

Late colonic metastases from ovarian carcinoma: report of two cases and review of the literature

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ABSTRACT

Introduction: Ovarian cancer is associated with high mortality and there has been little therapeutic progress in recent years. It has a high rate of peritoneal spread and recurrence. Solitary colonic metastatic implants are rare, difficult to diagnose, and have no defined treatment.

Objective: To describe two clinical cases of late colonic metastases from ovarian carcinoma.

Methods: We present two patients with a history of surgically treated ovarian cancer who developed colonic metastases eight and twenty years after the initial diagnosis.

Results: The diagnosis was based on imaging studies, tumor markers, and immunohistochemistry. The CK7+/CK20–immunophenotype was identified as an indicator of ovarian origin. Surgical treatment involving complete resection and regional lymphadenectomy was essential for controlling the disease in both patients. After follow-up periods of 36 and 48 months, no evidence of local or distant recurrence was observed.

Conclusions: Ovarian cancer can manifest with solitary metastases over time. Imaging may reveal distinctive features that could raise suspicion of the disease, differentiating it from primary colon cancer. Surgical treatment consists of organ resection and regional lymphadenectomy.

Keywords: Ovarian cancer; Colonic metastasis of ovarian cancer; Late metastasis

INTRODUCTION

Ovarian cancer is the seventh most lethal malignant neoplasm, and there has been little progress in therapeutic outcomes over the last three decades. This causes approximately 600,000 deaths per year worldwide. Approximately 70% of patients have disease spread to the peritoneum by direct extension at the time of diagnosis, and 60% of those patients experience recurrence.¹

Metastases in the colon are common in the context of intraperitoneal spread, however, solitary forms are much rarer and exceptional when they appear several years after initial treatment, as in the two cases that motivate this presentation.

CASE 1

A 66-year-old woman with a history of appendectomy in childhood, at age 46, underwent a total hysterectomy with bilateral salpingo-oophorectomy and omentectomy for ovarian cancer. She underwent postoperative chemotherapy and radiotherapy, although the drugs and doses used are unknown. She had oncological checkups for 20 years, and there was no recurrence.

During a colonoscopy to screen for colorectal cancer in a patient at average risk, an area of stenosis was

identified 30 cm from the anal margin, preventing the passage of the endoscope due to extrinsic compression. The tumor biomarkers CA-125, CEA, and CA 19-9 were within normal limits.

A high-resolution magnetic resonance imaging (MRI) scan was performed, revealing a polylobulated hypodense formation in the sigmoid colon with a cystic/mucinous appearance, suspected of being a peritoneal implant secondary to the ovarian history (Fig. 1). Virtual colonoscopy revealed luminal stenosis resulting from heterogeneous ovoid extrinsic compression with hypodense areas and calcifications, without a cleavage plane with the colon wall (Fig. 2).

A laparoscopic left colectomy with regional lymphadenectomy was performed. The pathological anatomy revealed metastatic infiltration of low-grade serous carcinoma of ovarian origin, with two positive lymph nodes. Immunohistochemistry revealed positivity for CK7, CK20, p16, and estrogen and progesterone receptors, and negativity for WT1.

Four courses of carboplatin were indicated as adjuvant treatment, but were not completed due to intolerance. At 48 months post-surgery, there is no evidence of recurrence.

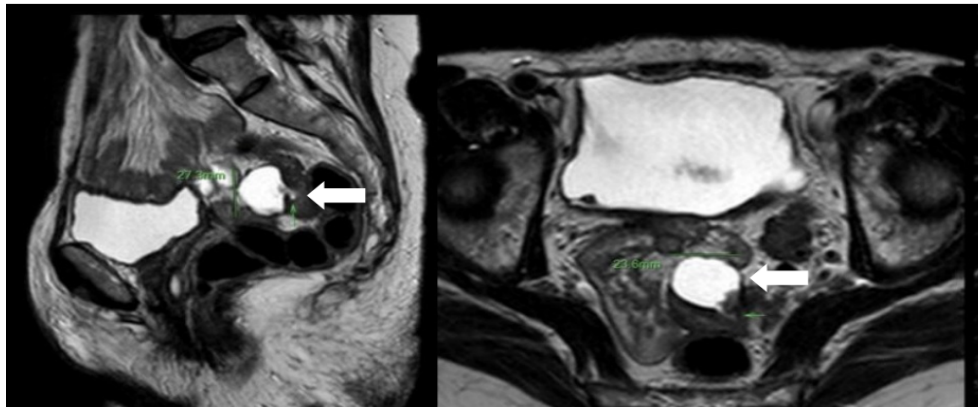


Figure 1. Case 1. The magnetic resonance imaging reveals a multilobulated lesion in the sigmoid colon, exhibiting hyperintensity on T2 and cystic or mucinous characteristics. An eccentric hypermetabolic solid area is identified, suggesting a peritoneal implantation secondary to a history of ovarian cancer (arrow).

