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COVID-19-associated pancytopenia and typhlitis

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ABSTRACT

Neutropenic enterocolitis is also known as typhlitis, is characterized by severe inflammation in the bowel loops. It is often seen in immunosuppressed patients, and it has high morbidity and mortality. Although the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) primarily affects the respiratory system and causes COVID-19 (Coronavirus Disease 2019), it may affect hematopoietic and gastrointestinal systems. Herein, we present a rare case of COVID-19-associated pancytopenia and typhlitis in a 60-year-old female who presented with abdominal pain. Contrast-enhanced abdominal computed tomography (CT) demonstrated the bowel wall thickening in the cecum and ascending colon compatible with enterocolitis. Moreover, the chest CT showed bilateral, peripheral, and multifocal ground-glass opacities, consistent with COVID-19 pneumonia. We also aimed to emphasize the laboratory, clinical, and CT findings of the patient.

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1. Introduction

Neutropenic enterocolitis, also known as typhlitis, is a rare but fatal complication of neutropenia. It is characterized by severe inflammation in the intestines, especially in the cecum ascending colon [1]. Typhlitis is often seen in patients with a severely compromised immune system due to aplastic anemia, hematological malignancy, solid organ transplantation, or patients receiving high-dose chemotherapy. It has a high morbidity and mortality rate [2,3]. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes COVID-19 (Coronavirus Disease 2019) and primarily affects the respiratory system [4]. Still, it has been shown that it may affect other systems, such as the hematopoietic system, and may cause lymphopenia, neutropenia, and rarely pancytopenia [5,6]. Moreover, reports of gastrointestinal system involvement in COVID-19 patients are rapidly increasing. Recently, Rehman and colleagues [7] reported a case of COVID-19 and neutropenic enterocolitis in an immunosuppressed patient with esophageal adenocarcinoma. Herein, we aimed to present clinical and radiological findings of a rare patient, who was not previously immunosuppressed, with COVID-19-associated pancytopenia and typhlitis.

2. Case report

A 60-year-old woman was admitted to the emergency department with complaints of abdominal pain, nausea, diarrhea, fatigue, and red blood in the stool, which were present for two days. The patient had a history of diabetes mellitus for 11 years, and she had been using oral antidiabetics (metformin and sitagliptin). Physical examination revealed tenderness in the right lower quadrant and bloody stool on rectal examination. The body temperature of the patient was found to be 37.1 degrees Celsius. One month ago, the patients' laboratory findings were within normal limits except for mild anemia (hemoglobin; 9.9 mg/dL, normal range; 11–14 mg/dL). Besides, the colonoscopy examination performed for screening two months ago was unremarkable. The laboratory test results in the current admission showed elevated c-reactive protein (286 mg/L, normal range; 0–5 mg/L), lactate dehydrogenase (304 U/L, normal range; 135–215 U/L) levels, and pancytopenia. The hemoglobin value was 7.8 mg/dL (normal range; 11–14 mg/dL), white blood cell count (0.27 K/uL; normal value, 4–10 K/uL), neutrophil count (0.01 K/uL; normal value, 4–10 K/uL), and platelet (15 K/uL, normal range; 150–410 K/uL). Other laboratory test results, including creatinine and liver function test results, were within normal limits.

Contrast-enhanced abdominal computed tomography (CT) was obtained with a suspicion of acute abdomen. Abdominal CT showed bowel wall thickening in the cecum and ascending colon and increased mucosal contrast enhancement in these segments. There were apparent pericecal fat stranding, mild abdominal free fluid, and multiple lymph nodes in the pericecal area (Fig. 1). The superior and inferior mesenteric arteries and veins were patent, and no thrombus was detected on CT. Moreover, CT sections passing through the lung bases showed peripheral, multifocal, patchy ground-glass opacities (GGO) in both lungs, highly suspicious of COVID-19 pneumonia during the COVID-19 pandemic. Then, Chest CT was obtained without intravenous contrast medium, and CT demonstrated that the GGO areas were widely distributed in both lungs (Fig. 2). The patient was accepted as typhlitis (neutropenic enterocolitis) with clinical and imaging findings, broad-

