Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

Neutropenic enterocolitis in aplastic anemia – a case report from Nepal

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Introduction and importance: Neutropenic enterocolitis (NE) is a life-threatening necrotizing enterocolitis, particularly in neutropenic patients.

Case presentation: We are presenting a case of a 22-year-old male who presented chief complaints of abdominal pain, reddish black stool, abdominal distention, and low-grade fever with laboratory and bone marrow findings suggestive of aplastic anemia. Computed tomography scan of the abdomen and pelvis with contrast was used to establish the diagnosis of necrotizing enterocolitis. Nonsurgical management including broad-spectrum antimicrobials, bowel rest, nasogastric suction, fluid and nutritional support, and blood product support, helped this patient to recover.

Clinical discussion: NE is a life-threatening inflammatory condition of the small and large intestines. Typical symptoms of NE include diffuse abdominal pain, fever, and watery or bloody diarrhea. Diagnosis of NE is done by clinical and imaging findings. Management of the primary disease is important to improve the ultimate survival of the disease.

Conclusion: Early identification and management of neutropenic enterocolitis help to reduce mortality.

Introduction

Neutropenic enterocolitis (NE) is a life-threatening, necrotizing enterocolitis, particularly in neutropenic patients. NE is a clinical entity that was first described in leukemic pediatric patients. It has been reported in individuals with hematologic malignancies such as leukemia, multiple myeloma, aplastic anemia, and myelodysplastic syndromes, as well as other immunosuppressive reasons like acquired immune deficiency syndrome (AIDS), solid tumor therapy, and organ transplantation. The pathophysiology of neutropenic enterocolitis is incompletely understood and likely involves a mix of elements, such as mucosal damage caused by cytotoxic medicines or other means, and significant neutropenia[1]. Gross and histologic studies can reveal gut wall thickening, discrete or confluent ulcers, mucosal loss, intramural edema, bleeding, necrosis, perforation, and depletion of inflammatory cells[2]. Polymicrobial infections are common[2]. The true incidence of neutropenic enterocolitis is unknown. The frequency of neutropenic enterocolitis appears to be increasing with the widespread use of cytotoxic agents. NE should be evaluated in the differential diagnosis of any severely neutropenic patient (absolute neutrophil count 500 cells/μl) with fever and abdominal pain[3]. The diagnosis of neutropenic enterocolitis is mainly made by detecting the distinctive computed tomography (CT) findings in neutropenic patients who arrive with fever and stomach pain[4]. Nonsurgical therapy with bowel rest, nasogastric suction, intravenous (i.v.) fluids, nutritional support, blood product support, and broad-spectrum antibiotics is a fair initial strategy in patients without complications (i.e. peritonitis, perforation, or serious bleeding)[5–7]. Surgery is normally avoided in patients with neutropenia and thrombocytopenia. Early identification and management of this condition helps to reduce mortality.

HIGHLIGHTS

- Awareness about neutropenic enterocolitis (NE).
- This study highlights the prevalence of the condition and its presentation.
- Management of NE.
- This study also highlights the importance of educational awareness about the disease and the importance of prompt diagnosis in further management.

Case presentation

A 22-year-old male presented with a 1-week history of mild-grade fever, abdominal pain, and loose, watery stools. On examination, vital signs were within normal limits, and there were no abnormal findings on physical examination. Laboratory investigations revealed a low platelet count of 55 000 cells/μl, a total leukocyte count of 1900 cells/μl (neutrophils 24% and lymphocytes 80%), and a hemoglobin of 9.6 g/dl. Serum iron profile, reticulocyte count, and vitamin B12 levels were within normal range. On further investigation, a peripheral blood smear showed 8%

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Annals of Medicine & Surgery (2023) 85:5728–5730

