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Incidental diagnosis of breast cancer in the pursuit of the treatment of intestinal obstruction

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ABSTRACT

Intestinal lipomatosis is rare and often asymptomatic but can present with intestinal obstruction. Occasionally, metastatic breast cancer is identified in the ovary before a breast primary is discovered. We report the case of a 50-year-old woman diagnosed with synchronous intestinal obstruction due to lipomatosis, and incidental ovarian metastases from breast cancer. The patient presented with a 12-day history of nausea, diffuse abdominal pain, and constipation. An abdominal x-ray showed air-fluid levels, and computed tomography documented small bowel distention. An explorative laparotomy was performed, which revealed small bowel distention, an obstructive lesion of the ileocecal valve, three terminal ileum lesions, ascites, and heterogeneous ovaries. Right ileocolic resection and left oophorectomy were performed. The pathological diagnosis revealed lipomatous submucosal lesion of the ileocecal valve and ileum, and 17 lymph nodes, which were all negative for malignant cells. The oophorectomy revealed ovarian metastasis from breast carcinoma. Ascitic fluid was positive for malignant cells. Mammography and breast/axillary ultrasonography showed a solid nodule of the left breast, ductal carcinoma, and multiple enlarged left axillary lymph nodes, which were positive for neoplastic cells. Immunohistochemical evaluation showed hormonal receptor positivity and C-erb2 negativity. Breast magnetic resonance imaging showed a 14 mm left nodule and a positron emission tomography scan revealed ^{18}F-FDG uptake in the left breast, left axillary lymph nodes, right ovary, and peritoneum. The tumor was staged as stage IV ductal breast carcinoma, cT1N1M1, Grade 2, Luminal B-like. The multidisciplinary oncological meeting proposed chemotherapy, and a re-staging breast MRI after chemotherapy, which showed a complete response. The patient started treatment with letrozole and remains disease-free 22 months after finishing chemotherapy.

Keywords
Lipomatosis; Intestinal Obstruction; Breast Neoplasms; Neoplasm Metastasis; Ovary; Peritoneum

INTRODUCTION

Diffuse intestinal submucosal lipomatosis is a sporadic condition with a few cases reported in the medical literature.[1] Usually, patients are asymptomatic, but these lesions may present as perforation, obstruction, ulceration, intussusceptions or bleeding.[2,3]

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Breast cancer is the most common malignancy in women worldwide, and is one of the leading causes of death among women,[4] with a reported incidence rate of 46.3% and a mortality rate of 13%.[5]

Metastatic breast cancer to the ovaries is not uncommon and represents 6-27.8% of all malignant ovarian tumors; however, it has been reported at autopsies in 50% of patients with breast cancer.[6,7]

Here, we report the case of a woman with synchronous intestinal lipomatosis that presented as an intestinal obstruction, and was revealed to be an incidental diagnosis of breast cancer metastatic to the ovary.

CASE REPORT

A 50-year-old Caucasian woman presented to the emergency department with a 12-day history of nausea, diffuse abdominal pain, and constipation. She experienced menopause at the age of 42. Her past medical history included morbid obesity (BMI of 44 kg/m^2), type 2 diabetes, arterial hypertension, hypercholesterolemia, and two cesarean sections. No relevant medical family history was informed. On physical examination, she presented a distended and tympanic abdomen, diffusely painful without guarding. The laboratory work-up showed a C-reactive protein of 29.9 mg/L (normal range <7.5 mg/L) with 13.1 × 10^3/µL leukocytes (normal range 4.5-11.0 × 10^3/µL), and a plain abdominal x-ray documented air-fluid levels. Abdominal and pelvic contrast-enhanced computed tomography (CT) showed a minor small bowel distension without parietal enlargement, without a clear obstructive etiology, and with normal colon caliber.

Conservative therapeutic measures for intestinal obstruction were unsuccessful; therefore, she underwent a laparotomy within 24 hours of admission. Surgical findings included an entire small bowel distention, an obstructive lesion of the ileocecal valve with retracting serosa and mesentery, three terminal ileum implants resembling carcinomatosis, moderate ascites, and heterogeneous ovaries. Accordingly, ileocolic resection and left oophorectomy were performed. Ascitic fluid was sent for cytologic evaluation.

The post-operative period was uneventful; however, she was re-admitted 2 weeks after discharge due to wound infection, which resolved with antibiotics and dressings.

The pathological diagnosis revealed a lipomatous submucosal lesion of the ileocecal valve and terminal ileum, and all 17 sampled lymph nodes were negative for malignant cells. The oophorectomy identified an ovarian metastasis from breast carcinoma (Figures 1 and 2). Ascites cytology was positive for malignant cells, which were most likely from an adenocarcinoma.

