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CASE REPORT

Colonic perforation in a nasopharyngeal carcinoma patient treated with fluorouracil: A case report

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Author contributions: Lu WJ and Li G wrote the manuscript; Gao L was involved in the patient's medical care, initiated and supervised the study, and wrote and revised the manuscript; all authors have given final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Abstract

BACKGROUND

Nasopharyngeal carcinoma (NPC) is a commonly encountered type of tumor. Fluorouracil (FU) is an effective treatment providing satisfactory oncologic outcomes in nasopharyngeal carcinoma patients. We describe a unique case of colonic perforation in an NPC patient treated with FU. Thus far, only two cases of intestinal perforation associated with FU treatment have been reported. We hope that the analysis of the relationship between the adverse effects of FU and physiological factors will help to reduce the incidence of colonic perforation in patients with nasopharyngeal carcinoma treated with FU.

CASE SUMMARY

A 67-year-old female patient suffered from NPC stage pT3N2M0. She had a history of three surgical procedures: Partial enterectomy, partial sigmoidectomy, and sigmoidostomy. After the administration of 2.75 g FU, a bloody stool appeared and the patient developed abdominal pain. Subsequent examination indicated colitis and intestinal perforation.

CONCLUSION

FU is a commonly used drug in NPC chemotherapy. The most common adverse effect of FU is gastrointestinal reaction, and the colonic perforation found here is thought to be caused by gastrointestinal mucosal injury consequential to the FU treatment. When selecting chemotherapy drugs, their side effects and the physical condition of patients should be considered, particularly in patients with a history of gastrointestinal surgery.

Key words: Chemotherapy; Nasopharyngeal carcinoma; Fluorouracil; Colonic perforation; Reaction; Case report

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Core tip: Intestinal perforation associated with fluorouracil treatment is very rare. The possible reason of the perforation in the case presented here is that the patient has undergone intestinal surgeries, her physical condition was poor, and the use of fluorouracil has damaged the intestinal mucosa. In general, patients with intestinal perforation require an immediate surgical treatment. However, the use of radiotherapy and chemotherapy in patients after intestinal surgery is challenging.

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INTRODUCTION

Fluorouracil (FU) is commonly used in nasopharyngeal carcinoma chemotherapy. A recent article by Fata *et al*[1] provides a reminder that FU does cause, directly or indirectly, gastrointestinal mucosal damage, and the awareness among oncologists of this problem and resulting complications is necessary. The current report presents a case of colonic perforation induced by FU in a patient with a history of three surgical procedures: Partial enterectomy, partial sigmoidectomy, and sigmoidostomy. Colonic perforation is a rare complication of FU therapy. So far, only two cases of intestinal perforation associated with FU treatment have been reported[2,3], and the uniqueness of the medical history of the patient presented here further highlights the clinical relevance of the current report.

CASE PRESENTATION

Chief complaints

A 67-year-old female patient felt left mandibular lymph node enlargement, accompanied by headache and tinnitus.

History of present illness

The left neck mass was found in May 2019, and the mass gradually increased, but she did not show symptoms of nasal congestion or nosebleed.

History of past illness

Seven years ago, she underwent partial enterectomy, partial sigmoidectomy, and sigmoidostomy.

Physical examination

On admission, the bilateral cervical lymph nodes of the patient were enlarged, and the swollen lymph node under the left jaw was the largest, with a size of 3.2 cm × 2.6 cm. She had no exophthalmos and no difficulty in deglutition or opening the mouth. No tenderness or rebound tenderness was found on abdominal palpation.

Laboratory examinations

Blood analysis (Figure 1) and urine analysis were normal on August 15, 2019. Chest X-ray, electrocardiogram, and arterial blood gas were also normal.

Imaging examinations

In August 2019, nasopharyngoscopy identified an undifferentiated non-keratinizing carcinoma. Additionally, magnetic resonance imaging of the nasopharynx, neck, and skull base documented bilateral thickening of the parapharyngeal wall and posterior parapharyngeal wall, and multiple lymph node metastases present bilaterally in the parapharyngeal space and the neck. These findings were consistent with nasopharyngeal carcinoma.

Further diagnostic work-up

Single-photon emission computed tomography/computed tomography revealed thickened mucous membranes in the bilateral and posterior parietal walls of the nasopharynx, with soft tissue mass shadows.

