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Metastatic Pancreatic Cancer Presenting as Bilateral Ovarian Masses

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Abstract

Patient with locally advancer pancreatic cancer was treated with neoadjuvant chemotherapy and chemo-radiation. Surveillance scans showed a left pelvic mass. Since the radiological findings were suggestive of a second primary, she underwent surgery and was found to have bilateral ovarian pancreatic cancer metastasis. The case is being reported to draw attention to this rare oligometastatic presentation that could be treated with curative intent.

Keywords

Pancreatic Cancer, Ovarian Metastasis

1. Background

Ovarian lesions observed on imaging can encompass a wide range of potential pathologies, from primary ovarian neoplasms to metastatic disease. Metastatic lesions constitute approximately 25% of all ovarian masses, with the most common sources being gastrointestinal and breast cancers [1]. Ovarian metastasis from pancreatic adenocarcinoma is exceptionally rare, with limited cases documented in the literature. 22% of all ovarian cancers are metastatic from non-gynecological cancers and of this pancreatic cancer is responsible for 5% - 12%. Such metastases often present diagnostic challenges, as they can mimic primary ovarian malignancies on imaging and initial examination, leading to potential misdiagnosis. Moreover, pancreas cancer is the most common spread by lymphatics to organs such as the liver, lungs, brain, and bones, with different outcomes and survival curves with each type of metastatic pattern [2].

We present a rare case of ovarian metastasis originating from pancreatic adenocarcinoma, underscoring the importance of thorough evaluation and ongoing surveillance for metastatic disease in pancreatic cancer patients, even after completion of treatment.

2. Case Presentation

A 58-year-old woman with no significant past medical history was presented to the emergency room in January 2023 for left lower quadrant abdominal pain, nausea, vomiting and a 12-pound weight loss over several weeks. She had been seen by her primary care provider and directed to go to the emergency room for further evaluation. Imaging in the emergency room showed a pancreatic mass measuring 3.8 cm × 2.1 cm. Endoscopic ultrasound revealed a pancreatic body mass and biopsy was consistent with adenocarcinoma. CA19-9 at diagnosis was 83.5. She was staged as borderline resectable pancreatic cancer, and the plan was for upfront systemic therapy followed by radiation and possibly exploration for surgery. She was treated with modified FOLFIRINOX, but experienced significant adverse effects, including cytopenia and diarrhea. Imaging three months after starting treatment showed stable disease. After developing anaphylaxis to oxaliplatin, treatment was adjusted to dose-modified FOLFIRI, which she continued for a total of 5 months. The cancer was still borderline resectable, so to increase her chances of resection with negative margins, she was treated with capecitabine and radiation. Genetic testing was negative. A distal pancreatectomy and splenectomy were performed in November 2023, with pathology demonstrating a 2.2 cm adenocarcinoma with perineural invasion, negative margins, and negative nodes, pT2N0.

Surveillance CT scan in January 2024 showed a left-sided complex pelvic mass measuring 4.2 cm × 3.2 cm. Subsequent PET CT and ultrasound confirmed the presence of a complex cystic mass in the left adnexa, presumably originating from the left ovary, and a new mildly thickened endometrium, as shown in **Figure 1**. CA-125 was 3. The patient underwent a salpingo-oophorectomy in April 2024 to remove suspected peritoneal metastases or a new adnexal cancer. Intraoperatively, she had a mildly enlarged right ovary but did not look suspicious for a metastasis. However, the surgical specimen revealed pancreatic cancer in the right ovary measuring 3.5 cm and in the left ovary measuring 8.1 cm.

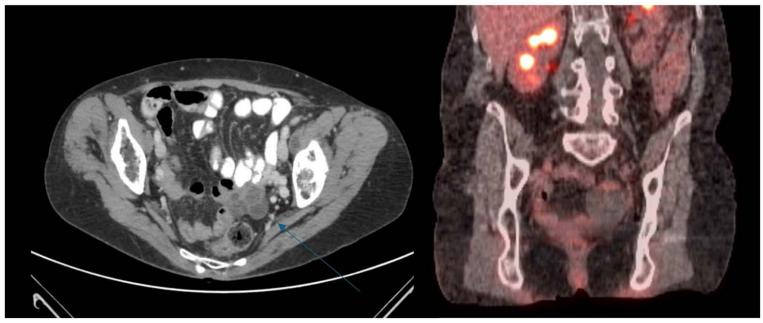

Figure 1. CT/PET images prior to surgery.