Received 21 June 2023; Accepted 7 September 2023

Published online 20 September 2023

http://dx.doi.org/10.1097/MS9.0000000000001322

atypical blast cells with normocytic normochromic anemia with leukopenia and thrombocytopenia. The occult blood test came out to be positive with subsequent normal ultrasonography findings. No active interventions were done during this time, and the patient was admitted for further workup. Thereafter, bone marrow aspiration and biopsy were performed, which revealed hypocellular marrow less than 10% for his age, with adipocytes replacing most of the marrow spaces. Parvovirus immunoglobulin M (IgM) positivity was highly consistent with recent infection. During his hospital stay, the patient complained of abdominal pain, reddish black stool, abdominal distention, and low-grade fever of 100°F, which was relieved by antipyretics. On abdominal examination, guarding and tenderness were present in the right iliac fossa, along with rigidity. Numerous petechiae were present on both upper and lower limbs. Initially, vital signs were normal; however, in a few days, there was a fall in the patient's blood pressure to 80/60 mmHg. A fluid resuscitation was done along with noradrenaline infusion, which increased the blood pressure to 110/80 mmHg. CT scan of the abdomen and pelvis with contrast was done, which showed diffuse bowel wall thickening suggestive of inflammatory changes in the terminal ileum, cecum, and ascending colon. A diagnosis of neutropenic enterocolitis was established based on clinical evidence and CT scan findings. After his diagnosis, the patient was put on a bowel rest. A nasogastric tube was placed as well, which relieved his abdominal distention. His lowest reported total whole blood count (WBC) was 600 cells/μl, in which neutrophils were 4 cells/μl during the hospital stay. Also, his platelets dropped up to 10 000 cells/μl of blood and hemoglobin 6.5 g/dl. Regular blood product transfusion was done to increase his blood counts during his hospital stay. Total parenteral nutrition was also initiated to maintain his daily caloric requirement. Following a blood culture and sensitivity report, the patient was started on broad-spectrum antibiotic therapy with piperacillin–tazobactam, cefepime, and metronidazole for 14 days. Despite the start of antibiotics, the patient still had recurrent episodes of fever, so Voriconazole, Bactrim, and Acyclovir therapy were started with a good response. Additional therapy with eltrombopag, filgrastim, and cyclosporine was also initiated. The symptoms subsequently reduced as the neutrophil count increased. The patient was thereafter transferred to a hematology isolation unit before being referred to a specialized institution for bone marrow transplantation. At the time of the follow-up, the patient had received bone marrow transplantation and was clinically better. He was discharged with regular follow-up appointments at the higher center.

Case discussion

NE, also known as necrotizing enteropathy, typhlitis, ileocecal syndrome, or cecitis, is a mainly cecal disease that has been observed in immunosuppressed cases. As the name suggests, it is a life-threatening inflammatory condition of the small and large intestine seen in conditions with decreased neutrophil count[1]. NE is a clinical entity that was first described in leukemic pediatric patients. It has been reported in individuals with hematologic malignancies such as leukemia, lymphoma, multiple myeloma, aplastic anemia, and myelodysplastic syndromes, as well as other immunosuppressive reasons like AIDS, solid tumor therapy, and organ transplantation[3,8]. The true incidence of NE is unknown. One systematic review published in 2005 suggested a pooled incidence of 5.6% in hospitalized adults with hematological malignancies, chemotherapy for solid tumors, and aplastic anemia[3,7,9]. The reported mortality also varies with rates as high as 50%. The pathogenesis of neutropenic enterocolitis is incompletely understood and likely involves a combination of factors, including mucosal injury by cytotoxic drugs or other means, profound neutropenia, and impaired host defense against invasion by microorganisms. The microbial infection leads to necrosis of various layers of the bowel wall[1,4]. The cecum is usually affected, and the process often extends to ascending colon and terminal ileum. The predominant cecal location is due to its distensibility and limited blood supply relative to the rest of the colon. Any severely neutropenic patient (absolute neutrophil count 500 cells/μl) presenting with fever and abdominal pain, typically in the right lower quadrant, has to have neutropenic enterocolitis taken into account in the differential diagnosis[10]. Additional signs and symptoms may include abdominal distension, cramps, tenderness, nausea, vomiting, watery or bloody diarrhea, and frank hematochezia[3,11]. Although paralytic ileus can occur, it is unusual. Peritoneal signs and shock suggest the possibility of bowel wall perforation. Stomatitis and pharyngitis may be present, indicating the existence of extensive mucositis. Sepsis is the leading cause of mortality related to bacterial translocation of the colonic wall, which can progress to multisystem organ failure. Common pathogens of NE are gram-negative bacilli, gram-positive cocci, anaerobes, and Candida (Table 1).