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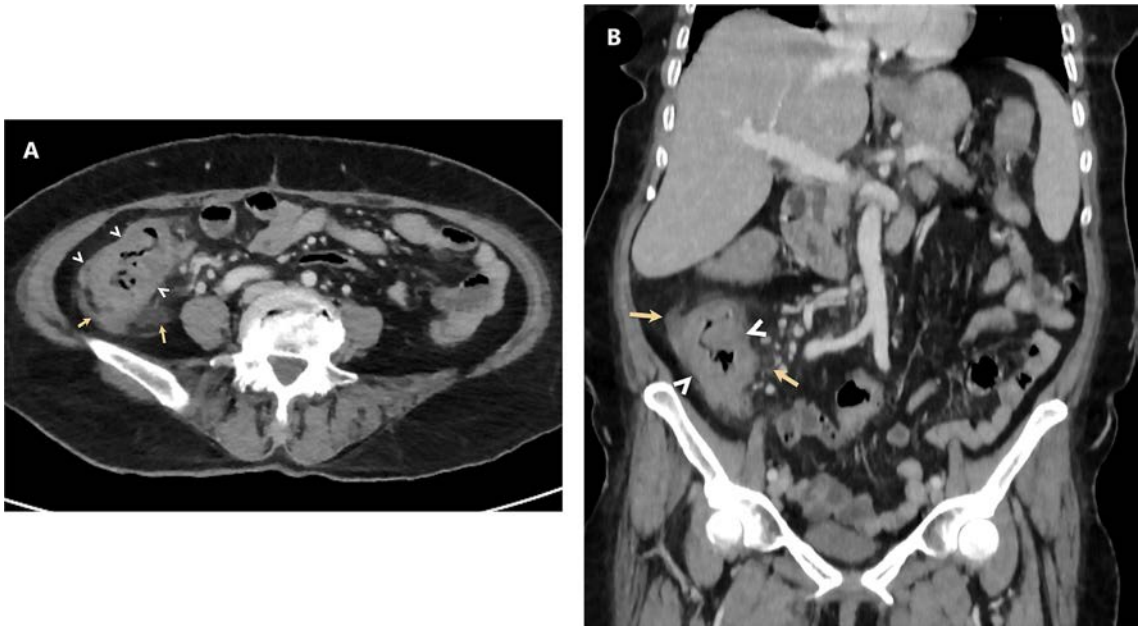

Fig. 1. (A) Axial, (B) coronal reformatted abdominal CT images obtained 40 s after administration of 80 mL of intravenous iodinated contrast medium demonstrate apparent wall thickening in the cecum and ascending colon (arrowheads) with pericecal fat stranding (arrows).

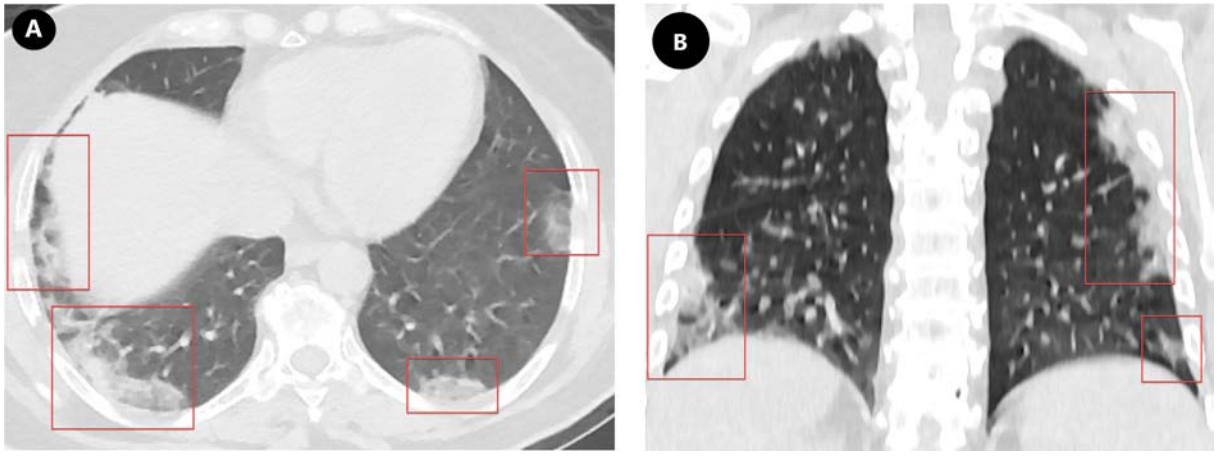

Fig. 2. (A) Axial, (B) coronal reformatted CT images of the chest obtained without administrating contrast medium show peripheral, multifocal, and patchy ground-glass opacities in both lungs (red rectangles).

