

Hemorrhagic episodes in hemophiliacs simulating abdominal surgical emergencies

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ABSTRACT

Hemophiliacs are subjected to develop episodes of spontaneous bleeding at different sites of the body, primarily the knees. On occasions, such episodes affect the abdomen. The picture engendered in such cases may mimic that of an abdominal emergency requiring surgical intervention. Such ill advised and unwarranted intervention may end with the patient's death. With the proper employment of radiology, the correct diagnosis may be reached and consequently, conservative treatment, in which factor VIII plays the major role, instituted. Here, we describe the clinical course of 2 patients with hemophilia A who suffered bleeding in the abdomen and were treated conservatively with a successful outcome.

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Hemophiliacs share with the general population the likelihood of developing abdominal surgical emergencies. The recognition that a bleeding episode might be the cause of a clinical picture mimicking acute abdomen,¹ would result in providing the appropriate treatment, and will therefore, help avoid unnecessary and often hazardous surgery in these unfortunate patients. In this report, we describe the clinical course of 2 cases of hemophilia A, presented to Assir Central Hospital with acute abdomen caused by a retroperitoneal bleeding episode. By reaching the correct diagnosis and instituting the appropriate replacement therapy, a response was obtained and surgery was thus avoided.

Case Report. Patient One. A 36-year-old male, a known hemophiliac (type A, factor VIII level 2%) with inhibitors (<2.0 Bethesda units) presented with severe pain in the left lower quadrant, which started one day earlier. The pain increased steadily with time and was associated with vomiting. A recent history of hematuria was obtained, and his past history was

remarkable for repeated hospital admissions for bleeding in different sites, mainly the knees. His family history showed that his brother succumbed to hemophilia several years ago. On examination, he was pale and in pain. His blood pressure was 90/60 mm Hg, the pulse rate was 97beat/minute and the temperature was 37°C. The abdominal examination revealed tenderness in the left flank with sluggish bowel sounds. The hemoglobin was 7.5 gm/dl, white blood cell count was 6900/ μ l, the liver function tests were normal, the prothrombin time (PT) was 17 seconds (control 17 seconds), and the activated partial thromboplastin time (APTT) was 112 second (control 30 seconds). An emergency ultrasound (US) examination revealed mild bowel wall edema with free fluid in the abdomen. Provisionally, a spontaneous bleeding episode attributable to his underlying disease was strongly suggested. The patient was kept under observation with nil orally, blood and factor VIII transfusion was started at a rate of 2000 units/12 hours. A few hours later, the patient went into shock and the blood pressure was not recordable with the appearance

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of a swelling in the left flank. At that point the patient was shifted to the intermediate care unit where resuscitation with blood and factor VIII concentrate was intensified. An emergency computerized tomography (CT) scan of the abdomen revealed a huge retroperitoneal hematoma on the left side, pushing the left kidney and bowel anteriorly and to the right, with free fluid in the abdomen (Figures 1 & 2). In addition, there was free fluid in the pleural spaces. With repeated blood transfusions and high doses of factor VIII concentrate, the patient was kept in a relatively stable hemodynamic state, and this continued throughout the main part of his hospital stay. Two days after admission, the patient developed extensive right hemothorax. Supplemental oxygen was needed to keep his partial pressure of oxygen (PO₂) within the normal range. Thoracocentesis was proposed, but the patient refused. On the 9th day, the patient started to mobilize fluids and the urine output increased much, his transfusion requirements and oxygen demands gradually decreased, and finally he was kept on room air with O₂ saturation of 96%. Three weeks after admission, he was discharged home, and 13 months later he remained relatively well, although the left flank mass did not decrease much in size. This management demanded high doses of factor VIII

concentrate, ranging between 2000 to 5000 units every 12 hours, his factor VIII assay ranged between 23-66%, his APTT fluctuated between as low as 46 seconds, and as high as 120 seconds (control 30 seconds), and his hemoglobin ranged from 3.3 to 11.9 gm/dl.

Patient 2. An 18-year-old male, who is known to have mild hemophilia A, presented with right lower quadrant pain of 2 days duration. The pain was accompanied with nausea. Except for mild hemophilia, his past history was unremarkable. On examination, he was tender in the right iliac fossa with rebound tenderness. Rovsing sign was also positive. The investigations revealed a hemoglobin level of 13.1 gm/dl and white cell count of 12,100/ μ l. His APTT was 120 seconds (control 30 seconds). The rest of the routine investigations were normal. Acute appendicitis was suspected. An US of the abdomen revealed a hematoma in the right iliac fossa involving the right iliopsoas muscle. The same finding was confirmed with CT scan of the abdomen (Figure 3). The hematoma was incriminated as the cause of his symptoms. Consequently, conservative treatment with factor VIII concentrate in a dose of 2000 units 12 hourly was started. The condition then improved and 2 days later, the patient was discharged home pain free.

