The European Research Journal
http://www.eurj.org
Case Report
e-ISSN: 2149-3189
DOI: 10.18621/eurj.370328

Neutropenic enterocolitis and colonic perforation in a patient with breast carcinoma treated with taxane-based chemotherapy: a case report and review of the literature

Aslıhan Demirel[1], Selçuk Kihtir[2], Gürkan Geceer[3], Safiye Koçulu[1], Esin Çevik[1]

[1]Department of Infectious Diseases and Clinical Microbiology, İstanbul Bilim University School of Medicine, İstanbul, Turkey
[2]Department of General Surgery, İstanbul Kadıköy Florence Nightingale Hospital, İstanbul, Turkey
[3]Department of Radiology, İstanbul Kadıköy Florence Nightingale Hospital, İstanbul, Turkey

;ABSTRACT

Neutropenic enterocolitis or typhlitis is one of the rare but high mortality acute complications of neutropenia that develops in immunosuppressed patients due to chemotherapy. It is a segmental cecal and ascending colon inflammation that can progress to necrosis and perforation. Although it is mostly observed in myelosuppressed and immunosuppressed patients, like those who have leukemia and lymphoma, it can also be observed in malignancies treated with myelosuppressive chemotherapy. It has been reported particularly in patients with solid tumors treated with taxane-based chemotherapy. In this article, a 40-year-old patient with invasive ductal breast carcinoma is presented, who was diagnosed with neutropenic enterocolitis and colonic perforation that developed 6 days after chemotherapy (Docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2). If neutropenic fever, abdominal pain, abdominal distension, and tenderness develops in a patient under taxane-based chemotherapy, neutropenic enterocolitis is a condition that must definitely be considered. It should be noted that it is possible to reduce mortality and morbidity by means of appropriate antibiotics and a timely surgical intervention.

Eur Res J 2018;4(3):231-234

Keywords: neutropenic enterocolitis, typhlitis, taxane-based chemotherapy

Introduction

Neutropenic enterocolitis (NE) or typhilitis is a serious complication of neutropenia characterized by segmental ulceration or inflammation with necrosis of ileum, caecum and ascending colon. It may be complicated with perforation and septicemia. It also appears as a complication of neutropenia that develops mostly in leukemia and lymphoma patients [1]. NE has also been identified in patients with solid tumors treated with new chemotherapeutic drugs and intensive immunosuppressive therapy [2]. It has been reported particularly in patients with solid tumors treated with taxane-based chemotherapy [3-8]. The clinical features consist of fever, watery diarrhea, and crampy abdominal pains, which are typical and not

Address for correspondence:
Aslıhan Demirel, MD., Assistant Professor, İstanbul Kadıköy Florence Nightingale Hospital, Department of Infectious Diseases, 34724 Kadıköy, İstanbul, Turkey.
E-mail: demirelaslihan@yahoo.com Phone and Fax: +90-216-4500303-3919
Received: December 23, 2017; Accepted: December 30, 2017; Published Online: January 5, 2018

specific to the disease. Reported mortality rate is 21% to 48%. When complications such as bleeding and perforation develop, surgical intervention should be applied without delay [1]. In this article, a case of breast cancer in which neutropenic enterocolitis and colonic perforation developed after docetaxel treatment, is presented.

Case Presentation

A 40-year-old female had undergone mastectomy two years ago, due to the diagnosis of ductal carcinoma in situ (DCIS), and then lesion developed under the flap. Pathological examination revealed invasive ductal carcinoma, and estrogen receptor was found to be 100% positive, while progesterone receptor and c-erb B2 were negative. The patient was admitted with abdominal pain to the hospital and was hospitalized. Six days before her admission, the patient had received a treatment involving docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2. In her physical examination fever was determined to be 37^{0}C (tympanic), her pulse was 120/minute, her blood pressure was 120/60 mmHg, and her respiratory rate was 19/minute. There was a minimal epigastric tenderness with deep palpation during the abdominal examination, peritoneal irritation was not detected. The laboratory studies revealed; leukocyte: 820/mm^3 (absolute neutrophil count: 150/mm^3), hemoglobin: 13.1 g/L, and platelet: 271.000/mm^3. The routine biochemical values were normal. No features that could explain the acute abdominal condition was found in any abdominal ultrasonography. Filgrastim 48MU was administered to the patient due to neutropenia. On the 9th day of her follow-up period, her fever was found to be 39^{0}C. Physical examination revealed abdominal guarding and rebound tenderness. C-reactive protein was 237 mg/L (normal range: 0-5 mg/L), the leukocyte count was 27.000/mm^3, and the absolute neutrophil count was 25.000/mm^3. The patient was consulted with infectious diseases. With the computerized tomography (CT) of the abdomen, wall thickening, and widespread abdominopelvic peritoneal fluid were found in the ascending colon, and most significantly in the caecum. In two localizations of the lower part of the caecum, the loss of wall continuity and neighboring peritoneal free air signs were found to be compatible with neutropenic enterocolitis (Figure 1). Oral intake of the patient was stopped, and intravenous hydration was initiated. With the prediagnosis of NE, meropenem (3×1gr, IV) and metronidazole (3×500mg, IV) was administered to the patient.

