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Case Report

An unusual presentation of Covid-19 in a patient with acute abdomen

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1. Introduction:

Covid-19 caused by SARS-CoV-2 is a multisystemic, complex disease, usually presenting as a localised upper respiratory tract infection. In severe cases it may spread to involve the lower respiratory tract and other organs, resulting in multi-organ failure. Emerging case reports have identified other presenting symptoms such as atypical respiratory symptoms, and progressive gastrointestinal symptoms in a subset of COVID-19 positive patients.

2. Case report

2.1. Clinical presentation

The 28-year-old male of South Asian ethnicity presented to the emergency department with a four-day history of fever, myalgia and localised pain in the right iliac fossa. He had a one-day history of passing loose stool following a period of two days of constipation. The patient had not received COVID-19 vaccinations which had not been made available to the public by the time he was admitted to hospital. No close infectious contacts were noted.

On examination, the patient was tachycardic (128 BPM) and febrile (38.0 °C). Blood tests revealed a neutrophilia (11.9×10^9), a markedly elevated C-reactive protein (117 mg/l), lymphopenia (0.5×10^9), normal platelet count (249×10^9), raised INR (1.4), raised fibrinogen (9.7 g/l). A CT scan demonstrated appendiceal thickening and enlarged mesenteric lymph nodes.

The patient was referred to the surgical team with a clinical suspicion of acute appendicitis and an emergency laparotomy was performed. Based on emergency COVID-19 intercollegiate guidance at the time, an open approach to appendicectomy was used [1]. The operation began with a right iliac fossa incision. Turbid fluid was noted within the pelvis. The appendix was retrocaecal and due to inadequate views, the operation was converted to a midline laparotomy. The appendix was removed in three fragments along with an enlarged mesenteric lymph node, and specimens were submitted for histological examination. The abdomen was washed out with 3L of warmed saline and the incision was closed. Following surgery, the patient was admitted to a surgical ward, and intravenous antibiotics and fluids were administered.

Approximately 24 h following surgery, the patient deteriorated. On examination he was tachypnoeic (26 breaths/min), hypoxic (saturation 88% on 2L of oxygen), normotensive, and mildly febrile (37.8 °C). Repeated arterial blood gases demonstrated persistent alkalosis (pH 7.46). CT chest, abdomen and pelvis demonstrated bilateral pleural effusions and volume loss in both lungs. There was also a pocket of fluid in Morison's pouch. The patient continued to deteriorate with a severe inflammatory response. He was intubated and admitted to the intensive care unit for presumed sepsis where he required oxygen and inotropic support with noradrenaline as well as continued antibiotic treatment. During the course of admission, three pharyngeal and nasal swabs were performed, and the results were negative for COVID-19.

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2.2. Histopathological examination and differential diagnosis

The appendix showed mild acute appendicitis with non-necrotising granulomata within reactive lymphoid follicles (Fig. 1). There was no significant transmural acute inflammation. The enlarged mesenteric lymph node showed severe widespread apoptotic necrosis, a prominent histiocytic infiltrate, and fibrinoid necrosis of blood vessels, microangiopathy, microthrombi, and an increased platelet aggregation highlighted by CD42b (Figs. 2, 3, 4). There was no significant neutrophilic infiltration of the lymph node. These unusual morphological changes raised the possibility of COVID-19, so a PCR was requested on the lymph node tissue and appendix and was positive for SARS-Cov-2 RNA, although during admission three nose and throat swabs for COVID-19 were negative.

The initial clinical suspicion of acute appendicitis appears appropriate given the localised right iliac fossa pain, blood tests, and radiology. A retrospective Alvarado score performed using the documented clinical history gives a score of eight out of a possible ten, implying a high likelihood of appendicitis. However, on histological examination of the appendix the features were unusual. Given the histology, several classically granulomatous infections were considered as part of the differential diagnosis. ZN, PAS and Grocott staining did not reveal any acid-fast bacilli, or fungi on histology.

The diagnosis of Yersiniosis was considered given the presence of granulomatous inflammation and mesenteric lymphadenitis. However, the granulomatous inflammation in Yersiniosis is typically necrotising, and neither the appendix nor the mesenteric lymph node showed necrotising granulomata.

Toxoplasmosis classically causes non-necrotising granulomata to form within lymphoid follicles as in this case. However, the presentation of extensive necrosis of the mesenteric lymph node would be an unlikely presentation, and PCR for toxoplasma performed on a blood sample was negative.

The possibility of primary infection with SARS-CoV2 was considered. The histological features of fibrinoid necrosis of blood vessels, microangiopathy, microthrombi, and increased platelet aggregation within the mesenteric lymph node were similar to the pulmonary findings in post-mortem case series of patients with COVID-19 [2].