The immunohistochemical evaluation revealed positivity for cytokeratin AE1/AE3, CK7 and hormonal

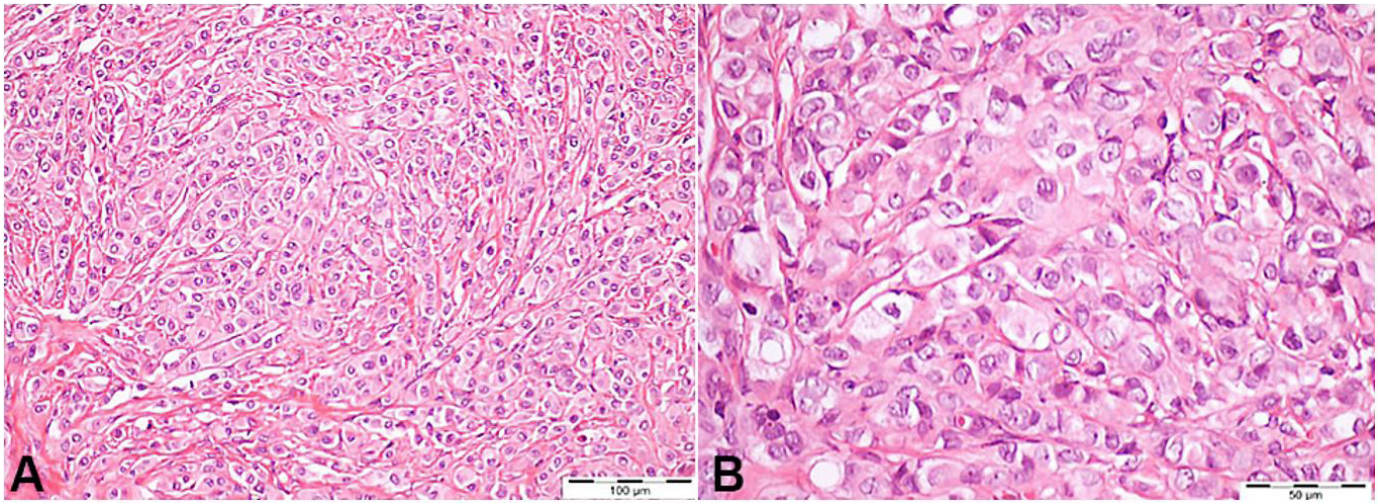

Figure 1. Photomicrograph of the ovary. **A –** Ovarian parenchyma almost entirely occupied by a proliferation of malignant epithelioid cells arranged in small nests and cords (H&E, 200x); **B –** Tumor cells were large, with irregular nuclei and prominent nucleoli (H&E, 400x).

