Respir Case Rep 2025;14(3):90-93 DOI: 10.5505/respircase.2025.32068

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.*

[1]Trakya University Faculty of Medicine, Edirne, Türkiye
[2]Şırnak State Hospital, Şırnak, Türkiye

[1]Trakya Üniversitesi Tıp Fakültesi, Edirne
[2]Şırnak Devlet Hastanesi, Şırnak

Submitted (Başvuru tarihi): 21.03.2025 **Accepted (Kabul tarihi):** 14.07.2025

Correspondence (İletişim): İlker Yılmam, Department of Pulmonary, Trakya University Faculty of Medicine, Edirne, Türkiye.

e-mail: drilkeryilmam@gmail.com

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).

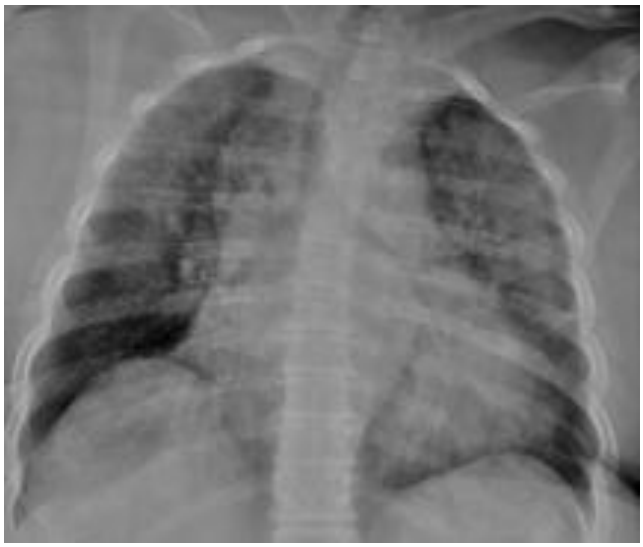

Figure 1: Chest X-ray at the time of admission

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.

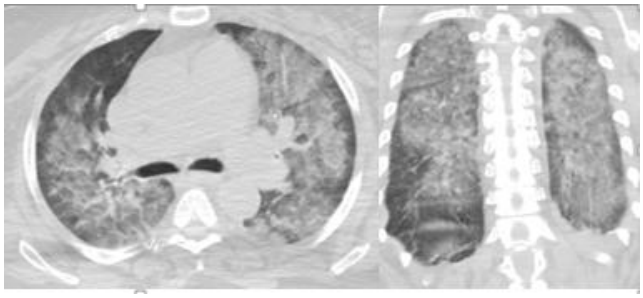

Figure 2: High-resolution computed tomography at the time of admission

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).

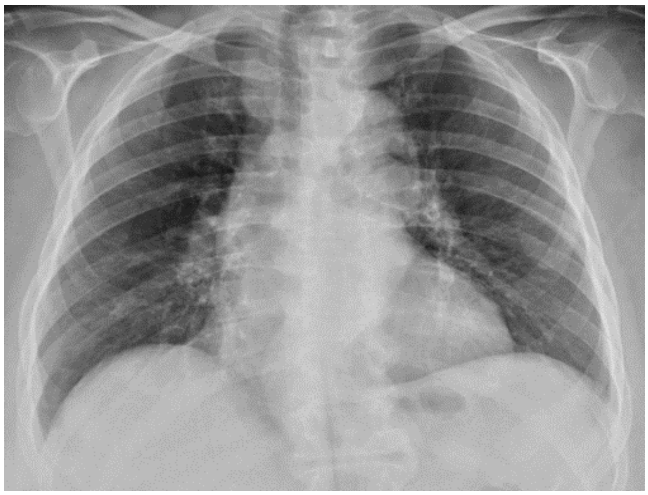

Figure 3: Chest X-ray after treatment

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.

REFERENCES

1. Shikdar S, Vashisht R, Zubair M, Bhattacharya PT. International Normalized Ratio: Assessment, Monitoring, and Clinical Implications. [Updated 2025 Feb 14]. Available from: https://www.ncbi.nlm.nih.gov/sites/books/NBK507707/
2. Erdogan D, Kocaman O, Oflaz H, Goren T. Alveolar Hemorrhage Associated with Warfarin Therapy: A Case Report and Literature Review. Int J Cardiovasc Imaging 2004; 20:155-9. [CrossRef]
3. Taşbakan MS, Özdemir Ö, Yıldız BS, Özerkan F, Bacakoğlu F. Varfarin Toksisitesi ve Amiodaron Tedavisi ile İlişkili İki Alveoler Hemoraji Sendromu Olgusu. Yoğun Bakım Dergisi 2010; 9:57-63.
4. Schreiber J, Knolle J, Kachel R, Schuck R. Differential Diagnosis of Diffuse Pulmonary Haemorrhage. Pneumologie 2006; 60:347-54. [CrossRef]
5. Aliyev D, Özer E, Şahin C, Özlü O. Diffusie Alveolar Hemorrhage-Complication of Warfarin Treatment. Comprehensive Medicine 2019; 11:53-57. [CrossRef]
6. Landefeld CS, Beyth RJ. Anticoagulant-Related Bleeding: Clinical Epidemiology, Prediction, and Prevention. Am J Med 1993; 95:315-28. [CrossRef]
7. Brown OL, Garvey JM, Stern CA. Roentgenogram of the Month. Dis Chest 1965; 48:525-6. [CrossRef]
8. Lee JH, Kim SW. Successful Management of Warfarin-Exacerbated Diffuse Alveolar Hemorrhage Using an Extracorporeal Membrane Oxygenation. Multidiscip Respir Med 2013; 8:16. [CrossRef]
9. Reisman S, Chung M, Bernheim A. A Review of Clinical and Imaging Features of Diffuse Pulmonary Hemorrhage. AJR Am J Roentgenol 2021; 216:1500-9. [CrossRef]
10. Homer RJ. Depositional Diseases of the Lungs. In: Grippi MA, Elias JA, Fishman JA, Kotloff RM, Pack AI, Senior RM, et al. eds.Fishman's Pulmonary Diseases and Disorders, Fifth Edition. McGraw-Hill Education; 2015.
11. Oymak FS, Tokgöz B, Akgün H, Gülmez İ, Erdoğan N, Demir R, et al. (2002). Alveolar Hemorrhage Syndromes; Clinical, Pathological and Imaging Features: Analysis of Eleven Patients. Turkish Thorac J 2002; 3:52-8.