

Apixaban Nedenli İzlenen Rektus Kılıf Hematomu Yönetimi ve Sonuçları

Management and Outcomes of Spontaneous Rectus Sheath Hematoma With Apixaban

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ÖZ

Giriş: Apixaban, kanama açısından hem aspirin hem de varfarine kıyasla daha güvenli görünen, nispeten yeni kullanılan bir oral faktör Xa inhibitörüdür. Literatürde apixaban ile ilgili bildirilen çok az yan etki vardır ve bunlardan biri de rektus kılıf hematomudur.

Olgu Sunumu: 78 yaşında kadın hasta karın ağrısı, öksürük ve nefes darlığı şikayetlerine ek olarak karın bölgesinde ekimoz ile hastanemiz acil servisine başvurdu. Özgeçmişinde hipertansiyon, astım, koroner arter hastalığı ve nonvalvüler atriyal fibrilasyon olduğu öğrenildi. Hasta nonvalvüler atriyal fibrilasyon nedeniyle 16 aydır apixaban tedavisi görüyordu. Çekilen abdominal ultrasonografi ve bilgisayarlı tomografide yaklaşık 30x40 mm boyutlarında rektus kılıf hematomu saptandı. Hasta konservatif olarak tedavi edildi, ancak solunum yetmezliği nedeniyle exitus gelişti.

Sonuç: Klinisyenler karın ağrısı olan hastalarda apixaban kullanan spontan rektus kılıf hematomunun farkında olmalıdır. Apixaban, güvenle kullanılabilen bir ilaç olmasına rağmen spontan kanama gibi komplikasyonlara yol açabilmektedir.

Anahtar kelimeler: Rektus abdominis, hematom, apixaban

ABSTRACT

Introduction: Apixaban is a comparatively newly used oral factor Xa inhibitor, which seems to be safer, compared to both aspirin and warfarin in terms of bleeding. There are very few reported apixaban related side effects in the literature, and one of them is rectus sheath hematoma.

Case Report: A 78-year-old female patient was admitted to the emergency service of our hospital with complaints of abdominal pain, cough, and dyspnea, and she also complained of ecchymosis in her abdominal region. Her medical history revealed that she had hypertension, asthma, coronary artery disease, and nonvalvular atrial fibrillation. The patient had been on apixaban for 16 months for nonvalvular atrial fibrillation. Abdominal ultrasonography and computed tomography revealed a rectus sheath hematoma of nearly 30x40 mm in size. The patient managed conservatively, but she died due to respiratory failure.

Conclusion: Clinicians should be aware of spontaneous rectus sheath hematoma in apixaban using patients with abdominal pain.

Keywords: Rectus abdominis, hematoma, apixaban

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Introduction

Apixaban, an oral factor Xa inhibitor, used in venous thromboembolic situations was approved by FDA in 2012 with the indication of reducing the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (1). Up to date this oral anticoagulant has also been indicated in prophylaxis of deep venous thrombosis (DVT) following hip or knee replacement surgery, treatment of DVT, treatment of pulmonary embolism (PE), and the reduction in the risk of recurrence of DVT and PE (1). The main advantage of this drug is that, no laboratory test is recommended to control the blood concentration of apixaban. It is advised that apixaban should not be co-administered with combinations of P-glycoprotein and strong cytochrome P450 3A4, such as ketoconazole, itraconazole, and ritonavir, or the recommended dose should be reduced by 50% (2). FDA approved a recombinant modified human Factor Xa (FXa) protein, inactivated zhzo (Adnexxa®), for reversal of the anticoagulant effect of apixaban in May 2018, however it has not been available in our country yet (3).

This oral factor Xa inhibitor is a comparatively newly used anticoagulant, and the reported adverse effects are yet very little in the literature and require to be reported. Rectus sheath hematoma may occur with anticoagulant agents both administered orally and subcutaneous. In the current literature there are very few reports on apixaban causing rectus sheath hematoma. We want to report and discuss a patient with rectus sheath hematoma associated with apixaban.

Case Report

A 78-year-old female patient was admitted to emergency service of our hospital with the complaints of abdominal pain, cough and dyspnea. She also complained of ecchymosis on her abdominal region. Medical history of the patient revealed hypertension, asthma, coronary artery disease and nonvalvular atrial fibrillation (AF). The patient had been on apixaban for 16 months for nonvalvular AF. Her abdominal examination revealed ecchymosis especially on the right side of the abdomen and a 4 cm palpable, painful, firm and non-pulsatile abdominal mass. The Fothergill sign was inconclusive. The patient was normotensive but she had AF, tachycardia (136 beat/min), and tachypnea (26 breath/min). Laboratory studies showed white blood cell count of $15 \times 10^3/\mu\text{L}$ with hemoglobin 15.3 gr/dL, hematocrit 53%, platelets $222 \times 10^3/\mu\text{L}$, and international normalized ratio 1.19. Blood urea nitrogen was 30 mg/dL, creatinine 0.84 mg/dl, lactate dehydrogenase 281 U/L. The other blood biochemical tests were within normal ranges. Abdominal ultrasonography (US) of the patient

