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Intestinal lymphangitis carcinomatosa related to ovarian cancer: Case report and review of the literature

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ABSTRACT

We present a 57-year-old woman with ovarian cancer that presented to the Emergency Room with a proximal small bowel obstruction. Exploratory laparotomy evidenced a thickened 10 cm extension of the proximal jejunum without bowel peristalsis, with stenotic enteric lumen, with a lesion apparently originating from its submucosal and muscular layers. The patient underwent an exploratory laparotomy with total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, small bowel resection and peritoneal biopsies. Final pathology and immunohistochemistry confirmed the intra-operative suspicion of lymphatic intestinal spread of malignant cells originating from a high grade serous carcinoma of ovarian origin. To the best of our knowledge, this is the first report in the literature of intestinal carcinomatous lymphangitis related to ovarian cancer, and the first report of involvement of the proximal portion of the jejunum.

1. Introduction

Lymphangitis carcinomatosa (LC) is defined as the diffuse involvement of metastatic malignant cells in lymph vessels (Bruce et al., 1996). The term 'Lymphangitis carcinomatosa' was first used in 1873 by Troisier to describe diffuse infiltration of malignant cells in the lymphatics of both lungs (Bruce et al., 1996).

Pulmonary LC is defined as the diffuse involvement of metastatic malignant cells in the pulmonary lymph vessels (Nakasono et al., 2006). It has been related to terminal stages of carcinomas originated from breast, stomach, lung, pancreas, prostate, cervix and colon cancers (Bruce et al., 1996; Nakasono et al., 2006). Extrapulmonary sites of LC are rare, and include the skin, the duodenum, and the bile duct (Burbano et al., 2018; Gabata et al., 1998; Hayes and Berry, 1992; Nakasono et al., 2006).

We perform a systematic review of the literature including all case reports about intestinal LC. To the best of our knowledge, this paper is the first case report of a woman with an intestinal LC related to ovarian cancer (OC) compromising a segment of the bowel other than the duodenum.

2. Case report

In July 2017, a 57-year-old woman was referred to our hospital with an abdominal computerized tomography (CT) scan performed about 7 months earlier showing a 3.5 cm mixed lesion in the left ovary, and inguinal lymphadenopathy. Physical exam was unremarkable, except by palpable bilateral inguinal lymphadenopathy (3 on the left and 1 on the right). CA-125 was 391.5 U/ml, and other tumor markers were normal. Abdominal magnetic resonance (MR) scan was performed, showing a mixed lesion of 3.7 cm in the left ovary, 1.2 cm endometrial thickness and inguinal lymphadenopathy. Inguinal lymph node core biopsy was negative for malignant cells. Colonoscopy and mammography were unremarkable.

Videolaparoscopy was performed showing a white liquid compatible with chylous ascites, lesions in the omentum were compatible with metastatic implants, and absence of mesenteric retraction or macroscopic changes in small and large bowels, and stomach. Left oophorectomy was performed and sent to frozen section analysis: diagnosis was undifferentiated malignant neoplasia, and could neither confirm carcinoma, nor rule out lymphoma. The patient was discharged on the

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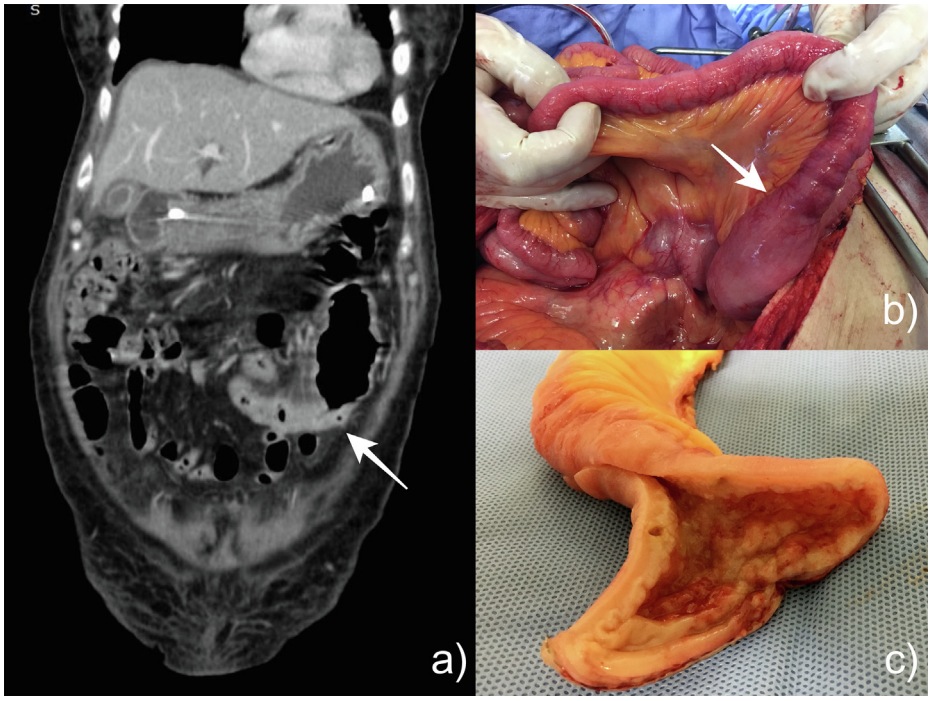

