



A 55-Years-Old Immunocompetent Woman with COVID-19 Infection Presented with Isolated Abdominal Symptoms due to Perforated Appendicitis: A Case Report

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Case summary

A 55-years-old immunocompetent woman had vomiting and abdominal pain on fifth day of fever. Then, it confined to right iliac fossa on 7th day of fever in spite of bowel rest, parenteral remdesivir, fluids & electrolytes therapy and antibiotics. Nasopharyngeal swab PCR was positive. Plain X-ray abdomen was compatible with paralytic ileus; ultrasound abdomen showed inflamed appendix. Laparotomy revealed an inflamed appendix with area of perforation and pus flakes in peritoneum; appendicectomy and peritoneal toilet were done. Polymorphonuclear infiltration in lamina propria in the histology of cut section of appendix. The postoperative period was uneventful; nasopharyngeal swab PCR was negative after 10 days treatment with remdesivir. She did not take steroids, tocilizumab or baricitinib.

Keywords: COVID-19 infection; perforated appendicitis; immunocompetent

Introduction

SARS-CoV2 can invade all cells in the body; no system in the body has been exempted. Though ACE receptors are distributed in brain, liver, heart, kidneys and gastrointestinal tract, the main affinity is respiratory tract; therefore, the commonest presentation

is the respiratory symptoms. On the other hand, gastrointestinal tract is less affected than respiratory tract; usual symptoms are nausea, vomiting, diarrhea and mild abdominal pain [1]. However, severe abdominal pain may be rare form. The gastrointestinal

presentations were found to be non-specific symptoms; they were combined symptoms with cough, sore throat, running nose and dyspnoea [2].

Gastrointestinal involvement is due to presence of ACE receptor in the intestinal wall giving rise to inflammation in intestinal wall: mucosa, submucosa and serosa. In addition, congestion and vasculitis of artery and vein of the intestine and mesentery aggravate inflammatory process in the intestinal wall leading to bowel gangrene and perforation. Moreover, the pathology may be direct cytopathic effect, thromboembolism or medication induced: steroids [3], IL6 inhibitor therapy [4,5] and Baricitinib [6]. Steroid therapy may mask typical clinical features leading to late diagnosis and surgical intervention. Rare side effect of IL6 inhibitor therapy was bowel perforation. Previous reports mentioned either inflammation or perforation of part of gastrointestinal tract: appendicitis [7], oesophagus perforation [8], gastric perforation [9], duodenal perforation, ileal perforation [10] and colonic perforation [11,12]. And their mortality rate was high [13] due to either late presentation [14] or delayed diagnosis as a result of atypical presentation. Moreover, stay-at-home orders and cancellation of non-emergent surgeries led to delay admission causing fatal complication- perforated appendicitis [15].

Case Presentation

A 55-years-old woman had vomiting and abdominal pain on fifth day of fever. She was immunocompetent; had no history of diabetes mellitus. She received 3 doses of COVID-19 vaccine; last vaccination in February 2022. On examination on admission, temperature was 101oF; pulse rate 90/minutes; respiratory rate 21/minutes; SaO2 95% on air; auscultation of lungs was normal; abdomen was soft; tenderness in epigastrium, right hypochondrium, right lumbar and right iliac fossa; no rebound tenderness or free fluids. Nasopharyngeal swab PCR was positive. Laboratory parameters revealed total WBC was upper normal limit $10.7 \times 10^9/L$ (reference range $4.0 \times 10^9/L$ - $11 \times 10^9/L$) (Neutrophils 85%, Lymphocyte 10%);

absolute lymphocyte counts was $0.72 \times 10^9/L$; hemoglobin was 12 gm%; platelets count was $300 \times 10^9/L$; blood urea was 14 mg/dl (10 – 30 mg/dl); serum creatinine was 0.6 mg% (<0.9 mg/dl); serum sodium was 134 mmol/L; serum potassium was 3.5 mmol/L; serum chloride was 97 mmol/L; serum aspartate aminotransferase was 23 mg/dl (<32 mg/dl); serum alanine aminotransferase was 89 mg/dl (<32 mg/dl); CRP was 13 mg/L (<5 mg/L); ferritin was 110 ng/ml (13-400 ng/ml); and serum amylase was 84 U/L (18-100 U/L). Chest radiograph was normal. First, she was treated as COVID-19 infection with acute gastroenteritis with liquid diet, parenteral remdesivir, fluids and electrolytes therapy and antibiotics. Then, she continued to have severe abdominal pain; tenderness in right iliac fossa was remarkable on 7th day of fever in spite of bowel rest. The abdomen became distended; then, she had frequent passage of loose motion.

