case report

Splenic abscess as a possible sequela of COVID-19: a case series

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Splenic abscess is an aggressive disease with a non-specific etiology and symptoms that are systemically detrimental. During the current COVID-19 pandemic, there has been a noted rise in the incidence of splenic abscesses. The aim of this article was to explore whether infection with the SARS-CoV2 virus increases the risk of developing splenic abscesses. We reviewed three cases with SARS-CoV-2 infection who developed splenic abscess. The clinical characteristics, treatment course, management and outcome are reported. We perceived that hypercoagulability status, superimposing infections and immunosuppression were related to SARS-CoV-2 infection. These were common factors in these three observed cases of splenic abscess as a complication related to the new viral pandemic. SARS-CoV-2 infection might be a risk factor in development of splenic abscess.

SIMILAR CASES PUBLISHED: To the best of our knowledge only one case similar to our case series was published.

Since the time of Hippocrates, splenic abscess has been described in terms of its natural history and prognosis.[1] A case series addressing splenic abscess was first published in 1885 by Grand Moursel, followed by multiple reports about the subject in the early 1890s, which were thought at the time to be related to typhoid fever and malaria.[2] In February 2020, coronavirus disease 2019 (COVID-19), caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was announced as a global pandemic.[3] Understanding this infection and its clinical manifestations and impact on human health is still being examined worldwide. The possibility of a correlation between COVID-19 and the development of splenic abscess is addressed in the present article. Population-based autopsy studies have established the incidence of splenic abscesses to be between 0.2% and 0.7%.[4] Splenic abscess is noted to be more predominant in males than females, with ratio of 2:1.[5] We are reporting three cases of splenic abscess in patients with COVID-19 infection (**Table 1**) with a hypothesis that COVID-19 infection increases the risk of splenic abscess formation.

CASE 1

A 55-year-old COVID-19-positive male, with known comorbidities, including diabetes mellitus, hypertension, chronic kidney disease, ischemic heart disease, and cerebrovascular accident, was admitted to hospital with SARS-CoV-2 infection and acute thrombotic cerebral ischemia, aphasia, and acute kidney injury. The patient exhibited abdominal pain on physical examination, in addition to high levels of inflammatory markers, with

Table 1. Summary of cases.

Case	Age (years)	Comorbidities	Length of stay (days)	Primary diagnosis	Treatment of splenic abscess	Outcome
1	55	Diabetes mellitus, hypertension, chronic kidney disease, ischemic heart disease	16	Stroke	Splenectomy	Death
2	34	None	21	Blunt abdominal trauma	Intravenous antibiotics	Abscess resolution
3	27	None	38	COVID-19 pneumonia	CT guided drainage followed by splenectomy	Recovered

a C-reactive protein level of 300 mg/dL. Abdominal computed tomography (CT) performed on the day after admission revealed a ruptured splenic abscess. He underwent urgent splenectomy with intraoperative findings of purulent peritonitis and a necrotic splenic remnant. Postoperatively, the patient's condition deteriorated according to chest radiography, which reflected severe COVID-related pneumonia. He was started on antiviral and immunoglobulin G treatment. The patient developed pulmonary embolism despite the administration of therapeutic anticoagulation. His condition progressed to multiorgan failure and he died on day 16. Culture samples obtained from the splenic abscess revealed *Streptococcus pseudopneumoniae*.

