Diagnosis is primarily based on characteristic radiological features, especially high-resolution computed tomography (HRCT) and ventilation-perfusion scintigraphy, while pathological confirmation is rarely required (4-7). SJMS is often misdiagnosed as chronic obstructive pulmonary disease (COPD) or pulmonary embolism (PTE) due to their overlapping clinical and radiographic features, leading to inappropriate or delayed treatment (8-10). We present the case of an adult male who undergone treatment for COPD for several years and who was admitted with suspected pulmonary embolism, but was subsequently diagnosed with SJMS following perfusion scintigraphy.

CASE

A 54-year-old male with a 15 pack-year smoking history was referred to our pulmonology outpatient clinic with a 10-day history of right-sided pleuritic chest pain, shoulder discomfort and exertional dyspnea, but no reported hemoptysis or fever. He had been diagnosed with chronic obstructive pulmonary disease (COPD) 5 years earlier based on symptoms of chronic cough and dyspnea, and had been intermittently treated with inhaled bronchodilators. The regimen had included a combination of indacaterol and glycopyrronium bromide, but the patient reported minimal symptomatic improvement, despite long-term use. Of note in his medical history was hospitalization for a lower respiratory tract at the age of 3–4 years, although the exact duration was not documented and no surgical intervention was performed. There was no history of tuberculosis, thromboembolic disease or relevant family history. The patient's vital signs were stable on physical examination, while auscultation revealed end-expiratory wheezing and markedly decreased breath sounds in the left lung. Oxygen saturation was 96% in room air, arterial blood gas: pH: 7.38, PaO_2: 81 mmHg and $PaCO_2$: 37 mmHg.Chest radiography demonstrated right hilar volume loss and decreased vascular markings in the left lung. Laboratory results revealed a D-dimer level of 1489 µg/L, CRP: 1.6 mg/L, and normal troponin and renal function. Pulmonary embolism was initially suspected in the emergency department due to the patient's acute pleuritic chest pain, exertional dyspnea and mildly elevated D-dimer level. Computed tomography pulmonary angiography (CTPA) was thus performed to exclude thromboembolic disease (Figure 1).

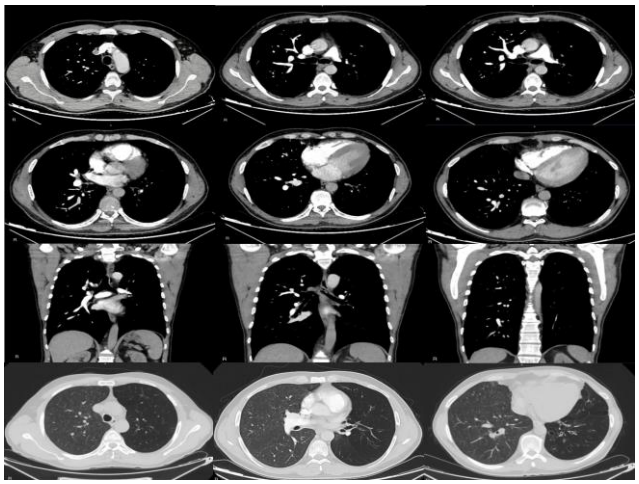

Figure 1: *Computed Tomography Pulmonary Angiography (CTPA) showing all lobes and segments of the right lung with features consistent with respiratory bronchiolitis, while the left lung demonstrates decreased attenuation and reduced broncho-vascular markings. Marked bronchial dilatation, bronchial wall thickening and peribronchial opacities that are particularly prominent in the lower lobe can be observed in both lobes, consistent with bronchiectasis*

The pulmonary arteries, including the main branches, were patent, and no significant thromboembolic event was detected in the distal subsegmental branches. Decreased density with reduced broncho-vascular markings was noted in the left lung, and the scan revealed centrilobular ground-glass opacities in the right lung, consistent with respiratory bronchiolitis, fibroatelectatic bands in the middle lobe and a subpleural air cyst in the right lower lobe. The left lung exhibited reduced volume, diffuses hypodensity, bronchiectasis, bronchial wall thickening and scattered ground-glass opacities that were most prominent in the lower lobe. Pulmonary function tests revealed an obstructive pattern with an FEV_1/FVC ratio of 65%, while transthoracic echocardiog-

raphy *demonstrated* normal biventricular function with no signs of pulmonary hypertension. A perfusion scintigraphy was performed using Tc-99m MAA to further investigate the asymmetrical radiological findings, demonstrating normal perfusion in the right lung, while the left lung showed a global perfusion deficit without segmental or subsegmental defects, consistent with unilateral hypoperfusion (Figure 2).

Based on the combined clinical, radiological and functional findings, the patient was diagnosed with SJMS, a condition likely attributable to his childhood respiratory infection. The initial diagnosis of COPD was reconsidered, and the patient was started on bronchodilator therapy tailored for SJMS-related airflow limitation, with a strong recommendation for smoking cessation and routine vaccinations. The patient reported symptomatic improvement at one-month follow-up. Given the absence of significant functional compromise, he was scheduled for continued outpatient follow-up without need for further intervention.