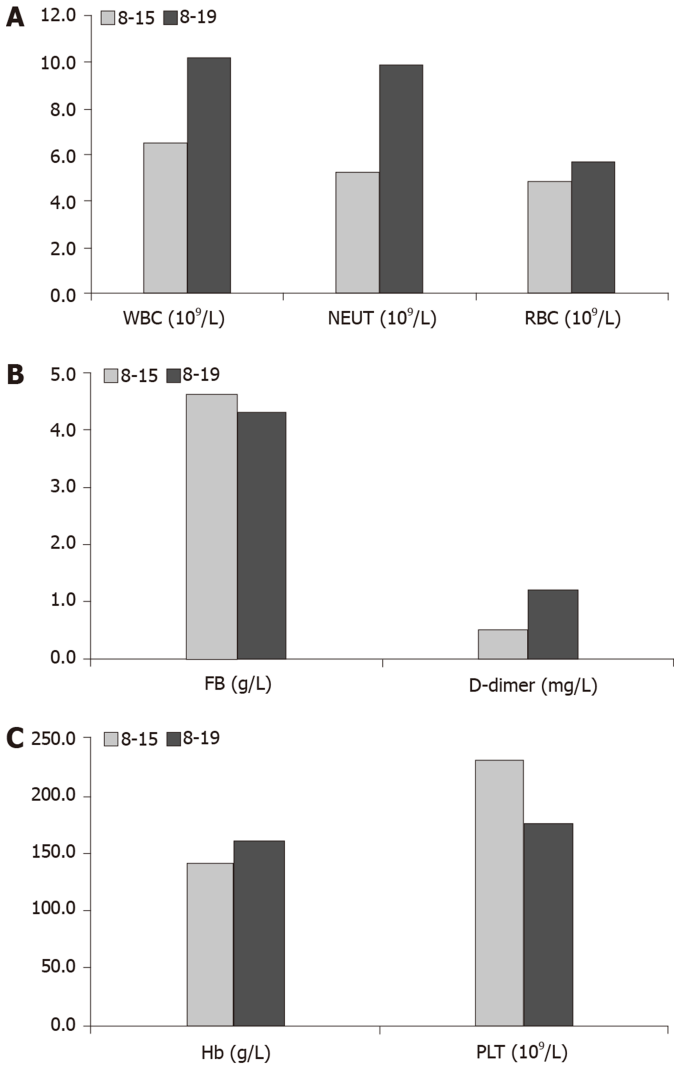

Figure 1 The values of white blood cells (WBC), neutrophils (NEUT), and red blood cells (RBC), fibrinogen (FB) and D-dimer, and hemoglobin (Hb) and platelets (PLT) before (August 15, 2019) and after the administration of fluorouracil (August 19, 2019). A: WBC, NEUT, and RBC; B: FB and D-dimer; C: Hb and PLT.

FINAL DIAGNOSIS

Based on the combination of imaging, clinical, and pathological results, the nasopharyngeal malignant tumor was diagnosed as pT3N2M0.

TREATMENT

The original treatment plan was to administer the TPF chemotherapy regimen (paclitaxel 180 mg + cisplatin 30 mg + FU 5 g). The first intravenous injection of 0.5 g FU was performed on August 16, 2019, and the remaining 4.5 g was divided into two intravenous doses. On August 19, 2019, after injecting the first of the remaining 2.25 g doses of FU, the patient developed abdominal pain and bloody stool. Of note, cisplatin and paclitaxel were planned to be given to the patient on that day, but they were not administered. Blood tests were performed, which showed an increase in D-dimer, white blood cells, neutrophils, red blood cells, and hemoglobin and a decrease in fibrinogen and platelets compared with the results obtained on August 15 (Figure 1). A computed tomographic scan (Figure 2) of the abdomen showed free intraperitoneal air. Colonoscopy revealed mucosal ulceration and erosion in the sigmoid colon and descending colon. The patient was immediately taken to the operating room for an emergent laparotomy. During the procedure, a perforation was found in the descending colon, and a large amount of exudate flowed out of the perforation. A partial colectomy was performed. Colitis was diagnosed based on pathologic examination of surgical specimens.