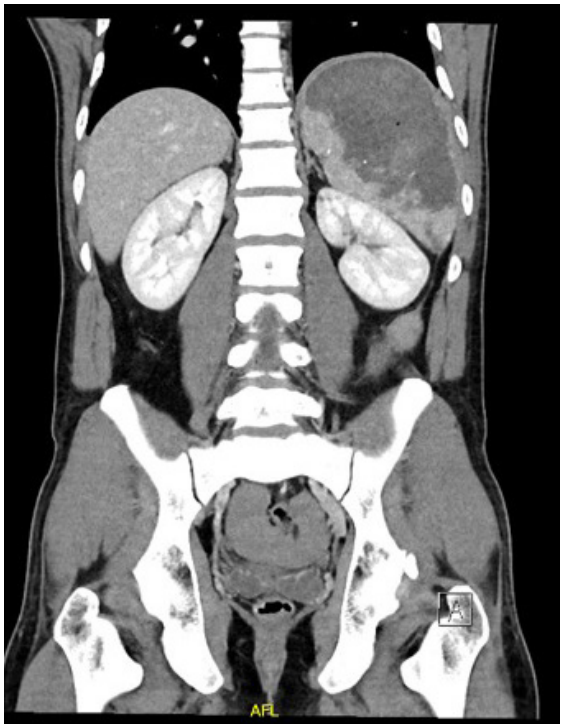

Figure 1. CT scan abdomen, coronal view showing splenic parenchyma with heterogeneous liquefaction changes and peripheral ring of enhancement with air locules within the parenchyma.

CASE 2

A 34-year-old male presented after a physical assault with complaints of left upper quadrant abdominal pain and vomiting for a few hours. Physical examination revealed a vitally stable healthy male with generalized abdominal tenderness and localized guarding of the left upper quadrant. CT of the abdomen revealed grade 4 splenic injury with active extravasation of contrast. Upon admission, the patient was confirmed to have SARS-CoV-2 infection. He underwent emergency arterial embolization of the splenic artery and remained clinically stable on dual therapy for SARS-CoV-2 infection (lopinavir/ritonavir (Kaletra, Abbvie Inc, North Chicago, IL, USA) and hydroxychloroquine. Fourteen days after the procedure, he experienced a spiking fever with high levels of inflammatory markers, with a C-reactive protein level of 62 mg/dL. Repeat CT of the abdomen with intravenous contrast suggested splenic abscess formation (**Figure 1**). The patient was started on an intravenous course of antibiotics consisting of meropenem and vancomycin for a total of 10 days. He remained vitally and clinically stable throughout his hospital stay and was discharged to the isolation center on day 21 due to his COVID-19 status.

CASE 3

A 27-year-old healthy male presented with a one-month history of cough, night sweats, and weight loss. He was admitted based on chest X-ray findings suspicious for tuberculosis. Further investigation revealed positivity for SARS-CoV-2 pneumonia, for which anti SARS-CoV-2 infection medications were administered (lopinavir/ritonavir [Kaletra] plus favipiravir [Avigan, FujiFilm, Tokyo, Japan]) for 10 days, along with piperacillin/tazobactam (Tazocin, Pfizer, New York, NY, USA) as an antibacterial. CT of the chest and abdomen with intravenous con-

trast performed as part of the investigation for fever to determine the source of sepsis (**Figures 2, 3**) revealed splenic artery thrombosis, large splenic abscess, and left iliac vein thrombus. Initially, the patient underwent CT-guided drainage for the abscess.

On day 11, post-drainage follow-up CT of the abdomen revealed a splenic abscess complicated by the development of a broncho-pleural fistula. Because the patient remained febrile with high levels of inflammatory markers, surgical intervention, including open splenectomy (**Figure 4**), was performed and an intercostal drain was inserted. The postoperative course was complicated, with pulmonary embolism managed medically. Culture of intraoperative abscess samples revealed *Prevotella oris* bacteria. A polymerase chain reaction (PCR) test performed on the same abscess sample was negative for COVID-19 protein.

DISCUSSION

Splenic abscess is defined as an infectious suppurative process involving identifiable macroscopic filling defects, either in the parenchyma of the spleen or the subcapsular space.[6] The most common clinical presentation of the condition is the triad of fever, left upper quadrant pain, and leukocytosis, listed according to the order of frequency of the findings.[7] Delayed diagnosis frequently occurs in individuals with splenic abscess, with median delays of up to 27.5 days from symptom onset to diagnosis.[6] A high index of suspicion is required for timely diagnosis and favorable outcomes. CT has high sensitivity and is the imaging modality of choice.[8] Pyogenic abscesses appear as hypodense lesions, ranging from 20 to 40 Hounsfield units, exhibiting enhancement of the outside-facing portion of the abscess wall.[9] Although the majority are unilocular, they can be multifocal in approximately 26% of cases.[9,10]