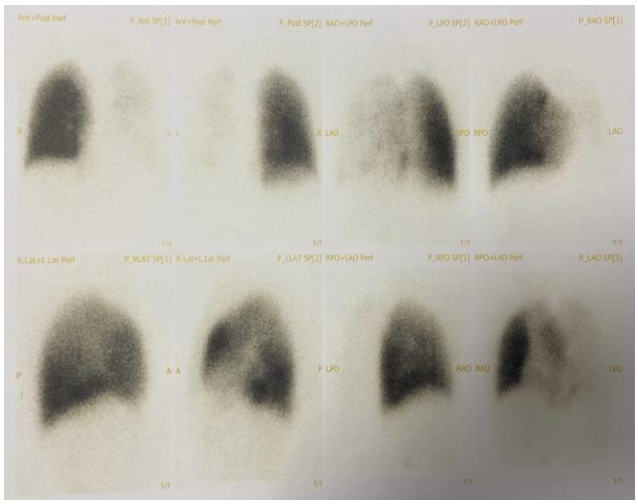

Figure 2: *Perfusion scintigraphy showing normal perfusion in the right lung without significant segmental or subsegmental defects. Perfusion scintigraphy showing absent perfusion in the left lung, and no parenchymal pathology on CT.*

DISCUSSION

Swyer-James-MacLeod Syndrome (SJMS) is a rare pulmonary disorder that was first described in 1953 by Swyer and James. The condition is characterized by unilateral hyperlucent lung, and while it is most frequent in the right lung, it can occasionally present with bilateral involvement (11). The pathogenesis involves post-infectious bronchiolitis obliterans, most commonly due to adenovirus subtypes B21, B3 or B7 in childhood, resulting in small airway obstruction and vascular hypoplasia (1,2). The history of severe lower respiratory tract infection during early life noted in our patient is a well-established risk factor for SJMS (2,3). In the original cases described by Swyer and James, spirometry typically demonstrated airflow obstruction associated with features of bronchiolitis obliterans (11), although there is evidence that SJMS may also be linked to the development of pulmonary hypertension in later stages of life (6,7). It should be kept in mind that SJMS can mimic acute pulmonary embolism (PTE), both clinically and radiographically. The sudden-onset dyspnea, pleuritic chest pain and hypoxemia symptoms common to PTE overlap with SJMS in patients with significant unilateral perfusion abnormalities. However, while PTE is an acute vascular event requiring immediate intervention, SJMS is a chronic condition with congenital or acquired pulmonary vascular underdevelopment. Differentiating between the two is essential, as misdiagnosis may lead to unnecessary anticoagulation or delayed appropriate management (9,10). In our case, the patient's acute chest symptoms and elevated D-dimer level initially raised suspicion for PTE, but further evaluation, including perfusion scintigraphy, pointed to the correct diagnosis. Another diagnostic pitfall is the misclassification of SJMS as COPD. Due to the presence of chronic cough, dyspnea and airflow limitation, patients with SJMS are often empirically treated for COPD without adequate imaging or pulmonary function evaluation. In our patient, bronchodilator therapy had been prescribed for presumed COPD for several years, but the lack of significant clinical improvement prompted further investigation. The spirometric pattern in SJMS often shows an obstructive component that, unlike COPD, is typically unilateral and associated with matched radiographic findings of lung volume loss, vascular attenuation and air trapping. Moreover, the progressive nature and systemic manifestations seen in classic COPD are usually absent in cases of SJMS. Previously reported cases have described patients treated for COPD for years until HRCT revealed unilateral hyperlucency and vascular hypoplasia consistent with SJMS (8), underscoring the importance of detailed history-taking and appropriate imaging in patients with atypical or treatment-refractory obstructive symptoms. HRCT remains the cornerstone of structural assessment, typically showing hyperlucency,

air trapping, bronchiectasis and vascular paucity in the affected lung. Ventilation-perfusion scintigraphy provides complementary functional information, characteristically demonstrating unilateral global hypoperfusion without segmental defects, a finding that helps distinguish SJMS from pulmonary embolism (6,7,9). The combined use of HRCT and scintigraphy can thus enhance diagnostic accuracy and prevent misinterpretation. The management of SJMS is usually conservative, tailored to symptom control and the prevention of complications. Treatments include inhaled bronchodilators, vaccination against influenza and pneumococcus, smoking cessation and pulmonary rehabilitation. Patients should also be followed for potential long-term complications such as recurrent pulmonary infections, hemoptysis and the gradual development of pulmonary hypertension (6,7). In selected cases with localized disease and recurrent infections, surgical interventions such as lobectomy may be considered (7). Our patient responded well to conservative measures with symptomatic improvement at follow-up.

CONCLUSION

Swyer-James-MacLeod Syndrome (SJMS) is a rare but important differential diagnosis in adults presenting with unilateral hyperlucent lung, chronic respiratory symptoms or perfusion abnormalities suggestive of pulmonary embolism. The presented case emphasizes the importance of a detailed history, advanced imaging (HRCT and perfusion scintigraphy) and pulmonary function tests for the establishment of a correct diagnosis. Clinicians should keep SJMS in mind when encountering patients with a history of lower respiratory infections in childhood and inadequate response to standard COPD therapy. Our report highlights the role of perfusion scintigraphy and HRCT in the diagnosis of this often-overlooked condition and in the prevention of misdiagnoses.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - S.K., E.T.P., E.T, M.K.; Planning and Design - S.K., E.T.P., E.T, M.K.; Supervision - E.T.P., E.T.; Funding - S.K., E.T.P., E.T, M.K.; Materials - S.K., E.T.P.; Data Collection and/or Processing - E.T.P., E.T, M.K.; Analysis and/or Interpretation - S.K., E.T.P.; Literature Review - S.K., E.T.P., M.K.; Writing - S.K., E.T.P.; Critical Review - E.T.P., E.T, M.K.

