

CASE REPORT

SARS-CoV-2 isolation from an appendix

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Abstract

Efforts to recognize SARS-CoV-2 infection have focused on respiratory symptoms such as cough and shortness of breath. Although it is also well known that SARS-CoV-2 infection can cause gastrointestinal symptoms such as abdominal pain, nausea, vomiting and diarrhoea, there are emerging reports of SARS-CoV-2 infection causing surgical pathology. We present the first case report of SARS-CoV-2 infection directly causing acute appendicitis, first suspected due to highly atypical histological features and later confirmed as polymerase chain reaction positive appendicular tissue sample.

INTRODUCTION

The aetiology of appendicitis is not completely understood. Coronavirus infection has not been associated with appendicitis, but SARS-CoV-2 has proven to infect a number of organs, with respiratory failure the most consistent feature of COVID-19. We present here a case report of a patient who presented with appendicitis during the COVID-19 pandemic.

CASE REPORT

A 28-year-old man presented to our hospital with fever, localized right iliac fossa pain and nausea. He is otherwise well with a past surgical history of chronic pilonidal sinus.

The patient was symptomatic for 5 days prior to presentation, when he developed fever ($>38.0^{\circ}\text{C}$) with rigours. He also reported loss of appetite and diarrhoea, with no associated blood or mucus.

Clinical examination revealed normal work of breathing and bilateral vesicular breath sounds. Cardiovascularly, the patient had a heart rate of 130 beats/min, blood pressure was normal and capillary refill time was <2 s. His Glasgow Coma Scale score was 15, blood glucose was 7.6 mmol/l and his temperature was

38.1°C . Abdominal examination revealed right iliac fossa tenderness on deep palpation. There was no guarding or evidence of peritonism.

Notable laboratory results include a leukocytosis and markedly elevated C-reactive protein. Lymphopenia was also demonstrated, which persisted for several days.

Imaging revealed an unremarkable chest radiograph. The report of the computed tomography (CT) scan of the chest, abdomen and pelvis is summarized in Table 1. Provisional diagnosis upon surgical consultation was acute appendicitis requiring surgery.

The COVID-19 pandemic has prompted anaesthetists and surgeons to reconsider safety in operating standards [1], due to the potential of aerosol generation. As such, this patient underwent an open appendectomy. An auto-amputated appendix was noted intraoperatively, necessitating conversion to midline laparotomy. The appendix specimen was sent for histology as per protocol.

The patient was successfully extubated at the end of surgery. Post-operatively, despite adequate analgesia with intravenous morphine, venous thromboembolism prophylaxis with dalteparin and antibiotics, his respiratory function declined.

Received: June 12, 2020. Accepted: June 26, 2020

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Table 1. Summary of CT scan as reported by radiologist

	Reports of CT chest, abdomen and pelvis (with contrast)
On day of presentation	<p>Chest: Lungs clear. No mass or lymphadenopathy. No other significant finding in the thorax.</p> <p>Abdomen and pelvis: There are inflammatory changes in the right iliac fossa with mild thickening of the proximal appendix. There are adjacent enlarged mesenteric lymph nodes. No appendicolith. No free gas. No collection. No bowel dilatation or other bowel lesion. Terminal ileum appears unremarkable. There is a trace of free fluid in the pelvis. No mass or lymphadenopathy. In the posterior basal cleft, the pilonidal sinus is noted, but there are no associated acute inflammatory changes or collection.</p> <p>Skeletal review: No vertebral collapse or lytic bony lesions seen.</p> <p>Conclusions: (i) Right iliac fossa inflammatory changes in association with features of mild acute appendicitis with localized lymphadenopathy. (ii) No evidence of associated perforation, collection, obstruction or other complications. (iii) Normal CT chest. (iv) No acute features associated with the known pilonidal sinus.</p>
3 days post-operatively	<p>Comparison is made with the preoperative scan on initial presentation</p> <p>Chest: Marked volume loss in both lower lobes with bilateral pleural effusions.</p> <p>Abdomen and pelvis: Right iliac fossa and midline scars are noted. There are bilateral basal pleural effusions with significant underlying volume loss in both lower lobes. The aerated lung bases are clear. The liver, gallbladder and ducts are normal. Normal adrenals, pancreas and spleen. Both kidneys are normal in appearance. Ureters are normal in calibre, bladder is thin walled and catheterized. Pelvic structures appear normal.</p> <p>There is a small quantity of fluid in the stomach. Multiple prominent small bowel loops are noted in the left and central abdomen. Terminal ileum is nondistended. There is fluid in the ascending colon and gas is seen in normal calibre transverse colon. Descending colon, sigmoid and rectum are collapsed.</p> <p>Once again, a number of prominent nodes are demonstrated in the ileocolic mesentery. Postsurgical changes noted around the region of the caecal pole.</p> <p>Fluid tracks up posteriorly, to lie in the right subhepatic space—in Morison's pouch. This fluid collection measures 8 × 8 × 3 cm. A single tiny dot of gas is noted posterior to the gallbladder, within this fluid collection.</p> <p>Elsewhere, there are very small quantities of fluid, in keeping with postsurgical change. No other collections.</p> <p>Conclusion: There is a pocket of fluid in the right subhepatic space—Morison's pouch—as described. Features of post-operative ileus.</p>

The minimal post-operative oxygen requirement escalated at Day 3 to high-flow nasal oxygen at 60-l flow with fraction of inspired oxygen at 0.9. The patient became cardiovascularly compromised with hypotension and tachycardia refractory to fluid resuscitation. The patient was reintubated and treated for septic shock.

