Case Report

Solitary Pancreatic Metastasis from an Ovarian Carcinoma: A Diagnostic Perplexity

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Abstract

Ovarian cancer presenting as an isolated pancreatic metastasis after years of treatment is extremely rare. Most such patients are easily misdiagnosed as a case of primary pancreatic cancer. We herein describe a unique case of posttreatment high-grade serous papillary ovarian carcinoma metastasizing to the pancreas that mimicked primary pancreatic cancer and caused a diagnostic dilemma. The approach to such a case, pathogenesis, differential diagnosis, management, and a brief literature review is also presented.

Keywords: *High-grade serous papillary ovarian carcinoma, immunohistochemistry, ovarian metastasis, pancreatic adenocarcinoma*

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Introduction

The majority of pancreatic malignant tumors are primary pancreatic neoplasms. Metastasis to the pancreas is unusual, accounting for an overall prevalence of 6%–11%. Primary tumors of the lung, breast, kidneys, gastrointestinal tract, prostate, and melanomas have been reported to spread to the pancreas.[1,2] However, epithelial ovarian carcinomas metastasizing to the pancreas is a very rare event with only a handful of such cases documented in the world literature.[3-8] We report an extremely uncommon case of solitary pancreatic metastasis from a high-grade serous papillary ovarian carcinoma occurring 9 years after the original resection of the primary ovarian tumor.

Case Report

A 60-year-old lady, G3 L3, with comorbidities of hypertension and diabetes had a prior history of stage 1V ovarian cancer diagnosed in July 2010. Staging of the disease showed involvement of the left ovary with bilateral pleural effusion, multiple enlarged enhancing cardiophrenic nodes, multiple omental deposits, and ascites. She was given neoadjuvant chemotherapy with three cycles of paclitaxel and carboplatin (P + C) and she underwent debulking surgery with total abdominal hysterectomy and bilateral salpingo-oophorectomy and omentectomy in November 2010. The histological report showed scanty residual viable high-grade serous papillary ovarian carcinoma with omental metastasis. The immunohistochemistry (IHC) highlighted the tumor cells to be positive for Wilms' tumor protein (WT-1), paired-box gene 8 (PAX8), CK7, p53, estrogen receptors (ERs) with a high Ki67 proliferation index (>70%). The tumor cells were negative for CK20, caudal type homeobox (CDX2), thyroid transcription factor (TTF-1), progesterone receptors (PRs), calretinin and breast cancer gene (BRCA1) as well as BRCA2. She was then given adjuvant chemotherapy three weekly intervals of P + C for three cycles till January 2011 and a good response was observed. Unfortunately, she had a recurrence in July 2013 with spleen hilum and left lumbar region metastasis. She received other cycles of chemotherapy (three cycles of P + C) followed by etoposide (21 cycles) as she developed intolerance to chemotherapy. Since July 2015, she was on regular follow-up. She did not present with any new complaints and signs or symptoms. Her general condition was good till the year 2018.

However, on regular follow-up in July 2019, her transabdominal sonography revealed a well-defined

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hypoechoic lesion measuring 3.9 cm × 2.1 cm in size in the pancreatic region of indeterminate etiology. Computed tomography scan of the abdomen showed a relatively well-defined heterogeneously enhancing lesion measuring about 4.6 cm × 3.3 cm × 3.2 cm involving the body of the pancreas and abutting the stomach [Figure 1]. A possibility of a primary tumor of the pancreas or metastasis from ovarian cancer to pancreas was rendered. All her laboratory tests were unremarkable. The patient underwent a distal pancreatosplenectomy and wedge resection of the stomach. Grossly, a primary tumor of 5 cm × 5 cm was identified in the body of the pancreas infiltrating the posterior wall of the stomach [Figure 2]. On subsequent, histopathological examination, the tumor was reaching up to the muscularis propria of stomach wall. It showed features of high-grade serous papillary adenocarcinoma which were morphological identical to the previous surgical resected specimen of the ovarian mass which she had in the year November 2010 [Figure 3]. IHC studies further showed the tumor to be positive for WT-1, PAX8, CK7, ER, and p53 while being negative for CK20, CDX2, TTF-1, PR, carcinoembryonic antigen, carbohydrate antigen 19–9, and calretinin indicating ovarian tumor as its origin [Figure 4]. Based on these histological and immunohistochemical findings, a final diagnosis of pancreatic metastasis from high-grade serous papillary ovarian carcinoma was made. Her postoperative course was uneventful. The patient is still under regular follow-up since 2019 and has no fresh complaints or any recurrences.

