Unusual massive gastric mucosal bleeding in a patient with dengue

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Introduction

Dengue has become one of the most important communicable diseases in Sri Lanka. 44,410 cases of dengue have been reported in Sri Lanka in 2012[1]. Gastrointestinal (GI) bleeding is a well recognised complication of dengue. However severe GI bleeding is usually seen in patients who develop shock, multi-organ failure and disseminated intravascular coagulation (DIC) or in those who have taken non-steroidal anti-inflammatory drugs (NSAIDs)[2]. Here we report a patient with dengue who had massive GI bleeding in the absence of any of the above contributing factors and we describe how timely administered conservative management could be life saving.

Case report

In November 2012, a previously healthy 17 year old boy was admitted to a private hospital in Wattala on the third day of a febrile illness. He also complained of severe headache, loose motions and faintishness. He did not have vomiting or bleeding manifestations at the time of admission. Before coming to the hospital he has taken treatment from a general practitioner. Prescribed drugs were paracetamol, domperidone, co-amoxiclav and fexofenadine. He gave a history of allergy to ibuprofen and had not taken any NSAIDs or steroids in the recent past. He did not have a history of peptic ulcer disease and has not been on anticoagulant therapy. He had never smoked or consumed alcohol.

The clinical examination on admission revealed an alert but ill patient with mild to moderate dehydration. His temperature was 101.1°F. There was no pallor, jaundice, skin rashes or flushing. His blood pressure (BP) was 100/70mmHg with no postural drop. Pulse rate was 80 beats per minute (bpm) and the pulse volume was normal. There was epigastric tenderness. The liver and spleen were not palpable and there was no free fluid in the abdomen. Respiratory system was normal with no evidence of pleural effusions. On admission, platelet count (PC) was 95,000/mm³, white cell count (WCC) was 2600/mm³. Hematocrit was 46.7% with hemoglobin of 15.5g/dl. Liver transaminases were normal [aspartate aminotransferase (AST)-47U/l, alanine aminotransferase (ALT) - 43U/l]. Dengue NS 1 antigen test was positive. It was done by SD BIOLINE Dengue NS 1 Ag rapid test which is an in-vitro immunochromatographic one step assay for qualitative determination (sensitivity-92.8%; specificity-98.4%).

Management at this stage consisted of fluid resuscitation with crystalloids and oral rehydration solution, symptomatic therapy with paracetamol and omeprazole and close monitoring. After resuscitation, initially high hematocrit dropped to 40.9% with hemoglobin of 14.2 g/dl. BP had risen to 110/70mmHg and pulse rate was 80bpm. Serial blood counts over the next 24 hours revealed further reduction of PC and WCC but the hematocrit remained around 40%.

Late on the 4th day of fever PC and WCC were 40,000/mm³ and 1400/mm³, respectively and hematocrit was 39.8%. Patient was febrile but was haemodynamically stable with adequate urine output. There were no features of fluid leakage. He had epigastric tenderness but there was no vomiting, hepatomegaly or bleeding manifestations. Few hours later, patient suddenly vomited 200-250 ml of fresh blood. The blood count done at the onset of bleeding showed a PC of 31,000/mm³. Liver transaminases have increased (AST - 346 U/1; ALT - 178 U/1) but prothrombin time (PT) and activated partial thromboplastin time (APTT) were normal.

Over the next 48 hours, patient had several episodes of massive haematamesis and melaena periodically. Persistent tachycardia above 100bpm continued throughout the 5th, 6th and 7th days and haematocrit continued to drop in spite of blood transfusions indicating continued active bleeding. With resuscitation systolic BP was maintained between 90-100mmHg. There was no narrowing of pulse pressure (i.e.≤20mmHg) at any point. Adequate urine output was maintained with no significant positive or negative balance. Patient was afebrile from the 6th day onwards. Lowest PC was recorded in the afternoon of the 5th day and it was 19,300/mm³. The lowest recorded hemoglobin level was 7.1g/dl. On the 6th day APTT

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was prolonged but the PT was normal. Highest levels of transaminases were recorded on the 8th day (AST - 458 U/1; ALT - 341 U/1) when patient was recovering from bleeding and serum bilirubin never went up. His serum creatinine and electrolytes remained normal. On the 6th day serum ionized calcium was low (0.9mmo1/1). But repeated ultrasound scan of the abdomen and chest did not reveal free fluids at any point.

Upper gastrointestinal endoscopy (UGIE) was considered on the 5th day but the patient vomited fresh blood just before the procedure and it was abandoned considering the risks associated with proceeding further. The UGIE was performed later on, on the 7th day when bleeding was settling. It revealed a diffuse gastropathy; altered blood was present in the stomach; there were no ulcers or erosions; the duodenum and the esophagus were normal.