2.3. PCR methodology

Formalin-fixed paraffin embedded tissue was cut at 10um thickness using a microtome. Upon sectioning, the section was allowed to curl, and 6 curled sections were placed in sample tubes for testing. Every effort was made to ensure the workspace is free from contamination. To that end, laboratory equipment was decontaminated using DNA Away solution and laboratory wipes.

The samples were sent to Micropathology Ltd a private Lab in Coventry and Corona RNA-SARS-CoV-2 was detected in both the appendiceal tissue and the mesenteric lymph node.

Bacterial 16S rRNA gene was not detected.

2.4. Outcome and follow-up

During his admission in intensive care, the patient underwent a further laparotomy to drain abdominal collections which were presumed to be driving his apparent sepsis. Bacterial cultures from post-surgical abdominal drains grew *Klebsiella* sp., *Enterococcus faecium*, and several anaerobic bacterial species which were treated with antibiotics.

The patient developed a poor ejection fraction which was deemed likely secondary to a myocarditis driven by sepsis. This subsequently improved following treatment with Levisimendan and IVIG.

A caecal perforation and associated haemorrhage were identified on CT imaging which was initially treated with antibiotics and supportive management. Following a large per-rectum haemorrhage, the patient underwent another laparotomy during which the large blood clot was removed and a pin-hole perforation in the caecum was sutured. A short segment of small bowel was removed due to a serosal tear, and a loop ileostomy was created.

Following the last surgery, the patient's condition began to improve. The patient was extubated, and his oxygen requirements decreased. Blood tests demonstrated a fall in inflammatory markers. Following a total of five weeks of admission to intensive care, he was discharged home and made a full recovery. Since discharge, the patient's ileostomy has been reversed and the patient remains well at the time of writing of this case report.

3. Discussion

COVID-19 usually manifests as a respiratory tract infection, however emerging worldwide data show that COVID-19 can present with a variety of clinical symptoms. Despite negative pharyngeal and nasal swabs, our patient developed features suggestive of COVID-19 including lymphopenia and bilateral consolidation on radiography. The pathological features of thrombotic microangiopathy, lymphocyte apoptosis, and lymph node fibrinoid necrosis are in keeping with morphological findings encountered in the lungs of COVID-19 patients in the literature [3].

Our case demonstrated a patient presenting with symptoms consistent with acute appendicitis. Suspicion of COVID infection was only considered following the unusual histological features seen within the mesenteric lymph node and appendix, which were reminiscent of features typically described in the pulmonary system in patients with COVID. In retrospect, the patient in this case demonstrated other features consistent with COVID infection including bilateral consolidation and blood tests including lymphopenia, raised CRP, raised INR, and raised fibrinogen [2].

An interesting feature in our case report is the negative repeated COVID-19 swabs despite a positive PCR test on the histological tissue

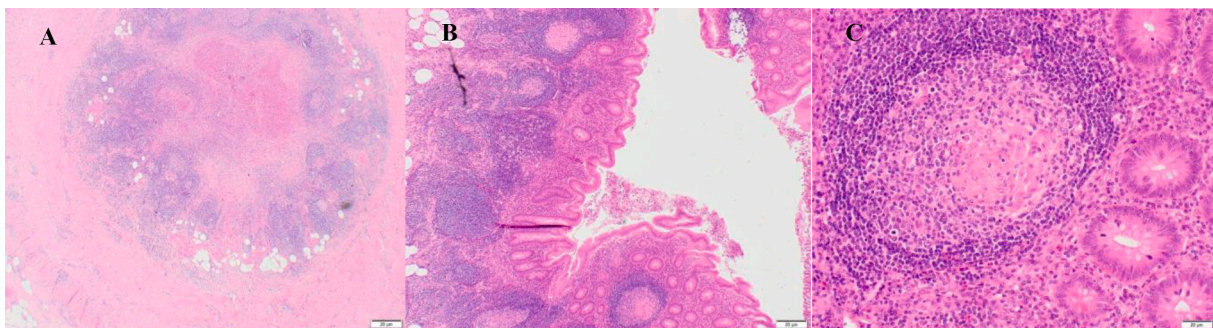


Fig. 1. Appendix showing mild acute inflammation and non-necrotising granulomata. A) $\times 2$ magnification. B) $\times 4$ magnification. C) $\times 20$ magnification showing a non-necrotising granuloma.

