

Splenic rupture after anticoagulant therapy in a patient with a history of COVID-19: a case report

Ruptura esplénica después de terapia anticoagulante en un paciente con antecedente de COVID-19: reporte de caso

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Abstract

We present the case of a 75-year-old man with a history of COVID-19 and splenic infarct treated with enoxaparin, who presented with intense abdominal pain and tomographic findings of free peri-splenic fluid and a hyperdense image in the spleen. An emergency laparotomy was performed, with findings of a splenic rupture at the vascular hilum. Spontaneous splenic rupture is a rare and fatal entity that should be suspected in a patient with history of COVID-19 who presents with acute abdominal pain after the administration of heparin.

Keywords: Anticoagulation. COVID-19. Splenic rupture. SARS-CoV-2.

Resumen

Presentamos el caso de un varón de 75 años con antecedente de COVID-19 e infarto esplénico tratado con enoxaparina, quien inició con dolor abdominal intenso y hallazgos tomográficos de líquido libre periesplénico, así como una imagen hiperdensa en el bazo. Fue sometido a laparotomía de urgencia, encontrando una ruptura esplénica a nivel del hilio vascular. La ruptura esplénica espontánea es una condición rara y potencialmente fatal, por lo que se deberá tener un alto índice de sospecha ante un paciente con antecedente de COVID-19 que inicie con dolor abdominal agudo posterior a la administración de heparina.

Palabras clave: Anticoagulación. COVID-19. Ruptura esplénica. SARS-CoV-2.

Introduction

The spleen is an intraperitoneal organ that plays a role in humoral and cellular immunity, red blood cell maturation, and the filtration of senescent blood products¹. Disease caused by SARS-CoV-2 has become a

global public health issue², and the predisposition to develop thrombotic disease is a common problem that needs to be detected and treated promptly to reduce morbidity and mortality³. COVID-19 induces a state of hypercoagulability and hyperinflammation due to increased production of systemic cytokines⁴; splenic

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infarction is an example of this, resulting from the occlusion of one or more branches of the splenic artery, compromising blood flow towards the spleen, causing ischemia, and resulting in necrosis^{1,4}.

Classically, splenic infarction presents with pain in the upper left quadrant that is exacerbated by palpation and may be accompanied by nausea and vomiting⁴. Diagnosis is established using contrast-enhanced computed tomography (CT), and management is often conservative. However, in cases of COVID-19 with a hypercoagulable and thrombotic state, anticoagulation is the cornerstone of treatment⁴. This report discusses the case of a patient who experienced spontaneous splenic rupture after receiving anticoagulation treatment for splenic infarction following COVID-19 and provides a review of the relevant literature currently available.

Case report

A 75-year-old man with a past medical history of systemic arterial hypertension and dyslipidemia diagnosed with SARS-CoV-2 infection (previously fully vaccinated) and treated with supplemental oxygen at 1 L/min, and a 14-day course of dexamethasone, prednisone, and apixaban as part of outpatient management. Afterwards, he presented to the ER with postprandial epigastric abdominal pain, without radiation, with a Numeric Analog Scale (NAS) intensity of 10/10, along with nausea and vomiting of gastric content. During the directed interview, he denied fever, or other symptoms. The physical examination at admission revealed a soft, depressible abdomen, tenderness to palpation in the epigastrium and left hypochondrium, without rebound tenderness, and normal active peristalsis. The lab test results showed thrombocytosis, leukocytosis with neutrophilia, hyperglycemia, hyperlactatemia, as well as elevated creatinine and D-dimer levels (2036 mg/dL). Therefore, further evaluation included a CCTA, which revealed a filling defect in the ascending aorta consistent with a thrombus and heterogeneous enhancement in the spleen suggestive of splenic infarction.

Consequently, in-hospital treatment was initiated with subcutaneous enoxaparin 60 mg every 12 hours. However, 48 hours after starting anticoagulant therapy, the patient experienced sudden abdominal distention, incapacitating mesogastric pain, nausea, vomiting, normocytic normochromic anemia, and metabolic acidosis with hyperlactatemia. A thoracoabdominal CT with IV contrast was requested

(Fig. 1) due to suspected bleeding, revealing abundant free perihepatic, perisplenic, and perigastric fluid, and a hyperdense image in the mid-portion of the spleen with contrast accumulation following administration, which was consistent with splenic rupture. Emergency exploratory laparotomy was deemed necessary. Intraoperative findings included 1.5 liters of hemoperitoneum, a 2 cm deep laceration at the splenic hilum, and a dissecting hematoma in retroperitoneal regions 1 and 2 (Fig. 2). Consequently, hemoperitoneum drainage, splenectomy (Fig. 3), abdominal cavity lavage and drainage with placement of a local hemostatic agent were performed. Histopathological examination (Figs. 4 and 5) revealed the presence of areas of multifocal hemorrhagic necrosis, congestion of red pulp, decreased white pulp, and the presence of blood clots without evidence of malignant neoplasm. The patient showed marked improvement in the postoperative period and was discharged 7 days after surgery.