The patient was managed medically in the intensive care unit. Blood and blood components were transfused and supportive therapy was given. The transfusion requirements were guided by the patient's clinical condition. In total, patient received 4 units of fresh whole blood and 13 units of packed red cells. He also received 17 units of platelets and 17 units of fresh frozen plasma. Intravenous normal saline was administered through out and the rate was adjusted according to the clinical parameters and the fluid balance status. During the period of active bleeding he was treated with esomeprezole 80mg intravenously as a stat dose followed by continuous intravenous infusion of 8mg/hour, intravenous tranexamic acid 1g 8hourly and intravenous vitamin K 10mg daily. Intravenous calcium gluconate was given to correct hypocalcaemia.

Apart from a transient bradycardia on the 9th and 10th days the recovery phase was uneventful. The patient was discharged from the hospital on the 13th day. On discharge he had a PC of 230,000/mm³, WCC of 5,200/mm³ and hemoglobin of 13.1g/d1. AST was 116 U/1 and ALT was 250 U/1. On subsequent follow-up after 2 weeks he was asymptomatic and the liver transaminases and the blood counts were within normal limits.

Discussion

Dengue is a complex and dynamic disease with a clinical spectrum that includes both severe and non-severe clinical manifestations[3]. The course of dengue illness classically has three phases, namely the febrile phase, the critical phase and the recovery phase. Plasma leakage leading to shock, severe haemorrhage

and severe organ impairment are the complications that could occur in the critical phase[2].

Major bleeding in patients with dengue, is almost always associated with shock since this, in combination with hypoxia and acidosis, can lead to multiple organ failure and advanced DIC. Massive GI bleeding may occur without prolonged shock when NSAIDs or steroids have been taken or with pre-existing peptic ulcer disease or with anticoagulant therapy[2].

There are only a few reports on the endoscopic findings in dengue patients with GI bleeding. In Taiwan endoscopic examination of 97 dengue patients with GI bleeding revealed hemorrhagic gastritis in 67%, gastric ulcer in 57.7%, duodenal ulcer in 26.8%, and esophageal ulcer in 3.1%[4]. In another study, among 26 dengue patients with GI bleeding, most had gastric or duodenal ulcers[5].

Prophylactic platelet transfusions to prevent any form of bleeding have not been shown to be effective in dengue even in the presence of severe thrombocytopenia[6]. Blood transfusion is life-saving and should be given as soon as severe bleeding is suspected or recognized with caution because of the risk of fluid overload[2]. There is little evidence to support the practice of transfusion of platelet concentrates and fresh-frozen plasma (FFP) when massive bleeding occurs in patients with dengue[2]. Nevertheless co-administration of higher ratios of plasma and platelets along with packed red blood cells (pRBC) help to prevent coagulopathy and this approach is associated with improved survival in patients with massive hemorrhage due to any cause[7]. There is some evidence for the usefulness of recombinant factor VII as adjunctive therapy in severe bleeding due to dengue in children[8].

Evidence is lacking for the effectiveness of endoscopic therapy in dengue patients with GI bleeding. Chiu YC et al have reported that, in dengue patients with peptic ulcer, endoscopic injection therapy is not effective[4]. In this study, after endoscopy patients who had injection therapy required more transfusions with pRBC and FFP than the control group.

The patient we report here had severe dengue according to the World Health Organization classification[2]. However his clinical course was unusual due to several reasons. Prior to the onset of major GI bleeding patient's haemodynamic status and hematocrit were stable. He did not have any feature of plasma leakage to indicate that he was in critical phase. The only warning sign of severe dengue he had prior to the onset of bleeding was epigastric tenderness.

The bleeding started at a relatively high platelet count and in the absence of evidence of shock, coagulopathy or DIC. Patient did not have any other risk factors for GI bleeding such as recent use of NSAIDs or steroids, anticoagulant use or history of peptic ulcer disease. UGIE did not reveal peptic ulcers or erosions and the massive bleeding which required 17 units of blood as replacement therapy was purely due to diffuse gastropathy. The slow oozing leading to collection of blood in the stomach manifested as periodic massive haematamesis and melaena. It was probably the slowness of the mucosal oozing which prevented him from going in to acute shock secondary to bleeding.

This case is a good example for the complex and unpredictable nature of dengue and illustrates that massive GI bleeding can occur even in the absence of generally identified risk factors. However when the bleeding started the platelet count was rapidly dropping despite the fact that the absolute count was relatively high. These findings highlight the need for close monitoring of all such patients even if the other warning signs are minimal. This case also shows that in patients with dengue, the usefulness of UGIE at the time of acute GI bleeding is limited. Benefits are minimal in cases like this as it cannot offer any effective therapy and the risks are high as any mucosal damage can lead to further bleeding because of platelet dysfunction. Furthermore this case highlights that timely and correctly administered conservative treatment with transfusion of blood components and supportive therapy alone is life saving for such patients even if the bleeding is massive.

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