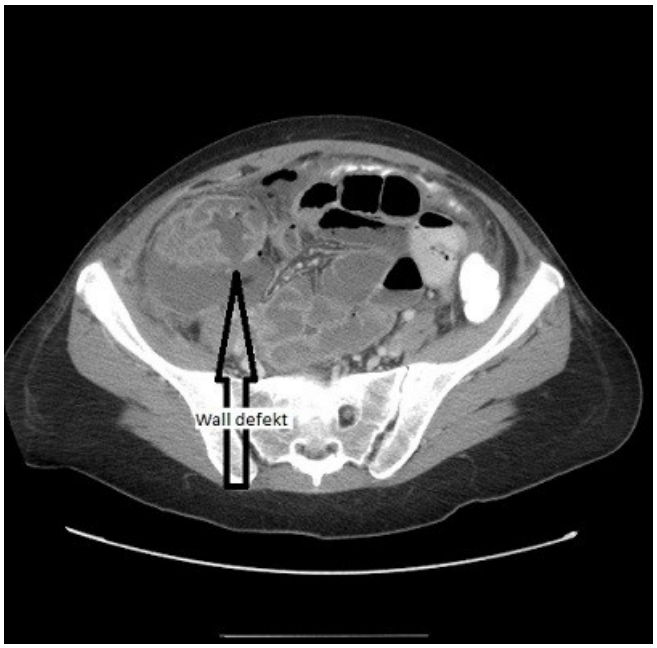

Figure 1. There is thickening of colon wall at ascendant colon, and it is most apparent at cecum as well diffuse ascites is seen most apparent at pericecal area. There is an area that the continuity of the colonic wall cannot be seen at proximal cecum near appendiceal root (arrow), and free air particles are also shown.

The general condition of the patient deteriorated, tachycardia and signs of peritoneal irritations developed. The patient was operated due to acute abdomen; cecal perforation was repaired and ileostomy was performed. No fever and abdominal pain developed after the operation and the patient was discharged on the 7th postoperative day. Additional doses of docetaxel were decided to be administered.

Discussion

Neutropenic enterocolitis is an intestinal inflammation rarely seen in cancer patients after chemotherapy. It is characterized by segmental ulceration of ileum, caecum and ascending colon as well as their inflammation with necrosis [1]. Clinically, certain initial symptoms can be observed such as fever, abdominal pain, nausea, vomiting, watery diarrhea that may sometimes leads to bleeding and polymicrobial sepsis. Abdominal rebound and defense can commonly be seen usually in the right upper quadrant, and sometimes in all quadrants;

however, it may not be detected in patients using steroids [7]. Similar clinical characteristics may also be observed in some other conditions such as appendicitis, Clostridium difficile colitis, intestinal invagination, ileus caused by vincristine, pancreatitis due to L-asparaginase, drug-induced cholestasis and cholecystitis, and fungal infections. Its pathogenesis is not fully known. It is most commonly observed after hematologic malignancies such as leukemia and lymphoma; however, it has been reported to be seen in patients with solid tumors treated with new chemotherapeutics and intensive chemotherapy [1, 2-10].

The agents most commonly associated with neutropenic enterocolitis are cytosine arabinoside, etoposide, and daunorubicin. Other influential agents include doxorubicin, methotrexate, vincristine, taxane-based chemotherapeutic agents, cyclophosphamide, and prednisone [2, 7, 9]. NE that developing after standard dose combination chemotherapy with nedaplatin and irinotecan for testicular tumor was reported by Takaoka *et al.* [2] for the first time. A search of the PubMed English literature between years 1993-2017 revealed NE cases developing taxane-based chemotherapy [3-8, 10]. Such complications can be observed in 0.1% of taxane-based chemotherapies [8]. In 1993, Seewaldt *et al.* [4] first reported an intestinal perforation that developed after paclitaxel therapy in an ovarian cancer patient. As in our case, there are five cases with NE that developing after the use of paclitaxel in the treatment of breast cancer [3, 5-8] (Table 1).

Symptoms usually observed within 10 to14 days after chemotherapy, when neutropenia is most obvious [7]. It is noticed that NE developed usually after 6-10th day of the chemotherapy. [3, 5-7]. In our case, NE developed on the 6th day after the first cycle. As in our case, all these cases of breast cancer, in which NE developed, taxane-based chemotherapy drugs have been used in combination with other chemotherapeutic agents (Doxorubicin, Cyclophosphamide, Epirubicin, 5% Fluorouracil) [3, 5-7].