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COVID-19 PCR (+) Neonatal Mortality: Case Series

COVID-19 PCR (+) Yenidoğan Mortalitesi: Olgu Serisi

Leyla Şero[1], Nilüfer Okur[2]

Abstract

We present here the clinical features of five infants who died in the neonatal period due to COVID-19, for which the medical records of COVID-positive pregnant women isolated in a third-level neonatal intensive care unit between December 2019 and October 2021 were evaluated retrospectively. Of the five cases, three were preterm, one had a great artery transposition and another underwent surgery for necrotizing enterocolitis. All of the cases experienced a gradual increase in respiratory distress, and none responded to remdesivir, intravenous immunoglobulin or steroid treatments. COVID-19 infection can be fatal in the neonatal period, especially in the presence of an underlying disease or comorbidities such as prematurity and congenital heart disease.

Keywords: *Covid-19, Newborn, Mortality.*

Öz

Bu çalışmanın amacı yenidoğan döneminde Covid-19 nedeniyle ölen beş bebeğin klinik özelliklerini paylaşmaktır. Aralık 2019 ve Ekim 2021 tarihleri arasında Covid-pozitif annenin bebeği olması nedeniyle üçüncü seviye yenidoğan yoğun bakım ünitesine izolasyon için kabul edilen hastaların tıbbi kayıtları retrospektif olarak incelendi. Beş olgunun üçü preterm, biri büyük arter transpozisyonu ve biri nekrotizan enterokolit nedeniyle ameliyat edilmişti. Tüm vakalarda solunum sıkıntısı giderek arttı. Hastaların hiçbiri remdesivir, intravenöz immünoglobulin ve steroidlere yanıt vermedi. Yenidoğan döneminde Covid-19 enfeksiyonu, özellikle altta yatan hastalık varlığında, prematürite ve konjenital kalp hastalığı gibi komorbiditelerde ölümcül olabilmektedir.

Anahtar Kelimeler: *Covid-19, Yenidoğan, Mortalite.*

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The novel 'severe acute respiratory syndrome coronavirus 2' (SARS-CoV-2) behind the coronavirus disease 2019 (COVID 19) pandemic resulted in severe illness in adult populations around the world. While pregnant women were considered at risk, neonatal infections have been rare. Early data indicated that older adults were at the greatest risk of severe disease and mortality, although pediatric cases (including neonates) have also been reported. That said, the number of documented cases among newborns is considerably lower than in adults (1,2). Respiratory viruses are rarely transmitted in utero, and while the vertical transmission of SARS-CoV-2 was initially considered unlikely, isolated case reports identified SARS CoV 2 RNA in amniotic fluid (3), placental tissue (4) and in the nasopharynx of neonates within 48 hours of birth, suggesting the possibility of congenital infection. The true rate of vertical transmission among infants born to SARS CoV 2–positive mothers remains unknown. In the present study we describe five cases of COVID-19-positive neonates, each of whom was born to a COVID-19-positive mother or father who died in a tertiary care pediatric hospital with a confirmed SARS-CoV-2 infection. Our article focuses on the clinical presentation, management and progression of these cases, highlighting the potential severity of COVID-19 in neonates.

CASE

Neonatal mortality among infants hospitalized at a rural tertiary referral center between December 2019 and October 2021 was reviewed, for which the institutional medical and perinatal death registries were accessed.

Inclusion Criteria:

- Live-born neonates with SARS-CoV-2 infection confirmed by PCR testing.
- Subsequent in-hospital death during the neonatal period.

Exclusion Criteria:

- Stillbirths.
- Suspected cases with negative PCR results.
- Infants who were transferred to other facilities prior to outcome ascertainment.

Clinical Management:

All infants were delivered in negative-pressure isolation rooms. The newborns were immediately separated from their mothers, all of whom had confirmed or suspected COVID 19 infection. Regardless of the neonatal symptoms, all infants underwent a SARS-CoV-2 PCR test at approximately 24 hours of life. If the initial result was negative or unavailable, a second test was conducted at 48 hours. Neonatal care was provided in accordance with institutional COVID-19 neonatal protocols, including respiratory support and pharmacologic interventions. Details of each case are presented below.

Case-1: A female newborn was delivered via cesarean section at 30 weeks' gestation weighing 1450 g. The mother had not received antenatal steroid treatment prior to delivery. The neonate developed respiratory distress, polycythemia and perinatal asphyxia immediately after birth. A cord blood gas analysis revealed a pH of 7.04, base excess of -19.7, lactate 16.6 mmol/L and bicarbonate 10.4 mmol/L. Chest X-ray revealed diffuse ground-glass opacities in the left lung (Figure 1).