revealed approximately 33x16 mm- and 13 mm-sized 2 adjacent hematomas on the right side of the epigastric region in the abdominal wall. Computerized tomography was used in order to determine the location, size and the extension of the hematoma, and revealed a rectus sheath hematoma of 30x40 mm in size in the right upper quadrant (Figure 1). The patient was hospitalized and followed up in intensive care unit with the diagnosis of apixaban-related rectus sheath hematoma. The patient was managed in multidisciplinary fashion, with the consultations and advices from pulmonary and chest diseases and cardiology clinics. Computed tomography of thorax revealed findings related with advanced stage of chronic obstructive pulmonary disease, and there was no sign of bleeding or pulmonary embolism. Apixaban was stopped and conservative treatment with analgesic, intravenous fluid resuscitation, and low molecular weight heparin (enoxaparin sodium, 40 mg/0.4 ml) was started. Additionally budesonide and ipratropium bromide/salbutamol inhalers and methylprednisolone were started for asthma attack. Hemodynamic parameters were followed closely. Decrease in hemoglobin value was not observed so erythrocyte replacement was not required in follow up. In control US, partials resorption of the hematoma was detected. The patient developed/continued to have tachycardia and tachypnea on the 3rd day of hospitalization, respiratory acidosis and an eventual asthma attack related respiratory arrest developed and mechanical ventilation was provided. Unfortunately, the patient died due to respiratory failure.

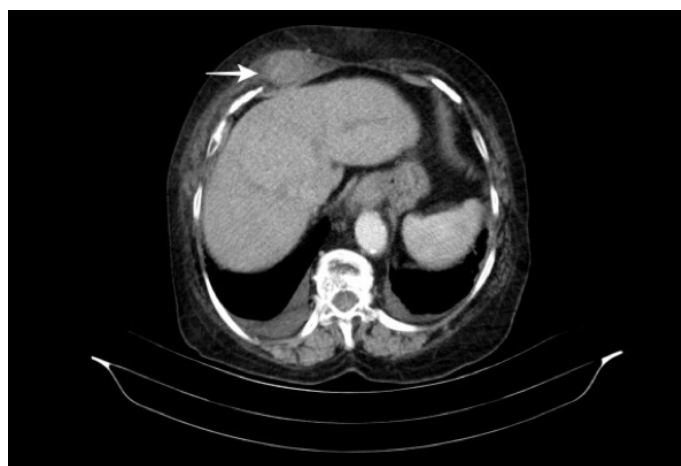


Figure 1. Computerized tomographic view of rectus sheath hematoma

Discussion

Apixaban is one of non-vitamin K oral anticoagulants that inhibits free and clot-bound factor Xa, and prothrombinase activity (4). It does not require coagulation monitoring routinely during follow up. FDA approved apixaban for reducing risk of stroke and systemic embolism associated with nonvalvular atrial fibrillation, prophylaxis and treatment of deep venous thrombosis and PE in 2012 (1). Bleeding is an adverse effect of the drug, but major bleeding is shown to be less than warfarin. In Aristotle study, apixaban was found to be related to low rates of clinically relevant nonmajor and major bleeding compared to warfarin (5). Apixaban was compared with aspirin in Averroes study and apixaban was found significantly related to low rates of bleeding also (6).

Rectus sheath hematoma is an uncommon cause of abdominal pain, and a significant complication in patients, receiving anticoagulant therapy. This type of hematoma is usually a self-limiting condition, yet it may still be fatal. Overall mortality rate of rectus sheath hematoma is reported to be 4% (7). Anticoagulant treatment is the most frequent predisposing factor for spontaneous rectus sheath hematoma. The other causes are coughing, pregnancy, previous or recent abdominal surgery, chronic kidney disease, steroid/immunosuppressive treatment and external trauma (8). Our patient was using a new generation oral anticoagulant and had severe coughing due to asthma. Generally, patients with rectus sheath hematoma without hemodynamic instability, expanding hematomas or symptomatic anemia may be managed conservatively. Rectus sheath hematoma associated with apixaban is a rare condition with limited numbered reports in the current literature. Aktas et al. reported a 71 year-old female patient with spontaneous rectus sheath hematoma who was using apixaban for nonvalvular atrial fibrillation. In this report the patient was also managed conservatively with removal of offending agent, fluid resuscitation and serial hemoglobin measurement and discharged on day 5 of admission with low dose apixaban (9). Gunasekaran and colleagues have also reported a 68-year-old obese patient with complaints of shortness of breath, cough, wheezing, and bilateral lower extremity pain and swelling (10). The patient in the related report had risk factors of thrombosis such as diabetes mellitus, hyperlipidemia, hypertension and total knee replacement surgery, and diagnosed with thrombus in the left common femoral vein. Rectus sheath hematoma was onset on day 3 of admission after 3 doses of apixaban. The patient was also managed conservatively, and only required 2 units of packed red blood cells (10). Elango et al. reported a 69-year-old woman with apixaban

associated rectus sheath hematoma. They also discontinued apixaban and the patient was managed conservatively (11). Just like these cases, our patient was a female and older than 68 years old. Another point in the formation of rectus sheath hematoma may be drug-drug interaction. Cytochrome p450(CYP)3A4 inhibitors effect the levels of FXa and increases the risk of bleeding (12). So possibility of drug interactions should be always be assessed. The patients in the literature were seem to be stable hemodynamically and only our patient died due to respiratory insufficiency. However the primary cause of the mortality was not rectus sheath hematoma, we think that the addition of the hematoma to multiple comorbid diseases contributed to the mortality.

Conclusion

Although apixaban is a new generation oral anticoagulant which seems to be safer compared to both aspirin and warfarin in terms of bleeding, rectus sheath hematoma may occur especially in elderly patients with comorbidities having risks of potential coughing. These patients should be managed multidisciplinary, and followed up closely. Clinicians should be aware of rectus sheath hematoma in the patients who are using apixaban and have complaints of abdominal pain.

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