Fig. 1. White arrows showing proximal jejunal stenosis (A: abdominal CT; B: intraoperative); Thickened 10 cm extension of the proximal jejunum with proximal jejunal and duodenal dilatation (B: white arrows); Jejunum specimen without mucosa or serosa involvement (C).

second postoperative day. Definitive histologic examination documented high grade serous OC.

The patient was readmitted to the emergency room 2 weeks later with clinical signs and symptoms of proximal small bowel obstruction. Abdominal CT scan was compatible with proximal small bowel obstruction, due to stenosis of the proximal jejunum just after the fourth duodenal portion (Fig. 1A). An exploratory laparotomy was performed, showing a thickened 10 cm extension of the proximal jejunum with stenotic lumen, without peristalsis or implants on the serosa. Apparently, the jejunal lesion was originating from its submucosal and muscular layers (Fig. 1B and C). Proximal small bowel resection, total hysterectomy, omentectomy, and resection of peritoneal implants in hepatic round ligament and bladder were performed, without any residual disease (optimal cytoreduction).

Pathology identified a tumor implant in the cortex of the right ovary, associated with tumor involvement of the uterus, and proximal jejunum. In the jejunum, macroscopic examination revealed luminal stenosis due to a white, annular, infiltrating tumor, measuring 7.2 cm in length, and microscopic examination showed tumor emboli in the lymphatics of the mucosa, submucosa and muscularis propria, associated with stromal invasion of these structures (Fig. 2A). No serosal involvement was identified in the jejunum. Serosal tumor implants were found on the round ligament and pre-vesical fat. An average endometrial thickening of less than 0.1 cm was evidenced, with endometrial hyperplasia without atypia. Immunohistochemistry (Fig. 2B) was positive for cytokeratin 7 (OV-TL 12/30), p63 (4A4), CA-125 (OC125), PAX-8 (MRQ-50), estrogen receptor (SP1), WT1 (6F-H2), and negative for cytokeratin 20 (Ks20.8), CDX2 EPR2764Y), Vilin (CWWB1) and GATA3 (L50-823). The immunohistochemical profile was compatible with metastatic involvement of the small intestine by high grade serous OC. Two weeks postoperatively, the patient develop a pleural effusion in right chest. Thoracentesis was compatible with chylothorax, and about 1000 ml were drained. Because of her clinical debilitation, the medical oncologist declined to prescribe chemotherapy at that time and the patient was discharged. Four months postoperatively, another admission in the emergency to treat pneumonia was necessary. The patient did not respond to antibiotic therapy and died in 2 weeks (about 11 months and 2 weeks since the initial CT).

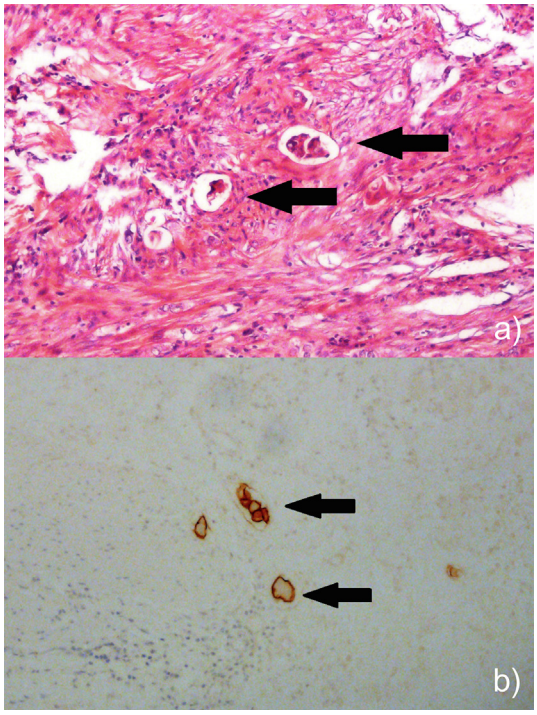

Fig. 2. HE (400×) showing lymphatic embolization of submucosal vessels (A; arrows); CA-125 immunohistochemistry (400×) showing positive nuclei in the lymphatic emboli (B; arrow).