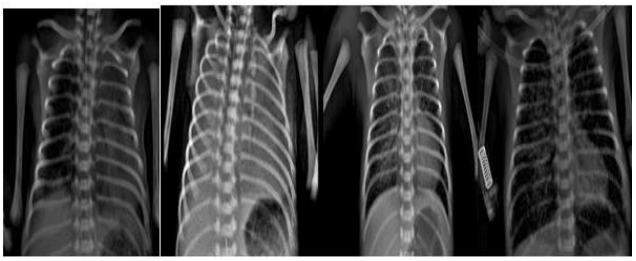

Figure 1: *Case 1 PA Chest X-ray*

The mother delivered at 30 weeks of gestation, and provided a positive nasopharyngeal PCR test at the time of delivery. The neonate's PCR test was positive on day 5. Initial management included partial blood exchange transfusion, the administration of three doses of exogenous surfactant and invasive mechanical ventilation. The infant's hematocrit was 74% at the time of birth, with increased plasma viscosity and thrombocytopenia. Clinical signs included slowed blood flow, features of polycythemia, respiratory distress and need for mechanical ventilation. An 80 ml/kg partial blood exchange was performed to alleviate symptoms, but the infant's condition deteriorated with worsening renal and hepatic function and the progression of radiographic

findings to bilateral opacities. Echocardiography (ECHO) detected a hemodynamically significant large patent ductus arteriosus (PDA), alongside poor thermal regulation, increased ventilatory requirements and decreased urine output. After failure of conservative management, two courses of ibuprofen were administered to close the PDA. The infant's escalating respiratory failure prompted the administration of broad-spectrum antibiotics (meropenem, vancomycin, amikacin) and inotropic support (dopamine), and the initiation of high-frequency oscillatory ventilation (HFOV). Pulmonary hypertension was observed, and sildenafil therapy was started. The infant's first two SARS-CoV-2 PCR tests (taken 48 hours apart) were negative but turned positive on day 5. Therapeutic interventions included remdesivir (loading dose 5 mg/kg followed by 2.5 mg/kg/day for 5 days), methylprednisolone (2 mg/kg/day) and intravenous immunoglobulin (IVIG) at 0.4 g/kg/day for 5 days. Despite aggressive treatment, the infant died on day 24 of life due to acute respiratory distress syndrome (ARDS) and multiple organ failure.

Case-2: A male neonate born via cesarean section at 34 weeks' gestation weighing 2400 g presented with cyanosis, respiratory insufficiency, tachycardia and low oxygen saturation. A cord blood gas analysis revealed pH 7.10, base excess -14.5, lactate 6.5 mmol/L and bicarbonate 15.1 mmol/L. Chest X-ray revealed bilateral opacification with pleural effusions, consistent with acute respiratory distress (Figure 2).

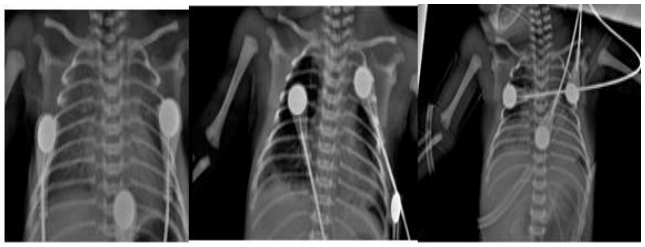

Figure 2: *Case 2 PA Chest X-ray*

The mother's PCR test was positive at the time of delivery, and the neonate's PCR test was also positive on day 0. Echocardiography confirmed the transposition of the great arteries (TGA). Invasive mechanical ventilation was initiated due to progressive hypoxia. An alprostadil (prostaglandin E1 at 0.1 µg/kg/min) infusion was given and an urgent balloon atrial septostomy was performed to improve systemic oxygenation. Additional management included surfactant therapy, cardiovascular support with milrinone and noradrenaline, and inhaled nitric oxide for pulmonary hypertension. Despite the interventions, the infant developed oliguria, hyperammonemia and acute renal failure, necessitating peritoneal dialysis, and his clinical condition had deteriorated further by day 3, complicated by massive pulmonary hemorrhage, ARDS and multi-organ failure. A SARS-CoV-2 PCR test was positive at this time. Despite maximal supportive care, the infant died on day 3 of life.

Case-3: A male neonate was born vaginally at 41 weeks' gestation weighing 3050 g, and developed respiratory distress, low oxygen saturation, shortness of breath and bilateral patchy infiltrates shortly after birth. Chest X-ray revealed diffuse ground-glass opacities in both lungs (Figure 3).

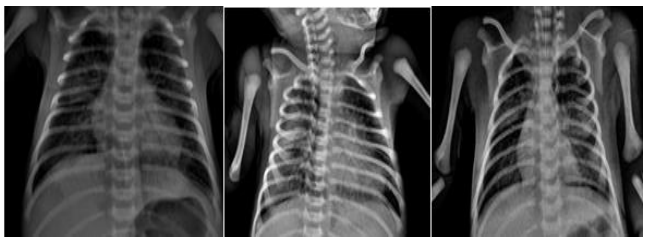

Figure 3: *Case 3 PA Chest X-ray*

PCR tests of the mother and father were negative and positive, respectively, while the neonate provided a positive PCR test 8 days after birth. Initial management included non-invasive respiratory support via CPAP and empirical antibiotics (ampicillin and amikacin). Despite treatment, his respiratory status worsened, and SARS-CoV-2 PCR testing returned positive. Treatment was escalated to invasive mechanical ventilation, with the addition of cefotaxime and the initiation of antiviral and immunomodulatory therapies including remdesivir, methylprednisolone and IVIG. Despite intensive care, the infant developed progressive ARDS, complicated by pulmonary hemorrhage and multi-organ failure, and died on day 13 postnatally.