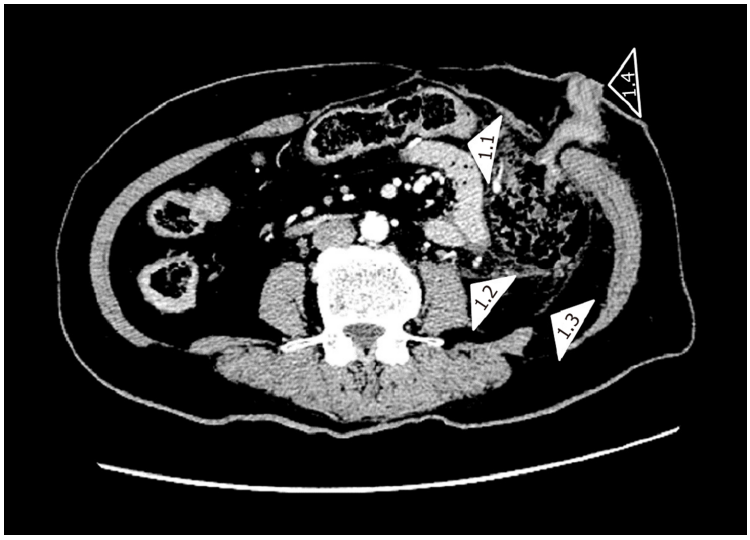

Figure 2 Computed tomography image of the abdomen documenting the inflammatory exudate (Δ) and enterostomy (▲) (August 19, 2019).

OUTCOME AND FOLLOW-UP

After the surgery, the patient was treated with antibiotics. She had diffuse abdominal tenderness to deep palpation. On presentation, her blood pressure was 122/83, pulse 85/min, temperature 37.1 °C, respiratory rate 18/min, and oxygen saturation 97%. The patient's condition gradually stabilized over a period of 24 d, but due to the intestinal damage, the induction chemotherapy had to be postponed. The patient and her family have expressed their understanding regarding the reason for postponing the original treatment plan.

DISCUSSION

Induction cisplatin-FU chemotherapy prior to definitive radiation improves freedom from distant metastases, disease-free survival, and overall survival in patients with locoregional stage IV nasopharyngeal carcinoma without increasing treatment-related morbidity[4]. In recent years, docetaxel, cisplatin, and FU-based induction chemotherapy has been widely applied in the treatment of locoregionally advanced nasopharyngeal carcinoma[5]. FU can effectively reduce the recurrence of tumors and prolong survival in patients with nasopharyngeal carcinoma, regardless of whether the surgery was performed.

However, the toxic and side effects of FU require careful consideration. The mechanism of adverse effects of FU involves a deficiency of the catabolic pathway, in which the drug competes with uracil, the naturally occurring pyrimidine, as an enzyme substrate. Dihydropyrimidine dehydrogenase (DPD, EC 1.3.1.2) is the initial and rate-controlling enzyme of the catabolism of endogenous pyrimidine and fluoropyrimidine nucleotides. DPD enzyme is expressed in most tissues, including the tumors, and is highly active in the liver and peripheral lymphocytes. The activity of DPD is highly variable among individuals. Low levels of DPD activity have been associated with an increased risk of toxicity during the FU treatment[6]. The most common adverse reaction triggered by FU is gastrointestinal tract response. The patient presented with colonic perforation, acute diffuse peritonitis, and acute infection, and these conditions were, to a large extent, associated with the use of FU. Surgical treatment of colonic perforation resulting from the administration of FU is crucial, and the prognosis depends essentially on the time to diagnosis. It is very important to increase the knowledge about intestinal perforation in order to improve the diagnostic accuracy[7].

Perforations of the colon are thought to be caused by damage to the gastrointestinal mucosa consequential to the treatment with FU. Gastrointestinal perforation is a known adverse event of bevacizumab[8-10], but it occurs only rarely during FU therapy[2,3]. In particular, descending colon perforation is less frequent than gastric and duodenal perforation. Because of the scarcity of reports of descending colon perforation in patients treated with FU, its frequency and mechanism are not

completely understood. It is possible that the patient had an enterostomy, and FU may be secondary to the inhibition of the methylation reaction catalyzed by thymidylate synthetase (EC 2.1. 1.45), which transfers a methyl group from N, N′-methylene-tetrahydrofolic acid to deoxyuridylic acid, contributing to the breakup of the gastrointestinal mucosa, which leads to intestinal perforation. Accordingly, we have a reason to believe that the colonic perforation presented in this case report was associated with the FU treatment.

In conclusion, although induction chemotherapy can improve the overall survival, side effects of drugs and the patient's physical condition should be all considered in selecting the optimal treatment modality, particularly in patients with a history of gastrointestinal surgery. The possibility of performing colonoscopy before chemotherapy should be taken into account in these patients.

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