PECTORAL MUSCLE HEMATOMA CAUSED BY ENOXAPARIN

ENOKSAPARİN TEDAVİSİ İLE OLUŞAN PEKTORAL KAS İÇİ KANAMA

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SUMMARY: Enoxaparin, which is a low molecular weight heparin, exerts its effect by inhibiting the activity of thrombin and acting as antifactor Xa. The rate of major hemorrhagic complications during enoxaparin treatment has been reported to be 1.9-6.5%. We present a 90-year-old male patient who had chronic obstructive pulmonary disease (COPD) in his background, who was admitted to hospital with pneumonia and acute respiratory failure. His neurological examination revealed left central facial paralysis with left hemiparesia. His cerebral computed tomography was normal and with his clinical informative data he was diagnosed with atherothrombotic acute ischemic stroke. Enoxaparin 60 mg (1.5 mg/kg/day) subcutaneously every 12 hours was initiated. A painful and tender mass lesion developed on the right pectoral muscle on the 20th day of treatment. Right pectoral muscle ultrasound and thoracal computed tomography revealed a hematoma 60 x 90 mm. There are reports about some patients that have developed hematoma inside the iliopsoas and rectus abdominis muscles, subdural hematoma, spontaneous hemothorax and retroperitoneal hematoma during enoxoparin treatment. However, intrapectoral hemorrhage has not been reported before.

Key Words: *Enoxaparin, Pectoral Muscle, Hematoma, Ultrasound, Computed Tomography.*

ÖZET: Bir düşük molekül ağırlıklı heparin olan enoksaparin etkisini trombin aktivitesini inhibe ederek ve antifaktör Xa etkisi göstererek yapar. Majör kanama komplikasyon oranı %1.9-6.5 olarak bildirilmiştir. Kronik obstrüktif akciğer hastalığı (KOAH) zemininde pnömoni ve akut solunum yetmezliği ile hastaneye kabul edilen ve nörolojik muayenesinde sol santral fasiyal paralizi ve sol hemiparezi bulunan 90 yaşında bir erkek olgu sunmaktayız. Bilgisayarlı beyin tomografisi normal olan vakada klinik bulgularla aterotrombotik akut iskemik strok tanısı düşünüldü. Enoksaparin subkütan olarak 60 mg (1.5 mg/kg/gün) her 12 saatte bir başlandı. Tedavinin 20'nci gününde sağ pektoral kas üzerinde ağrılı ve hassas kitle lezyonu gelişti. Sağ pektoral kas ultrasonografisi ve torokal bilgisayarlı tomografide 60x90 mm boyutunda kanama tesbit edildi Enoksaparin tedavisi esnasında iliopsoas ve rektus abdominis kas içi kanama, subdural kanama, spontan hemotoraks ve retroperitoneal kanama gelişen bazı olgular bildirilmiştir. Bununla birlikte pektoral kas içi kanama daha önce bildirilmemiştir.

Anahtar Kelimeler: *Enoksaparin, Pektoral Kas, Hematom, Ultrasonografi, Bilgisayarlı Tomografi.*

INTRODUCTION

Enoxaparin is a low molecular weight (4-5 kDa) heparin. It exerts its anticoagulant effect primarily by binding to antithrombin III. It also has an antifactor Xa effect similar to that of other low molecular weight heparins (1). Their interaction with antithrombin is mediated by a unique pentasaccharide sequence randomly distributed along the heparin chains. Binding of the pentasaccharide to antithrombin causes a conformational change in antithrombin that accelerates its interaction with thrombin and activated factor X by about 1000 times, and a pentasaccharide-containing heparin chain can inhibit the action of factor Xa simply by binding

to antithrombin and causing a conformational change (2). It is rapidly absorbed after subcutaneous administration and predominantly eliminated by the kidneys. Its optimal dose is 1-1.5 mg/kg/day for efficacy (1).

