

No SARS-CoV-2 detected in the vermiform appendix of a COVID-19 patient with appendicitis: a case report

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Case Report

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Abstract

Background:

SARS-CoV-2, the virus causing corona virus disease 2019 (COVID-19), has been demonstrated to infect the gastrointestinal tract and might therefore be a source of infection for the surgical team during abdominal operations. One of the most common surgical procedures performed is appendectomy. However, reports of virologic testing of appendiceal tissue specimens in COVID-19 patients are lacking. We sought to determine whether SARS-CoV-2 is present in the appendectomy specimen of a patient with COVID-19.

Case presentation:

A female patient presented to the emergency department of our tertiary care academic hospital with lower abdominal pain, fever, nausea, and vomiting. She was admitted to the gynecological floor because of suspected pelvic inflammatory disease. Due to worsening symptoms, a laparoscopy was performed the next day and a severely inflamed appendix was detected. Laparoscopic appendectomy was performed without complications. A few hours postoperatively, the patient was tested positive for corona virus disease 2019 (COVID 19). Real-time reverse transcription polymerase chain reaction analysis targeting the SARS-CoV-2 E-gene was performed on the appendectomy specimen. SARS-CoV-2 could not be detected. During her hospital stay, the patient developed mild respiratory symptoms while the postoperative course was otherwise uncomplicated.

Conclusions:

The absence of SARS-CoV-2 in the appendectomy specimen of our case adds to the preliminary available evidence indicating that appendectomy in COVID-19 patients with mild disease carries probably a low risk of infection by aerosols generated during the procedure.

Background

Since the emergence of the novel severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) in Wuhan (China) in December 2019, more than 7.5 million people have been infected worldwide and about 420.000 have died[1]. The disease caused by SARS-CoV-2 has been termed coronavirus disease 2019 (COVID-19), a predominantly respiratory illness with symptoms ranging from mild self-limited disease to acute respiratory distress syndrome (ARDS) and death[2]. When operating on patients with (suspected) COVID-19, there is concern for infection of members of the surgical team. Because SARS-CoV-2 has been demonstrated in stool specimens[3] and recent experimental data has robustly shown that SARS-CoV-2 can infect enterocytes[4], it is plausible that surgical manipulation of the gastrointestinal tract during laparoscopic procedures might generate infectious aerosols. Meanwhile, acute appendicitis is one of the most common emergencies in abdominal surgery and will continue to affect patients during the pandemic. We here report the case of a patient who underwent laparoscopic appendectomy and who

tested positive for COVID–19 several hours after the operation. For the first time we performed virologic testing to determine the presence of appendiceal SARS-CoV–2 infection. Clinical and laboratory data were retrieved from the files retrospectively.

Case Presentation

A 25-year old female presented to our emergency department at the end of March 2020 with lower abdominal pain, nausea, intermittent vomiting, and fever. The symptoms had lasted for 36 hours and the pain had progressed from mild lower abdominal discomfort to severe crampy pain. She reported dysuria and fever up to 38.6°C. There was no history of other illnesses. The patient appeared ill, the blood pressure was 127/84 mmHg, the heart rate 86 bpm, and the body temperature 38.4°C. Arterial oxygen saturation was 97% while the patient was breathing ambient air. The lower abdomen was painful on palpation and there was guarding and rebound tenderness in the right lower quadrant. The appendix could not be visualized by ultrasound imaging. Gynecological examination revealed no evidence for tubo-ovarian abscess formation. Laboratory testing was remarkable for leukocytosis of 29 exp9/l and for an elevated C-reactive protein level of 112 mg/l (normal range <5 mg/l). Because acute pelvic inflammatory disease was suspected, the patient was admitted to the gynecological floor and antibiotic treatment with cefuroxime, metronidazole, and doxycycline was started. Because of worsening abdominal pain, an explorative laparoscopy was performed on the next day. Intraoperatively, the appendix appeared severely inflamed with no sign of perforation. An appendectomy using a linear stapling device was performed without complications. Four hours postoperatively, the patient learned that her boyfriend had developed respiratory symptoms and that a friend of him had been tested positive for COVID–19. We performed oropharyngeal swabs and real time reverse transcription polymerase chain reaction (RT-PCR) analysis confirmed SARS-CoV–2 infection. The patient was transferred to a dedicated COVID–19 unit. The postoperative course was unremarkable. Mild respiratory symptoms developed but were self-limited. On the 5th postoperative day, the patient was discharged home and instructed to continue quarantine for a total of 14 days. Histopathological evaluation of the appendectomy specimen confirmed acute necrotizing appendicitis. Because surgery was performed without knowledge of the patient's COVID–19 infection, no special protective measures for the medical caregivers had been in place. Therefore, all patient contacts including the surgical team underwent repeated testing for SARS-CoV–2 during the following week. No infections were detected.

For virologic testing of the appendiceal specimen, ten slices of the proximal and of the distal portion of the formalin-fixed and paraffin-embedded appendix were cut. Deparaffinization was done by consecutive washes with xylene and ethanol. Following tissue homogenization and lysis (MagNA Lyser, Roche, Penzberg, Germany) nucleic acid extraction was performed (NucliSENS easyMAG, BioMerieux, Mary l'Etoile, France). Next, presence of SARS-CoV–2 specific RNA in the samples was assessed by a short-amplicon (113 bp) one-step real-time reverse transcription polymerase chain reaction (rt-PCR) targeting the viral E-gene[5] on a LightCycler 2.0 (Roche, Penzberg, Germany) instrument. Testing did not reveal SARS-CoV–2 in the vermiform appendix.

