CASE REPORT

Acute Abdomen: Unmasked the Bleeding Site in Severe Haemophilia A

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ABSTRACT

Haemophilia A is an inherited bleeding disorder, commonly involve soft tissues and joints. Gastrointestinal tract bleeding, are not uncommon but seldom highlighted. A 23-year-old male with underlying severe haemophilia A was presented with a generalised abdominal pain for 2 days, abdominal distension, diarrhoea and vomiting. He did not have any trauma to the abdomen. Abdominal examination revealed generalized tenderness with sign of guarding on palpation. Laboratory investigations revealed isolated, prolonged activated partial thromboplastin time (APTT) with normal total white blood cell count and haemoglobin level. In view of acute abdomen, which was not resolved by conservative treatment, an emergency laparotomy was done with FVIII concentrate and recombinant factor VII (rFVII) coverage. Intraoperative findings noted patchy gangrenous spots of about 30 cm in length in the small bowel. Histopathology examination revealed an evidence of haemorrhage within the submucosal and intramuscularis layer from the resected specimen. This case highlighted the possibility of gastrointestinal bleeding without prior trauma, which can be presented as acute abdomen in severe haemophilia patient.

Keywords: Hemophilia, Gastrointestinal bleeding, Bowel ischaemia

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INTRODUCTION

Haemophilia A is an inherited bleeding disorder caused by FVIII deficiency or dysfunction. It is inherited as X-linked with heterogeneous mutations in the factor VIII gene, which located at distal end of the long arm of the X-chromosome (1). Low level of these plasma glycoproteins will cause decreased and delayed thrombin generation, giving rise to significant defects in clot formation which lead to haemorrhagic diathesis. Bleeding manifestations commonly affect soft tissues, joints, and muscles (2). Sometimes severe haemophilia bleeding manifestation in other systems, including the gastrointestinal system, may occur. Acute small bowel ischaemia is a gastrointestinal emergency that requires prompt recognition and intervention to prevent subsequent complications, such as bowel infarction, perforation, and peritonitis, which are associated with high mortality.

CASE REPORT

A 23-year-old male with underlying severe haemophilia A was presented with generalized abdominal pain for 2 days, which was associated with bloating sensation, abdominal distension, diarrhoea and vomiting. The pain was colicky in nature, non-radiating and was resolved after defecation. He had history of passing out blackish stool a few days prior to admission. Otherwise, the patient informed that there was no history of trauma to the abdomen, hematemesis, fever or eating outside food. In addition, there was no recent intake of drugs (analgesic) prior to the admission. He was previously treated and followed up by Hospital Universiti Sains Malaysia (USM), but defaulted treatment 4 months prior to this presentation.

He was diagnosed with haemophilia A at the age of 2 years when he was presented with bruises on the chest and gluteal region. His mother also noted that he developed bruises at the injection site following vaccination. Full blood count showed normal platelet count (315 x 10^9/L). Initial coagulation profile showed isolated prolonged activated partial thromboplastin

time (APTT: 105.5 second) with complete correction when added with normal plasma in the mixing study. The FVIII level was less than 1%, and he was given FVIII replacement therapy. Since then, he had multiple episodes of hemarthrosis, especially at both elbows and right knee. Biweekly prophylactic FVIII infusion was started in 2014 before he lost to follow up in November 2016. He was diagnosed with Hepatitis C in 2014, but otherwise he was asymptomatic with the normal liver function test.

Physical examination showed mild dehydration and a stable vital sign. He has generalized abdominal tenderness with guarding. Laboratory investigations showed that the white blood cell count was 8.24 x10^9/L, haemoglobin was 12.2 g/dL, and platelet count was 334 x 10^9/L. APTT was 107.5 seconds and prothrombin time (PT) was 13.8 seconds. Factor VIII assay was less than 1%. Ultrasound examination showed the presence of minimal free fluid. Initial management with infusion of FVIII and rFVII plus analgesic did not relieve his pain despite of normalisation of his APTT. The screening for FVIII inhibitor was negative. He had undergone emergency laparotomy with infusion of FVIII and rFVII to secure haemostatic complication. Intraoperative finding showed patchy gangrenous of the small bowel (30cm) which was 180cm away from the ileocaecal junction. Small bowel resection with end-to-end anastomosis was done. Histopathological examination showed evidence of haemorrhage in the submucosal areas, extending up to the muscularis layer, with the tip of the villi appeared denuded and some showed shortening. However, there was no evidence of thrombosis, microorganisms, granuloma or malignancy in the histopathological specimen (Fig. 1a and 1b). Post-operative recovery was uneventful. He was well with no complication of clinical bleeding tendency. He received a total dose of 12,900 units of FVIII and 4 mg of rFVII, and was discharged 3 days post operatively. He was given an appointment for follow up at Surgical and Haematology clinics.