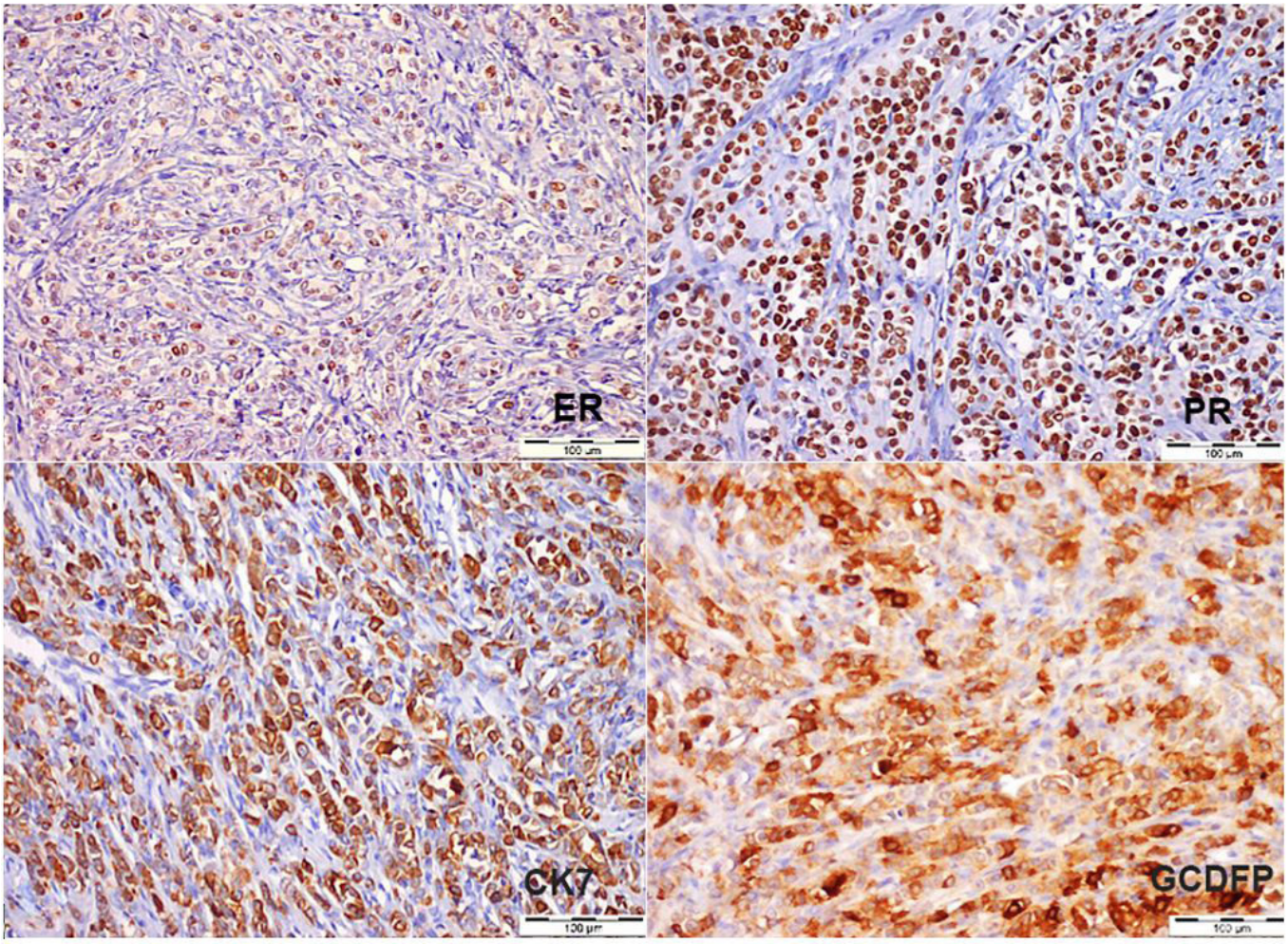

Figure 2. Photomicrograph of the ovary. Tumor cells showed immunoexpression of estrogen receptor (**ER**) in A, and progesterone receptor (**PR**) in B – intense staining in 75-100% cells, plus strong and diffuse immunoexpression of **CK7** in C and gross cystic disease fluid protein (**GCDFP-15**) in D.

receptors (HR) (75-100%), and negativity for CK20, e-cadherin, WT1, CA125, CDX2, and HER2 (score 0) (Figure 2).

A complementary study with mammography and ultrasonography of the breast and axilla was performed, which revealed a solid heterogeneous, spiculated nodule with 10 × 8 × 10 mm in the transition of the outer quadrants of the left breast, and multiple enlarged left axillary lymph nodes—the most prominent of which was 34 mm with metastatic features. Biopsies were performed, which revealed the presence of ductal carcinoma in the breast nodule. The fine-needle aspiration of the axillary lymph node was positive for neoplastic cells.

Histological findings were reviewed, and confirmed ovarian metastasis from ductal carcinoma of the breast. The immunohistochemical evaluation showed positivity for HR (75-100%), negativity for C-erb2 and Ki67 of 15-30%.

The upper and lower endoscopies were negative.

A thoracic, abdominal and pelvic CT scan and an abdominal and pelvic magnetic resonance imaging (MRI) scan showed a 14 mm left breast nodule, multiple enlarged left axillary lymph nodes, a right normal ovary, and uterine fibromas.

A positron emission tomography (PET) scan revealed ^{18}F-FDG uptake in the left breast, left axillary lymph nodes, right ovary, and peritoneum (Figures 3 and 4).

The baseline cancer antigen (CA)15.3 was 76.17 U/mL (normal range < 30 U/mL).

The tumor was assessed as a stage IV ductal breast carcinoma, cT1N1M1 (ovarian and peritoneal metastasis), Grade 2, Luminal B-like (HR+, HER2−).

