DOI: 10.14744/etd.2019.39114.

Manuscript Type: Case report

Title: Neoadjuvant Doxorubicin and Docetaxel in Breast Cancer Patients Applied Neutropenic Enterocolitis

Running Title: Neoadjuvant chemotherapy Applied Neutropenic Enterocolitis

Authors: Hatice Sarıkaya Aslan, Mevlüde İnanç

Institutions: Department of Internal Medicine, Kayseri Training and Research Hospital, Kayseri, Turkey

Address for Correspondence: Hatice Sarıkaya Aslan. Kayseri Training and Research Hospital - internal medicine, Kocasinan / Kayseri Kayseri 38010-Turkey

E-mail: hasirakaya@gmail.com

Cite this article as: Sarıkaya Aslan H, İnanç M. Neoadjuvant Doxorubicin and Docetaxel in Breast Cancer Patients Applied Neutropenic Enterocolitis. Erciyes Med J 2019; DOI: 10.14744/etd.2019.39114.

UNCORRECTED

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Sarıkaya Aslan H, İnanç M. Neoadjuvant Doxorubicin and Docetaxel in Breast Cancer Patients Applied Neutropenic Enterocolitis. Erciyes Med J 2019; DOI: 10.14744/etd.2019.39114.

©Copyright 2019 by Erciyes University Faculty of Medicine - Available online at: www.erciyesmedj.com

Abstract:

Neutropenic enterocolitis is an acute complication of neutropenia induced by chemotherapy, characterized by inflammatory processes involving colon and cecum that can lead to necrosis, hemorrhage, perforation and septicaemia. Usually this syndrome develops after cytotoxic drug use and fever and abdominal pain are the main symptoms. We present a case of typhlitis in a 38 year old female patient with breast cancer who received Doxorubicin and Docetaxel.

Introduction:

Neutropenic enterocolitis (NE) is a disease characterized by fever and abdominal pain, in which the target tissue is usually terminal ileum and cecum. Neutropenic enterocolitis is seen in cancer patients who develop neutropenia after chemotherapy. It is characterized by ulceration, necrosis, perforation developed in the retained intestinal segment and is usually mortal. Conservative treatment applied on time can provide healing without surgery, but it is frequently necessary to apply medical treatment together with surgical treatment. It has been shown to be most frequently associated with leukemia and lymphoma (1). Neutropenic enterocolitis is less common in solid tumors due to treatment-related short-term neutropenia, but has been shown to be associated with taxane-based chemotherapy (2). In patients receiving chemotherapy due to solid tumors, the incidence of NE has been reported as 5% and the mortality rate has been reported as 30-50% (3).

Case report:

A 38 years old female patient was diagnosed with left breast invasive ductal carcinoma 1.5 months ago. Magnetic Resonance Imaging of the patient revealed a mass of 14 × 10 mm in the left breast and 27 × 19 mm and 32 × 29 mm lymph nodes in the axillary region. Positron Emission Tomography-Computed Tomography (CT) scan showed left mammary and axillary involvement and neoadjuvant Doxorubicin and Docetaxel chemotherapy protocols were applied. Following chemotherapy, on the 10th day, she was admitted to the emergency

UNCORRECTED

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Sarıkaya Aslan H, İnanç M. Neoadjuvant Doxorubicin and Docetaxel in Breast Cancer Patients Applied Neutropenic Enterocolitis. Erciyes Med J 2019; DOI: 10.14744/etd.2019.39114.

©Copyright 2019 by Erciyes University Faculty of Medicine - Available online at: www.erciyesmedj.com