Discussion And Conclusions

Because gastrointestinal symptoms occur in 11 - 64% of COVID-19 patients[6-8], there have been early concerns during the current pandemic that the gastrointestinal system might be involved in the disease. Indeed, there is evidence that almost a third of all patients with COVID-19 and gastrointestinal complaints do not experience respiratory symptoms [7]. Early ex vivo experiments confirmed that SARS-CoV-2 can infect and replicate in enterocytes [4], and SARS-CoV-2 was demonstrated in stool specimen[3, 9]. In one study, SARS-CoV-2 was detected within enterocytes in biopsies taken from the esophagus, stomach, duodenum, and rectum of COVID-19 patients with severe disease [6] In another case report, SARS-CoV-2 was found in gastric, small intestinal, and rectal enterocytes of another COVID-19 patient with ARDS and bleeding from a gastric ulceration [9]. There is limited information regarding COVID-19 and acute appendicitis. While one report demonstrating SARS-CoV-2 in the peritoneal fluid of a patient with COVID-19 has been published[10], Ngaserin et al. reported recently that they could not detect SARS-CoV-2 in the peritoneal fluid of a COVID-19 patient with acute appendicitis[11]. Another case report recently described an appendectomy in a patient with COVID-19 but no investigations regarding the presence of SARS-CoV-2 in the appendix were performed [12].

Mechanistically, infection of gastrointestinal cells is most likely mediated by viral interaction with angiotensin converting enzyme 2 (ACE2), which serves as a functional receptor for SARS coronavirus [13] and which is expressed on gastrointestinal mucosal cells [14]. Currently, no evidence exists whether ACE2 is expressed in the vermiform appendix.

There are several caveats to our findings: first, our patient had only mild disease and it is likely that gastrointestinal involvement is more marked in severe cases and later stages of the disease course, as evidenced by the available studies involving gastrointestinal biopsies [6, 9]. Our patient had mild disease only, although we do not know with certainty if she was initially asymptomatic with regard to COVID-19. She had fever on presentation which we attributed to appendicitis, but it might also have been caused by COVID-19 even though respiratory symptoms were lacking. Like our patient, in a recent study most COVID-19 patients with fever had a body temperature in the range from 37.5°C-39.0°C[15]. Interestingly, there seems to be a significant number of patients who present with gastrointestinal symptoms only [6]. Two cases of COVID-19 patients with an appendicular syndrome as presenting complaint have been described, although appendicitis was not confirmed in either patient [16, 17]. In our case, however, appendicitis was confirmed laparoscopically and was certainly the cause for the gastrointestinal symptoms. As there are no reports of appendicitis caused by SARS-CoV-2 infection and since we did not find viral DNA in the appendectomy specimen, it seems unlikely that acute appendicitis could be part of the COVID-19 spectrum. Rather, our case highlights the concurrence of a common surgical emergency and COVID-19. In light of our data and of the recent failure to detect COVID-19 in the peritoneal fluid of a COVID-19 patient with acute appendicitis[11], we would consider the risk of infectious aerosol development during laparoscopic appendectomy in COVID-19 patients with mild symptoms to be relatively low. However, this is only one case report which clearly limits generalization and precautions such as appropriate personal protective equipment should be used whenever COVID-19 is suspected in a

patient, especially as infection of operating personal might result from other sources such as the respiratory system.

In summary, we could not demonstrate SARS-CoV-2 in the appendectomy specimen of a COVID-19 patient with acute appendicitis. This finding adds to the scarcely available evidence that the risk for aerosol-transmitted COVID-19 infection during laparoscopic appendectomy is probably low, at least in patients with mild symptoms. Testing of additional appendectomy specimens of COVID-19 patients should be performed in the future to confirm our findings.

List Of Abbreviations

COVID-19	Corona virus disease 2019
SARS-CoV-2	Severe acute respiratory syndrome – corona virus – 2
ARDS	Acute respiratory distress syndrome
(rt-) PCR	(real time) polymerase chain reaction

Declarations

Ethics approval and consent to participate

All procedures and studies involving our patient as described in this report were performed in accordance with the institutional and national ethics standards, founded on the 1964 Helsinki declaration and its later amendments. No formal ethics approval was necessary. The patient provided informed consent for all procedures described in the case report.

Consent for publication

The patient described consented in the publication of this case report. A written consent form is available.

Availability of data and materials

The corresponding author can be contacted if additional clinical information not reported in this publication should be needed.

Competing interests

BA has received honoraria from Novartis Pharma, Astra Zeneca, Amgen, and Roche Pharma. For the remaining authors no potential conflicts of interest exist.

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Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by B. Wolf, C. Pietsch, LC Horn, and GU Liebert. The first draft of the manuscript was written by B. Wolf and all authors commented on and critically revised the previous versions of the manuscript. All authors read and approved the final version of the manuscript.

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