Hemorrhage is a common complication experienced during antithrombotic treatment. In several studies, upon comparison with unfractionated heparin and warfarin, the incidence of hemorrhagic complications with enoxoparin has been reported to be lower (1). In several clinical studies, the incidence of major hemorrhagic complications was 1.9-6.5% and of minor ones was 20% (3). There have been reports about intrahepatic bleeding, intracranial bleeding, and bleeding into the iliopsoas and rectus abdominis muscles (1, 4, 5).

CASE REPORT

A 90-year-old patient presented with slurring of the speech and loss of power in the left arm and leg. His past medical history included hypertension and COPD. On physical examination, his temperature was 37.5°C, his blood pressure was 220/90 mmHg, his pulse rate was 94/min and arrhythmic, and he was tachypneic and hyperpneic. Upon auscultation, there were rales and ronchi at the base of the right lung. On neurological examination, the patient was conscious, cooperative and oriented. There were no signs of meningeal irritation. A cranial nerve examination yielded left central facial paralysis, while the other cranial nerves were intact. A motor examination demonstrated a 5-/5 muscle power deficit in the left upper and lower extremities. The plantar response was bilaterally flexor. Sensory and cerebellar system examinations were normal. A PA chest X-ray revealed pneumonic infiltration areas on the middle and lower zones of the right lung. In EKG there was atrial fibrillation with a low ventricular rate. His cerebral CT was normal. Renal function tests and other biochemical and hematologic parameters were within normal limits.

The patient was diagnosed with atherothrombotic acute ischemic stroke, pneumonia and acute respiratory failure due the underlying COPD. He was admitted to the intensive care unit, and was intubated secondary to respiratory failure. He was started on enoxaparin 1.5 mg/kg/day subcutaneously every 12 hours. It was injected subcutaneously into the left or right deltoid muscle regions in turns. Salbutamol (Ventolin) 4 x 1 nebula, ipratropium bromide (Atrovent) 4 x 1 nebula, aminophylline (aminocardol) 0.5 mg/kg/h and sultamicillin (Duocid) 4 x 1.5 g/day IV (14 days) were started. Doxazosine (Cardura) 2 mg/day, atenolol (Tensinor) 25 mg/day and isosorbide 5-mononitrate (Monoket) 40 mg/day were initiated. The patient was extubated on the 10th day of intubation. On the 20th day of enoxaparin administration a lesion causing pain, tenderness and warmness and a mass effect on the right pectoral muscle region 7 x 11 cm developed and continued to enlarge. The biochemical parameters of the patient did not change, and the coagulation studies were repeated. Hb fell to 8.1 g/dl from 11.6 g/dl and Hct decreased to 25% from 35.2%. Bleeding time was 9 min (N 2-9 min), prothrombin time (PT) was 14 sec, partial thromboplastin time (PTT) was 30 sec, and platelet count was 246,000/mm3. Fibrinogen and fibrin degradation products were normal. In the superficial ultrasound of the right pectoral muscle region, there was a well-defined, capsulated, hypoechoic cystic lesion with internal septations. With a thoracal CT scan the lesion was found to be consistent with a hematoma 60 x 90 mm in size (Fig. 1).

During the follow-up of the patient in the intensive care unit, there was no trauma history. Subcutaneous enoxaparin was withdrawn and 2 units of packed red cells were transfused. Hb was

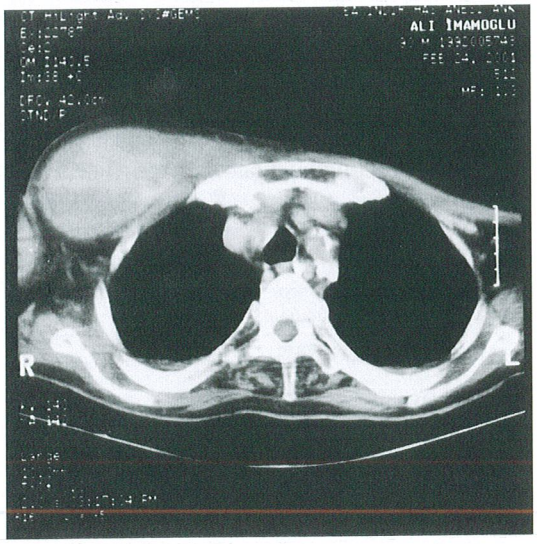

Fig. 1: Pectoral Muscle Hematoma was seen in thoracal computed tomography.