As seen in Figure 2, grossly, it is difficult to distinguish between ovarian primary mucinous tumors and metastatic mucinous tumors to the ovary. Cross sections display a multiloculated cystic tumor filled with mucin. On pathology evaluation as shown in Figure 3, ovarian cystic wall is lined by mucinous epithelium composed of atypical cells with nuclear enlargement, pseudo-stratification and mucinous cytoplasm. In some areas, the cells have deceptively bland cytological features mimicking ovarian mucinous cystadenoma. A few irregular glands in the underlying stroma demonstrate an invasive carcinoma. The specimen was also compared to the patient's prior pancreatectomy specimen showing similar tumor morphology.

Figure 2. Gross resection specimen.

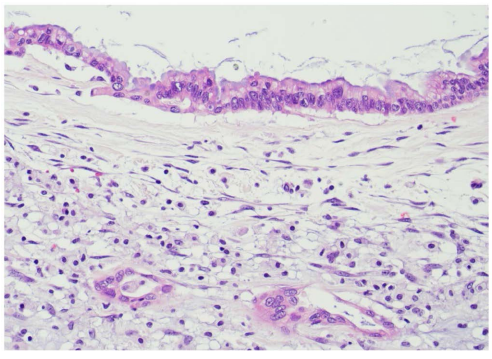

Figure 3. Hand E.

3. Discussion

Signed and informed consent was taken from the patient.

Ovarian mucinous carcinomas comprise 6% - 25% of primary ovarian carcinomas [3]. Among metastatic ovarian mucinous carcinomas, the most common source is the gastrointestinal tract. Most ovarian metastatic carcinomas have morphologic features that distinguish them from primary ovarian carcinomas. However, metastatic mucinous adenocarcinoma to the ovary can mimic primary ovarian mucinous carcinomas, causing a diagnostic dilemma and could lead to challenges in management. A less common source of metastatic mucinous adenocarcinoma to the ovary is pancreatic adenocarcinoma which in some series is estimated to be around 20% [3] [4].

Despite an algorithm to differentiate between primary versus metastatic ovarian tumors proposed by Seidman *et al.* demonstrating excellent diagnostic performance, it is not 100% specific [3]. The algorithm for general use to distinguish primary and metastatic tumors using the originally proposed criteria is bilateral tumors of any size, or unilateral tumor < 10 cm = metastatic and unilateral tumor > 10 cm = primary. Using this algorithm, 84% of all tumors were correctly classified, including 100% of primary tumors and 77% of metastatic tumors [5].

In their case series, Young *et al.* reported seven patients with mucinous tumors of the ovary that were metastases from adenocarcinoma of the exocrine pancreas [6]. Five out of the seven were explored primarily for the ovarian lesions and they were all found also to have peritoneal disease other than in the ovaries with pancreatic disease. Grossly, they had indistinguishable features from primary ovarian mucinous tumors [6].

The pathway for ovarian metastases from the pancreas remains unclear. Studies on ovarian metastases from the gastrointestinal tract suggest involvement of the ovarian stroma, but laterality does not correlate with the site of primary tumor [7].

Krukenberg tumors, a specific type of metastatic ovarian tumor often arising from GI cancers, provide additional insights. These tumors frequently exhibit lymph node metastases, which supports the hypothesis of retrograde lymphatic dissemination [8]. This mechanism underscores the ovary's potential role as a retroperitoneal organ involved in metastasis. Understanding these pathways is critical for improving diagnostic accuracy and treatment strategies for metastatic ovarian cancer.

In another series, Habib *et al.* describe a single institution series of ovarian metastases from pancreatic ductal adenocarcinoma [9]. Similar to this patient we describe, nine out of twelve developed metachronous ovarian recurrence during the surveillance period after a pancreatectomy. For those patients, the recurrence of free survival was 14.2 (IQR: 7.23 - 58.3) months. The OS for these nine patients was 44.6 (IQR: 18.6 - 82.9) months.

4. Conclusions

There remains no consensus on management strategy for this rare disease as much more evidence is required to support one treatment over another. Several studies

suggest a potential survival benefit of combining surgical resection and systemic therapy; however, the diagnostic dilemma remains crucial in determining what type of treatment to offer the patient [10] [11]. In a systematic review, Wang *et al.* found a total of five studies reporting 31 patients with metastatic pancreatic cancer to the ovaries [12]. However, only 9 of those 31 patients underwent pancreatectomy for their primary lesions. Moreover, there are newer studies suggesting a potential benefit of intraperitoneal chemotherapy with cytoreductive surgery [13].

Pancreatic adenocarcinoma is a highly lethal malignancy with limited treatment options, especially for patients presenting with advanced disease. This case highlights the critical importance of vigilant monitoring and consideration for metastatic spread to atypical sites, such as the ovaries, throughout the treatment journey. For selected patients, combined early surgical intervention and adjuvant chemotherapy may provide substantial benefits. At 18 months of follow-up, the patient remains alive, receiving quasi-adjuvant therapy with gemcitabine and capecitabine, with no evidence of disease recurrence.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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