Plain X-ray abdomen was compatible with bowel obstruction or paralytic ileus as there were multiple air fluid levels with dilated small and large intestine. (Figures 1 & 2) Ultrasound abdomen showed inflamed appendix. The blood tests on next day were as follows: total WBC count was rising ($12.2 \times 10^9/L$; Neutrophils 85%) and the serum electrolytes became normal (serum sodium 138 mmol/L; serum potassium 3.8 mmol/L; serum chloride 100 mmol/L). Then, both tenderness and rebound tenderness in right iliac fossa were distinct in the evening of 7th day of fever. Therefore, urgent laparotomy was done as localized peritonitis with appendicitis was possible in view of physical findings; it revealed burst inflamed appendix and pus flakes in peritoneum; appendectomy and peritoneal toilet were done. (Figures 3-5) Polymorphonuclear infiltration in the lamina propria with congestion of vessels were seen in the histology of cut section of appendix. (Figures 6-9) Postoperative period was uneventful; nasopharyngeal swab PCR was negative after 10 days of remdesivir therapy. She did not receive steroids, IL-6 inhibitor (tocilizumab) or baricitinib.



Figure 1: Abdomen Xray (Supine) showing dilated bowel loops (diameter of small bowel was 2.8 cm and large bowel was 5.6 cm) more of central location.



Figure 2: Abdomen Xray (Erect) showing multiple air-fluid levels suggestive of bowel obstruction or paralytic ileus.



Figure 3: Pus in the peritoneum and base of appendix.



Figure 4: Inflamed appendix and area of perforation at the base of appendix.



Figure 5: View after appendectomy.

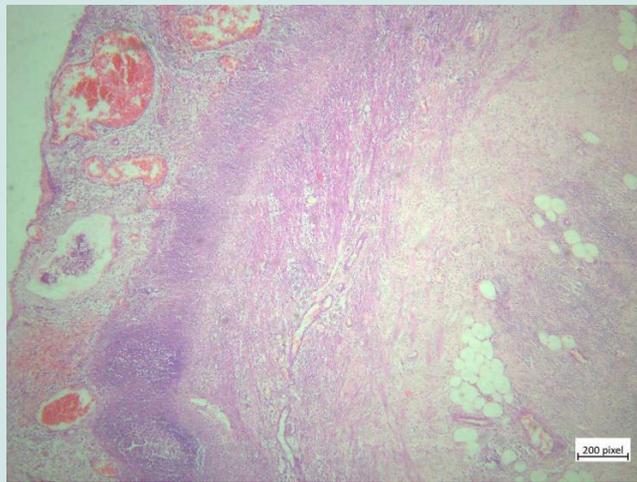


Figure 6: Prominent lymphoid follicles and congested areas in section of appendix (H&E) (10x).

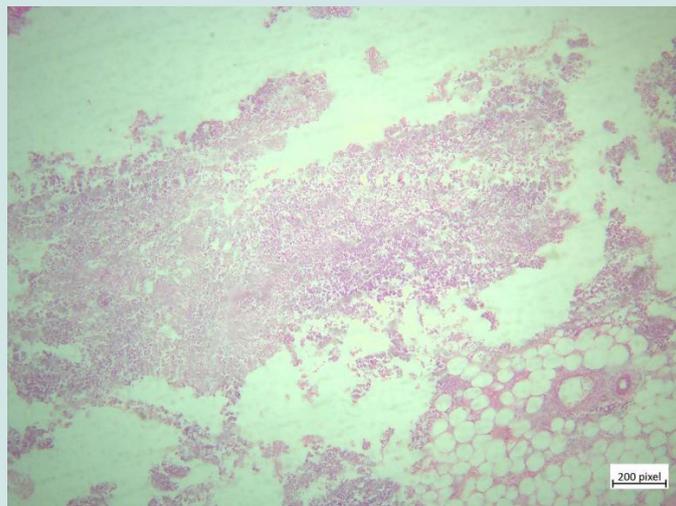


Figure 7: Sheets of inflammatory cells and necrosis at the site of perforation (H&E) (4x).

