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Case Report / Olgu Sunumu

Edoxaban-related Spontaneous Renal Hematoma: A Case Report

Edoxaban Kullanımına Bağlı Spontan Renal Hematom: Olgu Sunumu

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Özet

Edoxaban faktör Xa'yı doğrudan baskılayan bir oral antikoagülan ilaçtır. Daha az ilaç etkileşimi ve rutin izleme ihtiyacını ortadan kaldırması nedeniyle; inme profilaksisi, venöz tromboemboli profilaksisi/tedavisi, akut koroner sendromların sekonder profilaksisi için hastalara daha iyi tedavi alternatifleri sağlamıştır. Kullanımı arttıkça klinisyenlerin potansiyel tedavi riskleri ve komplikasyon yönetiminden daha fazla haberdar olmaları gerekmektedir. Bu makalede, atriyal fibrilasyon nedenli inme profilaksisi için edoxaban kullanan hastada gelişen spontan renal hematom bildirilmektedir. Hemodinamik destek sağlanan, görüntülemeler ile izlenen ve multidisipliner açıdan tedavi ve takip kararları alınan hasta tüm çabalara rağmen hayatını kaybetti. Kanama pıhtılaşma değerlerini değiştirmedikleri için acil servise başvuran kanamalı hastalarda bu ilaçların kullanım anamnezi dikkatli alınmalıdır. Vakamızda da gösterildiği gibi kullanımları sırasında gelişebilecek ölümcül komplikasyonlar için tedavi algoritmaları geliştirebilmek için daha geniş vaka serilerine ve olgu sunumlarına ihtiyaç vardır.

Anahtar Kelimeler: Edoksaban, major kanama, böbrek, hematom.

Abstract

Edoxaban is an oral anticoagulant drug that directly inhibits factor Xa. It is used for stroke prophylaxis, venous thromboembolism prophylaxis / treatment, and secondary prophylaxis of acute coronary syndromes. Drug interactions with edoxaban are rare and there is no need for routine blood monitoring. Clinicians should be more aware of potential complications and complication management, as they are prescribed quite frequently. In this article, a spontaneous renal hematoma in a patient using edoxaban for atrial fibrillation-induced stroke prophylaxis is reported. The treatment and follow-up decisions were made by the multidisciplinary team and the patient died despite all efforts. The use of these drugs should be carefully questioned in patients with bleeding who apply to the emergency room because they do not change the coagulation parameters. Larger case series and case reports are needed to develop treatment algorithms for fatal complications that may occur during their use.

Keywords: Edoxaban, major bleeding, kidney, hematoma.

INTRODUCTION

Edoxaban is an oral anticoagulant drug that directly inhibits factor Xa. It prevents factor Xa from separating prothrombin into thrombin. Instead of increasing the activity of antithrombin like heparin, they are directly linked to factor Xa (1). New oral anticoagulant agents (NOAC), such as dabigatran, rivaroxaban, apixaban, and edoxaban, provided quite good treatment alternatives for stroke prophylaxis, venous thromboembolism (VTE) prophylaxis / treatment, and secondary prophylaxis of acute coronary syndromes in patients with non-valvular atrial fibrillation (NVAF). Like other direct oral anticoagulants, drug interaction with edoxaban is rare compared to vitamin K antagonists. These drugs are gaining popularity due to their predictable pharmacokinetic profiles and no need for routine blood monitoring (2).

NOACs have a variable effect on vitamin K-dependent clotting factors, so coagulation parameters are unreliable (3). Clinicians should be more aware of potential complications and complication management, as they are prescribed quite frequently. In this article, a spontaneous renal hematoma in a patient using edoxaban is reported.