CT and ultrasound (US) are the radiological methods used for diagnosis. It is likely to observe thickening of the intestinal wall, inflammatory mass in the right lower quadrant, caecum enlargement, pericaecal fluid, and inflammatory changes in the pericaecal tissue [7, 8]. CT is the most preferred

Table1. Summary of reported cases of neutropenic enterocolitis associated with docetaxel

Authors	Cancer	Patient	Chemotherapy regimen	Date of onset of symptoms	Symptoms	Outcome
Ramsing *et al.* [3]	Breast cancer	66-year-old, female	Docetaxel Cyclophosphamide	7th day of chemotherapy	Generalized abdominal pain, fever, rigors and vomiting	Operated because of perforation, released on postoperative 7th day
Sodhi *et al.* [5]	Breast cancer	38-year-old, female	Fluorouracil Epirubicin Cyclophosphamide given, later on changed with Docetaxel	7th day after Docetaxel	Acute abdomen, diarrhea and shock	Operated because of perforation, get well postoperative
Taşköylü *et al.* [6]	Breast cancer	40-year-old, female	Docetaxel Cyclophosphamide Doxorubicin	10th day of chemotherapy	Generalized abdominal pain and fever	Neutropenic enterecolitis, get well after antibiotic regimen
Oehadian *et al.* [7]	Breast cancer	61-year-old, female	Docetaxel Cyclophosphamide Doxorubicin	6th day of chemotherapy	Abdominal pain and vomiting	Operated because of perforation, released on postoperative 7th day
Rolston *et al.* [8]	Breast cancer	NA	NA	NA	NA	NA

NA = not available

method because it is considerably lower (15%) than that of US (23%) and plain radiography (48%) [7]. A wall thickness greater than 10 mm and its association with intestinal perforation are negative factors for prognosis [9]. In our case, the wall thickness in the ascending colon, and most significantly in the caecum was found to be 16 mm and peritoneal free air signs were regarded as a bowel perforation associated with NE.

In the follow-up and treatment period of NE, patients should be monitored on a daily basis, and should be fed intravenously after stopping their oral intake. In case of clinical deterioration, the patient should be assessed in terms of perforation or necrosis, and then a surgical treatment should be considered accordingly [1]. It has been reported that complications requiring surgical intervention can be encountered in 5% of patients diagnosed with NE [6]. However, most of such cases are cases with hematologic malignancies. NE-related perforation was reported in 3 patients with solid tumors treated with taxane-based chemotherapy [3, 5, 10]. According to our knowledge, our case is the 4th case in the literature in which perforation developed.

Conclusions

In conclusion, NE should be definitely considered in differential diagnosis of abdominal pain in neutropenic patients. Although perforation is rarely seen in neutropenic patients with solid tumors, it should be kept in mind and the patient should be followed-up carefully. It is noteworthy that mortality and morbidity can be reduced by means of appropriate antibiotics and a timely surgical intervention.

Informed consent

Written informed consent was obtained from the patient for the publication of this case report.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

[1] Machado NO. Neutropenic enterocolitis: A continuing medical and surgical challenge. N Am J Med Sci 2010;2:293-300.
[2] Takaoka E, Kawai K, Ando S, Shimazui T, Akaza H. Neutropenic colitis during standard dose combinaton chemotherapy with nedaplatin and irinotecan for testicular cancer. Jpn J Clin Oncol 2006;36:60-3.
[3] Ramsingh J, Bolln C, Hodnett R, Al-Ani A. Neutropenic enterocolitis affecting the transverse colon: an unusual complication of chemotherapy. BMJ Case Rep 2014;2014:bcr2014204035.
[4] Seewaldt V, Cain JM, Greer BE, Tamimi H, Figge DC. Bowel complications with taxol therapy. J Clin Oncol 1993;11:1198.
[5] Sodhi KS, AiyappanSK, Singh G, Prakas M, Khandelwal N. Colitis and colonic perforation in a patient with breast carcinoma trated with taxane based chemotherapy. Indian J Cancer 2011;48:134-5.
[6] Yapar Taşköylü B, Gökçen Demiray A, Aksoy P, Yaren A, Gököz Doğu G, et al. [Neutropenic enterocolitis after adjuvant chemotherapy: a case report]. Pamukkale Tıp Dergisi 2013;6:96-9. [Article in Turkish]
[7] Oehadian A, Fadjari TH. Neutropenic enterocolitis in breast cancer patient after taxane-containinig chemotherapy. Acta Med Indones 2008;40:29-33.
[8] Rolston KV. Neutropenic enterocolitis associated with docetaxel therapy in a patient with breast cancer. Clin Adv Hematol Oncol 2009;7:527-8.
[9] Cartoni C, Dragoni F, Micozzi A, Pescarmona E, Mecarocci S, Chirletti P, et al. Neutropenic enterocolitis in patients with acute leukemia: Progmostic significance of bowel wall thickening dedected by ultrasonography. J Clin Oncol 2001;19:756-61.
[10] Colucci G, Thaler W, Dejaco H, Marsoner H, Grones A. Colonic rupture in a patient on combination chemotherapy for metastasized carcinoma of the esophagogastric junction. Case report and review of the literature. Onkologie 2005;28:204-6.