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The Beneficial Aspect of Ulinastatin in Severe Sepsis Due to Splenic Rupture

KEYWORDS: Splenic rupture, Sepsis, Ulinastatin.

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ABSTRACT *A 57 year old man underwent an uneventful colonoscopy for black stool with weakness. Three hours later, he had a syncopal episode . Hemoglobin dropped from an initial level from 12.4 g/dL to 7.9 g/dL. Abdominal CT revealed a 12.8 × 11 × 13 cm splenic hematoma with splenic rupture . ECG showed sinus tachycardia. 2D Echo revealed no RWMA, Grade 1 diastolic dysfunction. He was treated for loss blood by bloos transfusion with support of i/v fluids and colloids, antibiotics along with supportive medicines. Massively raised WBC counts was treated with support of two to three broad spectrum antibiotics . Despite of all medical therapy patient did not improved then as per studies we started inj Ulinastatin with same antibiotic support. After 4 days at stable condition, he was shifted to surgical unit and subsequently spleenectomy was performed successfully. After spleenectomy, he became stable with no recurrence of syncope.*

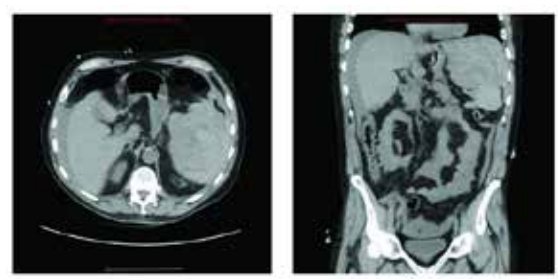
Introduction

Splenic rupture is a rare, catastrophic complication of colonoscopy and an exceptional cause of syncope. This injury is believed to be from direct trauma or tension on the splenocolic ligament . We describe a case of syncope as the initial manifestation of splenic rupture after colonoscopy. Clinicians should consider syncope, lightheadedness, and drop in hemoglobin in absence of rectal bleeding following a colonoscopy as possible warning signs of imminent or emergent splenic injury. Studies suggest that treatment with ulinastatin may reduce mortality in refractory severe sepsis in humans. Ulinastatin is a highly selective serine protease inhibitors that act on only a few steps in the multipronged inflammatory response involved in the pathogenesis of sepsis.

Case Report

A 57 year old man underwent an uneventful colonoscopy for black stool with weakness. Three hours later, he had a syncopal episode . He denied postictal confusion or bowel/bladder incontinence. He described mild, poorly localized abdominal discomfort following the second syncopal episode. Blood pressure was 98/56 mm Hg on admission without a postural change, heart rate: 125 beats/min; respirations: 33/min; oral temperature: 34.6 degree C;pulse oximetry: 98% on room air.General: An approximately 51 Kg, Head and neck are normal, JVP was not raised.The heart is tachycardic, regular, and without murmurs. His lungs are clear with rapid respiratory pattern . The neurologic examination reveals normal mentation, intact cranial nerves, intact motor strength and sensation, and normal reflexes. No tremor is noted.There are no other pathological findings on Pulmonary Embolism. He had a third syncopal event in the Emergency Department two hours after arrival.

Hemoglobin dropped from an initial level from 12.4 g/dL to 7.9 g/dL. Abdominal CT scan revealed a 12.8 × 11 × 13 cm splenic hematoma with splenic rupture (Figures 1 and 2). ECG showed sinus tachycardia. 2D Echo revealed no RWMA, Grade 1 diastolic dysfunction.Other Lab investigation revealed, WBC counts 34,280 per cubic millimeter of blood, 93% polymorphs, raised serum creatinine 4.48 mg/dl, urea 67 mg/dl, raised SGOT and SGPT level and raised CRP level.



Abdominal CT scan revealed a 12.8 × 11 × 13 cm splenic hematoma with splenic rupture

(Figure 1: Axial view of splenic rupture and hematoma, Figure 2: Coronal view)

He was treated for loss blood by bloos transfusion with support of i/v fluids and colloids, antibiotics along with supportive medicines. Massively raised WBC counts was treated with support of two to three broad spectrum antibiotics . Despite of all medical therapy patient did not improved then as per studies we started inj Ulinastatin with same antibiotic support. After 4 days at stable condition (stable BP, HR improved WBC counts , renal and liver functions), spleenectomy was performed successfully. After spleenectomy, he became stable with no recurrence of syncope.

