

SPONTANEOUS LIVER RUPTURE ASSOCIATED WITH LOW-MOLECULAR-WEIGHT HEPARIN THERAPY

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We present a rare case of a patient with spontaneous liver rupture, who was treated with anticoagulant therapy due to pulmonary embolism. The patient was diagnosed in the emergency department with deep vein thrombosis of his left leg and bilateral pulmonary embolism. He was admitted to the medical intensive care unit and low-molecular-weight heparin (enoxaparin) therapy was introduced. After the third dose, the patient started complaining of right shoulder and chest pain, and 3 hours later, when the patient was put in the sitting position, there was sharp drop of blood pressure, the patient lost consciousness, stopped breathing and pulse was impalpable. He was resuscitated for 4 minutes, after which he regained consciousness and complained of pain in the right shoulder, chest and right upper abdominal quadrant. Emergency abdominal ultrasonography showed free fluid in the abdomen, and computed tomography showed liver hemorrhage and liver capsule rupture. The patient was transferred to the operating theater, where liver hemostasis and perihepatic packing were performed. This case report shows the extent of possible adverse effects of anticoagulant therapy, even in patients with short duration of therapy and with no prior blood clotting disorders. Prompt diagnosis and treatment of spontaneous liver rupture are crucial in favorable resolution of this complication.

KEY WORDS: anticoagulant therapy, low-molecular-weight heparin, pulmonary embolism, spontaneous liver rupture

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INTRODUCTION

Spontaneous liver rupture is a rare condition, which has been described in patients with comorbidities such as benign and malignant liver tumors, acute fatty liver, hemolysis, elevated liver enzymes and low platelet count syndrome (HELLP syndrome), amyloidosis, systemic lupus erythematosus, pregnancy, and has been associated with high morbidity and mortality (1). Spontaneous liver hematomas are rare in patients without prior liver disease, however, there have been several cases reported, some linked to the usage of anticoagulant therapy or dual antiplatelet agents (2-5), and spontaneous liver ruptures in such patients are ever rarer (6,7). We describe a case of spontaneous liver rupture in a patient treated with low-molecular-weight heparin (LMWH) due to pulmonary embolism.

Spontaneous liver hematomas are treated conservatively in hemodynamically stable patients (8). On the other hand, liver ruptures leading to hemodynamic instability need to be treated surgically. Hemostasis of the liver can be achieved in several ways, including hepatic suture, perihepatic packing, cauterization, topical hemostatic agents, or even hepatectomy (6,9,10).

CASE REPORT

An 85-year-old male presented to the emergency department (ED) with clinical signs of left leg deep vein thrombosis. He complained of left leg pain and swelling during the previous 2 days, and his grandson mentioned he had had difficulty breathing for the last 3 weeks. He suffered from rheumatoid arthritis, osteoporosis

with compressive fractures of thoracic and lumbar vertebrae (Th 9-Th 12, L1-L3), arterial hypertension, and prostate adenoma. He was a non-smoker and did not consume alcohol, had a decreased appetite, but no complaints of urinary or bowel functions. On physical examination, the patient was afebrile and hemodynamically stable, blood pressure 130/90 mm Hg, heart rate 81/min, oxygen saturation 99%. There was a 3-cm difference in circumference between his left and right calf. His left calf was painful upon palpation, but there was no erythema. Other findings of physical examination were unremarkable. Electrocardiogram (ECG) showed sinus rhythm with left bundle branch block. Laboratory findings demonstrated a slightly lower level of hemoglobin (125 g/L), normal prothrombin time (99%), elevated lactate dehydrogenase (277 U/L), and very high D-dimer levels (>4.47 mg/L).

Once the diagnosis of left leg deep vein thrombosis was confirmed by color doppler ultrasonography, computed tomography pulmonary angiography was performed. The patient's Wells score for pulmonary embolism was 6 (moderate probability), modified Geneva score was 11 (high probability), and could not be excluded according to the *Pulmonary Embolism Rule-out Criteria* (PERC) as the patient was older than 50 years and presented with unilateral leg swelling. Angiography confirmed the diagnosis of bilateral pulmonary embolism. The patient was admitted to the medical intensive care unit and treatment with LMWH (enoxaparin) was initiated. He received the first dose of enoxaparin 80 mg subcutaneously (s.c.) in the emergency department at 5 pm, according to his weight of 70 kg. On the next day, he received another dose of 80 mg s.c. at 5 am, and the third dose of 60 mg s.c. at 4 pm. The third dose was reduced by the treating doctor in the intensive care unit. Approximately one hour after the application of the third dose, the patient started complaining of right shoulder and chest pain. The ECG was unremarkable, and the patient's pain subsided after analgesic and antihypertensive therapy. Three hours later, when the patient was put in the sitting position, there was sharp drop of blood pressure and the patient lost consciousness, stopped breathing and pulse was impalpable. He was resuscitated for 4 minutes. Medical team performed chest compressions and bag-valve-mask ventilation, administered intravenous fluids and one dose of intravenous epinephrine. The patient regained consciousness rapidly and complained of pain in the right side of his chest, right shoulder and right upper abdominal quadrant. Laboratory findings showed a decrease in hemoglobin level (from 117 g/L in the morning to 107 g/L), prothrombin time value (from 90% in the morning to 83%), and activated partial thromboplastin time (from 37 s in the morning to 29 s), which all were still within the reference values. Emergency abdominal ultrasonography showed free fluid in the perihepatic