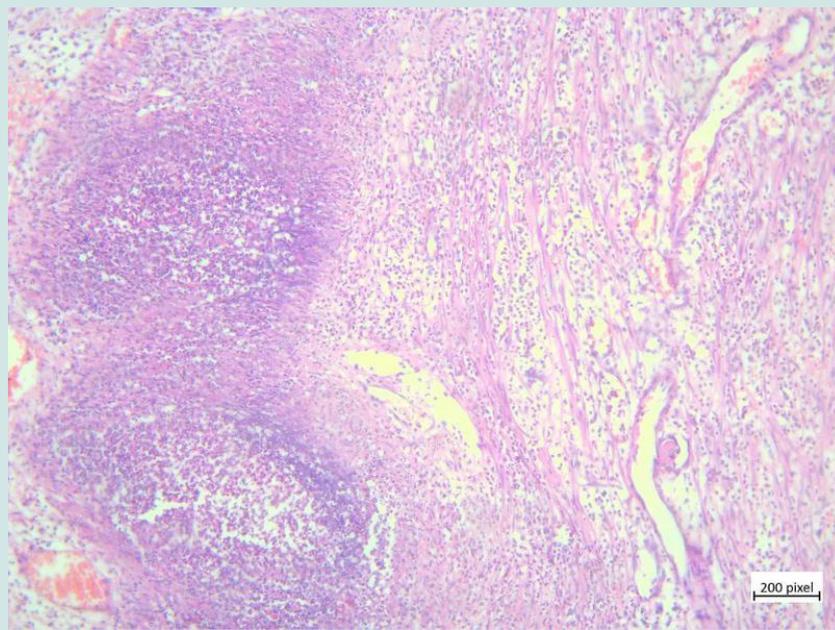


Figure 8: Enlarged lymphoid follicles with polymorphonuclear infiltration in cut section of appendix (H&E) (40x).

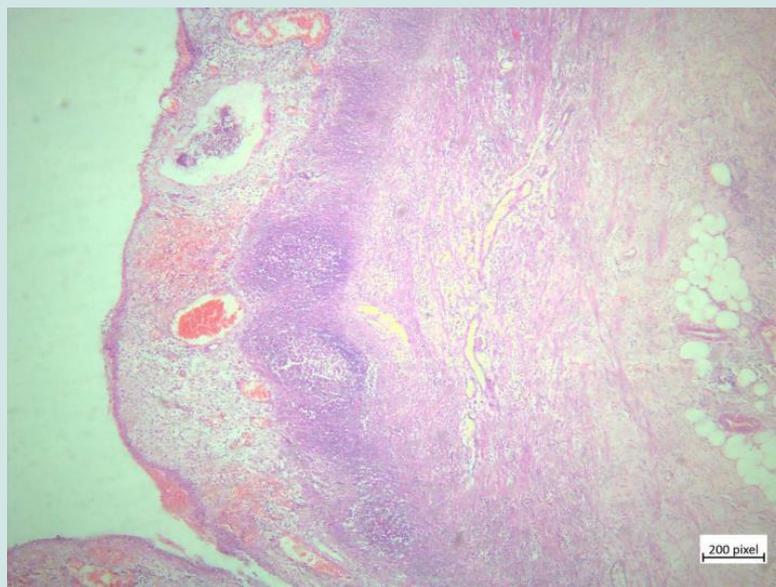


Figure 9: Enlarged lymphoid follicles, congested vessels with polymorphonuclear infiltration in cut section of appendix (H&E) (10x).

Discussion

The commonest presentation of COVID-19 infection is respiratory symptoms, varying from mild flu like symptoms to severe fatal pneumonia. Combination of gastrointestinal symptoms (nausea, vomiting and abdominal pain) plus respiratory symptoms was seen in 20% of cases [16-18] and the severity of abdominal pain was usually mild; presentation with abdominal symptoms without respiratory manifestation is rare (Hellinger JC et al., 2020). This patient was rare form as she was presented with acute severe

pain in abdomen; she did have neither cough nor throat pain.

Regarding the review on the site and pattern of pain in abdomen with severity of COVID-19 infection, those having pain/tenderness in upper part of abdomen (epigastrium and right hypochondrium) were found to be associated with severe COVID-19 infection (dyspnea, low SaO₂ and severe COVID-19 pneumonia) (Balaphas et al., 2022) and they had poor outcome compared to those having pain/tenderness in lower part of abdomen. Contrary to their finding, this patient had pain/tenderness in both upper and lower

abdomen and her oxygen saturation was normal; chest radiograph was normal too.