Discussion

Splenic rupture is a life-threatening condition⁵, and traumatic etiology is much more common than spontaneous splenic rupture, which is an extremely rare situation associated with pre-existing diseases or conditions⁵⁻⁷, including neoplasms (30%), infections (30%), inflammatory diseases (15%), drugs (10%), and idiopathic causes (7%), among others⁷. In a systematic review and meta-analysis, Aubrey-Bassler and Sowers⁸ analyzed 613 cases of spontaneous splenic rupture and found that the most frequently observed abnormalities were splenic infarction, splenic cysts, and hamartomas, while the drugs most widely reported as direct causes are anticoagulants and thrombolytics, which have been regularly and systematically prescribed since the beginning of the COVID-19 pandemic.

Heparin is indicated for the prevention and treatment of thromboembolic events, being thrombocytopenia the most widely reported adverse event to date (10%), while bleeding, especially in surgical sites towards the retroperitoneum, is the most serious event⁹. Spontaneous splenic rupture following the use of IV heparin is extremely rare, and the mechanism by which it occurs is not yet fully understood^{6,8,9}. According to Ghobrial et al.⁹ only 4 cases of spontaneous splenic rupture due to the use of IV heparin and 1 case due to subcutaneous enoxaparin have been reported to this date⁹.

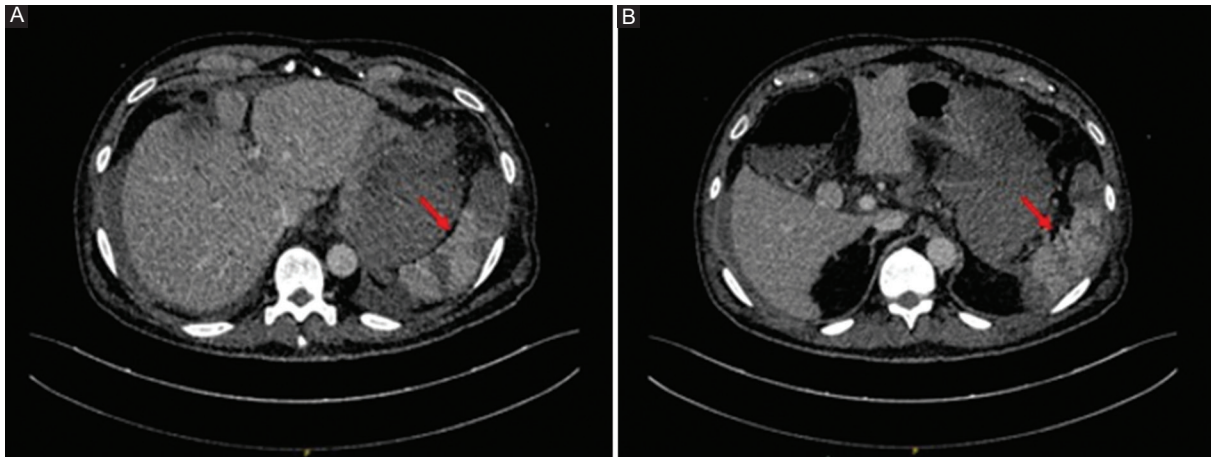


Figure 1. Computed tomography of the thoracoabdominal region with IV contrast. **A:** cross-section at 9th rib level in the arterial phase. **B:** cross-section at 11th rib level in the arterial phase. Hyperdense images (red arrows) occupying nearly 50% of the splenic parenchyma and enhanced after IV contrast administration, which is consistent with blood extravasation due to splenic rupture.

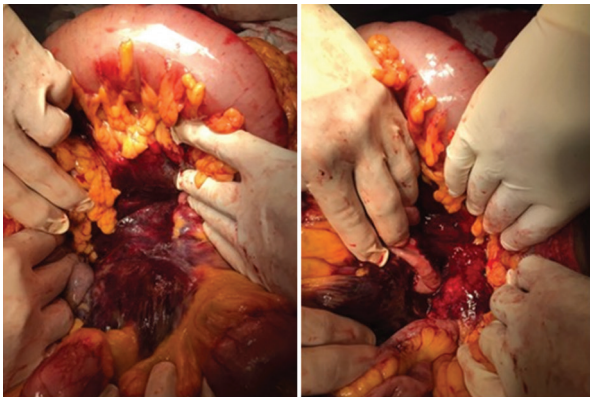


Figure 2. Intraoperative findings. Splenic rupture with hematoma infiltration of the mesocolon and mesentery due to dissecting retroperitoneal hematoma.



