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# Neutropenic Enterocolitis Following Autologous Stem Cell Transplantation: A Compelling Clinical Case Report Written With the Assistance of ChatGPT

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#### **Abstract**

Neutropenic enterocolitis (NE) is a rare and life-threatening condition that typically occurs in patients with hematologic malignancies undergoing intensive chemotherapy, radiation therapy, or bone marrow transplant regimens, predisposing them to profound neutropenia. NE can have a nonspecific clinical presentation and mimic other gastrointestinal disorders such as appendicitis, diverticulitis, or inflammatory bowel disease but is associated with very high morbidity and mortality if not diagnosed and treated promptly. We present the case of a middle-aged female with a recent diagnosis of follicular lymphoma who developed neutropenic enterocolitis after undergoing induction chemotherapy for an autologous stem cell transplant (ASCT). In this article, we provide a literature review of neutropenic enterocolitis and highlight the importance of a prompt diagnosis and management, given its high mortality rate.

Categories: Internal Medicine, Radiology, Gastroenterology

**Keywords:** post-autologous stem cell transplantation enterocolitis, enterocolitis, artificial intelligence, neutropenic enterocolitis, chatgpt

## Introduction

Neutropenic enterocolitis (NE), also called typhlitis, poses a severe threat to individuals with compromised immune systems. This life-threatening condition is distinguished by the extensive, circumferential thickening of the proximal colon, primarily impacting the cecum. The precise pathophysiological mechanisms driving NE are still not comprehensively understood, but it is thought to stem from damage to the intestinal mucosa caused by cytotoxic chemotherapy, radiation, or leukemic infiltration [1]. Left untreated, the mortality rate of NE ranges from 50% to 100% [2,3], underscoring the urgent need for a prompt, accurate diagnosis and management. To further elucidate the clinical features of NE in a patient population, we present a compelling case of a middle-aged female who developed NE following induction chemotherapy for an autologous stem cell transplant (ASCT).

#### **Case Presentation**

A 53-year-old female with a history of follicular lymphoma was admitted for an ASCT. This patient was initially diagnosed with follicular lymphoma a year before admission when she presented with a right groin mass. Imaging revealed multiple lymph nodes in the right common iliac, external iliac, and inguinal region distribution. An excisional biopsy confirmed low-grade lymphoma with positive CD10 of germinal B-cell origin, and the patient achieved complete disease remission following three cycles of bendamustine and rituximab. However, several years later, a surveillance positron emission tomography-computed tomography (PET-CT) scan indicated disease progression in the right calf area, and a tibia bone biopsy confirmed lymphoma recurrence. The patient received three cycles of rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP), resulting in complete remission.

During her ASCT preparative regimen with carmustine, etoposide, cytarabine, and melphalan (BEAM), the patient experienced severe complications. On the fifth day of hospitalization, she became hypotensive and febrile and developed 6-8 watery bowel movements. Her condition rapidly deteriorated, and she was transferred to the intensive care unit, where she was treated with vasopressors and broad-spectrum antibiotics for febrile neutropenia. Stool studies were negative for infectious agents. On abdominal X-ray, the patient was found to have distended small and large bowels (Figure 1), and an abdominal/pelvic computed tomography (CT) scan revealed pneumatosis coli with mesenteric venous and intrahepatic portal veins gas, indicative of colonic necrosis and severe nonspecific adynamic ileus (Figure 2A-2B and Figure 3A-3B). Laboratory results revealed pancytopenia with a WBC count of  $<0.1 \times 10^9$ /L (absolute neutrophil count:  $0.3 \times 10^9$ /L), indicating severe neutropenia.

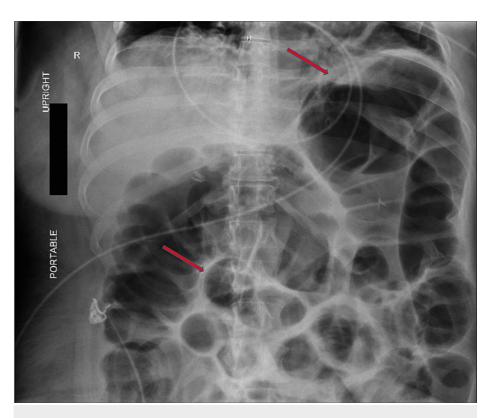


FIGURE 1: Abdominal X-ray demonstrating small and large bowel distention (red arrows).