department due to bloody diarrhea and abdominal pain. She had fever at 39˚C, widespread abdominal tenderness and bloody diarrhea. Ultrasonography revealed wall thickening at cecum location. The laboratory findings were WBC 0.65, neutrophil 0.37, hemoglobin 12.3, platelet 183000. There were over 10 bowel movements per day. There was no evidence of perforation while wall thickening was observed at cecum in a CT scan of the abdomen (Fig. 1, 2). The patient was admitted as neutropenic enterocolitis. Oral feeding was stopped and antibiotherapy was initiated at a dose of 1 × 400 mg in a loading dose of parenteral nutrition solution, Granulocyte-colony stimulating factor (GCSF), meropenem 3 × 1 gr, teicoplanin 2 × 400 mg. IV potassium replacement was performed for 5 days due to lack of potassium associated with gastrointestinal loss of the patient. On the third day of her admission, the patient's oral feeding was opened due to recovery from neutropenia, abdominal tenderness and bloody diarrhea. On the 6th day of admission, she recovered from the bloody diarrhea. GCSF therapy was discontinued when the number of neutrophils reached 5000. There was no growth in stool, urine and blood cultures during the hospital admission. The clinical and radiological findings of the patient were completely improved and the patient's antibiotic treatment was completed in 14 days. There was no complication in the patient who continued the combination of doxorubicin and docetaxel.

Discussion:

Neutropenic enterocolitis is a rare but serious necrotizing inflammation of the intestine that can occur after chemotherapy in cancer patients. Docetaxel demonstrates high anti-tumor activity in solid tumors. Docetaxel, applied at a dose of 100 mg / m2 for 3 weeks, as we have in our case, develops neutropenia in 70-90% of patients. In our present case, NE was developed as a result of combined treatment of Docetaxel and Doxorubicin. Unlike Dumitra and colleagues, because the patient was quickly given antibiotic treatment and neutropenia was detected early, there was a decline in NE before the surgical procedure (4). Similar to our case, there are cases in the literature where NE is developed by combination chemotherapy and controlled by medical therapy (5). Neuropenic enterocolitis is most commonly developed by Gram negative

UNCORRECTED

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Sarıkaya Aslan H, İnanç M. Neoadjuvant Doxorubicin and Docetaxel in Breast Cancer Patients Applied Neutropenic Enterocolitis. Erciyes Med J 2019; DOI: 10.14744/etd.2019.39114.

©Copyright 2019 by Erciyes University Faculty of Medicine - Available online at: www.erciyesmedj.com

bacilli, Escherichia coli and Klebsiella species, however in our case, no growth was detected in urine and blood cultures (6). It has been observed in most cases reported in the literature that NE develops when docetaxel and other chemotherapeutic drugs are used together in the same way as in our case (7). In literature, as a result of disturbance of circulation due to distention tendency, cecum is the most frequently affected intestinal segment (8). In a patient with a diagnosis of neutropenic enterocolitis, the presence of a complication that requires urgent surgical intervention should be excluded. First of all, oral feeding of the patient should be stopped and intravenous feeding should be started. Then, antibiotic therapy, especially with anaerobic activity, should be given and treatment should be continued until the clinical findings disappear (8). Despite intensive medical treatment; surgical intervention should be considered in patients with persistent bleeding, perforation, and clinical worsening (9). Continuation of chemotherapy without complete healing increases the risk of developing new NE (10). For this reason, chemotherapy should not be started before the treatment is completed.

Conclusion:

When patients with chemotherapy have neutropenia and bloody diarrhea, NE should be considered, diagnosis should be made early and treatment should be started quickly. Otherwise, morbidity and mortality increase in patients.

Figures:

Figure 1: CT image of intestinal wall thickening

Figure 2: CT image of wall thickening in the cecum

UNCORRECTED

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Sarıkaya Aslan H, İnanç M. Neoadjuvant Doxorubicin and Docetaxel in Breast Cancer Patients Applied Neutropenic Enterocolitis. Erciyes Med J 2019; DOI: 10.14744/etd.2019.39114.

©Copyright 2019 by Erciyes University Faculty of Medicine - Available online at: www.erciyesmedj.com

Kaynaklar:

1. Portugal R, Nucci M. Typhlitis (neutropenic enterocolitis) in patients with acute leukemia: a review.Expert Rev Hematol. 2017 Feb;10(2):169-174.
2. Rochigneux P, Schleinitz N, Ebbo M. Acute myositis: an unusual and severe side effect of docetaxel: a case report and literature review. Anticancer Drugs. 2018 Jun;29(5):477-481.
3. Duceau B, Picard M, Pirracchio R, Wanquet A. Neutropenic Enterocolitis in Critically Ill Patients: Spectrum of the Disease and Risk of Invasive Fungal Disease. Crit Care Med. 2019 May;47(5):668-676.
4. Dumitra S, Sideris L, Leclerc Y Leblanc G, Dubé P. Neutropenic enterocolitis and docetaxel neoadjuvant chemotherapy. Ann Oncol 2009; 20(4): 795-6.
5. Oehadian A, Fadjari TH. Neutropenic enterocolitis in breast cancer patient after taxane–containing chemotherapy. Acta Med Indones 2008 ; 40(1): 29-33.
6. Rodrigues FG, Dasilva G, Wexner SD. Neutropenic enterocolitis. World J Gastroenterol. 2017 Jan 7;23(1):42-47.
7. Vergara-Fernández O, Trejo-Avila M, Solórzano-Vicuña D. Factors associated with emergent colectomy in patients with neutropenic enterocolitis.Langenbecks Arch Surg. 2019 May;404(3):327-334.
8. Youngs J, Suarez C, Koh MBC. An unusual presentation of neutropenic enterocolitis (typhlitis). Lancet Infect Dis. 2016 May;16(5):618.
9. Mourad N, Michel RP, Marcus VA. Pathology of Gastrointestinal and Liver Complications of Hematopoietic Stem Cell Transplantation. Arch Pathol Lab Med. 2019 Mar 6.
10. Rolston KVInfections in Cancer Patients with Solid Tumors: A Review. Infect Dis Ther. 2017 Mar;6(1):69-83.

UNCORRECTED

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Sarıkaya Aslan H, İnanç M. Neoadjuvant Doxorubicin and Docetaxel in Breast Cancer Patients Applied Neutropenic Enterocolitis. Erciyes Med J 2019; DOI: 10.14744/etd.2019.39114.

©Copyright 2019 by Erciyes University Faculty of Medicine - Available online at: www.erciyesmedj.com

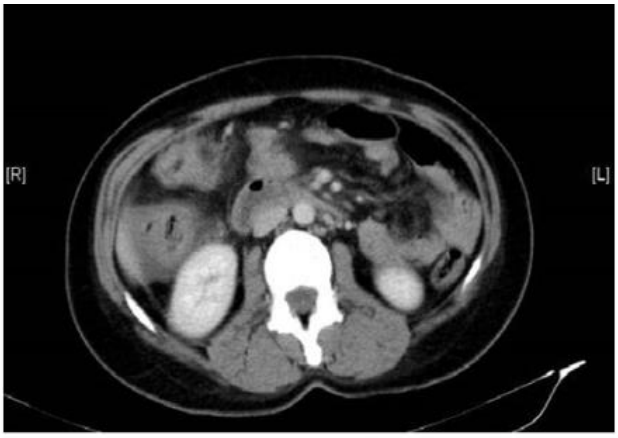

Figure 1: CT image of intestinal wall thickening

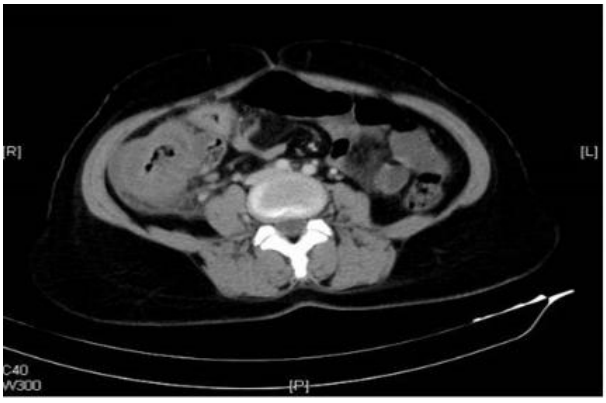

Figure 2: CT image of wall thickening in the cecum

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Sarıkaya Aslan H, İnanç M. Neoadjuvant Doxorubicin and Docetaxel in Breast Cancer Patients Applied Neutropenic Enterocolitis. Erciyes Med J 2019; DOI: 10.14744/etd.2019.39114.

©Copyright 2019 by Erciyes University Faculty of Medicine - Available online at: www.erciyesmedj.com