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A case of pseudomembranous colitis associated with paclitaxel and carboplatin chemotherapy for vulvar cancer

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Summary

Introduction: Pseudomembranous colitis is inflammatory disease of the colon with symptoms that may range from loose stool in the mildest cases to toxic megacolon (fever, nausea, vomiting, and ileus) and colonic perforation (rigid abdomen and rebound tenderness) in the most severe cases. In the last decades the causative relationship of cytotoxic and targeted antineoplastic agents with pseudomembranous colitis is increasingly recognized among cancer patients. *Material and Methods:* Here in the authors present a case of metastatic squamous vulvar cancer that developed pseudomembranous colitis after treatment with the combination of chemotherapy (paclitaxel and carboplatin). *Results:* The actual rate of paclitaxel-containing chemotherapy induces pseudomembranous colitis is not simple to determine and probably underestimated, as most relevant studies were conducted on a small scale. Methotrexate, cisplatin, cleomycin are the most common agents associated *Clostridium difficile* infection. Pseudomembranous colitis, whatever the chemotherapy usually appears soon after its administration, with watery stool that soon becomes bloody and affects almost equally men and women with a mean age of 58.64 years. *Conclusions:* Combination or single-agent chemotherapy are associated with pseudomembranous colitis. Clinicians need to have a high index of suspicion and the combination of the clinical picture with the characteristic findings on a colonoscopy and stool cultures can help in the prompt diagnosis. Pseudomembranous colitis can be reversible with appropriate supportive treatment and discontinuation of the causative factors.

Key words: Pseudomembranous colitis; Stool culture; Colonoscopy; Diarrhea; Chemotherapy.

Introduction:

Chemotherapeutic drugs induce gastrointestinal toxicity, diarrhea being the most common (10%), but the cases that are associated with pseudomembranous colitis in existing medical literature are scarce [1]. *Clostridium difficile* is a *Gram*-positive spore-forming bacteria, related to antibiotic-associated colitis. The disruption of normal intestinal flora benefits the colonisation of *Clostridium difficile* which releases toxins inducing inflammation and mucosal damage [2].

Case Report

The present case refers to a 78-year-old woman, having squamous vulvar cancer with inguinal and iliac lymph nodes and metastasis to the lungs receiving palliative treatment with paclitaxel 75/m^2 and carboplatin (AUC: 5). Ten days after her eighth cycle of chemotherapy, she visited the Emergency Department complaining about abdominal pain, fever, bloody, and watery stool that had lasted for about a week. She did not take any antibiotics but, on her own initiative, she took loperamide for three days assuming that her symptoms were generated by chemotherapy, without of course any benefit [3]. She had high serum LDH levels (1,021 IU/L), thrombocytopenia (65,000/μL) and the abdominal X-ray demonstrated dilatation of the colon, but not toxic megacolon. Stool cultures and enzyme immunoassay (EIA) for *Clostridium difficile* toxins A and B were both positive. A colonoscopy revealed diffuse Pseudomembranes in the sigmoid and descending colon and the biopsy confirmed the diagnosis (Figure 1). Oral vancomycin was administrated (1 g/day for 14 days) and the patient was discharged with complete resolution of her clinical findings 38 days afterwards.

Discussion

An uncommon case of paclitaxel associated with pseudomembranous colitis is reported. Paclitaxel blocks microtubule depolymerization and causes the formation of bundles of microtubules, thereby arrests mitosis and may facilitate proliferation of *Clostridium difficile* [4]. Among patients receiving standard regimens of paclitaxel-containing chemotherapy, 20% are likely to be hospitalized at least once with symptoms of nausea, vomiting, diarrhea, and dehydration, but the actual rate of chemotherapy related *Clostridium difficile*-associated diarrhea is not simple to determine and probably underestimated, as most relevant

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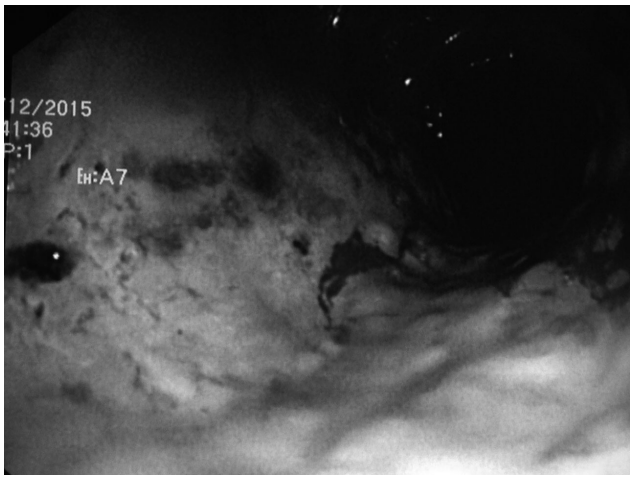

Figure 1. — Endoscopic appearance of the sigmoid colon showing diffuse pseudomembranes with hemorrhage.