Discussion

Splenic injury due to colonoscopy is rare and believed to be due either to direct trauma or to tension on the splenocolic ligament .Risk factors include a pathologic spleen or splenomegaly; anticoagulation; smoking; inflammatory bowel disease; therapeutic or difficult colonoscopy; intra-abdominal adhesions secondary to prior surgery, trauma, or an inflammatory process. The most common symptoms are abdominal pain (93%), usually left-sided, as well as left shoulder pain (Kehr's sign: 88%) , which was absent in this patient. Kehr's sign is believed to be due to distention of the splenic capsule or irritation of the left hemi-diaphragm.

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Delayed or missed diagnosis is common. Syncope without abdominal pain, our patient's clinical presentation, is not a typical initial manifestation of splenic rupture. Mild, nonspecific abdominal discomfort due to air insufflation is typical after colonoscopy and may occur in the setting of benign radiographic findings . Our patient's pain was delayed; his discomfort was mild and not localized to the left upper quadrant. Thus, association of syncope with a ruptured spleen was not an easy diagnosis A nonruptured hematoma or walled-off rupture after colonoscopy may occur without suspicious abdominal complaints.

Contrast-enhanced abdominal CT is vital in diagnosing splenic rupture but was performed only after three syncopal episodes had occurred—almost ten hours after the first episode. Other imaging findings in splenic trauma in addition to rupture include subcapsular hematoma, splenic laceration, perisplenic clot, and hemoperitoneum . Ultrasonography has also been used successfully in some patients. Selected cases without free rupture into the peritoneum can be observed and treated nonoperatively. Rare case reports describe successful splenic artery embolization

Ulinastatin is a highly selective serine protease inhibitors that act on only a few steps in the multipronged inflammatory response involved in the pathogenesis of sepsis like coagulation (tissue factor pathway inhibitor, activated protein C, thrombomodulin, and antithrombin III), complement cascade (C1 inhibitor), or neutrophil elastase . In contrast, ulinastatin inhibits a wide variety of pro-inflammatory serine protease enzymes including trypsin, thrombin, kallikrein, plasmin, cathepsin, neutrophil elastase, neutrophil protease-3, and coagulation factors IXa, Xa, XIa, and XIIa . It is likely that it may attenuate the Systemic inflammatory response by acting at multiple sites. Studies have shown that patients with sepsis treated with ulinastatin have lower serum levels of pro-inflammatory markers like TNF-α, IL-1α, IL-4, IL-6 and C-reactive protein, while levels of anti-inflammatory cytokine IL-10 was significantly higher . It also reduces thrombomodulin levels and decreases endothelial dysfunction .

Besides reduction in 28-day all-cause mortality, ulinastatin also showed beneficial effects on some secondary endpoints in the present study like new-onset organ dysfunction. Although the duration of vasopressor use was similar in the two groups, ventilator-free days were significantly higher in the ulinastatin group (19.4 vs. 10.2 days), suggesting faster recovery from severe sepsis. This also translated into a shorter mean hospital stay in the ulinastatin group. No infusion-related adverse effects were seen in the present study. Adverse effects with ulinastatin are rare and were reported in 0.84 % of patients in a Japanese study . These included increased transaminases (0.36 %), eosinophilia or leucopenia (0.16 %), rash (0.13 %), gastrointestinal symptoms (0.08 %), fever (0.02 %), and local irritation at the injection site (0.02 %).

Another prospective, double-blind, randomized, placebo-controlled trial of ulinastatin in patients with severe sepsis showed that 2,00,000 units of ulinastatin i/v twice daily for 5 days was associated with a reduction in 28-day all-cause mortality 7.3 versus 20.3 % in the placebo control group. A few small studies, published in Chinese-language journals, have shown lower mortality in patients treated with ulinastatin . A small Korean study showed that mortality was lower in patients with severe sepsis treated with ulinastatin (18.6 vs. 27 % in the control group) .

Conclusion

Splenic rupture is an exceptional and life-threatening complication of colonoscopy. Splenic rupture is in turn an unusual cause of syncope, so diagnosis requires a high index of suspicion that may be absent. In that particular situation with refractory of multiple broad spectrum antibiotics, ulinastatin have good role in control of sepsis and recovery of multiorgan failure status. Studies suggest that ulinastatin have key role in patients with severe sepsis investigated a novel therapy directed against the systemic inflammatory response.

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