Recombinant Activated Factor VII Treatment of Life-Threatening Rectus Sheath Hematoma in a Patient Receiving Enoxaparin, Aspirin, and Clopidogrel: A Case Report

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ABSTRACT

Rectus sheath hematoma is a rare complication of anticoagulant therapy. We have described the case of a 78-year-old woman with unstable angina who developed a life-threatening rectus sheath hematoma during treatment with antiplatelet drugs and enoxaparin. The patient had underlying diseases of hypertension and triple vessels disease status post coronary artery bypass graft. She was admitted initially with an asthmatic attack. Three days later, she developed unstable angina and thus received aspirin, clopidogrel, and enoxaparin. After the fifth dose of enoxaparin, she developed progressive suprapubic pain with a newly palpable mass, anemia, hypotension, and oliguria. Abdominal computed tomography revealed a rectus sheath hematoma sized 15 cm., (about 2,000 mL by volume). Her coagulogram was normal. Despite rapid fluid resuscitation, packed red cell transfusion (1,300 mL), platelet transfusion, and protamine sulfate injection, the patient's hemodynamic status remained unstable. Finally recombinant activated factor VII (rFVIIa) injection improved her hemodynamic status and stabilized her hemoglobin level without a thrombotic complication. This case report provides evidence of the benefit of rFVIIa use as a part of the treatment of refractory bleeding from enoxaparin.

Keywords: Enoxaparin, rectus sheath hematoma, rFVIIa

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CASE REPORT

A 78-year-old woman with a previous history of hypertension and triple vessels disease was admitted with an asthmatic attack and bronchitis. She had had progressive dyspnea and non-productive cough for 3 weeks before admission. On physical examination, her temperature was 37.8°C, her blood pressure (BP) 160/90 mmHg, her regular pulse 120 beats per minute and her respiratory rate (RR) 24 breaths per minute, and expiratory wheezes diffusely. The jugular veins were 3 cm above the sternal angle. Her cardiac examination showed the point of maximal impulse at the 6th intercostal space in the anterior axillary line, no heaving, normal heart sounds, and no murmur. A few days after treatment with a bronchodilator, dexamethasone and clarithromycin, her clinical symptoms improved. Three days after admission, she developed angina with increased dyspnea. Electrocardiogram showed ST depression in lead V1-V6 with dynamic change whereas her cardiac enzyme was normal. She received aspirin 325 mg/day, clopidogrel 75 mg/day, and enoxaparin 1 mg/kg (60 mg) subcutaneously every 12 hours (creatinine clearance was 40 ml/min) for unstable angina therapy.

Eight hours after the fifth dose of enoxaparin, she suddenly developed progressive suprapubic pain. The physical examination showed the BP of 80/35 mmHg, the pulse 70 beats per minute, the respiratory rate 24 breaths per minute, mild pallor and mild dyspnea. Chest and cardiovascular examination were normal, but abdominal examination found a large palpable suprapubic mass with later on large ecchymoses at her suprapubic area, on both flanks, and back (Fig 1).

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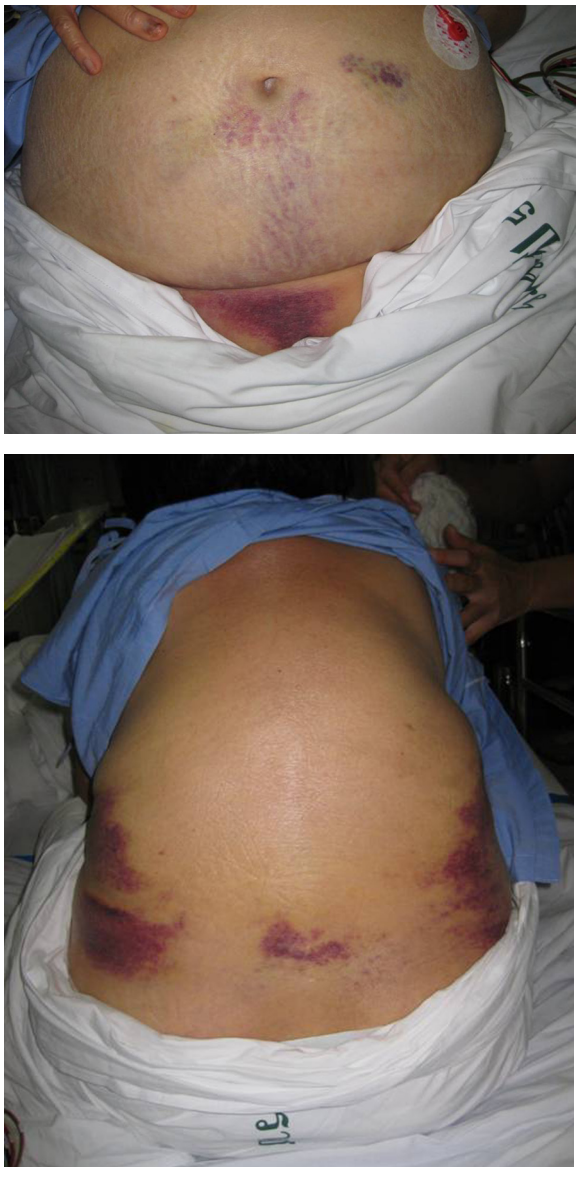

Fig 1. Ecchymoses at suprapubic area, both flanks, and back.