Case-4: A 19-day-old male neonate, born vaginally at 38 weeks' gestation with an uneventful perinatal course, presented with stage 3A necrotizing enterocolitis (NEC) requiring surgical intervention. The infant had significant perinatal asphyxia (Apgar scores 3, 5, and 6; pH 6.8; base excess –23.1 mEq/L), which likely contributed to intestinal ischemia and NEC. Histopathological

examination of the resected bowel revealed transmural necrosis, inflammatory cell infiltration and bacterial colonization. The mother provided a positive PCR test at delivery, while the neonate's PCR test was positive on day 3. Preoperative SARS-CoV-2 PCR testing was positive. Post-surgery, the neonate was intubated and transferred to our tertiary neonatal intensive care unit (NICU) for ongoing management. Upon admission, portal venous thrombosis was detected on Doppler ultrasonography, leading to the initiation of low-molecular-weight heparin (LMHW) therapy. Broad-spectrum antibiotics (meropenem, vancomycin and amikacin), antiviral therapy (remdesivir), methylprednisolone and IVIG were also administered. Although the infant's SARS-CoV-2 PCR tests were initially negative at birth, subsequent tests during hospitalization were positive. Over the following days, liver function and coagulation parameters deteriorated, and thrombocytopenia developed. Platelet transfusions and fresh frozen plasma were provided as needed. Despite aggressive management, the patient suffered massive pulmonary and gastrointestinal hemorrhages on day 25 of life (NICU day 6) as well as acute respiratory distress syndrome (ARDS) and multiorgan failure, leading ultimately to death (Figure 4).

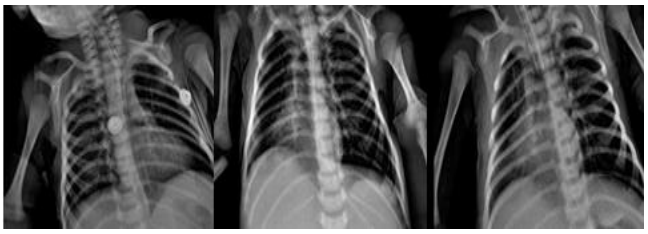

Figure 4: *Case 4 PA Chest X-ray*

Case-5: A male neonate born vaginally at 28 weeks' gestation weighing 1150 g presented immediately after delivery with respiratory distress, complications related to prematurity, perinatal asphyxia and a small patent ductus arteriosus (PDA). The mother provided a positive PCR test at delivery, while the neonate's PCR test was positive on day 0. On day 6, the infant developed life-threatening complications, including massive pulmonary hemorrhage, metabolic acidosis, anemia and thrombocytopenia. Endotracheal intubation was performed, and blood cultures revealed Acinetobacter baumannii bacteremia. The SARS-CoV-2 PCR tests remained positive throughout hospitalization. The infant was treated with broad-spectrum antibiotics, including meropenem, vancomycin and amikacin, as well as inhaled colistimethate (colimycin). Supportive care included transfusions of platelets and red blood cells, as well as fresh frozen plasma. Despite intensive management, the infant succumbed to massive pulmonary hemorrhage on day 10 of life, complicated by ARDS and multiple organ failure secondary to COVID-19 (Figure 5). Table 1 presents a summary of the demographic and clinical characteristics of the five cases, while Table 2 presents the key laboratory findings.

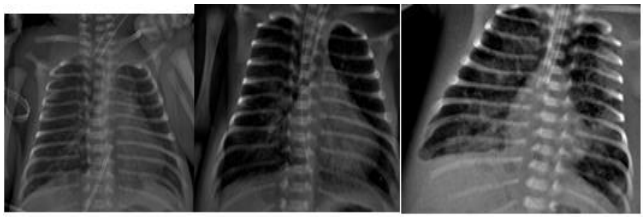

Figure 5: *Case 5 PA Chest X-ray*

Table 1: *Clinical Characteristics and Outcomes of Neonatal COVID-19 Cases*

	Case 1 BY	Case 2 BK	Case 3 BO	Case 4 EK	Case 5 BT
Maternal age(years)	34	26	24	17	22
Gestational age at delivery (weeks)	30	34	41	38	28
Comormidities (GDM, HPD, PE, Hypothyroidism)	NR	NR	NR	NR	NR
Maternal nazopharingeal PCR	Positive	Positive	Negative (father's positive)	Positive	Positive
Mode of delivery	Cesarean	Cesarean	Vaginal	Vaginal	Vaginal
Birth weight (g)	1450	2400	3050	3070	1100
Apgar score (1'/5')	3/5	3/7	8/8	3/5	5/7
Resuscitation requirement (yes/no)	Yes	Yes	No	No	Yes
Neonatal nasopharyngeal PCR	Positive	Positive	Positive	Positive	Positive
Sex	Female	Male	Male	Female	Male