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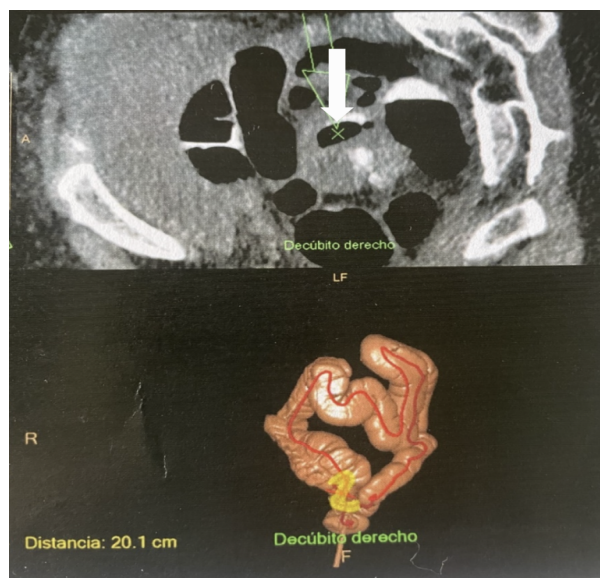


Figure 2. Case 1. The virtual colonoscopy reveals luminal stenosis resulting from extrinsic ovoid compression. The lesion is heterogeneous, with hypodense areas and calcifications. There is no cleavage plane between the lesion and the colonic wall.

CASE 2

An 80-year-old woman with diabetes underwent a total hysterectomy with bilateral salpingo-oophorectomy and omentectomy for ovarian cancer at the age of 65. The patient received adjuvant therapy consisting of paclitaxel and carboplatin. Three years later, a sigmoid colon tumor was detected, and the patient underwent a 5 cm segmental resection of the colon, a biopsy of a bladder nodule, and a resection of the residual omentum. The pathological examination revealed the presence of ovarian metastases in the colon and omentum, as well as an inflammatory nodule in the bladder.

One year later, the patient exhibited adenopathy above the inferior mesenteric artery, necessitating additional surgical intervention. The pathological examination confirmed once again metastasis of ovarian adenocarcinoma.

Eight years later, she presented with symptoms indicative of intestinal occlusion. Therefore, a colonoscopy was performed, which revealed a lesion occupying 90% of the lumen 15 cm from the anal margin. A biopsy of the lesion revealed normal colonic mucosa. The tumor markers CEA, CA 19-9, and CA 125 were found to be within normal limits. A MRI scan revealed a lesion on the colon wall, accompanied by adenopathy in the mesorectum. A new laparotomy was performed, during which a 5-cm tumor at the rectosigmoid junction was resected, and a primary anastomosis was performed 7 cm from the anal margin. The pathological anatomy revealed metastasis of high-grade serous ovarian carcinoma, with two of 14 positive lymph nodes. Immunohistochemistry revealed positivity for CK7, p16, PAX-8, WT1, and estrogen and progesterone receptors, and negativity for CK20, p63, and chromogranin (Fig. 3).

Adjuvant therapy with paclitaxel and carboplatin was indicated; however, treatment had to be suspended due to severe leukopenia.

Months later, a positron emission tomography (PET-CT) scan revealed two nodules in the posterobasal region of the right lung. A video-assisted thoracoscopic lobectomy was performed. Subsequent pathological examination confirmed that metastases originated from an ovarian adenocarcinoma.

At the 36-month follow-up, the patient exhibited no signs of recurrence.

DISCUSSION

Epithelial ovarian carcinoma constitutes 85 to 90% of malignant ovarian neoplasms. The disease is characterized by its tendency to spread through direct invasion, which can result in peritoneal carcinomatosis. This often leads to fatal outcomes, including death from ascites and intestinal obstruction. Metastasis through vascular

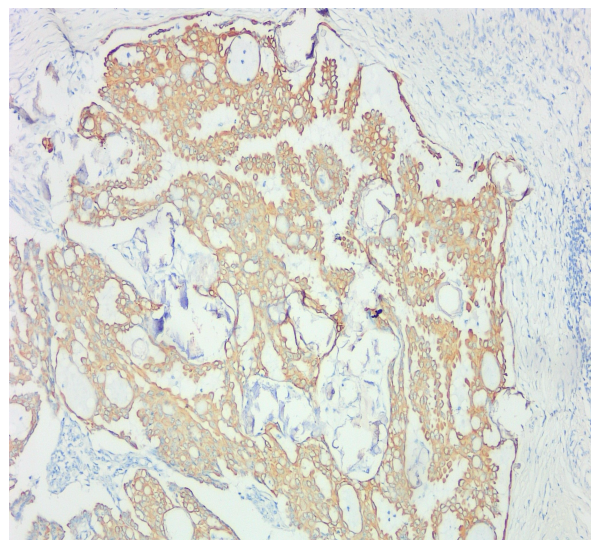


Figure 3. Case 2. Immunohistochemical staining of the metastatic lesion. CK7 positivity is identified.