CASE REPORT

A seventy-three-year-old male patient came to the emergency room because of his right flank pain that started ten hours ago. The patient without a previous surgical history did not describe any trauma. He also had no hematuria and fever. He had diagnoses of diabetes mellitus and hypertension. Edoxaban 60 mg/day was prescribed by the cardiologist because the patient was diagnosed with atrial fibrillation 1 month ago. The patient had no renal failure (creatinine 0.76 mg / dL) and liver dysfunction (bilirubin 0.81 mg / dL, ALT 41 U / L, AST 32 U / L).

In contrast-enhanced thorax and all abdominal computed tomography, pericardial effusion reaching 15 mm in its widest part and subcapsular collection reaching 35 mm in the thickest part of the right kidney were detected. The collection had an appearance consistent with hyperdense hemorrhage. Also it caused external compression to the right kidney and displaced the kidney medially. Widespread densities (6 cm) are observed in the right perinephric and pararenal areas and were interpreted primarily in favor of hemorrhage. Spread from these areas towards retroperitoneum (Fig.1a,1b).

The patient was recommended to remain immobile and consulted to interventional radiology. In angiography performed by interventional radiology; the right renal artery and its branches were seen and there was no bleeding area. In the first 48 hours of hospitalization, seven units of erythrocyte suspension transfusion were performed, but he did not have hypotension and tachycardia. The patient was re-evaluated with second contrast-enhanced CT. Bilateral pleural effusion and subcapsular hematoma measuring 44.8 mm in its thickest part of the right kidney were seen. During his five-day follow-up at the urology clinic, 13 units of erythrocyte suspension and 4 units of fresh frozen plasma transfusion were needed (Fig.2) Due to the use of edoxaban, he was consulted to cardiology, but switching to low molecular weight heparin was not recommended. Cardiologist suggested discontinuation of the edoxaban 24-48 hours before surgery but the patient was at high risk for surgery.

Surgery was planned for the patient and edoxaban was discontinued, but pulmonary embolism was suspected due to dyspnea, desaturation, and fever. Low molecular weight heparin was switched to 2 x 0.6 mg in the patient with D-Dimer 4.13 mg / L and pulmonary embolism could not be ruled out clearly. On the fourth day of hospitalization, thoracic CT angiography showed pleural fluid, which measured 69 mm in the right lung and 17 mm in the left. There was a passive atelectatic appearance secondary to effusion in lower lobes, there was no clear finding in favor of embolism in the pulmonary arteries. Pulmonary medicine consultation was requested for the patient because he had cold sweating, dyspnea, cough and fever. Antibiotherapy (meropenem and linezolid) was started due to the pre-diagnosis of heart failure and pneumonia. Fluid loading was avoided by furosemide infusion (Fig.3a,3b). Respiratory rate was 32 and bilateral breathing sounds were heard spasmodically on physical examination. When respiratory acidosis (ph: 7.33, pco2: 61) was detected in the arterial blood gas, he was transferred to the intensive care unit. Then he died due to heart failure and pneumonia.

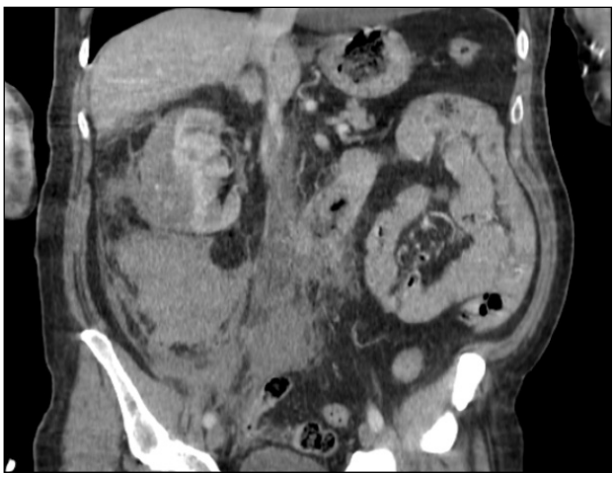

Figure 1a. Contrast-enhanced computed tomography image in the emergency department (coronal section)