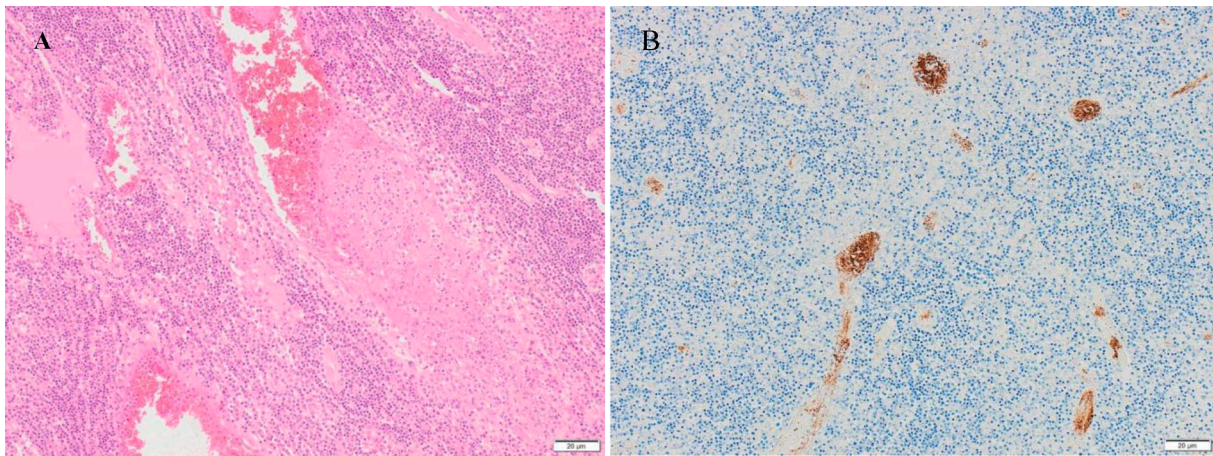


Fig. 2. A) A lymph node showing microangiopathy and small vessel thrombosis ($\times 10$ magnification). B) CD42b immunostaining highlights increased platelet aggregation ($\times 10$ magnification).

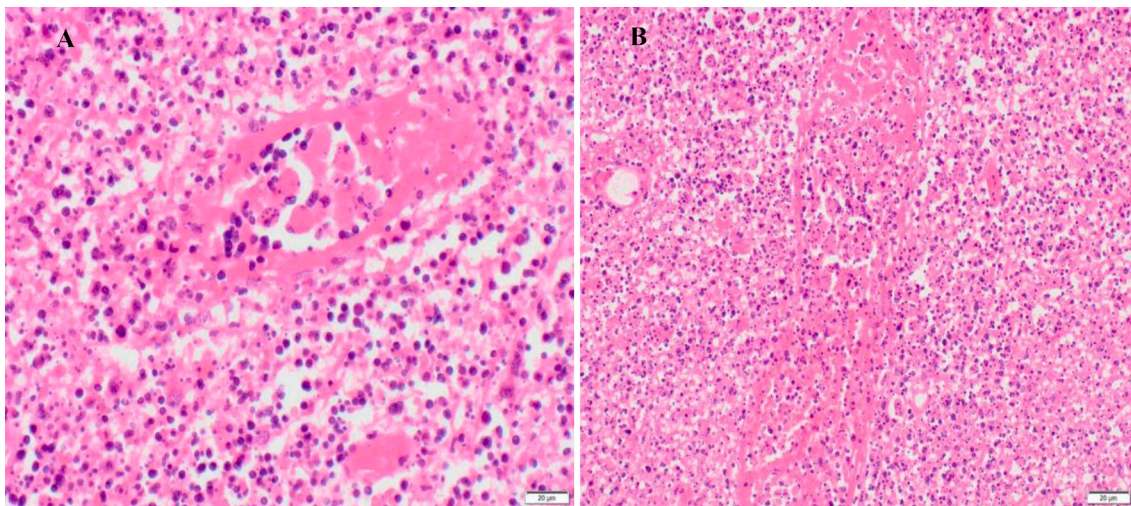


Fig. 3. A + B) A lymph node showing fibrinoid necrosis of small vessels A) $\times 40$ magnification. B) $\times 20$ magnification.



Fig. 4. A lymph node showing severe necrotising lymphadenitis.

samples. A similar case of a 33-year-old man presenting with severe abdominal pain and diarrhoea has been reported in the BMJ. In this case report, early nasopharyngeal airway (NPA) swabs were also negative. The patient showed bilateral consolidation on CT of the thorax, and later

developed severe respiratory symptoms requiring intensive care admission [4].

In several case reports, NPA swabs have been consistently negative in symptomatic patients who later tested positive for COVID-19 on PCR [5]. There appears to be an association with gastrointestinal presentations of COVID-19 and negative NPA swabs [6].

