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Case Report

Case Report: Acute Hemorrhagic Colitis Following Doxorubicin Chemotherapy

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Abstract

Systemic treatments employed in oncology, including cytotoxic agents and targeted therapies, often lead to gastrointestinal side effects. The severity of colitis and its potential complications necessitate prompt diagnosis and appropriate management.

We present the case of a 70-year-old, he was diagnosed since May 2023 for a dedifferentiated liposarcoma on the 10th left rib put on chemotherapy based on D-Rubicin 90mg; and who presented five days after the first course of treatment a severe bloody diarrhea with haemodynamic instability; the patient benefited from an upper and lower digestive endoscopy having objectified revealed two ulcers with thickened irregular margins and fibrinous background, centered on regenerative areas. Biopsies confirmed subacute colitis with non-specific epithelial abnormalities; doxorubicin was halted, and the patient was kept under clinical surveillance with transfusion and corticosteroid enema with good clinical improvement.

Keywords: Acute Hemorrhagic, Colitis, Doxorubicin, Chemotherapye

Introduction

Post-chemotherapy colitis is a recognized complication of treatment for solid or hematological cancers, frequently linked to chemotherapy-induced neutropenia as a key contributing factor [1]. However, instances of non-neutropenic colitis have been documented, prompting inquiries into the potential direct toxicity of the administered drugs. Doxorubicin (doxorubicin hydrochloride), a potent cytotoxic anthracycline antibiotic derived from Streptomyces peucetius var. caesius, exerts its anticancer and toxic effects through various mechanisms [2]. Complications associated with doxorubicin are diverse; concerning the digestive tract, adverse effects may range from nausea and vomiting to mucosal inflammation, stomatitis, abdominal pain, bleeding in the digestive tract, colitis, and diarrhea. Hence the importance of regular monitoring of patients undergoing chemotherapy and effective, yet delicate, management of complications.

Observation

Mr A.K, aged 70, was admitted to emergency for management of hemorrhagic shock; he was diagnosed since May 2023 for a dedifferentiated liposarcoma on the 10th left rib (12cm transversely, 15cm vertically). He received first course with chemotherapy Under D-RUBICIN 90mg, antiemetics, and methylprednisolone 120mg every 3 weeks, five days after the first treatment course, the patient experienced severe bloody diarrhea. He was admitted to an intensive care unit, the clinical examination revealed PS 2, BMI 11.6, GCS 15, low blood pressure (7/4mmhg), tachycardia (115 puls/min), apyrexia, slightly tender abdomen, and a soft left hypochondrium mass (approx. 16cm). No inflammatory signs, hepatomegaly, or splenomegaly were noted. Rectal examination revealed active fresh blood.

The biological work-up showed anemia (normocytic normochromic hemoglobin 7g/dl, initially 13g/dl), hyperleukocytosis

(18400/mm3, predominantly neutrophils at 12000/mm3), correct platelet count (420000), and prothrombin rate at 100%. C-reactive protein levels were normal, and tests for Clostridium difficile toxin and coprocultures were negative.

after the patient's hemodynamic stabilization, an abdominal angioscan (Figure 1,2) was performed showed a large dedifferentiated liposarcoma in the left hypochondrium (18*12*18cm) and hypodense hepatic lesions in segments IV and VIII; The was no extravasation of contrast medium; with regular, symmetrical rectal thickening endoscopic exploration was carried out, starting with a fibroscopy (Figure 3,4) that returned normal and we completed by colonoscopy, revealed two ulcers with thickened irregular margins and fibrinous background, centered on regenerative areas (Figure 5,6).

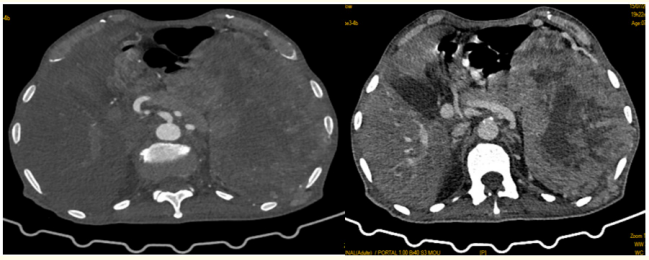

Figure 1 and 2: Scans showing dedifferentiated liposarcoma without extravasation.

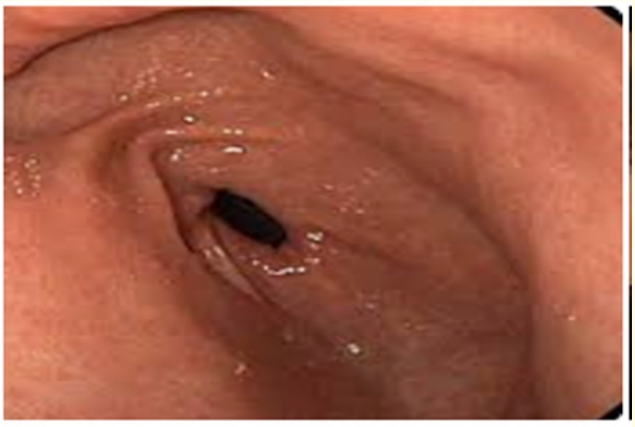

Figure 3: Normal gastric mucosa without bleeding.

