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CASE REPORT

Painless neutropenic enterocolitis in a patient undergoing chemotherapy

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ABSTRACT

Case Description A 60-year-old man developed painless neutropenic enterocolitis after induction chemotherapy for newly diagnosed acute myelogenous leukemia. The patient had recurrent fever while neutropenic, without experiencing abdominal pain or tenderness on physical examination. His diagnosis was delayed by the fact that he had no localizing symptoms.

Discussion Neutropenic enterocolitis is a common complication, generally occurring in patients who are severely neutropenic; the condition presents with fever and abdominal pain. No cases of painless neutropenic enterocolitis have yet been reported. Review of the literature shows that patients can develop this condition in the absence of fever and, sometimes, neutropenia. Furthermore, few comprehensive studies or reviews have investigated the utility of computed tomography imaging in identifying a source for abdominal pain in neutropenic patients with fever.

Summary Many potential causes of febrile neutropenia should be considered in chemotherapy patients.

Key Words Enterocolitis, neutropenia, fever, painless enterocolitis

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INTRODUCTION

Neutropenic enterocolitis (NE), commonly referred to as typhlitis, is a necrotizing inflammatory condition of the mucosal barrier of the intestine, often occurring in individuals with febrile neutropenia (FN). A diagnosis is suspected when a patient develops fever and abdominal pain with severe neutropenia. Neutropenic enterocolitis is a lethal condition requiring prompt diagnosis and treatment with intravenous antibiotics. Diagnostic imaging ensures accurate diagnosis of the condition. Delay in diagnosis and treatment can lead to significant morbidity and mortality in patients who are already immunocompromised. We report the first case of NE presenting with fever but without abdominal pain in a patient undergoing chemotherapy.

CASE DESCRIPTION

The only complaint presented by our patient, a 60-year-old man with acute myelogenous leukemia, was back pain, thought to be attributable to leukemic infiltration. His pain improved with initiation of induction chemotherapy, and no pain medication was required after that point. On admission, he was also diagnosed with hypertension, with systolic blood pressures ranging consistently between 150 mmHg and 160 mmHg. His blast count was 17% on peripheral blood smear. Bone marrow biopsy showed 90% blasts, with nearly absent tri-lineage hematopoiesis. He underwent induction therapy with 7 days of cytarabine and 3 days of daunorubicin.

On days 1–6 of chemotherapy, the patient reported feeling well, without any abnormal symptoms. By day 6 of treatment, complete blood counts indicated that he was severely neutropenic, with an absolute neutrophil count (ANC) of less than 0.5×10^9/L. The morning of day 6, the patient reported 2 episodes of melena, but denied any abdominal pain or tenderness on exam. He had no evidence of mucositis or odynophagia. Other than fatigue, he had no other complaints and was otherwise well-appearing.

Gastroenterology consultation was obtained, and given the neutropenia and resolution of melena, no further diagnostic evaluation was recommended at that time. Laboratory testing revealed an ANC of 0.2×10^9/L, hemoglobin 7.4 g/dL, and platelet count 10×10^9/L. Bleeding was speculated to be the result of an upper gastrointestinal source in the setting of thrombocytopenia. The patient received transfusions of platelets and packed red blood cells.

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The evening of day 6, the patient had a single recorded fever at 38.6°C, with blood pressure at 107/60 mmHg. Again, the patient reported no symptoms. He had a right arm peripherally-inserted central venous catheter that showed no erythema, a urinalysis without pyuria, chest radiography without evidence of airspace disease, and blood cultures that were negative for bacterial growth. Given his relative hypotension and fever, vancomycin and cefepime were started for treatment of FN.

After the patient's initial fever, he remained afebrile for 1 week. After 72 hours without bacterial growth from blood cultures, vancomycin was discontinued. On day 13 of treatment, the patient developed a temperature of 38.7°C, and labs revealed an ANC of 0.0×10^9/L. Blood cultures and urine cultures were again negative for bacterial growth. The patient had been tolerating his meals without nausea or vomiting. He had no abdominal pain, bloating, or distention, and no further episodes of melena. He had not requested medication for pain since the beginning of his hospital stay. Physical exam of the abdomen was negative for tenderness or guarding. Despite reinitiation of vancomycin, the patient continued to have fevers intermittently over the next 3 days. His antimicrobial coverage was expanded to include voriconazole, and consultation by the infectious disease team was obtained. QuantiFERON (Qiagen, Hilden, Germany), cryptococcal antigen, (1→3)-β-D-glucan, and galactomannan testing were negative.