spectrum antibiotic therapy (intravenous meropenem 3 g/day, metronidazole 2 mg/day, and teicoplanin 800 mg/day) was initiated. A few hours after the CT exam, the patient's general condition deteriorated, and hypoxia, hypercarbia was detected in the arterial blood gas. No malignant cells were observed in the peripheral smear, and in the serum protein electrophoresis, gammopathy was not detected. The oropharyngeal swab test was positive for COVID-19, and *Escherichia coli* was found in the blood culture obtained from the patient, and the patient died on the third day of hospitalization.

3. Discussion

Typhlitis (neutropenic enterocolitis) is a rare and life-threatening inflammatory disorder of the intestinal system and typically seen in immunocompromised patients. Patients usually present with right lower quadrant abdominal pain, mild fever, and severe neutropenia [1,2]. In the pathophysiology of the disease, mucosal damage is found with a superimposed bacterial infection. Pathological manifestations of typhlitis range from mucosal inflammation to transmural necrosis and may be further complicated by intestinal perforation or sepsis. Early diagnosis is of great importance because progression in typhlitis is associated with high morbidity and mortality [3-5]. Abdominal CT is beneficial in diagnosing typhlitis and can demonstrate circumferential bowel wall thickening and edema in the relevant bowel segments (usually in the cecum and ascending colon) and peri-intestinal fat-stranding. Moreover, bowel wall thickening is the most sensitive imaging finding and is sufficient to suggest typhlitis diagnosis in the correct clinical and laboratory findings [1,2,7]. Rehman et al. [7] recently reported an immunosuppressed patient with COVID-19 and typhlitis, whose general condition deteriorates rapidly. Similarly, the clinical condition deteriorated rapidly in the present case, and the patient was died. However, the present case had no history of malignancy or immunosuppressant therapy. According to the findings in these cases, necrotizing enterocolitis (typhlitis) progresses very rapidly in COVID-19 patients and causes

mortality. Therefore, early recognition of these patients is of great importance. Typhlitis is treated conservatively with broad-spectrum antibiotics and parenteral nutrition. In case of failure of conservative treatment or the presence of complications such as bowel perforation, surgery can be performed [7,8].

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes COVID-19 (Coronavirus Disease 2019) and primarily affects the respiratory system [4]. However, it has been shown that it may affect many other systems, such as the hematopoietic system, and may cause lymphopenia, neutropenia, and rarely pancytopenia—only a few cases in the English literature report pancytopenia associated with COVID-19 [5,6]. In the present case, while the previous month's laboratory values were within normal limits, sudden onset pancytopenia was likely caused by bone marrow suppression and probably associated with SARS-CoV-2 infection, as the patient had no evidence of malignancy or use of immunosuppressive drugs.

In a recent meta-analysis of 4234 COVID-19 patients, it has been reported that 17.6% of COVID-19 patients have gastrointestinal system symptoms at initial admission [9]. The most frequently reported imaging finding in COVID-19 patients with gastrointestinal involvement is thickening and hyperemia in the intestinal wall. Moreover, pneumatosis intestinalis, bowel perforation, intussusception, and portal venous gas has been rarely demonstrated [9]. Carvalho and colleagues [10] reported a 71-years-old female patient with COVID-19 and hemorrhagic colitis. On abdominal CT, they found bowel wall thickening in the ascending, transverse, descending, and sigmoid colon [10]. Hemorrhagic colitis should be considered in the differential diagnosis in non-neutropenic COVID-19 patients with long segment bowel wall thickening.

In conclusion, the present case has demonstrated the association of COVID-19 pneumonia, pancytopenia, and typhlitis. The pancytopenia possibly occurred due to bone marrow suppression with SARS-CoV-2 infection, and CT findings are useful in diagnosing both COVID-19 pneumonia and typhlitis. Since the early diagnosis of gastrointestinal involvement of SARS-CoV-2 is of great importance, emergency physicians should be aware of this entity during the pandemic period in patients presenting with gastrointestinal symptoms.

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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.

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