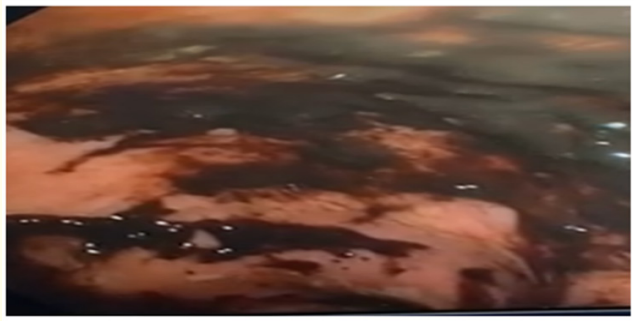

Figure 4: Colonic mucosa lined with red clotted blood.

Biopsies confirmed subacute colitis with non-specific epithelial abnormalities without inflammatory infiltrate; without CMV inclusion. A corticosteroid enema resulted in clinical improvement and no recurrence of bleeding. In collaboration with the oncologist, doxorubicin was halted, and the patient was kept under clinical surveillance with transfusion and corticosteroid enema. A switch to another treatment line was planned upon stabilization of the patient's condition.

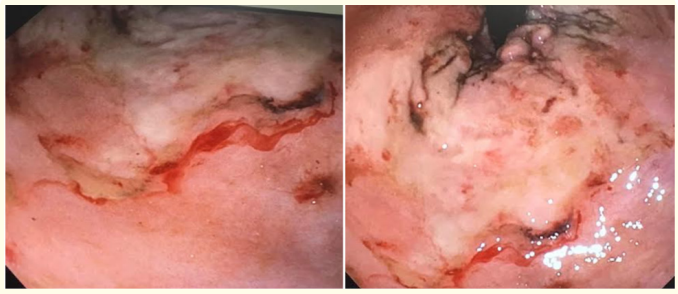

Figure 5 and 6: Rectal bleeding ulcer mucosa without bleeding.

Discussion

Anthracycline toxicity describes the toxic consequences of anthracycline-class medications. Anthracyclines, such as doxorubicin and epirubicin, are potent chemotherapy agents employed in managing various hematological and solid malignancie [3]. Anthracyclines are a key component in hematological chemotherapy regimens treating lymphoma, where doxorubicin, arguably the widest-used anthracycline, features in the CHOP (cyclophosphamide, hydroxydaunorubicin [doxorubicin], Oncovin® [vincristine], prednisone) and ABVD (Adriamycin® [doxorubicin], bleomycin, vinblastine, dacarbazine) protocols [4].

The primary anticancer mechanism of action of anthracyclines is disruption of the topoisomerase-II enzyme (TOP2) stable intermediates, leading to a state of ever-increasing DNA damage. Other mechanisms, including the impact of reactive oxygen species, interference within intercalation, and chromatin damage, have also been proposed as anticancer mechanisms [5]. All the proposed mechanisms lead to preferential apoptosis in rapidly replicating cells, impacting slowly replicating or quiescent cell types less significantly.

The most prominent, well-studied, and clinically concerning toxicity associated with anthracycline chemotherapy is type-1 cardiotoxicity, a dose-dependent, irreversible, cumulative cardiomyocyte cell death that leads to the development of dilated cardiomyopathy and subsequent cardiac failure [6,7]. Likely, anthracycline exposure may also increase the risk of secondary cancer and lead to gonadal failure, but these impacts are not as well documented [8]. Liver, gastrointestinal tract, renal, and bone marrow toxicity may also occur but are often reversible; it is likely some degree of hepatic necrosis does occur with anthracycline administration, which may develop chronicity, but this occurs in doses well above that of cardiomyocyte death [9].

Patients exposed to anthracycline chemotherapy are much more likely to die from their underlying malignancy before anthracycline toxicity presents a threat to life. More than 95% of patients with cancer treated with anthracycline chemotherapy die from their underlying malignancy rather than developing anthracycline toxicity, and cardiac death contributes to 0.7% all-cause mortality. [10] At 1 year following anthracycline treatment, 98% of cases where toxicity develops will be clinically apparent.

In our case, the diagnosis of acute colitis secondary to Doxorubicin can be considered probable according to the criteria of Bégaud., *et al*. [11]. supported by the following reasons: a) the highly suggestive five-day delay after Doxorubicin administration; b) a favorable outcome following treatment discontinuation; c) the absence of alternative causes for colitis, particularly infectious ones. However, despite negative coprocultures for Clostridium difficile toxin and bacteriological cultures of colonic biopsies, the possibility of an infectious colitis with an unidentified pathogen cannot be definitively ruled out.

Moreover, other reported cases of doxorubicin-associated colitis further support this association. Doxorubicin (doxorubicin hydrochloride) is a potent cytotoxic anthracycline antibiotic known for causing major side effects, including neutropenia, severe skin and mucous membrane damage, diarrhea, hypersensitivity reactions, and gastrointestinal hemorrhage [12,13]. Acute diarrhea was observed in 38% and 42% of patients treated with this cytotoxic agent respectively.

Conclusion

The complications of chemotherapy have a prognostic impact and their management is a major challenge; chili hemorrhagic colitis induced by doxorubicin remains a rare entity but does exist. This is why all hepatogastroenterologists must be able to manage the digestive complications of chemotherapy in an emergency context, knowing that the quality of their prevention and treatment has a prognostic impact.

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