10.4 g/dl and Htc was 32.8%. By the end of 1 week, the edema, warmness and size of the hematoma had all decreased. Hematoma completely resolved after a 2-month follow-up period.

DISCUSSION

Low molecular weight heparins, like enoxaparin, are different from "unfractioned heparin" in several ways. In addition to having a more predictable bioavailability and a longer biologic half-life, low molecular weight heparins also have dose-dependent activity and inhibit the binding of platelets to fibrinogen and endothelium. Increasing the dose can magnify these effects and can increase the risk of bleeding. In addition, abnormal renal function, advanced age, and the effect of combining nonsteroidal anti-inflammatory drugs with enoxaparin may potentiate its effects (5).

In several studies, upon comparison with unfractionated heparin and warfarin the incidence of bleeding complications with enoxoparin has been reported to be lower (1). In 3 large series covering 2143 coronary artery disease patients receiving 40 mg/day enoxoparin, the major complication rate was 1.9-6.5% and the minor complication rate 20% (3). In a comparative study with unfractionated heparin by the Enoxacan Study Group, in 555 patients who had undergone cancer surgery and who were receiving enoxaparin for the prophylaxis of deep vein thrombosis, the major complication rate was 4.1% (6). The specific hemorrhagic complications were intrahepatic and intracranial bleeding, bleeding into the rectus abdominis and iliopsoas muscles (1) and an increase in postoperative site bleeding (7). Other non-hemorrhagic complications included local skin reactions, thrombocytopenia and hyperpotassemia (1).

In the literature, there are reports about hematomas in the rectus abdominis and iliopsoas muscles related to the use of LMW heparin. Barry et al. identified a hematoma in the rectus abdominis muscle in 2 patients receiving LMW heparin at a dose of 1-1.5 g/kg (8). Tsapatsaris et al. reported a 63-year-old patient who had steroid dependent COPD and who was followed-up in the intensive care unit due to pneumonia and acute respiratory failure. This patient was receiving 5000 units of LMW heparin, 3 times a day. On the 10th day of treatment, there was a hematoma in the rectus abdominis muscle not accompanied by coagulation test abnormalities. The hematoma decreased in size after 1 week and there was complete resorption after 2 months (7).

Antonelli et al. reported hematomas in the abdominal wall in 2 patients receiving enoxaparin. The first patient was receiving enoxaparin due to non-Q wave MI at a dose of 2 x 80 mg/day; the second had undergone abdominal aortic aneurysm surgery and was using enoxaparin at a dose of 2 x 30 mg/day. Both patients had bleeding of the abdominal wall 10 days after and their serum potassium levels were 6.1 meq/l and 8.3 meq/l, and serum creatinine levels were 5.4 mg/dl and 6.7 mg/dl, respectively. Hyperpotassemia was thought to be related to the resorption of the bleeding (1). Another patient, who had a blockade of the lumbar plexus, received prophylactic enoxaparin for deep vein thrombosis at a dose of 2 x 30 mg/day. On the 14th day of this treatment, the patient had right hip pain, and motor deficit of the right quadriceps, adductor and flexor muscles. CT revealed hematoma in the psoas muscle. PT was 13.6 sec, PTT was 26 sec, and platelet count was 431,000/mm3. The treatment was stopped and the patient had total correction of the motor deficit after 4 months (4). Davies et al. reported patients who developed hemorrhages in the rectus abdominis and iliopsoas muscles during oral anticoagulant (warfarin) and subcutaneous heparin administration with both normal and high INR values (9).