Figure 3. Product of splenectomy. Weight of 255 g and measurements of 13.0 cm × 9.5 cm × 2.0 cm. The external surface is wine-red, smooth, and shows evidence of splenic rupture at the vascular hilum (white arrow), spreading into the splenic parenchyma.

The most common symptom of spontaneous splenic rupture is abdominal pain in the upper left quadrant. Most cases occur in men between the 5th and 7th decades of their life^{6,9}. Other common clinical signs include abdominal distention, tenderness to palpation, abdominal rigidity, hypotension, and Kehr's sign (left shoulder pain)^{7,9}. Additionally, there is often significant bleeding because the spleen is a highly vascularized organ^{6,7}. According to Gedik et al.⁶ more than half of the patients develop hemorrhagic hypovolemic shock if not treated promptly. Computed tomography is the imaging modality of choice for diagnosis in stable patients as it provides information on the severity of splenic injury, while ultrasound can be used in unstable patients to visualize free fluid in the abdominal cavity with a sensitivity of 90%⁷.

In Gedik et al.'s study⁶, 43 out of a total of 131 patients diagnosed with spontaneous splenic rupture, were managed conservatively, and 88 underwent surgery. Of the patients managed conservatively, 40 died, compared to the 33 deaths reported in those patients who underwent surgery. Therefore, management should be aggressive, with early surgical intervention and hemoderivative support^{6,7}. Unlike patients with traumatic splenic rupture, who may prefer conservative treatment to preserve splenic function or splenorrhaphy as a repair technique, patients with spontaneous rupture will always require splenectomy for resolution^{7,10-12}. When the spleen exceeds 1000-2000 g, as in the case presented here, laparoscopic



Figure 4. Histopathological study, macroscopic description: Solid and smooth splenic parenchyma, interspersed with irregular dark brown areas (red arrows), suggestive of hemorrhagic necrosis involving approximately 50% of the splenic parenchyma.

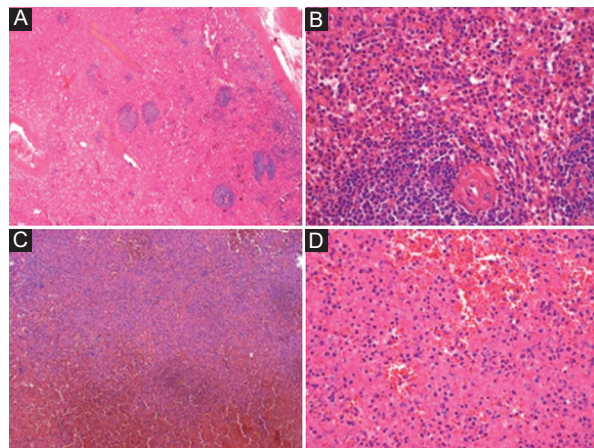


Figure 5. Histopathological study, microscopic description, hematoxylin, and eosin staining. **A:** 4x objective, congested splenic tissue. **B:** 40x objective, splenic tissue with decreased white pulp and congestion of red pulp invading lymphoid follicles. **C:** 10x objective, splenic tissue with multifocal hemorrhagic necrosis. **D:** 40x objective, splenic tissue with multifocal hemorrhagic necrosis.

splenectomy becomes technically complicated, so an open procedure would be indicated¹³.

Emergency exploratory laparotomy is justified if there is hemodynamic instability, or if the patient requires > 4 units of blood over 48 hours⁷. Additionally, all patients undergoing splenectomy should be vaccinated vs encapsulated microorganisms (*Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae*) to prevent post-splenectomy infections, which have been reported in 5% of the cases and have a mortality rate of up to 50%¹³. Thromboembolic complications, if present, often include deep vein thrombophlebitis or pulmonary or portal system embolism¹⁴.

The postoperative mortality rate ranges from 3% to 15%, depending on the patient's hemodynamic status^{15,16}.

Conclusions

Splenic rupture, regardless of its etiology, is a life-threatening condition. Spontaneous splenic rupture is extremely rare and sparsely reported in the medical literature. We presented the case of a 75-year-old man with a history of COVID-19 who experienced a spontaneous splenic rupture following treatment with enoxaparin for splenic infarction. Physicians should maintain a high level of suspicion for any patient with a history of COVID-19 and acute abdominal pain following heparin administration. Timely diagnosis and treatment of spontaneous splenic rupture are essential to reduce morbidity and mortality associated with this condition.

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Conflicts of interest

None declared.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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