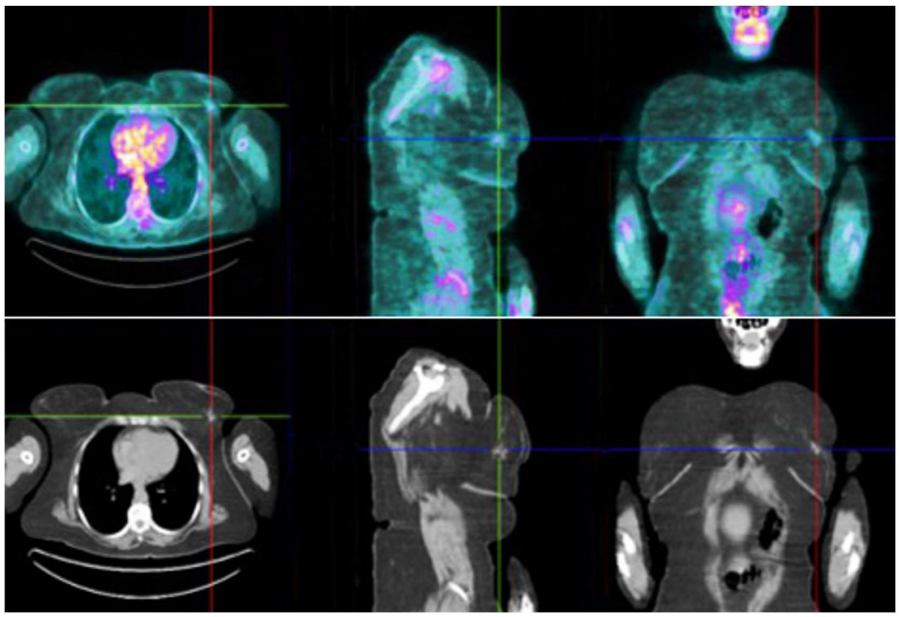

Figure 3. PET scan showing ^{18}F-FDG uptake in the left breast.

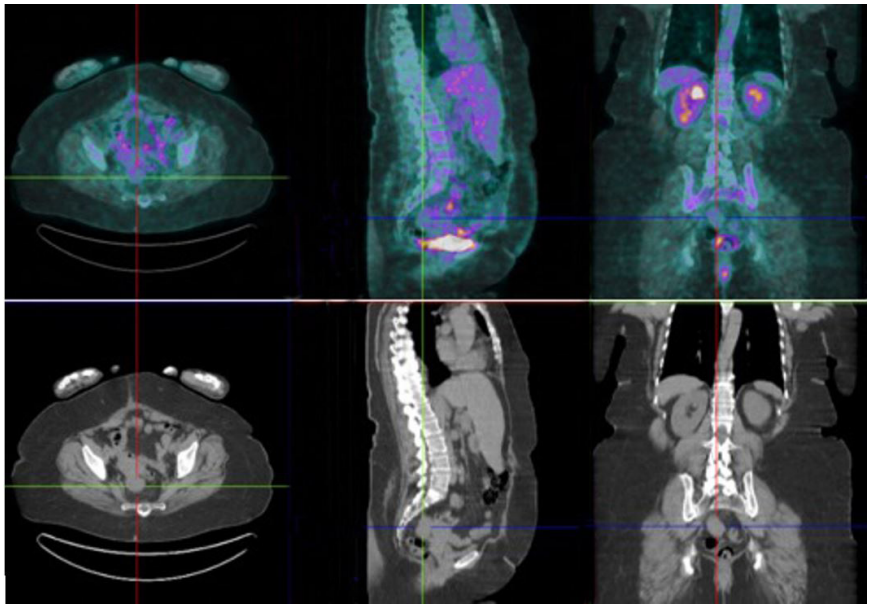

Figure 4. PET scan showing moderate ^{18}F-FDG uptake in right ovary area and less uptake posteriorly and inferiorly, which could be peritoneal implants.

The patient was referred to an oncological center and evaluated in a multidisciplinary oncological meeting, which proposed palliative chemotherapy. The patient completed six cycles of doxorubicin and cyclophosphamide with good tolerance. The re-staged breast MRI and PET scan showed complete response, and CA15.3 had dropped to 17.81 U/m.

After re-evaluation by the multidisciplinary oncological meeting, the patient started hormonal treatment with letrozole, and now remains in complete remission 22 months after the end of chemotherapy.