Diagnosis of NE is done by CT, which can show features of bowel wall thickening, mesenteric stranding, bowel dilatation, mucosal enhancement, and pneumatosis[4]. Both oral and i.v. contrast should be given when feasible. However, oral contrast is sometimes not tolerated in patients with severe gastrointestinal tract symptoms, and i.v. contrast is typically avoided in patients with renal insufficiency. Plain X-ray films, while nonspecific, can be used to detect free air. Colonoscopy is a relative contraindication due to the risk of cecal perforation. A high discordance rate exists between clinical and diagnostic findings of NE, which might also be due to the fact that endoscopic examination and surgical resection might not be possible in all cases. Some important differential diagnoses of NE are nonspecific chronic and acute colitis, ischemic colitis, graft-versus-host disease-associated colitis, CMV (cytomegalovirus) colitis, malignancy relapse, drug-induced

Table 1

Diagnostic criteria for neutropenic enterocolitis[a]

Type of criteria	Finding	Remarks
Major	Neutropenia	ANC $<500 \times 10^9$ cells/l
	Bowel wall thickening on CT exam or US exam	> 4 mm (transverse scan) thickening in any segment of the bowel for at least 30 mm length (longitudinal scan)
	Fever[b]	> 38.3 (oral or rectal)
Minor/nonspecific	Abdominal pain	> 3 on a visual analog scale (1–10)
	Abdominal distension	
	Abdominal cramping	
	diarrhea	
	Lower GI bleeding	

ANC, absolute neutrophil count; CT, computerized tomography; GI, gastrointestinal; US, ultrasound.
[a]Adapted from Nesher and Rolston[8].
[b]Fever may be absent in a minority of patients, and some may even be hypothermic – Major criteria.

colitis, and acute appendicitis[12]. NE is mostly underdiagnosed with diagnosis made in postmortem examination. Prompt diagnosis is the key to management and a decrease in the mortality rate of NE. Therefore, NE should be considered in cases of immunosuppressants who present with above-mentioned signs and symptoms. Management of the primary disease is important to improve the ultimate survival of the disease. A reasonable initial strategy is nonsurgical management with bowel rest, nasogastric suction, i.v. fluids, nutritional support, blood product support (packed red blood cells and fresh frozen plasma as needed), and broad-spectrum antibiotics in patients without complications (such as peritonitis, perforation, or severe bleeding)[5–7]. The recommended antibiotic regimen includes piperacillin–tazobactam and cefepime plus metronidazole for 14 days[5,6]. Surgery is normally avoided in patients with neutropenia and thrombocytopenia; however, in cases of free perforation or other conditions that cannot be managed medically (such as prolonged bleeding despite correction of coagulopathy and cytopenias), surgical intervention is advised[6]. As this is an article of a case report of a single patient, it may not be generalizable to other cases of neutropenic enterocolitis.

Conclusion

NE is a life-threatening inflammatory condition of the intestine seen in conditions with a decreased neutrophil count. The frequency of neutropenic enterocolitis appears to be increasing with the widespread use of cytotoxic agents. It is usually diagnosed by detection of the characteristic CT findings in neutropenic patients presenting with fever ,abdominal pain, and tenderness. Prompt diagnosis of the condition is key to management, and management of the primary disease is important to improve the ultimate survival of the disease.

Ethical approval

Ethics approval is not required for case reports in our institutes. The authors of this case report are from Bir Hospital, Manipal Teaching Hospital, and Nepalese Army Hospital, Nepal. The consent of this case report has been taken from the patient in their native language, all the conditions and the process have been explained to the patient properly and also explained their authority to decline and withdraw from the study at any given moment.

Patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Source of funding

The authors did not receive any funds to conduct the study.

Author contribution

J.S.: study concept, editor, writing the paper, and design; A.A.: study concept, writing the paper, and design; A.B.: history taking and consent from the patients; D.G.: case presentation and reviewing the paper; S.S.: editing and reviewing the paper; A.M.: data collection and editing.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

Research registration unique identifying number (UIN)

Not applicable.

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Provenance and peer review

The paper was not invited.

Data availability statement

Data sharing is not applicable to this article.

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