Given the possibility of mucormycosis in the setting of a neutropenic patient with ongoing fevers, liposomal amphotericin B was started, and voriconazole was discontinued. Diagnostic imaging was performed to identify a source for the fevers, and computed tomography (CT) imaging of abdomen and pelvis showed marked inflammatory changes involving the cecum and terminal ileum, consistent with NE (Figure 1). On the day of the CT imaging, ANC was still noted to be 0×10^9/L. Cefepime was changed to piperacillin–tazobactam and liposomal amphotericin B was stopped. Intravenous antibiotics were continued until the patient's ANC exceeded 0.5×10^9/L for 48 hours, and after that time, treatment was transitioned to ciprofloxacin and metronidazole for a total of 14 days after count recovery.

FIGURE 1 Abdominal computed tomography image for the patient with neutropenic enterocolitis of the ileocecal junction. Significant pericolonic stranding surrounds the ileocecal junction, with bowel-wall edema characteristic of neutropenic enterocolitis.

DISCUSSION

Neutropenic enterocolitis is a gastrointestinal disease process affecting children and adults with severe neutropenia. Early recognition and early treatment are vital to preventing adverse outcomes. Historically, NE has been associated with the ileocecal junction; however, NE affecting other parts of the colon have been reported[1,2]. The pathophysiology of the condition is commonly thought to be multifactorial. Factors that have previously been theorized to lead to NE include exposure to cytotoxic chemotherapy agents, involvement of the anatomic site with malignancy, bacterial translocation, and mucosal ischemia from poorly vascularized parts of the intestine[3]. All those characteristics can be found in fragile immunocompromised individuals, putting them at risk for NE.

Neutropenic enterocolitis is a disease process commonly considered when a patient develops FN. The clinical hallmarks of NE include fever and abdominal pain, but abdominal distention, bloating, and diarrhea have also been reported as associated signs and symptoms[4,5]. Neutropenic enterocolitis is most commonly reported to affect patients undergoing chemotherapy, but it has also been seen in patients who develop neutropenia in other conditions such as chronic neutropenia and infection with HIV[6,7]. When NE is suspected, the diagnosis is made by CT imaging, which can show pericecal fluid and bowel wall thickening[3]. Some authors have attempted to provide diagnostic criteria for early diagnosis and intervention in immunocompromised patients. Gorschlüter *et al.*[8] suggested utilizing the classic presentation of fever and abdominal pain, but also including the radiographic finding of bowel-wall thickening for diagnosis in the neutropenic patient[8]. Without abdominal pain, it is challenging to localize an intra-abdominal infectious source in a neutropenic patient with fever. The symptoms in our patient created such a conundrum, leading to a delayed diagnosis of NE.

A review of the literature showed no prior cases of individuals presenting without abdominal pain or tenderness; however, atypical symptoms and scenarios have been documented. In one case of NE, a 4-year-old girl with a diagnosis of acute lymphoblastic leukemia undergoing chemotherapy reported abdominal distention and pain, but did not report fever[9]. The patient was severely neutropenic at the time of discovery. Early in her hospitalization, she developed a fever that resolved several days before her diagnosis and the presentation of abdominal symptoms. Abdominal radiographs showed free air in the intraperitoneal cavity, and the patient required intestinal resection and repair for intestinal perforation. In a separate case, a 72-year-old man with fever, nausea, vomiting, and right lower quadrant abdominal pain was found to have bowel-wall thickening of the cecum, as well

as pericolonic inflammatory stranding, all suggestive of NE, but in a non-neutropenic patient[10]. That patient had no evidence of acquired immunodeficiency or malignancy on laboratory reports. Those findings suggest that, although necrotic bowel-wall thickening occurs mostly in patients in an immunocompromised state, it can also sometimes occur in patients without that risk factor.

Imaging by CT can play a useful role in managing patients with persistent FN. One study showed that, compared with standard chest radiography, CT was able to diagnose approximately twice the number of pneumonia cases[11]. Despite the common use of CT imaging in FN patients, only one study in pediatric oncology patients with FN reviewed the utility of CT scans of various parts of the body. Interestingly, abnormal results were more commonly seen with CT of the chest than with CT of the abdomen (47% vs. 18%)[12]. The authors of the latter work also found that CT imaging of the abdomen was negative in 93% of their asymptomatic patients[12]. However, because of the retrospective nature of the analysis, it is difficult to determine how many asymptomatic FN patients were examined by CT. The use of abdominal CT in the present case of painless NE suggests that, in situations of recurrent FN without identifiable cause, CT might help in identifying a source of infection. Future studies are required to look at this specific question.

CONCLUSIONS

Early recognition of NE is vital to prompt treatment and reduction of morbidity and mortality. Review of the literature shows that not all patients with NE will present with the classical features of fever and abdominal pain. This case of painless NE illustrates the need to generate a broad diagnostic differential, and to consider CT of the abdomen in asymptomatic FN patients.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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