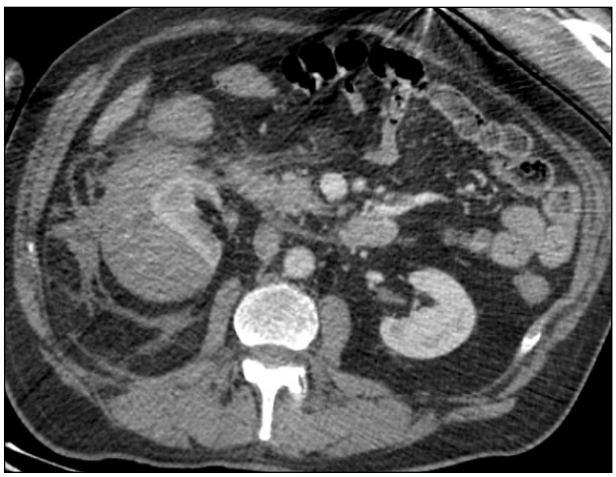

Figure 1b. Contrast-enhanced computed tomography image in the emergency department (axial section)

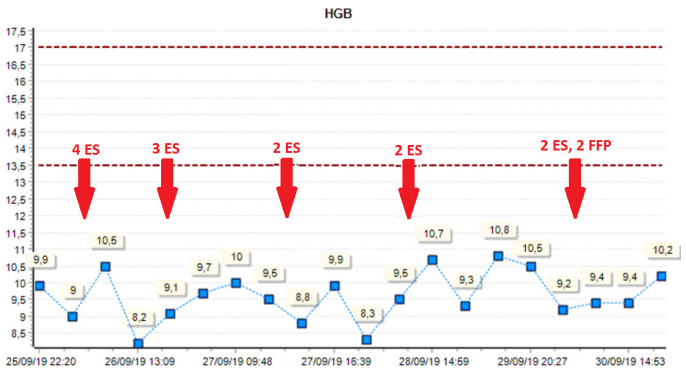

Figure 2. Hemoglobin (g / dl) level graph during follow-up in the urology service for 5 days. (ES: erythrocyte suspension transfusion , FFP: fresh frozen plasma transfusion)

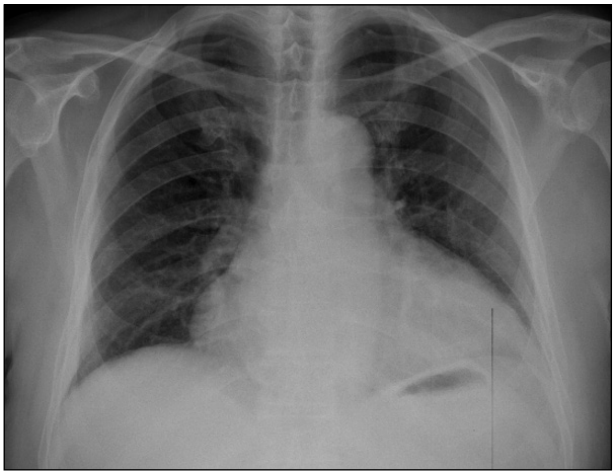

Figure 3a. Chest x-ray (PA) in the emergency department

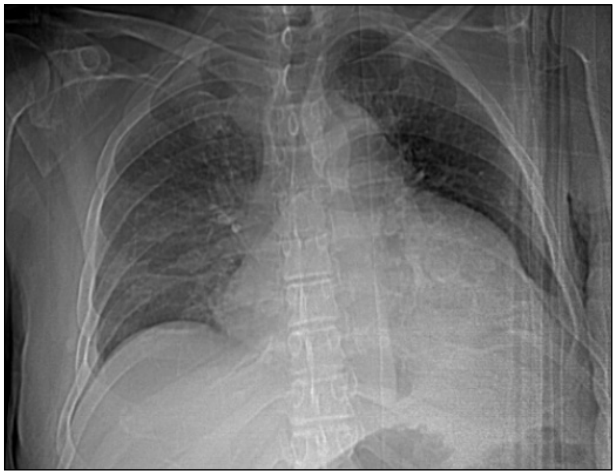

Figure 3b. On the 5th day of follow-up, chest x-ray (PA) before transfer to the intensive care unit