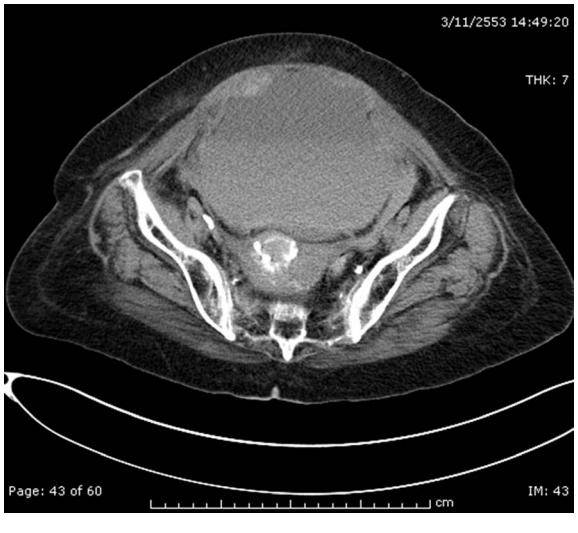

Fig 2. CT of whole abdomen showed a large rectus sheath hematoma.

Abnormal laboratory data were decreased hematocrit (40.7 (two days ago) to 31.8 percent) and increased serum creatinine (1.3 to 1.6 mg/dL). Her coagulogram was normal (PT 11.9 seconds, aPTT 24.7 seconds). Emergent abdominal computed tomography (CT) revealed a large rectus sheath hematoma anterior to her urinary bladder in which unclotted blood level was seen due to the remaining anticoagulant effects. This hematoma was approximately 15 cm in diameter and its total volume was about 2,000 ml (Fig 2).

Fluid replacement therapy was given rapidly to stabilize hemodynamics. Three hours later, central venous pressure (CVP) was accessed by venesection and the initial pressure was 4 cm. To partially reverse the anticoagulant effect of enoxaparin, 30-mg of protamine sulfate was injected. Six units of platelet concentrates were given in order to correct the antiplatelet effect of aspirin and clopidogrel. The patient was not given fresh frozen plasma (FFP) because of the fear that FFP contained antithrombin which is the substrate of enoxaparin and hence can enhance the anticoagulant effect of residual enoxaparin.

After six hours of resuscitation, 4,000-ml normal saline and 4-units of packed red cell (PRC) and platelet concentrates (340 ml) were given, but they could not restore her hemodynamic instability. Her BP was still 90/60 mmHg, CVP 5 cm and her urine output was only 40 ml. Repeated hematocrit after 3-units of PRC transfusion was 32.3%. Repeated coagulogram after aggressive blood transfusion showed a normal result.

Eventually, we injected recombinant activated factor VII (rFVIIa) 6,000 µg (105 µg/kg) intravenously. Control of bleeding and stability of hemodynamic status were achieved within 3 hours after rFVIIa injection with her BP 147/82 mmHg and urine output of 30 ml/hour 6 hours later. Fluid therapy could be discontinued on the next day with a stable hematocrit of 30 percent. No thrombotic complications were observed. Her hematoma size was stable. Finally, she was discharged 6 days later.

DISCUSSION

Rectus sheath hematoma (RSH) is a rare, but serious condition. The incidence among patients receiving anticoagulants is unclear. Risk factors include advanced age, systemic anticoagulant, minor abdominal trauma and cough.[1,2] In this case, the potential risk factors were advanced age, cough and enoxaparin which have been relatively overdosed when compared with the creatinine clearance. Accidental intramuscular enoxaparin injection may be responsible for hematoma formation and anticoagulants may contribute to its extension[3]. RSH can develop owing to direct muscular damage or tearing in one of the superior or inferior epigastric vessels. RSH can be managed conservatively, although, in patients with hemodynamic instability or expanded hematoma, surgical intervention or embolizations are recommended.[4,5] Protamine can partially neutralize the anticoagulant effect of low-molecular-weight heparin (LMWH).[6] Fresh-frozen plasma (FFP) will not be useful because of the inhibitory activity of LMWH. Furthermore, FFP contains antithrombin which is potentiated by both unfractionated heparin (UFH) and LMWH. Thus, FFP will not correct the anticoagulant effect of either UFH or LMWH and may, in fact, worsen the bleeding problem.[7] Use of rFVIIa in order to achieve hemostasis for uncontrolled RSH has been previously reported.[8] The rFVIIa works locally by directly forming a complex with

exposed tissue factor on subendothelial cells. This complex activates factors IX and X generating small amounts of thrombin which activate factors V and VIII and platelets perpetuating thrombin burst generation. The action of rFVIIa is limited to the site of injury and tissue factor exposure. This is useful with either surgical or non-surgical bleeding from a raw surface or without feeding vessels.[9] Recommendations of rFVIIa use for refractory bleeding are based on reported cases data with a lack of randomized controlled trials.

Examples of situations recommended for rFVIIa use include postpartum hemorrhage, uncontrolled post-operative bleeding especially cardiac surgery, uncontrolled bleeding due to a traffic accident, massive non-surgical bleeding with multi-transfusion and uncontrolled bleeding due to coagulopathy or anticoagulants.[10,11] Recent data shows that rFVIIa can effectively reverse the anticoagulant effect of newer therapies especially argatroban and bivalirudin.[12,13] This suggests that rFVIIa may be an effective option widely recommended in patients with any refractory anticoagulant bleeding complication.

CONCLUSION

This case report provides the evidence of the benefit of rFVIIa use as a part of the treatment of refractory rectus sheath bleeding from enoxaparin.

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