Sudden Onset Abdominal Wall Swellings in Patient of Liver Cirrhosis

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Spontaneous hematomas in cirrhotic patients are uncommon. Severe coagulopathy in advanced hepatic disease is characterized by both coagulation factor deficiencies and accelerated fibrinolysis. Hyperfibrinolysis in cirrhosis is a result of excess fibrin breakdown leading to defective hemostasis. We present a case of spontaneous hematomas with an acute drop in hemoglobin level, in a patient with cirrhosis which was due to primary hyperfibrinolysis. (J CLIN EXP HEPATOL 2012;2:283–285)

CASE REPORT

A 50-year-old male with significant ethanol consumption presented with jaundice of 15 days duration, ascites and pedal edema of 5 days duration and, melena of 4 days duration. He had not experienced any physical trauma and was not receiving antiplatelet agents or anticoagulants. Subsequent investigations revealed that he had alcoholic hepatitis with portal hypertension related ascites. Gastrosocopy showed pigment based duodenal ulcer (Forrest class IIc). His Child-Pugh classification was category C, with a score of 10.

On day 3 of admission, he developed pain and swelling in right iliac fossa. Ultrasonography revealed heterogeneous collection in anterior abdominal wall suggestive of hematoma. The same evening he complained of pain and swelling in left iliac and lumbar region, which on ultrasonography revealed an irregular heterogeneous echo texture collection in the anterior abdominal wall of the left iliac fossa measuring $11.8 \times 5.3 \times 7.9$ cms with 260 cc volume suggestive of hematoma (Figures 1 and 2). Next day he developed back muscle hematoma.

Blood investigations revealed drop in hemoglobin from 8.3 g/dl to 4.8 g/dl, platelet count was 1.5 lacs. Coagulation profile revealed normal activated partial thromboplastin time (aPTT), prothombin time elevated by 3 s, D-dimer of 2050 ng/ml, serum fibrinogen level was 175 mg/dl (normal 220–496 mg/dl), factor VIII level was 140 IU/dl (normal

50–150 IU/dl) and euglobin lysis test less than 60 min (normal 90–120 min). Other coagulation parameters were normal. Schistocytes were negative on study of peripheral smear. He received supportive treatment which consisted of transfusion of 4 pints packed red blood cells, tranexamic acid (dose: 1 g thrice a day) which is plasminogen activation inhibitor and fibrin breakdown and prophylactic antibiotics (amoxicillin + clavulanic acid). Patient improved symptomatically during hospital stay. On follow up 3 months later, near complete resorption of hematomas was seen.

DISCUSSION

We report a rare case of primary hyperfibrinolysis syndrome which is defined by an elevated D-dimer or fibrin degradation products (FDPs) levels and/or markedly shortened clot lysis time. The above criteria have been found to predict subsequent clinical hemorrhage¹ of which spontaneous intramuscular and subcutaneous hematomas are a manifestation. Violi et al² found a relationship between hyperfibrinolysis (FDPs over 10 mcg/ml) and fatal bleeding. Hyperfibrinolysis correlated positively with the severity of underlying liver disease (the Child-Pugh classification).³ APTT prolongation is a significant risk factor of death.¹ Alcoholic cirrhosis is the most common etiology found in hyperfibrinolysis with liver disease.

Sugiyama et al⁴ reported a 56-year old with alcoholic cirrhosis, who was admitted with shock and anemia. Evaluation of anemia which included EGD, colonoscopy and upper abdominal computed tomography did not identify the cause for shock and anemia. He died on the 10th day of admission. Autopsy showed bilateral iliopsoas hematomas. In the same report Sugiyama et al⁴ reviewed eight cases of spontaneous muscle hematoma associated with liver cirrhosis. Of these cases, four involved the rectus abdominis muscle, three iliopsoas, and one involved the gluteus maximus, the biceps femoris and the pectoralis muscles. The three patients with iliopsoas hematoma

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Abbreviations: aPTT: Activated partial thromboplastin time; FDPs: Fibrin degradation products; tPA: Tissue plasminogen activator; PAI-1: Plasminogen activator inhibitor 1; TAFI: Thrombin-activatable fibrinolysis inhibitor; DIC: Disseminated intravascular coagulation; EACA: Epsilon amino-caproic acid