DISCUSSION

The use of new oral anticoagulant drugs is increasing day by day due to its advantages such as not requiring INR follow-up and less interaction with other drugs. The use of these drugs should be carefully questioned in patients with bleeding who apply to the emergency room because they do not change the coagulation parameters. There are many studies in the literature comparing the safety of these drugs in terms of bleeding risk. As far as we know, spontaneous renal hematoma is reported for the first time in a patient using edoxaban with normal kidney and liver functions.

In a study comparing patients using edoxaban and warfarin for venous thromboembolism prophylaxis, clinically significant bleeding was observed in 8.5% (major bleeding 1.4%) in edoxaban users and 10.3% (major bleeding 1.6%) in warfarin users. There was no statistically significant difference between the two groups in terms of major bleeding, and retroperitoneal bleeding was observed in four patients (<0.1%) using warfarin (4). In the ENGAGE AF–TIMI 48 study, which included a total of 21105 patients, the number of patients with fatal bleeding in the group using warfarin, edoxaban 60 mg and edoxaban 30 mg were 65, 35 and 24, respectively. Treatment with edoxaban has been associated with less fatal bleeding, less bleeding-related complications (5). In the comparison study in which new oral anticoagulants were given to 42411 patients and warfarin to 29272 patients, more gastrointestinal bleeding was detected in the NOAC group compared to warfarin. (RR 1.25, p = 0.04). New oral anticoagulants have also been shown to reduce mortality (RR 0.90, p = 0.0003) and intracranial bleeding (RR 0.48, p <0.0001) (6). It should also be noted that; in the study of ENGAGE AF-TIMI 48, gastrointestinal bleeding was observed more frequently in edoxaban group than warfarin group in patients over 75 years of age (7). In the literature, bleeding in the gallbladder, cerebral hemorrhage, spontaneous hemopericardium, hematoma in the tympanic membrane have been reported in patients using edoxaban (8-11).

In a comparative study between DMAH and edoxaban against malignancy-associated venous thrombosis, the major bleeding incidence for edoxaban at doses of 60 mg/day or higher was 6.9%. This incidence is significantly higher than the 4% detected for low molecular weight heparin. In addition, major bleeding from the urogenital system was noted in five patients (1%) using edoxaban in this study, but did not cause death (12). In the study of Beyer-Westendorf J et al., 1776 patients using rivaroxaban were followed for 2 years. Bleeding was detected in 42.9% of the patients and major bleeding in 6.1% of this group. Surgical or interventional treatment was needed in 37.8% of patients with major bleeding (13).

All new oral anticoagulants are excreted through the kidney to a certain percentage (edoxaban 35%, rivaroxaban 35%, apixaban 25%). Therefore, it should be remembered that dose adjustment may be required in people with kidney failure (14). Since there was no renal failure in our case, no dose adjustment was required. In the study of Scaglione et al., it has been shown that in patients with normal renal function, NOAC drugs will be decrease to an ineffective concentration after five half-live time from the last dose. For edoxaban, whose half-life is 6-11 hours, this period varies between 1.3-2 days (15).

Current guidelines support the use of prothrombin complex concentrate (PCC) to reverse the anticoagulation effect of vitamin K antagonists such as warfarin before emergency procedures or life-threatening bleeding (16). On the other hand, the use of PCC in patients taking NOAC is not explicitly supported by any guidelines. It may reverse the anticoagulation effect of NOAC, but evidence is still limited (17).

CONCLUSION

The use of new oral anticoagulant drugs is increasing day by day. However, as shown in our case, larger case series and case reports are needed in terms of fatal complications that may occur during use.

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