Typical causes of splenic abscess are summarized under five categories that include metastatic spread

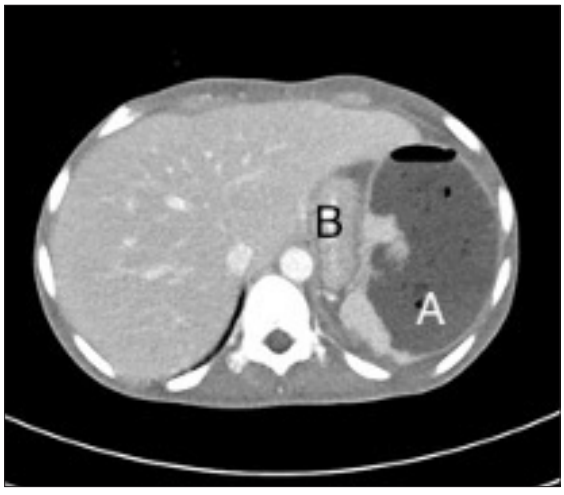

Figure 2. A: spleen with liquefaction and necrosis, B: stomach.

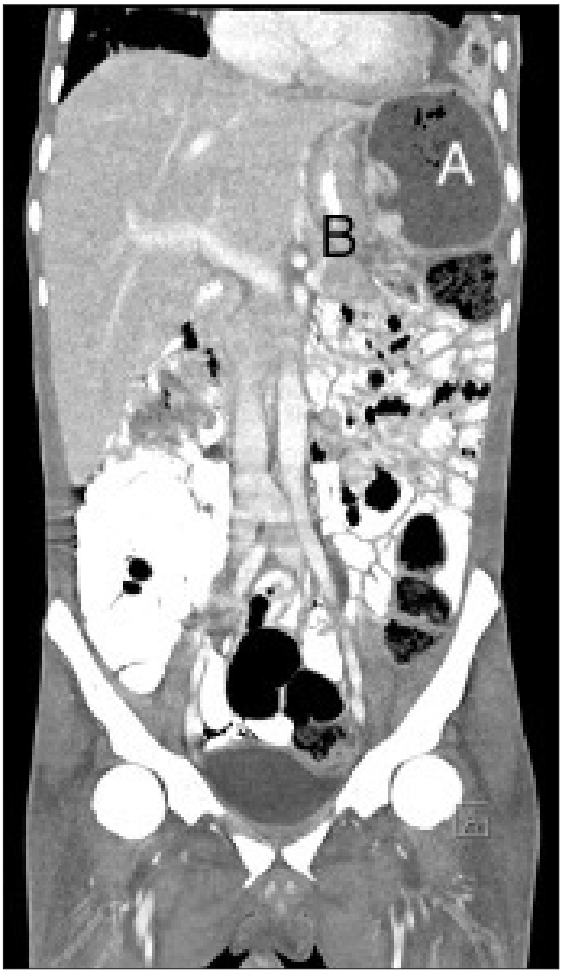

Figure 3. CT scan abdomen, coronal view A: spleen with liquefaction and necrosis, B: stomach.

Figure 4. Intraoperative specimen of resected spleen.

from septic foci, including intravenous drug use; endocarditis, *salmonella* infection, osteomyelitis, tuberculosis, dental extractions, and infected intravascular devices; spread from adjacent organs (through pancreatic abscess, gastric and/or colonic perforations); infection of splenic infarct (seen in hemoglobinopathies including sickle cell disease and splenic artery embolization); splenic trauma; and immunocompromised status including cancer, diabetes mellitus, alcoholism, immunosuppressive treatment, and/or liver cirrhosis.[11]

Our proposed hypothesis of SARS-CoV-2 infection and subsequent COVID-19 as a hypercoagulable status that increases venous thrombotic events is attributed to multiple factors such as inflammation, SARS virulence, immobility, and other factors that support the formation of microthrombi[12] within the splenic parenchyma at the arteriole level, which provides rich media for septic foci to evolve and develop an abscess along with low immunological status of SARS-CoV-2 infection. On the other hand, patients undergoing treatment with high doses of anticoagulant(s) as per COVID-19 guidelines[13] are at risk for bleeding of approximately 6% with heparin and low molecular weight heparin use.[14] Splenic bleeding and hematoma formation are part of this complication that may lead to superinfection and abscess formation.