Cardiac impairment was further observed on echocardiography, demonstrating severe left ventricular dysfunction with an ejection fraction of 20–25%. Alongside raised troponin of 148 ng/l, this was suggestive of myocarditis.

This deterioration prompted further imaging (Table 1). Chest findings were either normal or atypical of COVID-19 on both chest CT's and respiratory decline was attributed to inadequate analgesia and derecruitment. The abdominal collection was the most likely source of sepsis. A further laparotomy and washout procedure was conducted as source control. Abdominal drain samples were negative for acid-fast bacilli but were positive for *Klebsiella pneumoniae*, *Enterococcus faecium* and *anaerobes* (Table 2). Whilst progressing well from a ventilatory perspective, the

patient developed overt haemorrhage from the right pelvic drain necessitating a third laparotomy following which the patient was discharged to the ward.

Three nasopharyngeal and throat swabs were negative for SARS-CoV-2. The histopathology report mentions unusual macroscopic and microscopic appearances, possibly pertaining to the virus (Table 2). A paraffin tissue sample of the associated lymph node was sent for polymerase chain reaction (PCR) analysis. This was later reported as positive for SARS-CoV-2.

To our knowledge, this is the first reported case of SARS-CoV-2 isolation from an appendix specimen.

DISCUSSION

It is well established that SARS-CoV-2 can be isolated from rectal swabs and faeces, even in patients who do not display respiratory symptoms and are negative for SARS-CoV-2 in nasopharyngeal and throat swabs [2]. Digestive symptoms attributed to COVID-19 include nausea, vomiting, diarrhoea, abdominal pain and change

Table 2. Microbiology, virology and histopathology results

	Specimen	Result
Bacteriology	BAL	Microscopy—AFB negative. MC&S—No growths.
	Abdominal drain fluid	Microscopy—AFB negative. MC&S—Gram stain: WBC ++, organisms not seen, no growth aerobically/anaerobically.
	Abdominal drain fluid	MC&S—Gram stain: WBC+, organisms not seen, culture: <i>E. faecium</i> , <i>K. pneumoniae</i> , anaerobes.
	Lung pleural fluid	Microscopy: AFB not seen.
	Blood culture	Aerobic and anaerobic samples negative in a total of seven samples sent at different periods during admission.
	Sputum	No growths.
	MC&S	
	CVC line tip	Negative in two CVC tips.
	MC&S	
	Arterial line tip MC&S	No growths.
Virology	Novel coronavirus swab	Negative in three throat swabs.
	Appendix tissue PCR	Bacterial 16S rRNA gene: not detected.
		Coronavirus RNA-SARS-CoV-2: detected.
	Appendiceal lymph node PCR	Bacterial 16S rRNA gene: not detected.
		Coronavirus RNA-SARS-CoV-2: detected.
	Mycoplasma serology	<i>Mycoplasma pneumoniae</i> IgM negative.
	Toxoplasma IgG	Detected.
	Toxoplasma IgM	Not detected.
	HBsAg test	Not detected.
	Hepatitis C antibody	Not detected.
	HIV 1 and 2 antibodies	Not detected
Urine	Urine	No growths in five specimens taken at different periods during admission.
	Culture	
	<i>Pneumococcal</i> antigen	Not detected.
	<i>Legionella pneumophila</i> antigen	Not detected.
Histopathology	Appendix microscopy report	All the appendix has been embedded and histological sections show a mild acute appendicitis with focal mucosal ulceration associated with occasional noncaseating granulomata in the wall but no transmural inflammation seen. A focal foreign body giant cell reaction to faecal material is present. Sections from the separate nodular tissue fragments reveal an enlarged mesenteric lymph node with severe mesenteric necrotizing lymphadenitis associated featuring apoptosis, occasional micro thrombi, fibrinoid necrosis of the blood vessels, perivascular lymphocytic inflammatory infiltrate (highlighted on CD4 and CD8) and a histiocytic component with prominent nucleoli and clear cytoplasm. Increased platelets aggregation is seen highlighted by CD42b. Special stains for acid-fast bacilli and fungi are negative. No dysplasia or malignancy present and no parasites identified.
	Appendix histology report	Acute appendicitis with a severe unusual mesenteric lymphadenitis and suppurative necrotizing reaction. The differential diagnosis includes <i>Yersinia enterocolitis</i> and Crohn's disease; however, due to the prominent areas of apoptosis, micro thrombi and fibrinoid necrosis, the possibility of COVID19 aetiology needs to be ruled out. A PCR on paraffin tissue sections of the lymph node and appendix have been requested and will be reported later.