Table 1: *Continued*

Time to positive PCR (days from delivery)	0	0	8	3	0
Maternal mortality	NR	Yes	NR	NR	NR
Clinical signs and symptoms	Severe polycythemia, thrombocytopenia, inflammation (elevated CRP, PCT, ferritin, LDH), metabolic acidosis, bleeding risk (prolonged PT/INR, elevated D-dimer), severe azotemia, severe hypoxemia, pulmonary hemorrhage; liver dysfunction (elevated AST, ALT, bilirubin, hypoalbuminemia)	Severe mixed acidosis, respiratory failure, cyanosis, massive pulmonary hemorrhage, renal failure, perinatal asphyxia, mild anemia and thrombocytopenia, high bleeding risk, liver dysfunction, and hyperammonemia.	Shortness of Breath, Decreased Oxygen Saturation, Dyspnea, Congenital Pneumonia	Severe anemia, thrombocytopenia, coagulopathy, severe renal and liver failure, respiratory failure, metabolic acidosis, NEC stage 3a, portal vein thrombosis, and massive pulmonary and gastrointestinal hemorrhage.	Severe anemia, critical thrombocytopenia, metabolic acidosis, multiorgan failure with severe renal and liver dysfunction, respiratory failure with possible pulmonary and GI hemorrhage, suspected NEC, and hyperkalemia.
Administered drugs and treatment	Surfactant (3 courses), Allopurinol Parsiyel Exchange transfusion, İbuprophen, Meropenem, Vancomycin, Amikacin, Dopamin, Sildenafil	Alprostadil Surfactant, Milrinone, Dopamine, Noradrenalin, inhale Nitric Oksit, Carnitine, Coenzim Q Sodyum Benzoat Peritoneal Dialise, Atrial Septostomi	Ampisilin, Amicasin Sefotaksim,	Meropenem, Vancomycin, Amikacin	Meropenem, Vankomisin, Amikasin, Colimycin
Antiviral therapy, remdesivir	+	-	+	+	-
Ritonavir	-	-	--	-	-
HFOV ventilation	+	-	+	+	+
IVIG treatment	+	-	+	+	-
Corticosteroids (methylprednisolone)	+	-	+	+	-
Respiratory support (HFOV/MV)	HFOV	MV	HFOV	HFOV	HFOV
Main findings of Echocardiography	Large PDA, pulmonary hypertension	c-TGA, perimembranous VSD(3 mm) restrictive PFO	PFO	PFO	Small PDA
Hospital stay(days)	29	3	13	25	10
Day 1, neonatal SARS-CoV-2 RNA (RT-PCR) nasopharyngeal swab	Negative	Positive	NR	Negative	Positive
Day 2-5, neonatal SARS-CoV-2 RNA (RT-PCR) nasopharyngeal swab	Negative	NR	NR	Negative	Positive
Day >5 , neonatal SARS-CoV-2 RNA (RT-PCR) nasopharyngeal swab	Positive	NR	Positive	Positive	Positive
Time of neonatal SARS-CoV-2 RNA (RT-PCR) nasopharyngeal swab positivity, day	14	1	11	19	1
Additional complications or comorbidities	Neonatal asphyxia, prematurity, Grede1 germinal matrix hemoragy	Trasposition of great arteries (ballon atrial septostomy), prematurity	Neonatal pneumonia,	Nekrotizan enterokolitis with colostomy	Neonatal asphyxia, prematurity, periventricular leukomalacia
Neonatal outcomes	Death	Death	Death	Death	Death

Abbreviations: GDM (Gestational Diabetes Mellitus), HFOV (High-Frequency Oscillatory Ventilation), HPD (Hypertensive Disorders in Pregnancy), IVIG (Intravenous Immunoglobulin), MV (Mechanical Ventilation), NEC (Necrotizing Enterocolitis), NR (Not Reported), PE (Preeclampsia), PDA (Patent Ductus Arteriosus), PM (Prematurity), PFO (Patent Foramen Ovale), TGA (Transposition of the Great Arteries), VSD (Ventricular Septal Defect).

DISCUSSION

The clinical course of neonates infected with SARS-CoV-2 remains an area of active investigation, given the severe outcomes and high mortality observed in some cases. In the present study we describe five COVID-19-positive neonates, each born to a COVID-19-positive mother or father, who died while hospitalized in a pediatric tertiary care hospital. This case series highlights the compounded risks associated with prematurity, congenital heart disease (CHD) and immune immaturity in the presence of neonatal COVID-19 infection. Most neonates with SARS-CoV-2 infection are either asymptomatic or present with mild symptoms, and generally result in favorable outcomes (5). That said, severe manifestations can occur, especially in neonates with underlying comorbidities such as prematurity, CHD and immune dysregulation. The mortality rate observed in the presented series is alarmingly high. In a study by Oncel et al. (6) of 120 neonates born to COVID-19-positive mothers, only four of the sample tested positive themselves, suggesting that vertical transmission is a rare event; however, the potential for vertical transmission should not be ignored, especially in cases with severe neonatal infections. The early PCR positivity recorded in Cases 1, 2, and 5 in the present study is suggestive of intrauterine transmission. Premature infants are particularly susceptible to respiratory viral infections, including respiratory syncytial virus (RSV), rhinovirus and parainfluenza viruses, which may exacerbate the clinical course of COVID-19 (7–11). The underdeveloped pulmonary structures and immature immune responses associated with such cases can contribute significantly to poor outcomes. Antigen-specific adaptive response is known to be diminished in neonatal immune systems, leaving preterm infants vulnerable to severe viral infections (11). Furthermore, the immaturity of the respiratory system in infants complicates the management of COVID-19, often leading to rapid respiratory failure (12). Of the five cases presented here, three were born preterm, predisposing them to early respiratory failure due to surfactant deficiency, underdeveloped lungs and immaturity of the immune system. These infants exhibited early respiratory distress, requiring intensive care, and the immaturity of the pulmonary and immune systems, in combination with the SARS-CoV-2 infection increased the risk of adverse outcomes substantially. One neonate developed septic shock due to an Acinetobacter baumannii infection, further complicating clinical management. Bacterial co-infections, particularly with pathogens such as Acinetobacter species, are known to worsen outcomes in the immunocompromised and preterm neonates (8). Although Acinetobacter is not a common neonatal pathogen, its involvement in hospital-acquired infections has been noted, especially among mechanically ventilated infants or those receiving prolonged antibiotics (9). Fetal inflammatory response syndrome (FIRS) has been identified as a critical pathophysiological mechanism contributing to acute respiratory distress syndrome (ARDS) in neonates born to mothers infected with SARS-CoV-2. FIRS is characterized by elevated pro-inflammatory cytokines, including IL-6 and TNF-a, which can provoke an exaggerated neonatal immune response, and such dysregulated inflammations can lead to endothelial injury, alveolar inflammation and, ultimately, ARDS. The neonatal cytokine storms associated with SARS-CoV-2 infection have been reported to cause severe respiratory distress, hypoxemia and multi-organ failure (13-16). When combined with prematurity, this inflammatory cascade creates a vicious cycle of pulmonary dysfunction and systemic inflammation, significantly increasing the mortality risk.