and perisplenic areas. Subsequently performed computed tomography of the abdomen showed irregular lateral contour of the right liver quadrant with active bleeding from at least 2 peripheral subcapsular blood vessels with rupture of the liver capsule and free fluid around the liver, spleen and in the pelvis (Fig. 1). No apparent cause of the bleeding was visible (such as tumors or arteriovenous malformations). The patient's history clearly demonstrated that he had not sustained any trauma prior or after being admitted to the hospital. The on-call abdominal surgeon was consulted and the patient was transferred to the operating theater. Abdominal exploration showed hematomas located in the subhepatic and perisplenic regions, and around the greater omentum. The source of diffuse bleeding was located in the 6th and 7th liver segments. The procedure of perihepatic packing was applied several times, and the Pringle maneuver in duration of 15 minutes each was performed 2 times. An absorbable hemostat, sealant matrix coated with fibrinogen and thrombin, and hemostatic powder were applied once more before performing perihepatic packing.

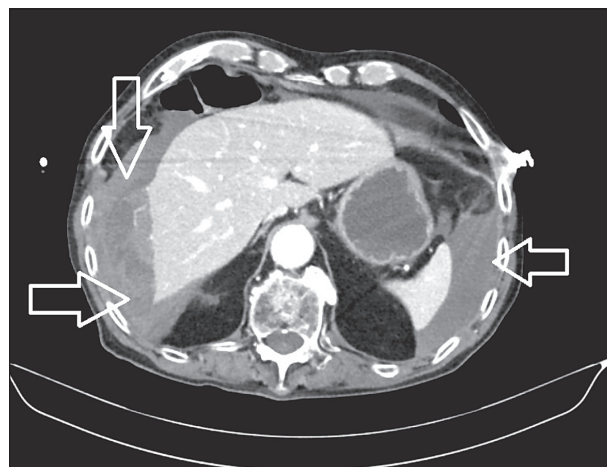


Fig. 1. CT of the abdomen showing liver capsule rupture and free fluid around the liver and spleen (arrows).

DISCUSSION

We present a case of an elderly male patient without any liver disease or blood clotting disorders, treated with LMWH due to bilateral pulmonary embolism who suffered spontaneous liver rupture on the second day of anticoagulant therapy. The patient first complained of right shoulder and chest pain. Several hours later, he was found to be hemodynamically unstable and in need of resuscitation measures. It is our strong opinion that the liver hemorrhage was spontaneous indeed, rather than caused by the resuscitation measures, as the patient had the aforementioned complaints prior to development of hemodynamic instability and loss of

consciousness. A similar case is described in the literature; a patient was found to have a large subcapsular liver hematoma after deterioration of her condition and subsequent resuscitation, on the third postoperative day after renal transplant (11). It is well known that anticoagulant therapy bears an increased bleeding risk, although it has been shown that a fixed dose of LMWH has a reduced incidence of major hemorrhage during initial treatment of venous thromboembolism and is superior over unfractionated heparin (12). Other than trauma, another situation where liver hematomas are frequently described is pregnancy due to preeclampsia, hemolysis, elevated liver enzymes, and low platelet syndrome, which was not the situation in this case (8,10,13). Although few, there also are cases described in the literature of spontaneous liver ruptures in male patients denying trauma and without any history of anticoagulant use (14).

CONCLUSIONS

Low-molecular-weight heparins are widely used and are fairly safe. However, this case report shows the extent of possible adverse effects and bleeding risks, even in patients with short duration of anticoagulant therapy and with no prior blood clotting disorders. Hemodynamically unstable patients and those on LMWH therapy developing hemorrhagic shock should be assessed for bleeding complications, especially the uncommon presentations, as prompt diagnosis and treatment are crucial in favorable resolution of this complication.

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SAŽETAK

SPONTANA RUPTURA JETRE POVEZANA S PRIMJENOM HEPARINA NISKE MOLEKULARNE MASE

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Prikazujemo slučaj bolesnika kod kojega je došlo do pojave spontane rupture jetre, a koji je bio liječen antikoagulacijskom terapijom zbog plućne embolije. Bolesniku je u hitnoj službi dijagnosticirana duboka venska tromboza lijeve noge te obostrana plućna embolija. Primljen je u Jedinicu intenzivne medicine te je započeto liječenje heparinom niske molekularne mase (enoksaparin). Nakon primljene treće doze bolesnik se počeo žaliti na bolove u desnom ramenu i prsnom košu te je 3 sata nakon toga, nakon postavljanja u sjedeći položaj, došlo do naglog pada tlaka, izgubio je svijest, prestao disati, a puls nije bio palpabilan. Nakon reanimiranja u trajanju od 4 minute došao je svijesti i žalio se na bolove u desnom ramenu, prsnom košu i gornjem desnom kvadrantu trbuha. Učinjenim ultrazvukom abdomena verificirana je slobodna tekućina u abdomenu, a kompjutoriziranom tomografijom krvarenje iz jetre i ruptura jetrene čahure. Hitno je premješten u operacijsku dvoranu gdje je učinjena hemostaza i tamponada jetre. Prikaz ovoga bolesnika ukazuje na opseg mogućih neželjenih učinaka antikoagulacijske terapije, čak i kod bolesnika koji su kratkotrajno na antikoagulacijskoj terapiji i ne boluju od poremećaja zgrušavanja krvi. Pravodobno postavljanje dijagnoze spontane rupture jetre i primjena odgovarajuće terapije ključni su u poželjnom rješavanju navedene komplikacije.

KLJUČNE RIJEČI: antikoagulacijska terapija, nisko-molekularni heparin, plućna embolija, spontana ruptura jetre