Ultrasound is the initial diagnostic tool in such cases. If there is diagnostic difficulty CT should be used. When a CT scan is obtained earlier in the course, the presence of hyperdense areas favor the diagnosis of hematoma. The fluid level within the hematoma due to layering of the hematocrit are a charateristic sign of anticoagulant-related hematomas. If the clinical history is not clear enough, CT findings can be interpreted as an abscess or a tumor. In such an instance, magnetic resonance imaging (MRI) may be necessary to demonstrate the presence of a hematoma. If Th1 sequences are obtained within 2 to 3 weeks, there will be a characteristic ring appearance, which results from the paramagnetic effect of Hb degradation. This

results in the differential diagnosis of hemorrhage due to other causes (9). The patient had respiratory problems, and so he was intubated and mechanically ventilated. Since we did not have a portable ventilatory device we were not able to perform thoracal MRI scanning. We think that thoracal CT was in accordance with his physical findings and so we considered the lesion on thoracal CT a hematoma.

Although there are cases of hematoma in the iliopsoas and rectus muscles, subdural hematoma, spontaneous hemothorax and retroperitoneal hematoma in the literature due to the administration of enoxaparin (10,11), pectoral muscle hematoma has not been previously reported in patients receiving a therapeutic dose of enoxaparin. If a decrease in Htc or blood pressure is experienced during enoxaparin treatment, the source of the hemorrhage should be investigated. In such a case the possibility of a hematoma in the pectoral muscle should be considered and it should be added to the list of potential complications of the administration of LMW heparin.

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REFERENCES

1. Antonelli D, Fares L, Anene C. Enoxaparin associated with huge abdominal wall hematomas: A report of two cases. The Am Surg 2000; 66: 797-800.
2. Weitz JI, Ed (by): Wood JJ. Low-molecular-weight heparins; Drugs therapy. The New England Journal of Medicine 1997; 337: 688-698.
3. Noble S, Spencer CM. Enoxaparin: A review of its clinical potential in the manegement of coronary artery disease. Drugs 1998; 56: 259-272.
4. Staff D, Heudebert G, Young MJ. Hematoma of the rectus abdominis manifested as severe pain in the right lower quadrant. South Med J 1991; 84: 1275-1276.
5. Klein SM, D'Ercole F, Greengrass RA, Warner DS. Enoxaparin associated with psoas hematoma and lumbar plexopathy after lumbar plexus block. Anest 1997; 87: 1576-1579.
6. ENOXACAN Study Group. Efficacy and safety of enoxaparin versus unfractionated heparin for prevention of deep vein thrombosis in elective cancer surgery: a double-blind randomized multicentre trial with venographic assessment. Br J Surg 1997; 84: 1099-1103.
7. Tsapatsaris NP. Low-dose heparin: A cause of hematoma of rectus abdominis. Arch Intern Med 1991; 151: 597-599.
8. Canova CR, Fischler MP, Reinhart WH. Effect of low-molecular-weight heparin on serum potassium. Lancet 1997; 349: 1447-1448.
9. Barry T., Butt J, Awad ZT. Spontaneous rectus sheath hematoma and an anterior pelvic hematoma as a complication of anticoagulation. Am J Gastroenterol 2000; 95: 3327-3328.
10. Davies RS, Goh GJM, Curtis JM, Meaney JF, Lewis-Jones HG. Abdominal wall haematoma in anti-coagulated patients: The role of imaging in diagnosis. Austr Rad 1996; 40: 109-112.
11. Mrug M, Mishra PV, Lusane HC, Cunningham JM, Alpert MA. Hemothorax and retroperitoneal hematoma after anticoagulation with enoxaparin. South Med J 2002; 95: 936-938.
12. Olson S, Rossato R, Guazzo E. Acute subdural haematomas and enoxaparin. J Clin Neurosci 2002; 9: 256-259.