A case series by Poggiali et al. (2020) [7] reported on 10 patients diagnosed with COVID-19 who presented to hospital with gastrointestinal symptoms such as abdominal pain and vomiting or diarrhoea, and a fever. As with our case, the majority of patients had a raised C-reactive protein, and lymphopenia.

By endoscopic assessment mucosal damage has been identified within gastrointestinal mucosa, and histological examination has revealed lymphocytic and plasma cell infiltration within the lamina propria of stomach, small intestine, and rectum in patients with COVID-19 [8]. Interestingly, a cross-sectional study of 203 patients in Hubei, China, found that almost 2% of COVID-19 patients demonstrated abdominal pain, and approximately 6% of patients experienced gastrointestinal symptom as their only complaint [9].

A single-centre retrospective case series by Saeed et al. (2020) analysed medical reports of all patients who were admitted to the hospital with abdominal pain [10]. They found that 9/76 patients admitted over a 14-day period tested positive for SARS-CoV-2. Of note, 6/9 patients

demonstrated unilateral or bilateral ground-opacities on pulmonary CT scan despite having no respiratory symptoms at presentation, like with the patient in our case study. These six patients differ from ours in that their abdominal and pelvic CT scans were normal. In five of these cases, incidental findings on pulmonary CT scan prompted the consideration and further investigations into the possibility of COVID-19 infection. Of the three patients in the case series who had normal pulmonary CT scans, abdominal CT demonstrates one case of cholecystitis, one case of appendicitis, and one case of ileus. This series do not report on histological findings of these patients.

Gahide et al. (2020) describe three patients presenting with acute abdominal pain who were identified to have COVID-19 after ground-glass opacities were found in their lung bases during an abdominal CT scan. The identification of incidental radiological pulmonary changes appears to be a recurring feature in several case studies, despite the apparent absence of chest symptoms [10,11]. This mirrors the findings of Saeed et al., and those of our case study.

Abdominal pain is uncommon in COVID-19, however a literature review by Lin-Man et al. (2021) estimated the prevalence of abdominal pain to be between 1.9% and 14.5% [12]. The authors also suggest that mesenteric lymph node enlargement could potentially represent a mechanism of abdominal pain in COVID-19 patients. Our case study would support this hypothesis.

A reported feature of patients with gastrointestinal symptoms of COVID-19, not highlighted by this case, is raised liver enzymes [6]. This feature is corroborated by an autopsy case study which demonstrated microscopic features of microvascular steatosis and mild lobular and portal inflammation [8].

Gastrointestinal symptoms, while not classical, have been well-recognised as possible presenting symptoms of COVID-19. However, presentation with a clinically 'acute abdomen' is unusual in the literature. There are rare case reports in the literature which have reported similar findings. A report published in *ID Cases* describes a 40-year-old female presenting with a clinical picture of appendicitis that later developed symptoms consistent with COVID infection, but unlike our case had a positive COVID nasal and pharyngeal swab and radiologically showed a normal appendix without lymphadenopathy. Furthermore, this case lacked the histological data present in our case [13].

A possible mechanism of action for intestinal injury by SARS-CoV-2 is the high expression of ACE2 receptors within the intestinal tract. ACE2 mRNA expression is known to exceed that in the lung 100-fold. Reduced absorption of tryptophan within the intestinal tract due to ACE2 inhibition has also been implicated in the intestinal damage. A murine model of ACE2 deficiency demonstrated a high susceptibility of intestinal inflammation following chemical irritation [8].

4. Conclusion

COVID-19 caused by SARS-CoV-2 is a multisystemic, complex disease, usually presenting as a localised upper respiratory tract infection. In severe cases it may spread to involve the lower respiratory tract and other organs, resulting in multi-organ failure. Emerging case reports have identified other presenting symptoms such as atypical respiratory symptoms, and progressive gastrointestinal symptoms in a subset of COVID-19 positive patients [14].

Rare case reports have identified presentations of COVID-19 as possible acute appendicitis and acute abdomen in children, an uncommon manifestation of the virus [15,16]. We report an unusual presentation of COVID-19 in a 28-year-old adult who presented to the emergency department with a 'clinical appendicitis' and histological evidence of inflammation.

Our case demonstrates an important differential in the presentation of acute abdomen in the current pandemic. This case also highlights the

important learning point that NPA swabs may miss COVID-19 diagnoses in patients, especially those presenting with gastrointestinal symptoms.

5. Ethics statement

The case report has been completely anonymised to protect patient confidentiality, and patient consent has been obtained for publication of a case report.

Ethics and consent statement

The case report has been completely anonymised to protect patient confidentiality, and consent has been obtained for publication of a case report including digital histopathology images in a journal by the patient.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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