Observational studies investigating COVID-19 report that concomitant or secondary bacterial infection has been scarcely and/or inconsistently reported, with a frequency of 4.8–15% in the larger series of COVID-19 published to date.[15] It appears that when the immune system is severely damaged and becomes inefficient due to lymphopenia and CD8-positive T cell exhaustion, it tries to compensate by triggering a "cytokine storm," which could potentially lead to complications.[16] Abscess formation secondary to sterile procedures has also been proposed.[16] The development of splenic abscess post-embolization remains an infrequent complication. Indications for splenic artery embolization begin with splenic trauma in a hemodynamically stable patient experiencing platelet disorders to improve the platelet count, and both carry a low risk of developing an abscess. A study involving 18 patients who underwent splenic artery embolization for severe pancreatitis-related splenic artery hemorrhage reported complications in the majority of cases with splenic abscess.[17] They speculated that the direct cause of this complication was the state of immunosuppression after a long disease course.[17] COVID-19 can have similar sequela(e) on the body when compared with acute pancreatitis in terms of systemic inflammatory response and multiorgan involvement.[18] A recent study reported that *Streptococcus* and *Staphylococcus* were the most common organisms isolated in splenic abscess. Historically, *Salmonella* species, gram-negative *Escherichia coli*, and *Enterococcus* species plus fungal infections were the leading causes of splenic abscesses.[19]

The emergence of SARS-CoV-2 heralds a new causative organism that has not been previously reported in association with splenic abscess in the literature. Regarding Case 3 (**Table 1**), *Prevotella oris* species was cultured from both splenic abscesses drained radiologically and from excised splenic tissue. *Prevotella oryzae* is a gram-negative, anaerobic bacterium that has been associated with oral infections.[19] Furthermore, to support the super infection theory, for Case 3, a PCR test for COVID-19 protein from splenic pus did not detect the virus protein. Although expression of SARS-CoV-2 in abscess/pus fluid is yet to be studied, the sensitivity of such tests may not be reliable. On the other hand, formal bacterial culture was positive for unusual organisms, as mentioned earlier.

The optimal management strategy for splenic abscess remains controversial; to date, the traditional surgical approach involving splenectomy has been the treatment of choice, as reported in the first case of splenic abscess in a patient with SARS-CoV2 infection.[20] Presently, specific centers consider antibiotics alone as a sufficient treatment option, which is supported by case series with success rates of 75%.[6] Fluid culture and sensitivity analysis of the drained abscess must be performed, being aware that COVID-19 positivity may be associated with unusual causative organisms. Considering the expansion of image-guided drainage of intra-abdominal abscesses, minimally invasive interventions have significant advantages in preserving the function of the remaining spleen. However, percutaneous drainage is less effective in COVID-19-positive patients due to multiple factors, including limited mobility caused by isolation in a single room, which decreases the intra-abdominal pressure gradient and the role of gravity, which makes drainage inadequate. Other factors are fear of close contact and dealing with body fluids of positive cases; both create obstacles to completing care of the patient, including wound drainage. Delayed diagnosis, surgical intervention, and immunocompromised status have been reported to increase splenic abscess-related mortality (0–24%).[21] SARS-CoV-2 infection may have an association with the development of splenic abscess that might be related to hypercoagulability, exhausted immunity and superinfection. However, clinical and histopathological studies are needed to define a clear pathophysiological association between the diseases Early diagnosis and rapid management are essential for optimal outcome.

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