Table 1. — *Cases in the literature with confirmed pseudomebranous colitis after chemotherapy.*

Patient no.	Diagnosis	Regimen	Years old	Cycle	Presenting symptoms	Stool culture	CD toxin	Previous Antibiotics	Response (clinically, radiologically)	Refs.
1	Colon	5-FU	59M	N/A	N/A	Negative	ND	none	CR	7
2	Ovary	CDDP, CPA, 8 VP-16	65F	N/A	Bloody stool on the day after onset of diarrhea negative	-		IPM, fluconazole	CR	7
3	Ovary	CDDP, DOX, CPA	56F	N/A	Bloody stool was seen two days after onset of diarrhea	Negative	+	none	CR	7
4	H&N	CPT-11	68M	N/A	N/A	Negative	ND	IPM, fluconazole	Death	7
5	Papillary serous adenocarcinoma of the ovary	Paclitaxel, carboplatin	66F	2	Severe epigastric pain, nausea, vomiting, diarrhea and fever	N/A	+	N/A	Death	8
6	IIIc endometrial cancer	Paclitaxel, carboplatin	50F	1	Massive bloody and watery stool was seen 14 days after onset of diarrhea	Positive	None	N/A	CR	9
7	Br.Ca.	Paclitaxel	N/A	N/A	N/A	Positive	N/A	none	CR	10
8	GCT	Bleomycin, cisplatin, vinblastine	26M	1	Abdominal cramping, mild diarrhea	Positive	Positive	None	CR	11[1]
9	Pancreas	Capecitabine and docetaxel	83M	1	Diarrhea and painless melena	Negative	Negative	None	CR	12
10	NSCLC	Carboplatin and docetaxel	47M	3	Febrile neutropenia, odynophagia, mucositis, diffuse abdominal pain and severe bloody diarrhea	Positive	Positive	None	CR	12
11	Br.Ca	Cisplatin and docetaxel	41F	2	Abdominal cramps and severe watery diarrhea that quickly became bloody	Negative	Negative	None	CR	12
12	V.Ca.	Carboplatin and paclitaxel	78F	8	Abdominal pain, fever and bloody and watery stool	Positive	Positive	Positive	CR	Current case

Patients with pseudomebranous colitis after chemotherapy. CR: complete response, NSCLC: non-small cell lung cancer, mBr.Ca: metastatic Breast cancer, GCT: germ cell tumour, V.Ca: vulvar cancer F: female, M: male, CDDP: cisplatin, CPT-11: irinotecan hydrochloride, 5-FU: fluorouracil, VP-16: etoposide, CPA: cyclophosphamide, DOX: doxorubicin hydrochloride, IPM, imipenem/cilastatin, N/A: Not assessed. [1]continued chemotherapy

studies were conducted on a small scale. Anand and Glatt [5] after reviewing 23 cases of chemotherapy-related *Clostridium difficile* concluded that methotrexate was the most common agent, but others chemotherapeutic treatments like cisplatin, bleomycin etc. were also associated. Husain *et al.* [6] associated *Clostridium difficile* infection with high-dose treatment regimens [4], with regimens containing paclitaxel [5], and its associated steroid premedication [6], and with concurrent exposure to antineoplastic and antimicrobial therapy [6]. Finally, as noted in Table 1, pseudomembranous colitis caused from chemotherapy usually appears soon after its administration, with watery stool that soon becomes bloody. It affects almost equally men and women (5/12 males and 7/12 females) with a mean age of 58.64 (men male age 56.6 and female age 60.33) years.

Conclusions

Pseudomembranous colitis related to treatment with paclitaxel is an uncommon case in clinical practice and literature. The combination of the clinical symptoms and characteristic findings in colonoscopy can help in the prompt diagnosis and management of this clinical entity. Clinicians need to have a high index of suspicion and request stool culture and enzyme immunoassay (EIA) for *Clostridium difficile* toxins A and B when the syndrome is suspected.

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