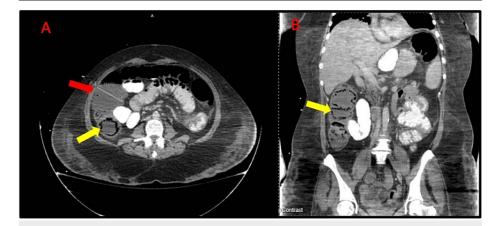


FIGURE 2: A: Initial CT (axial view) of the abdomen demonstrating pneumatosis coli (yellow arrow) and colonic distension (red arrow). B: CT scan (coronal view) showing pneumatosis coli of the ascending colon (yellow arrow).

CT: computed tomography

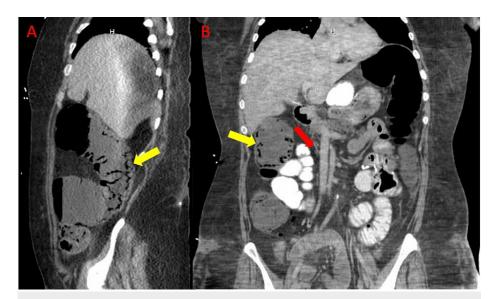


FIGURE 3: A: CT (sagittal view) redemonstrating pneumatosis coli of the ascending colon (yellow arrow). B: CT (coronal view) demonstrating gas in the mesenteric veins (red arrow).

CT: computed tomography

The patient was treated with broad-spectrum antibiotics, antifungals, and antivirals, and repeat imaging showed a near-complete resolution of pneumatosis coli of the right colon (Figure 4). Our patient recovered quickly due to prompt diagnosis and treatment; therefore, no surgical intervention had to be carried out.

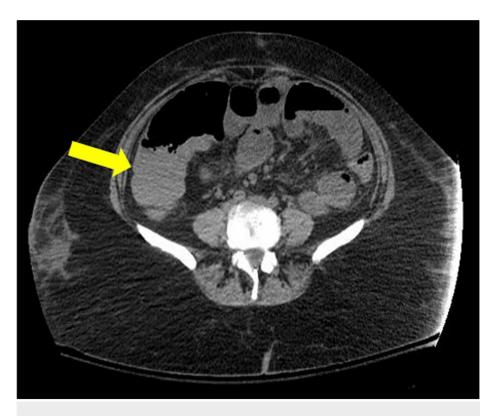


FIGURE 4: Posttreatment follow-up abdominal CT scan (axial view) that demonstrates resolution of pneumatosis coli with persistent distended bowel loops (yellow arrow).

CT: computed tomography

#### **Discussion**

NE is a rare but potentially life-threatening condition that occurs most commonly in neutropenic patients. The prevalence of NE varies among different patient populations, with reports ranging from 0.8% to 26% [4]. Gorschlüter et al. reported a 5.3% pooled incidence rate of NE in adults hospitalized for the treatment of hematologic malignancies or solid tumors, although noting this figure to be an underestimate [4]. NE is more common in patients with hematologic malignancies, particularly those with acute myeloid leukemia and non-Hodgkin lymphoma who receive intensive chemotherapy regimens [5]. However, NE has been reported in association with several chemotherapy regimens, including those that contain cytarabine, anthracyclines, and platinum agents [2]. NE may also occur in patients receiving radiation therapy or immunosuppressive therapy. The incidence of NE is also higher in patients with prolonged neutropenia, as well as those with additional risk factors such as hypotension, sepsis, and the use of antibiotics.

NE has also been reported in patients with other underlying conditions that cause neutropenia and immune suppression, such as severe infections, autoimmune diseases, and bone marrow failure syndromes [5]. Additionally, NE has been observed in patients receiving immunosuppressive therapy for organ transplantation and those with congenital neutropenia or cyclic neutropenia. The exact mechanism by which NE develops in these conditions is not well understood, but it is thought to result from injury to the intestinal mucosa due to a combination of factors such as cytotoxic agents, immunosuppression, and altered gut flora [5]. The clinical presentation and management of NE may differ depending on the underlying condition and the severity of the neutropenia.