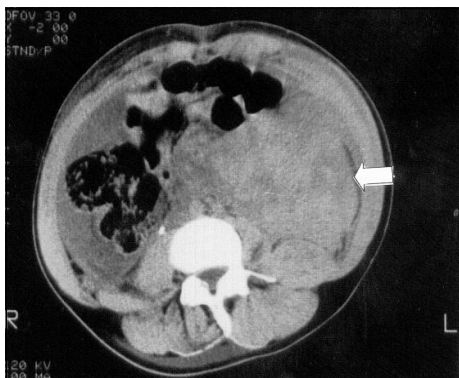


Figure 1

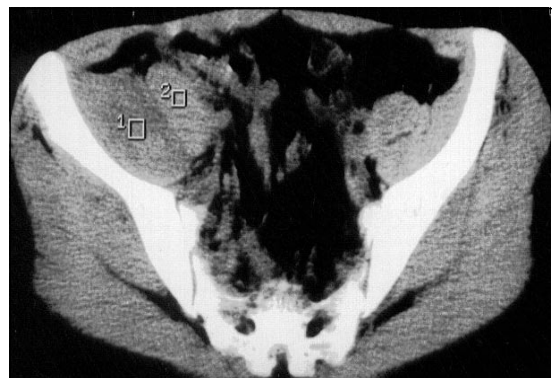


Figure 3

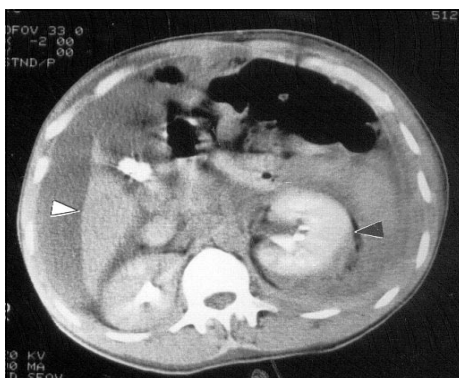


Figure 2

Figure 1 - Extensive retroperitoneal hematoma on the left side (arrow), pushing the intestine to the right of the abdomen.

Figure 2 - The left kidney (black arrow head) seen displaced anteriorly by the hematoma. The distal part of the right lobe of the liver (white arrow head) is seen surrounded by blood.

Figure 3 - The right iliacus (1) and psoas major (2) seen swollen by the hematoma.

Discussion. Classical hemophilia (hemophilia A) is a disease of males. The failure to synthesize factor VIII in normal proportions is inherited as a sex linked recessive trait. Spontaneous mutations account for almost 20% of cases. The incidence of the disease is approximately 1:10,000 to 1:15,000 population, and the clinical manifestations can be extremely variable. Characteristically, the severity of clinical manifestations is related to the degree of deficiency of factor VIII. Retroperitoneal bleeding may follow lifting of a heavy object or strenuous exercise. Hypovolemic shock may occur, as the amount of blood loss that can take place in this setting is enormous. The management of such cases is based on appropriate transfusion therapy and avoidance of surgical treatment.¹ A small proportion of patients with hemophilia A (10-20%) develop inhibitors to factor VIII. These are usually immunoglobulin G antibodies, and they complicate therapy, the actual level of the inhibitor can be quantified using a Bethesda assay.² The management of bleeding episodes in such patients presents a major therapeutic challenge to clinicians.^{3,4}

Acute abdominal pain in a hemophiliac should be approached as hemorrhage until proven otherwise. Diagnostic imaging can define areas of hemorrhage. The ability to support patients with factor replacement and avoid unneeded exploratory surgery means that recognition, diagnosis and treatment can lead to a major decrease in morbidity and mortality.⁵ Until recently, bleeding from any site in hemophiliac patients with inhibitors indicated a bleak prognosis.⁶ There are few therapeutic options available for managing such patients. In the presence of serious bleeding and a low initial antibody titer, a large dose of factor VIII calculated to overcome the inhibitor and temporarily raise the concentration of factor VIII may be given.² The use of porcine factor VIII, which differs from the human protein in regions that contribute to antigenicity,⁷ may be effective where the antibody titer against human factor VIII is very high.⁸ Newer methods include prothrombin complex concentrate, activated prothrombin complex concentrate, activated factor VII and more recently, activated recombinant human factor VII. These agents can bypass functional deficiencies of factor VIII in hemophilia A or factor IX in hemophilia B.⁴ Of all the treatment options, recombinant activated factor VII (rVIIa), is emerging as the treatment of choice for treating such patients in both the elective and emergency situations³ and a variety of elective major surgical procedures have been recently reported under its cover.⁹⁻¹¹ In the elective situation, tolerance to factor VIII inhibitors can be achieved by the long-term daily infusion of large amounts of factor VIII. The tolerance thus obtained lasts for years in approximately 80% of patients.¹²

In the first case, a hemophiliac with inhibitors, the absence of history of trauma aided by US and CT

scanning enabled a diagnosis of spontaneous bleeding in the retroperitoneum to be established. The presence of inhibitors made the treatment remarkably difficult. Of all the options listed above, the only available one was to infuse high doses of factor VIII, and although this did not succeed initially, as evidenced by expansion of the hematoma and extension of the bleeding into the thorax, we persisted with it and eventually, hemostasis was achieved. Triggered by the rapid expansion of the hematoma and the presence of free blood in the abdomen, there was an urging desire to intervene surgically aiming at evacuating the hematoma and checking the source of bleeding, but this was strongly resisted and certainly, this was one of the reasons that led to the successful outcome.

The second case presented with the picture of acute appendicitis. The utilization of US revealed the correct diagnosis. There are similar instances in which a small bowel hematoma in a hemophiliac caused a picture simulating acute appendicitis, the diagnosis was reached with abdominal US, and the condition has been termed pseudoappendicitis.⁵

In conclusion, bleeding in hemophiliacs can disguise as acute abdomen necessitating operation. In the absence of trauma, bleeding should be assumed to consist of capillary ooze. The employment of diagnostic radiology and appropriate replacement therapy enables a successful outcome to be achieved. Where the more recent therapeutic options are inaccessible, the presence of inhibitors does not preclude repeated transfusions of factor VIII to control bleeding. This option is particularly valid for non-specialized centers, and third world countries with limited access to the more sophisticated and certainly more expensive agents.

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