Cases 1, 3, 4 and 5 in the present study were placed on high-frequency oscillatory ventilation (HFOV) due to the need for elevated mean airway pressures (>12 mmHg) and the presence of pulmonary hemorrhage. HFOV increases alveolar recruitment and minimizes barotrauma by delivering rapid, small tidal volumes at a constant mean airway pressure, thereby reducing dependence on conventional mechanical ventilation and preventing ventilator-induced lung injury (17,18). The precise control of mean airway pressure is critical in COVID-19-associated ARDS (19), and the avoidance of excessive tidal volumes and pressures is important in this setting (20).

Congenital heart disease has been shown to increase the risk of severe COVID-19 outcomes in neonates, mirroring the findings in pediatric and adult populations. Children with CHD hospitalized with COVID-19 have higher rates of mechanical ventilation, respiratory failure and acute kidney injury (20). Two neonates with CHD in the presented series experienced rapid respiratory and circulatory deterioration that was attributable to

the combined stress of viral infection and the underlying cardiac lesions, and developed myocardial injury, arrhythmia and refractory hypoxemia, underscoring the potential for additional complications arising from SARS-CoV-2 infection in neonates with pre-existing cardiac defects (20). This aligns with a case series in which two deaths were reported among nine pediatric CHD patients infected with COVID-19, both of whom had complex cardiac anomalies (aortic stenosis, hypoplastic left heart syndrome) (20).

Table 2: *Laboratory Findings of Cases*

Parameter	Case 1	Case 2	Case 3	Case 4	Case 5	Normal range
White Blood Cell Count ($x10^9$/L)	27,16	16,78	12,27	33,10	26,26	4-10
Red Blood Cell Count ($\times10^{12}$/L)	6,01	4,32	4,58	4,18	4,67	3,5-5,5
Hemoglobin (g/dL)	21,9	15,3	14,3	8,7	7,7	10-16
Hematocrit (%)	74,2	48,2	48,2	26,4	24,1	55-68
Platelet Count ($\times10^9$/L)	65	186	254	14	9	150-450
Neutrophil Count ($\times10^9$/L)	7,29	9,73	5,92	31,26	1,73	2-7
Lymphocyte Count ($\times10^9$/L)	2,68	4,86	4,58	0,44	0,87	0,8-4,0
Blood Urea Nitrogen (BUN) (mg/dL)	120	17	14	104,8	192	5-20
Creatinine (µmol/L)	1,17	0,83	0,46	1,75	1,12	0,3-0,7
Creatine Kinase (CK) (U/L)	1512	1720	-	450	4639	24-172
Aspartate Aminotransferase (AST) (U/L)	175,3	186,4	81	917,9	211,1	5-34
Alanine Aminotransferase (ALT) (U/L)	212,9	23,1	13,9	189,6	24,4	0-55
Albumin (g/L)	21	18	25	17	17	32-53
Total Bilirubin (mg/dL)	8,28	3,34	1,27	7,18	10,53	0,2-1,2
Direct Bilirubin (mg/dL)	1,09	0,46	0,54	4,09	5,59	0-0,5
Lactate Dehydrogenase (LDH) (U/L)	4294	1231	-	6000	3056	5-746
Sodium (mmol/L)	144	138	140	160	154	135-145
Potassium (mmol/L)	5,02	4,76	4,46	2,74	8,83	3,7-5,9
Ferritin (µg/L)	3755	-	-	1333	-	0-10
Procalcitonin (ng/mL)	2,92	-	0,985	-	4,32	<0,5
D-Dimer (µg/mL)	3,29	-	-	8,7	-	<0,5
Fibrinogen (mg/dL)	206	-	-	296	-	125-300
C-Reactive Protein (CRP) (mg/L)	41,5	2	11,5	125	239	<2
Prothrombin Time (PT) (sec)	15,8	28,7	-	25,2	-	9,5-13,5
Activated Partial Thromboplastin Time (aPTT) (sec)	52,2	94,2	-	46,3	-	<65
International Normalized Ratio (INR)	1,72	2,58	-	2,34	-	<1,3

Table 2: *Continued*

pH	6,34	6,15	6,76	6,78	6,89	7,35-7,45
PCO_2 (mmHg)	146,8	169,2	108,8	84,3	70,5	38-42
PO_2 (mmHg)	19,6	12,8	12,9	22,7	28,1	75-100
HCO_3^- (mEq/L)	10,4	9,4	18,3	6,3	6,1	22-28
Base Excess (BE) (mEq/L)	-17,3	-21,9	-16,1	-21,4	-23,1	-4+4
Lactate (mmol/L)	16,48	16,76	9,33	26	23	0,26-2,21
Oxygen Saturation (%)	25,7	19,3	46	30,5	34,2	94-100