Severe abdominal pain associated with COVID-19 infection is challenging for clinicians as it is difficult to differentiate from surgical causes of acute abdomen [19,20]. This patient had vomiting and abdominal pain on fifth day of fever. Initial abdominal examination revealed diffuse tenderness over epigastrium, right hypochondrium, right lumbar area, right iliac fossa and suprapubic area; all were suggestive of acute gastroenteritis. Forty-eight hours later, even with bowel rest, anti-viral treatment and antibiotics, the patient continued to have pain in whole abdomen; it finally localized in right iliac fossa. This is the main reason for reporting case, close observation on changes in abdominal examination gives the diagnosis- acute appendicitis. Although there were reports on atypical presentation of acute appendicitis, this patient had more of typical presentation. Close observation and serial abdominal examination in patients with COVID-19 infection was paramount important not to miss diagnosis as well as to avoid unnecessary surgery and complications. However, it was relatively high risks for health care workers.

Clinical diagnosis of appendicitis is mainly based on history and physical examination; it is supported by neutrophil leukocytosis in full blood count. However, ultrasound examination and CT scan usually give high diagnostic yield. Negative appendectomy rate was reduced with the aid of CT scan in COVID-19 pandemic [21]. One report mentioned that CT scan of abdomen was very informative in diagnosis of acute abdomen in patients with COVID-19 infection [22]. However, CT scan of abdomen was not performed in this case as resources were limited. Therefore, clinical acumen of treating physician was extremely important, combination of continuing severe abdominal pain, localized tenderness in right iliac fossa and neutrophil leukocytosis.

In fact, it is not easy to monitor changes in abdominal features unlike serial SaO₂ measurement in COVID-19 treatment center. It required an experienced hand for diagnosis as well as for surgery. Late diagnosis or missed diagnosis can lead to fatal complications, perforation and peritonitis. Besides, unnecessary surgery leads to iatrogenic morbidity and mortality to both patient and healthcare professionals working in operative areas. Furthermore, appendectomy is challenging in COVID 19 infected patients with acute appendicitis as it includes high surgical risks for the patients, as well as hazards for healthcare professionals who are exposed to SARS CoV 2. In addition, the inflammatory changes intestine, appendix, mesentery and vasculitis may be ongoing after appendectomy; the process of healing could not be guarantee with parenteral remdesivir. The anti-inflammatory agents like steroids and IL-6 inhibitors like Tocilizumab were contraindicated in this case. In some studies, antibiotic treatment appeared to be a safe first-line therapy in unselected patients with acute appendicitis without COVID-19 infection [23]. Before COVID-19 pandemic, conservative treatment (fluids and antibiotics therapy) was comparable with appendectomy [24] in treating acute appendicitis; however, in

COVID-19 era, it was rarely mentioned that conservative treatment (fluids, antibiotics therapy and parenteral remdesivir) was equally effective as appendectomy [25]. In this patient, bowel rest and parenteral antibiotics had been tried for 48 hours; presence of severe pain as well as localized tenderness and rebound tenderness in right iliac fossa (localized peritonitis) were the indication for surgery. This highlighted the importance of physical signs and close observation to detect new findings, reasons for case reporting.

COVID-19 infection may cause bowel gangrene and perforation. The etiology of bowel inflammation and perforation were multifactorial; direct cytopathic effect, thromboembolism or medication induced [13], veno-occlusive disease within the appendix [26], the microcirculatory thrombosis in the mesentery vessels due to COVID-19-related coagulopathy [27]. In this patient, inflamed mucosa, prominent lymphoid follicles, polymorphonuclear infiltration and congested vessels were seen in histology, no evidence of thrombosis or vasculitis.

Conclusion

Clinical presentation with respiratory symptoms is the commonest presentation in COVID-19 infection. However, COVID-19 infection may present with pure gastrointestinal symptoms or in combination with respiratory symptoms. Those having abdominal symptoms should be carefully monitored for features of acute abdomen as clinical presentation may not be typical. A high index of clinical suspicion of acute appendicitis is important if tenderness is confined to right iliac fossa. If CT scan is not accessible, combination of neutrophil leukocytosis and ultrasound findings in a patient having tenderness in right iliac fossa give high probability for diagnosis of acute appendicitis. Good clinical acumen with close observation is necessary for early diagnosis and surgical intervention.

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Ethical Approval

Our institution does not require ethical approval for reporting cases.

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Informed Consent

The informed consent for publication in this article was obtained from a patient.

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