The diagnosis of NE can be challenging, as symptoms can be nonspecific and overlap with other common complications of chemotherapy, such as infectious diarrhea and neutropenic fever. However, early recognition of NE is critical, as prompt diagnosis and treatment can significantly improve outcomes [1]. Conservative management, which includes bowel rest, parenteral nutrition, and broad-spectrum antibiotics, is the standard of care for most patients with NE and has been shown to improve outcomes and reduce the need for surgery. In addition to bowel rest and broad-spectrum antibiotics, supportive care may include aggressive fluid resuscitation, blood product transfusions, and close monitoring for complications such as perforation or sepsis.

Surgical intervention in NE is not always required and should be considered a last resort in patients who do

not respond to conservative management or develop complications such as perforation, abscess, or uncontrolled bleeding. The decision to perform surgery is based on the clinical presentation, severity of symptoms, and imaging findings. In a study of 329 patients with NE, conservative management was successful in 69% of cases, and only 31% required surgery [2]. Another study reported a success rate of 80% for conservative management, with surgery needed in 20% of cases [6].

Untreated NE has a high mortality rate ranging from 50% to 100%, which is why early recognition and management are essential for improving patient outcomes [7,8]. With appropriate treatment, the mortality rate decreases to 30%-50% [7,8]. Mortality is often attributed to complications such as sepsis, bowel perforation, and multi-organ failure. The mortality risk is higher in patients with more severe disease, longer duration of neutropenia, older age, and comorbidities. The use of prophylactic antibiotics in neutropenic patients with cancer has also been shown to reduce the incidence of NE and the need for surgical intervention. However, the role of prophylactic antibiotics in patients undergoing autologous stem cell transplant is still controversial and requires further study.

Given the high mortality rate of NE, physicians caring for neutropenic patients should have a low threshold for considering NE in the differential diagnosis of gastrointestinal symptoms, particularly in patients receiving intensive chemotherapy or ASCT. In our patient's case, NE was diagnosed based on imaging findings and clinical presentation. The successful management of NE in our patients highlights the importance of early diagnosis and prompt, targeted interventions in improving clinical outcomes in this challenging population.

Below are screenshots (Figure 5 and Figure 6) showing the utilization of ChatGPT to produce comprehensive insights into the disease and to enhance the language and structure of the existing case report's paragraphs.

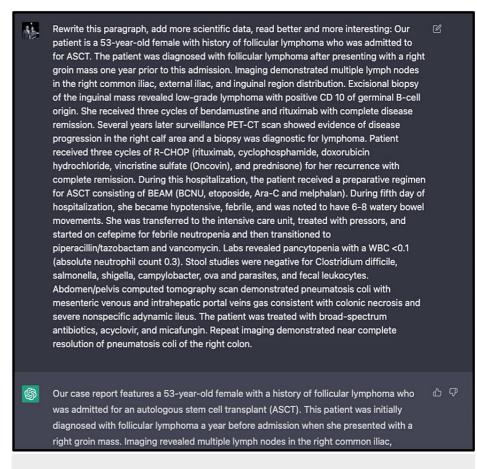


FIGURE 5: Screenshot #1 showing how ChatGPT is used in writing the case report.



Add more information to this paragraph from scientific papers, discussing neutropenic enterocolitis, typical presentations of neutropenic enterocolitis, the prevalence of the disease, and frequency of neutropenic enterocolitis in patients receiving autologous stem cells transplant: This case highlights the importance of having a broad differential diagnosis when assessing a patient with profound neutropenia and gastrointestinal symptoms. The current standard of care in treating NE consists of early diagnosis, bowel rest, broad-spectrum antibiotics, or if complications develop, surgical intervention. We believe physicians caring for patients receiving chemo/immunotherapy agents should have low threshold for NE as prompt diagnosis and

management are key to a better outcome especially given the high mortality associated with NE.