COVID-19-related coagulopathy is a recognized complication in adults and children with CHD (18). This hypercoagulable state, driven by endothelial injury and systemic inflammation, predisposes the patient to thrombotic events, as observed in Case 4, who developed portal vein thrombosis and bleeding complications. Neonates with ARDS and SARS-CoV-2 infection are particularly susceptible to severe hemorrhage due to inflammation-induced vascular fragility and impaired hemostasis. These factors likely contribued to the pulmonary hemorrhages preceding the deaths of several infants in this series (8,9). The combined effects of hypoxemia and systemic inflammation due to SARS- CoV-2 infection can impair intestinal perfusion, promote mucosal ischemia and exacerbate inflammatory injury, thereby increasing the risk and severity of necrotizing enterocolitis (NEC) (13–16). Previous studies have reported cases of term neonates with confirmed perinatal COVID-19 who developed NEC, similar to Case 4 in the present study, highlighting SARS-CoV-2-induced intestinal ischemia and inflammation as a potential mechanism (16). Although vertical transmission remains rare, our findings, and those of other studies, indicate that neonates can test PCR-positive early in life, likely due to intrauterine or intrapartum transmission. This is supported by the early PCR positivity recorded in Cases 1, 2 and 5. Conversely, the delayed PCR positivity recorded in Cases 3 and 4 is likely due to peripartum or nosocomial postnatal exposure, possibly from infected healthcare workers or family members. In all cases, either the mother or father developed COVID-19 symptoms and tested positive postpartum, suggesting lateral transmission in addition to vertical routes. These findings underscore the complexity of SARS-CoV-2 transmission in neonates and emphasize the need for rigorous infection control, including both postnatal screening and the vigilant monitoring of the vertical and horizontal transmission routes.

Study Limitations

This case series has several limitations, including the small sample size and single-center design, both of which restrict the generalizability of the findings. The lack of uniformity in the timing of PCR tests and the methods used may have affected diagnostic accuracy, particularly concerning vertical transmission. Furthermore, the absence of placental and amniotic fluid testing limits the definitive evaluation of in utero transmission. Furthermore, the lack of maternal vaccination data and long-term neonatal outcome data precludes the assessment of the potential protective effects of the vaccine.

CONCLUSION

Neonatal SARS-CoV-2 infections can have fatal consequences, especially in infants with underlying vulnerabilities such as prematurity or congenital heart disease. The immaturity of the immune and pulmonary systems of infants predisposes them to rapid respiratory deterioration, thrombotic complications and multi-organ failure. Early recognition, aggressive respiratory support, careful coagulopathy monitoring and multidisciplinary management are essential for the improvement of outcomes. Clinicians should maintain a high index of suspicion for COVID-19 in neonates, even when the initial PCR results are negative, and particularly in those with such risk factors as prematurity or comorbidities.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - L.Ş., N.O.; Planning and Design - L.Ş., N.O.; Supervision - L.Ş., N.O.; Funding - L.Ş., N.O.; Materials - L.Ş., N.O.; Data Collection and/or Processing - L.Ş., N.O.; Analysis and/or Interpretation - N.O., L.Ş.; Literature Review - L.Ş., N.O.; Writing - L.Ş., N.O.; Critical Review - L.Ş., N.O.

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Erratum: Pulmonary Carcinosarcoma: A Case Series of Seven Patients and Review of the Literature

Pulmoner Karsinosarkom: Yedi Hastalık Olgu Serisi ve Literatürün Gözden Geçirilmesi

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In the article "Pulmonary Carcinosarcoma: A Case Series of Seven Patients and Review of the Literature" published in Respiratory Case Reports 2025;14(1):7-11 was inadvertently published with the following paragraphs missing.

Case 6: A 61-year-old chronic smoker with a 30-year smoking history presented with right-sided chest pain. The patient had a WHO performance status of 2, and oxygen saturation was 96% in ambient air. Chest CT revealed a tissue mass in the right upper lobe extending into the mediastinal region measuring approximately 8 cm, and bilateral pulmonary nodules were also noted that were suggestive of secondary lesions (Figure 5). Bronchoscopy revealed two small lesions at the entrance to the right main bronchus. A biopsy confirmed the diagnosis of pulmonary carcinosarcoma, and an extension assessment revealed distant metastases to the adrenal glands and liver. The patient was referred for chemotherapy, but was lost to follow-up.

Case 7: A 58-year-old chronic smoker with a 40-year smoking history presented with acute abdominal pain localized to the right hypochondrium, accompanied by persistent vomiting and weight loss. Although the clinical examination was normal, computed tomography (CT) confirmed an adrenal incidentaloma and revealed multiple pulmonary nodules of a secondary nature. A whitish lesion was identified during the bronchoscopy that was noted to obstruct the dorsal segment of the culmen. A histopathological examination confirmed a diagnosis of pulmonary carcinosarcoma, and an extension assessment indicated the presence of metastases in the brain and liver. The patient was subsequently referred for chemotherapy, but succumbed to the disease due to the advanced IVB classification stage.

RESPIRATORY CASE REPORTS

Author Index of Respiratory Case Reports Volume Fourteen, 2025

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