DISCUSSION

Gastrointestinal (GI) haemorrhage occurs in 17.5% to 25.0% of haemophiliac patients and causes death in 4% of the overall population (3). Patients are usually presented with melaena or rectal bleeding, and rarely cause bleeding in the small intestinal wall. In haemophilia, GI pathology especially duodenal or gastic ulcers, bleeding from unknown site, and gastritis, are the most common cause of GI bleeding, as compared to the underlying coagulation disorder itself (4). Therefore, based on clinical presentation of acute abdomen, the underlying GI pathology needed to be excluded first.

Intramural bleeding of small intestine is commonly due to blunt trauma to the abdomen. However, spontaneous intramural small bowel hematoma in non-traumatic case is rare, and there has been several risk factors related to this condition including haemophilia. In this case, intramural bleeding had occurred in the small intestine, leading to ischemic bowel. The most possible cause could be due to rupture of the terminal arteries as they enter the muscle layer of the intestinal wall (5). This haemorrhage dissects the wall between the muscularis mucosae and the muscle layers. In the absence of trauma, spontaneous GI bleeding can be associated with other factors, such as infection with Helicobacter pylori, the use of non-steroidal anti-inflammatory drugs (NSAIDS) or may be due to the development of an inhibitor. In this reported case, he had no trauma, neither recent exposure to NSAIDS nor a sign of infection. Moreover, the FVIII inhibitor was not detected. Rate of infection with Helicobacter pylori were reported to be equal between haemophilia and non-haemophiliac patient, however the risk of bleeding were increased in haemophilia patients. Test for Helicobacter pylori was not done in this patient as it was not upper gastrointestinal bleeding. Therefore, after excluded the common GI pathology and considering prolonged APTT with low FVIII level, bleeding due to factor deficiency was considered.

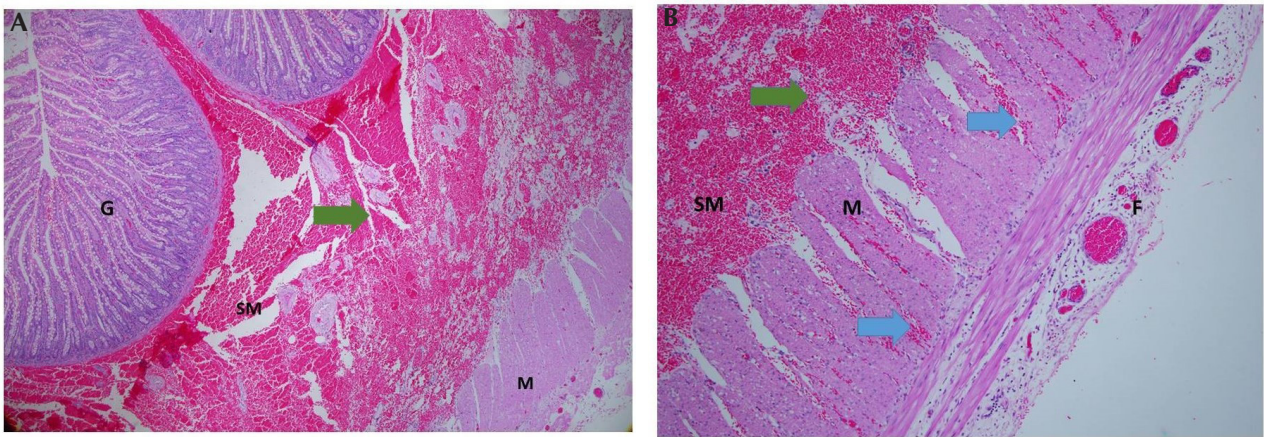

Figure 1: (A) and (B): Part of jejunum exhibiting submucosa and intramuscular haemorrhage. G: Colonic Gland, SM: Submucosa, M: Muscularis Layer, F: Pericolic Fat → Submucosa Haemorrhage → Intrmural/Muscular Haemorrhage

Most of the haemophilia patients with GI bleeding are treated conservatively with factor concentrates and computed tomography scan (CT scan) monitoring before embarking on surgery. The initial treatment is to give FVIII concentrates with the aim of increase its levels more than 80% in the acute stage, and to continue with maintenance treatment to keep FVIII around 50% for 14 days. However, if the bleeding cannot be controlled, activated prothrombin complex concentrate (APCC) or recombinant factor VIIa (rVIIa) may be considered. However in our case, based on the clinical judgement, laparotomy was done to prevent further complication that was related to bowel ischemia and gangrenous after adequate coverage with factor concentrates. The prevention of patient with occult GI bleeding is important to avoid recurrent episodes. Therefore, he was scheduled for proper prophylaxis treatment and monitoring of FVIII inhibitor during follow up.

CONCLUSION

This case highlights the possibility of GI bleeding without prior trauma, which can be presented as acute abdomen in a severe haemophiliac patient. Even though conservative medical treatment is the treatment of choice in most cases, early surgical approach in acute abdomen may be implemented if necessary with proper adjunctive therapy to prevent complications in haemophiliac patients.

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