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Figure 1 Abdominal wall swellings.

and two of the four patients with rectus abdominis muscle hematoma died. The mortality rate of muscle hematoma associated with hyperfibrinolysis in cirrhosis is 75%.⁴ This is higher than the rates in hemophilia and on anticoagulants.⁴

Fibrinolysis (the degradation of fibrin) is regulated by different factors that either activate the process (eg, tissue plasminogen activator [tPA] and urokinase plasminogen activator) or act as antiactivators (eg, plasminogen activator inhibitor 1 [PAI-1] and alpha-1 plasmin inhibitor). Thrombin-activatable fibrinolysis inhibitor (TAFI), another plasma protein, has been recently identified. It is synthesized by the liver and plays an important regulatory role in fibrinolysis. Upon activation by thrombin or plasmin, it

is converted to an enzyme TAFIa with carboxypeptidase B-like activity that inhibits fibrinolysis through the removal of C-terminal lysine's from partially degraded fibrin. Any imbalance in the fibrinolysis pathways may lead to hypofibrinolysis or hyperfibrinolysis.⁵ In patients with cirrhosis the fibrinolytic pathway is activated by an increased endothelial release of t-PA, decreased hepatic clearance of t-PA, decreased TAFI, and decreased synthesis of α 2- antiplasmin and plasminogen activator inhibitor.³ Hyperfibrinolysis may affect formation of the platelet plug through an increase in von Willebrand factor and glycoprotein Ib and IIb/IIIa degradation; it may reduce platelet adhesion; or it may cause early disruption of the hemostatic plug that consequently increases the risk of additional bleeding.⁵

Primary hyperfibrinolysis is diagnosed by elevated FDPs and shortened euglobin lysis test. Other coagulation parameters are normal including aPTT and prothrombin time. Euglobin lysis time is a modified plasma clot lysis time and measures increased plasminogen activation. Disseminated intravascular coagulation (DIC) may resemble hyperfibrinolysis findings in patients with cirrhosis. Hyperfibrinolysis is characterized by elevated factor VIII, a relatively stable platelet count, low fibrinogen level, absence of schistocytes on peripheral smear and absence of the multiorgan failure frequently associated with DIC.⁵ Our patient had normal aPTT and FDPs <10 mcg/ml, which are good prognostic signs in hyperfibrinolysis in cirrhosis.

Treatment of hyperfibrinolysis is supportive which includes maintaining hemoglobin with transfusion of

Figure 2 USG showing muscle hematoma.

packed red blood cells. It also includes therapies that inhibit plasminogen activation and fibrin breakdown. Epsilon amino-caproic acid (EACA), a synthetic derivative of the amino acid lysine is effective and safe in treating patients with bleeding in accelerated fibrinolysis. It binds reversibly to the lysine-binding site of plasminogen and blocks the binding of fibrin.⁶ Tranexamic acid produces an antifibrinolytic effect by competitively inhibiting the activation of plasminogen to plasmin. It is also a weak non-competitive inhibitor of plasmin. These properties make possible its clinical use as an antifibrinolytic in the treatment of both general and local fibrinolytic hemorrhages. It has an action mechanism similar to, but about 10 times more potent in vitro, than that of EACA. It was used in dose of 1 g thrice a day. Aprotinin is a serin-protease inhibitor that reduces fibrinolytic activity by inhibiting plasmin and kallikrein. It has been used in post liver transplantation cases. Antifibrinolytic agents are potentially associated with two important complications: the development of thromboembolic events and acute renal tubular necrosis.

In general, spontaneous intramuscular or subcutaneous hematomas are not recognized as one of the bleeding complications occurring in cirrhotic patients. Considering the high mortality rate despite early diagnosis, spontaneous

hematomas should be recognized in the differential diagnosis in the rare but clinically important bleeding complication of cirrhosis, especially in cases of alcoholic cirrhosis. APTT and FDPs levels can be used for prognostication of patients in hyperfibrinolysis with cirrhosis.

CONFLICTS OF INTEREST

All authors have none to declare.

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