spread is less common (16%), and the organs most commonly affected are the pleura (33%), liver (26%), lung (15%), and spleen.^{1,2} Solitary metastases in the colon account for 1% of colorectal tumors. The diagnosis of these conditions is frequently made in patients with neoplasms originating in the lung, ovary, breast, prostate, kidney, and melanoma. Those originating in the ovary account for between 4 and 6% of cases and are more prevalent in the left colon, although they have also been observed in the cecum.³⁻⁵

The classification of colonic metastases is determined by the route of spread, which may be hematogenous, lymphatic, or contiguous (peritoneal implants). In the latter case, the serosa of the colon is initially involved, followed by infiltration of the muscular wall and, finally, the mucosa. Embolic forms are extremely rare and manifest via the bloodstream or lymphatic system. Zigelboim et al.⁶ reported a case of recurrence of epithelial ovarian carcinoma as an intraluminal colonic lesion, polypoid in shape with preservation of the serosa. Consequently, the origin was considered hematogenous due to embolization in the submucosal network.

In the cases presented, the pathophysiological mechanism of metastasis was peritoneal invasion. Pathological anatomy confirmed invasion of the colonic wall from the serosa and subserosa without mucosal involvement.

The interval between the initial diagnosis of primary ovarian cancer and the subsequent development of colonic metastasis typically ranges from 1 to 22 years, with a median of 9 years and an average age of 58.8 years.^{3,4}

In our cases, the duration of the disease-free interval was extensive, which can complicate diagnosis. In the first patient, the disease-free interval was 20 years, while in the second, after metastasis to the colon at 3 years, the recurrence-free interval was 8 years.

The presentation is consistent with that of colorectal cancer. A medical history of treatment for ovarian cancer, irrespective of the duration of progression, should raise suspicion of metastasis. Direct visualization during colonoscopy can contribute to suspicion in cases of a protruding lesion with intact mucosa.

Tumor markers (CEA, CA 19-9, and CA 125) can be useful, however, normal results do not necessarily rule out metastasis. Imaging procedures can guide the diagnosis, as observed in our patients.⁷

The histological distinction between primary colon adenocarcinoma and metastatic ovarian adenocarcinoma can be challenging. Immunohistochemical studies of CK7 and CK20 are beneficial in this regard. In the study by Loy et al.,⁷ a CK7-positive/CK20-negative immunophenotype exhibited 100% specificity for differentiating primary ovarian carcinoma from metastatic colon carcinoma. A CK7-negative/CK20-positive immunophenotype exhibited a 99% specificity in differentiating metastatic colon carcinoma from ovarian carcinoma. Although less specific than CK immunostaining, positivity for CA-125, estrogen receptors, and progesterone receptors is indicative of primary ovarian carcinoma. Conversely, positivity for MUC2 and CDX2 is associated with primary colon cancer.

Cytoreductive surgery is the standard treatment for advanced ovarian cancer, and, based on this criterion, solitary metastases have been treated by segmental resection.

However, O'Hanlan et al.⁸ conducted a study on 100 patients who underwent intestinal resection for ovarian cancer. Notably, of the 33 patients who underwent mesenteric resection, 70% exhibited positive lymph nodes. In both cases presented, positive lymph node invasion was observed. Consequently, we support the recommendation of at least 5 cm of longitudinal resection, as previously outlined by these authors.

Overall survival in ovarian cancer with colon metastases may be acceptable. The DESKTOP III study demonstrated that patients who underwent secondary cytoreductive surgery had a higher likelihood of survival, particularly when the interval to first recurrence was prolonged. The survival benefit was observed only in patients who underwent complete tumor resection. Currently, selecting appropriate patients is essential, prioritizing those with a high probability of achieving complete resection. The primary factors that contribute to resectability include: an interval of more than six months without platinum treatment, a satisfactory overall health status, a complete resection during the initial surgery, the absence of a substantial ascites volume (>500 mL), the absence of unresectable lesions as determined by imaging, and the absence of surgical contraindications.⁹

CONCLUSIONS

Solitary and late metastases of ovarian cancer to the colon and rectum are rare, even many years after initial treatment, and require a high index of clinical suspicion. Colonoscopy, CT, and MRI allow the identification of lesions with particular characteristics that can be differentiated from primary colorectal cancer. Immunohistochemistry is a fundamental component of the diagnostic process. In selected patients, complete resection with locoregional lymphadenectomy, followed by adjuvant treatment, offers the best oncological control and prolonged survival.

Contributions:

JIP: Bibliographic research and topic updates. JPS: Development and study of pathological anatomy specimens. RGI: Patient data management and development. YZ: Design, writing, and layout. AMM: Scientific advice and review.

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