3. Discussion

There are some descriptions of pulmonary LC in the literature, being the first one credited to Gabriel Andral in 1829 (Doyle, 1989). The term LC is usually mistaken as a synonymous of its pulmonary manifestation.

Table 1
Cases of lymphangitis carcinomatosa in abdominal organs.

N	*Ref*	*Year*	*Age*	*Primary tumour*	*Organ with Lymphangitis*	*Clinical Manifestation*	*Survival (days)*
1	Subramanian et al. (2014)	2014	44	Gallbladder	Duodenum	None	180
2	Nakasono et al. (2006)	2006	71	Stomach	Duodenum	None	162
3	Nakasono et al. (2006)	2006	74	Pancreas	Duodenum	None	81
4	Nakasono et al. (2006)	2006	53	Unknown	Duodenum	None	80
5	Nakasono et al. (2006)	2006	73	Pancreas	Duodenum	None	64
6	Gabata et al. (1998)	1998	63	Stomach	Bile duct wall	Cholestasis	Not reported
7	Present study	2017	57	Ovary	Proximal jejunum	Intestinal Obstruction	163

N number of patients; *Ref* bibliographic reference; *Year* if informed is year of the case occurred (if not, the year of publication); *Survival* time in days estimated since lymphangitis diagnosis.

Extrapulmonary sites of LC are rare, and include the skin, the duodenum, and the bile duct (Burbano et al., 2018; Gabata et al., 1998; Hayes and Berry, 1992; Nakasono et al., 2006).

The etiology of LC remains unknown, but some theories have been suggested (Bruce et al., 1996; Murin, 1997; Raja et al., 2010; Subramanian et al., 2014): one suggest that tumor embolize through hematogenous metastasis, producing obliterative endarteritis, and subsequently extends through the vascular walls into the perivascular lymphatics; while another theory hypothesizes that tumor spreads via the lymphatics. Nonetheless, both mechanisms might be involved simultaneously (Bruce et al., 1996; Murin, 1997).

After a systematic literature search of the databases PubMed and Cochrane Central Register of Controlled Trials (search date 20-05-2020) using the search terms “lymphangitis”[MeSH Terms] OR “lymphangitis”[All Fields]) AND carcinomatosa [All Fields], 139 citations were identified. After screening all abstracts, 3 citations were selected (Gabata et al., 1998; Nakasono et al., 2006; Subramanian et al., 2014), 2 reporting on patients with intestinal LC (Nakasono et al., 2006; Subramanian et al., 2014) and 1 on patient with bile duct wall LC (Gabata et al., 1998). Until today, the primary tumors related to intestinal LC reported were pancreatic (2 cases), gallbladder, gastric, and unknown. There is only 1 case reported of lymphatic bile duct wall stricture in a patient with gastric cancer. The data is summarized in Table 1. There is no intestinal LC related to OC reported in the English literature. There was no clinical manifestation of LC in 71.4% (5/7) of the patients. The median age at diagnostic was 63, with a median survival of 121.5 days.

LC is often associated with poor cancer prognosis (Klimek, 2019). There are only few reports of intestinal involvement with variable primary sites published (Nakasono et al., 2006; Subramanian et al., 2014), making the prognosis analysis unfeasible. It is possible that OC extrapulmonary lymphangitis can achieve better prognosis if properly treated. Unfortunately, our patient died before chemotherapy.

4. Conclusion

In conclusion, our report demonstrates an unusual pattern of OC metastasis: embolization of intestinal lymphatic vessels, with subsequent stromal invasion. To the best of our knowledge, this is the first report in the literature of intestinal carcinomatous lymphangitis related to OC, and the first report of jejunal bowel segment with intestinal lymphangitis. Although rare, it is possible that intestinal LC is being underestimated in medical literature.

CRediT authorship contribution statement

Ricardo Pedrini Cruz: Conceptualization, Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Gustavo Peretti Rodini:** Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Margarete Duarte da Rosa:** Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Vinicius Duarte Cabral:** Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Eduardo Cambruzzi:** Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Gabriella Ferrandina:** Formal analysis, Writing - review & editing. **Reitan Ribeiro:** Formal analysis, Writing - review & editing.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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