Neutropenic enterocolitis (NE), also known as typhlitis, is a rare but potentially fatal condition that occurs in neutropenic patients, particularly those undergoing intensive chemotherapy or hematopoietic stem cell transplantation. It is estimated to occur in 2-15% of patients undergoing autologous stem cell transplant (ASCT) and is associated with a mortality rate of 50-100% if left untreated. NE typically presents with fever, abdominal pain, and watery diarrhea, and is characterized by diffuse circumferential mural thickening of the proximal colon, primarily in the cecum. Other reported presentations include ileus, peritoneal signs, and shock. The pathophysiology of NE is not well understood, but it is believed to result from mucosal injury caused by cytotoxic chemotherapy, radiation, or leukemic infiltration. The prevalence of NE in ASCT recipients varies widely in the literature, ranging from 0.9% to 9.8%, with higher rates reported in patients undergoing multiple courses of chemotherapy. The diagnosis of NE can be challenging, as symptoms can be nonspecific and overlap with other common complications of chemotherapy, such as infectious diarrhea and neutropenic fever. However, early recognition of NE is critical, as prompt diagnosis and treatment can significantly improve outcomes. In addition to bowel rest and broad-spectrum antibiotics, supportive care may include aggressive fluid

FIGURE 6: Screenshot #2 showing how ChatGPT is used in writing the case report.

#### **Conclusions**

In conclusion, this case report highlights the challenges that can arise during ASCT for patients with a history of follicular lymphoma. The patient in this report developed hypotension, febrile neutropenia, and diarrhea, which was later confirmed with the diagnostic imaging to be NE and resolved following prompt and effective treatment. This case underscores the importance of close monitoring and prompt intervention for patients undergoing ASCT and the potential for serious complications related to febrile neutropenia and abdominal issues. This information is valuable for healthcare providers as they care for patients undergoing ASCT and strive to minimize the risk of complications. Further research is needed to determine the best strategies for preventing and managing these complications in patients undergoing ASCT.

# **Additional Information**

#### **Disclosures**

**Human subjects:** Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

#### **Acknowledgements**

We would like to extend our gratitude to ChatGPT and its creators, as this endeavor would not have been possible without its collaboration. This platform allowed us to write a comprehensive literature review of the latest information on neutropenic enterocolitis. ChatGPT was used predominately to help consolidate the author's thoughts in writing this case report to produce a report that has comprehensive insights on the

disease and to enhance the language and structure of the existing case report's paragraphs. Using preexisting information written by authors, questions were phrased and rephrased until the output from AI was felt to have addressed the author's question appropriately. Despite the efficiency, vast access to internet resources, and the ability to produce comprehensive writing, ChatGPT is limited in providing sources for its statements. ChatGPT could not provide references for its writing, which is reflected in our discussion section. We hope that with future iterations of ChatGPT, this drawback to academic research writing could be addressed.

#### References

- Belmoufid N, Daghri S, Driouich S, Nadi A, Bouanani N: Neutropenic enterocolitis as a complication of autologous stem cell transplant in patients with multiple myeloma: a case series. Cureus. 2022, 14:e24475. 10.7759/cureus.24475
- Machado NO: Neutropenic enterocolitis: a continuing medical and surgical challenge. N Am J Med Sci. 2010, 2:293-300.
- Xia R, Zhang X: Neutropenic enterocolitis: a clinico-pathological review. World J Gastrointest Pathophysiol. 2019, 10:36-41. 10.4291/wjgp.v10.i3.36
- Gorschlüter M, Mey U, Strehl J, et al.: Neutropenic enterocolitis in adults: systematic analysis of evidence quality. Eur J Haematol. 2005, 75:1-13. 10.1111/j.1600-0609.2005.00442.x
- Nesher L, Rolston KV: Neutropenic enterocolitis, a growing concern in the era of widespread use of aggressive chemotherapy. Clin Infect Dis. 2013, 56:711-7. 10.1093/cid/cis998
- Saillard C, Zafrani L, Darmon M, et al.: The prognostic impact of abdominal surgery in cancer patients with neutropenic enterocolitis: a systematic review and meta-analysis, on behalf the Groupe de Recherche en Réanimation Respiratoire du patient d'Onco-Hématologie (GRRR-OH). Ann Intensive Care. 2018, 8:47. 10.1186/s13613-018-0394-6
- Cartoni C, Dragoni F, Micozzi A, et al.: Neutropenic enterocolitis in patients with acute leukemia: prognostic significance of bowel wall thickening detected by ultrasonography. J Clin Oncol. 2001, 19:756-61. 10.1200/JCO.2001.19.3.756
- 8. Moran H, Yaniv I, Ashkenazi S, Schwartz M, Fisher S, Levy I: Risk factors for typhlitis in pediatric patients with cancer. J Pediatr Hematol Oncol. 2009, 31:630-4. 10.1097/MPH.0b013e3181b1ee28