AFB, acid fast bacilli; MC&S, microscopy culture and sensitivities; WBC, white blood cells; CVC, central venous catheter; BAL, bronchial alveolar lavage; IgM, immunoglobulin M; IgG, immunoglobulin G; HBsAg, hepatitis B surface antigen.

in appetite [3]. Our patient presented with four of the latter symptoms and displayed no respiratory symptoms pertaining to the virus.

SARS-CoV-2 may invade the intestinal wall due to high expression of viral receptor ACE2 in the gut wall, thereby impairing barrier function and allowing microbial translocation [2, 3]. This yields a number of hypotheses.

We argue that SARS-CoV-2 is the causative agent of appendicitis in this patient. The highly atypical histological appearance of the appendix specimen, particularly the occasional micro thrombi, fibrinoid necrosis of the blood vessels and perivascular lymphocytic inflammatory infiltrate in the specimen points towards the influence of SARS-CoV-2. These findings are represented in several reports of lung specimens, where lymphocytic infiltration and fibrinous micro thrombi are prominent features [4, 5]. The positive PCR result further supports our diagnosis.

In addition, haematological and biochemical parameters were highly suggestive of COVID-19-induced sepsis; sustained lymphopenia, raised ferritin (5352 µg/l), troponin (148 ng/l) and creatinine kinase (200 iu/l maximally) and myocarditis have all been reported in SARS-CoV-2 infection [6].

Route of transmission to the appendix is undetermined. The presence of SARS-CoV-2 RNA in stool samples of patients with gastrointestinal symptoms alludes to the possibility of faeco-oral transmission [2]. Infection may additionally enter the gastrointestinal tract via oropharyngeal contamination, also enabling bacterial translocation and appendicitis.

Another hypothesis is that the presence of SARS-CoV-2 in the gastrointestinal system was coincidental, with appendicitis resulting from an appendicolith forming concomitantly with infection. The CT and macroscopic biopsy appearances have not substantiated this suggestion.

We argue that SARS-CoV-2 may cause other surgical problems pertaining to inflammation. In addition, given its propensity to cause thromboembolic complications, bowel ischaemia is another distinct possibility. In keeping with this, acute pancreatitis, acute cholecystitis, gastrointestinal bleeding and bowel ischaemia have been reported in patients critically ill due to COVID-19 [7]. Another reported complication is haemorrhagic colitis [8]. Thus, a higher index of suspicion for surgical problems is required in patients with SARS-CoV-2 infection.

CONCLUSION

To our knowledge, this is the first report of SARS-CoV-2 gastrointestinal infection causing appendicitis. This adds to the body of evidence implicating SARS-CoV-2 in surgical complications. Given that SARS-CoV-2 has been discovered to affect multiple tissues, we propose that during the pandemic, biopsy and tissue specimens should be studied for the typical findings associated with COVID-19 and if present, specimens should be sent for detection via PCR.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Royal College of Surgeons of England RC of S of E. *Updated Intercollegiate General Surgery Guidance on COVID-19* [Internet]. 2020. <https://www.rcseng.ac.uk/coronavirus/joint-guidance-for-surgeons-v2/> (23 May 2020, date last accessed).
2. Hindson J. COVID-19: faecal-oral transmission? *Nat Rev Gastroenterol Hepatol* 2020;17:259.
3. Han C, Duan C, Zhang S, Spiegel B, Shi H, Wang W, et al. Digestive symptoms in COVID-19 patients with mild disease severity: clinical presentation, stool viral RNA testing, and outcomes. *Am J Gastroenterol* 2020;116:916–23.
4. Dolhnikoff M, Duarte-Neto AN, de Almeida Monteiro RA, Ferraz da Silva LF, Pierre de Oliveira E, Nascimento Saldiva PH, et al. Pathological evidence of pulmonary thrombotic phenomena in severe COVID-19. *J Thromb Haemost* 2020;18:1517–9.
5. Wichmann D, Sperhake J-P, Lütgehetmann M, Steurer S, Edler C, Heinemann A, et al. Autopsy findings and venous thromboembolism in patients with COVID-19. *Ann Intern Med* 2020.
6. Doyen D, Mocerri P, Ducreux D, Dellamonica J. Myocarditis in a patient with COVID-19: a cause of raised troponin and ECG changes. *Lancet* 2020;395:1516.
7. Kaafarani HMA, Moheb ME, Hwabejire JO, Naar L, Christensen MA, Breen K, et al. Gastrointestinal complications in critically ill patients with COVID-19. *Ann Surg* 2020;272:61–2.
8. Carvalho A, Alqusairi R, Adams A, Paul M, Kothari N, Peters S, et al. SARS-CoV-2 gastrointestinal infection causing Hemorrhagic colitis. *Am J Gastroenterol* 2020;115:942–6.