DISCUSSION

Primary small intestinal tumors are uncommon, which account for about 1% of all gastrointestinal tumors, and primary lipomas of the small intestine are rare.[8] The incidence rate of detection of intestinal

lipomatosis at autopsy ranges from 0.04% to 4.5%.[2] Lipomas of the intestine may be solitary, or multiple and encapsulated, or diffuse, discrete, non-capsulated lobules of adipose tissue, called lipomatosis. In 90% of the cases they are localized in the submucosa, but occasionally they extend into the muscularis propria, while up to 10% are subserosal.[9]

The colon is the most common site (65-75%) of lipoma location followed by the ileum.[10] No predilection site has been mentioned for lipomatosis in the literature.[11]

The age of presentation is highly variable, ranging from the neonatal period to the seventh decade of life.[3] No gender differences are observed.[12] Most intestinal lipomas are asymptomatic, but they can sometimes precipitate a surgical emergency, especially when the ileocecal valve and small intestine are affected.[13] The most frequent presenting symptom is abdominal pain.[14]

The etiology of lipomatosis is yet to be established. Hypothetical etiological factors include embryonic displacement of adipose tissue; degenerative disease with disturbance of fat metabolism; post-chemotherapeutic fat deposition; chronic irritation, such as chronic inflammatory bowel disease; low-grade infection; and hamartomatous syndromes.[15]

Clinical diagnosis may be difficult, but a pre-operative CT scan may be of value to characterize large submucosal masses, and to show the specific nature of a mass and the extent of disease.[1]

Plain abdominal films are non-specific and commonly demonstrate the presence of multiple air-fluid levels, which is suggestive of mechanical obstruction.[1]

The intraoperative appearance of the lesion can be confusing, and it may be difficult to exclude carcinoma on gross appraisal during surgery.[1] This is similar to our case, which resembled ileocecal carcinoma or ileal carcinomatosis.

Ovarian metastases from breast cancer generally reflect advanced breast disease,[4] and in most cases are bilateral.[16] The challenge of diagnosing a malignancy metastatic to the ovary is that the clinicopathological characteristics vary and the morphology can be different from the corresponding primary tumor.[17]

In this case, metastatic breast cancer was identified in the ovary before the primary breast tumor was suspected. The primary neoplasm may be quite small, and detailed imaging may be necessary for its detection.[18] Lobular carcinomas are known to spread to the ovary more frequently than ductal carcinomas, but because ductal cancer is considerably more common, most diagnostic challenges are posed by tumors with a ductal morphology.[7]

Metastatic involvement of the peritoneum in the setting of breast cancer is rare.[19] Therefore, it is mandatory to exclude other primary tumors, such as gastric and colorectal cancer, which more frequently present with peritoneal carcinomatosis. In this case, other etiologies were excluded with endoscopic studies, CT, MRI, and PET scans.

Patients with metastatic breast cancer are unlikely to be cured of their disease with any treatment.[20]

The removal of the primary tumor in patients with stage IV breast cancer has not been associated with prolongation of survival, with the possible exception of bone-only disease, being considered only in selected patients to improve quality of life.[20] Deviations to this approach may be made on a case-by-case basis in a multidisciplinary setting, although these instances are exceptional.

Complete remissions from systemic chemotherapy are uncommon, and, indeed, only a small fraction of complete responders remain progression-free for a prolonged period (being mostly those with oligometastatic disease or low-volume metastatic disease).[20] The patient reported herein started chemotherapy and experienced a substantial response. However, such tumors expressing hormonal receptors should start with hormonal/endocrine therapy, even in cases of visceral disease. Chemotherapy should be reserved for non-responders or for patients with a high tumor burden, or whenever rapid disease/symptoms control (e.g. a visceral crisis) is needed.[20] Furthermore, even in patients who progress after first-line endocrine therapy, there are now targeted agents (e.g. the CDK4/6 inhibitors), which can be added to endocrine therapy, with good long-term survival results.[20]

The median survival for patients with stage IV breast cancer is 18-24 months, although the range extends from only a few months to many years.[21]

CONCLUSION

Intestinal lipomatosis is rare and frequently asymptomatic, but occasionally it can present as an intestinal obstruction and should be kept as a differential diagnosis in unusual cases. Pre-operative image findings and even intra-operative macroscopic findings can be misleading; therefore, histologic evaluation will confirm the diagnosis. Ovarian metastasis eventually can be an incidental finding and be identified before the primary breast tumor. Metastatic involvement of the peritoneum in breast cancer patients is rare; thus, it is important to exclude other primary tumors. Stage IV breast cancer should be managed with endocrine therapy, targeted therapy and/or chemotherapy, depending on the hormonal receptors and the C-erb2 status, plus the patient's comorbidities, performance status, response to previous treatments, tumor burden, and associated symptoms. Our patient presented a rare cause of intestinal obstruction, a not-so-common case of ovarian and peritoneal carcinomatosis from breast cancer, and a rare case of complete response after chemotherapy in stage IV luminal breast cancer.

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The patient signed an informed consent form. The paper is in accordance with the institutional ethical research committee.

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