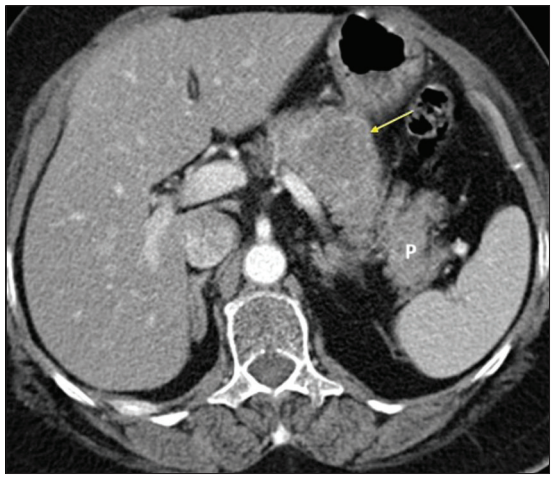

Figure 1: Axial contrast enhanced computed tomography image showing a well-defined heterogeneously enhancing lesion (arrow) in the body of the pancreas (P), suspicious for either a primary pancreatic neoplasm or metastasis

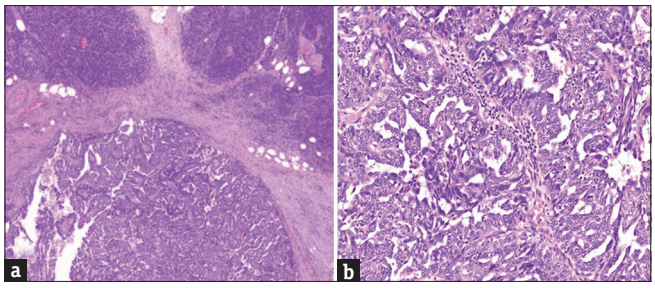

Figure 3: (a) Tumor surrounded by adjacent benign pancreatic tissue (H and E, ×100), (b) High grade papillary tumor (H and E, ×400)

Discussion

Ovarian cancers are commonly diagnosed gynecological malignancies worldwide with serous carcinoma of the ovary being one of the most common diagnosis of ovarian epithelial tumors.[9] It is important to recognize that while these neoplasms may seem to be localized to the peritoneal cavity in a

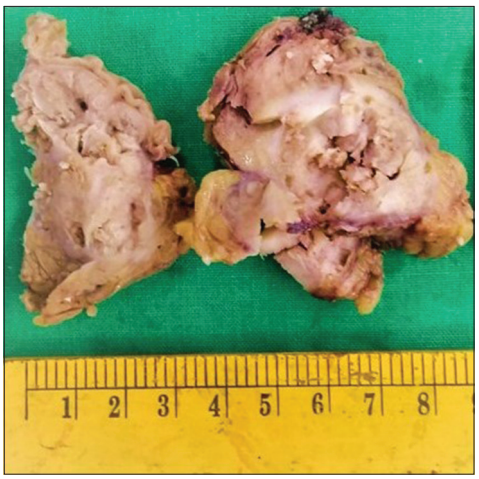

Figure 2: Resected specimen showing a tumor within the pancreas

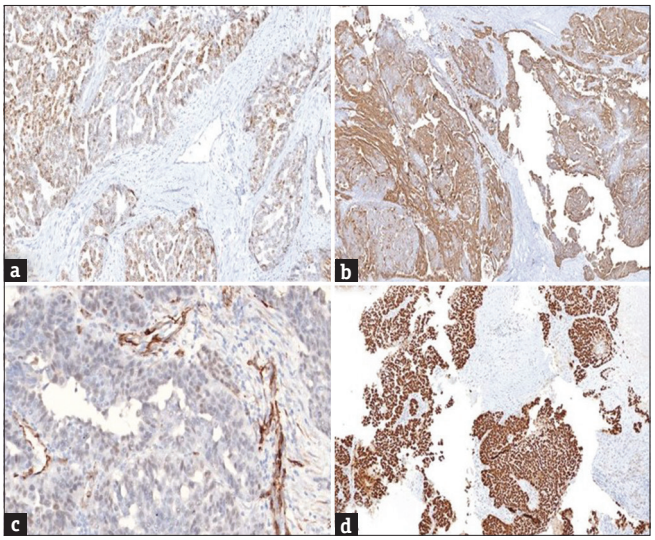

Figure 4: Photomicrographs showing immunohistochemical profile of the tumor cells. (a) Nuclear positivity for paired-box gene 8 (immunohistochemistry [IHC]; ×200), (b) Positive membranous expression of CK7 (IHC, ×100), (c) Focal and distinct nuclear staining for Wilms' tumor protein (IHC, ×400), (d) Diffuse strong nuclear positivity of p53 mutated protein (IHC, ×100)

majority of cases, distant metastasis is still a common occurrence.

Nevertheless, metastasis to the pancreas is an extremely rare event, with an overall incidence of approximately 3.8%.[3,10] Ovarian cancer metastasis to the pancreas is an even rarer entity. However, the first case was reported by Schumacher in 1993, describing ovarian adenocarcinoma metastasis to the pancreas.[7] While the pancreatic head is the most common site of metastasis, in this particular case, the tumor was significantly impacting the body of the pancreas. It is usually believed that ovarian cancer spreads through the intraperitoneal route of dissemination, although it may also metastasize through the lymphatic channels and the hematogenous route.[3] However, in the present case, we assert that the pancreatic metastasis resulted from direct extension from the retroperitoneal area, given the patient's previous history of malignant ascites due to recurrent ovarian tumor.

Distant metastasis may occur at any time of ovarian cancer throughout its course. Nevertheless, the median interval time between the diagnosis of ovarian cancer and documentation of distant disease has been reported as 15–44 months in the literature.[3] In our case, it was determined 108 months following a curative surgical treatment of primary ovarian cancer and 72 months from the secondary recurrence. Researchers have found that the longer survival observed in patients with prolonged interval time between the diagnosis of ovarian cancer and detection of distant metastasis probably indicate a biologically indolent course of such tumors.[11]

Our patient did not exhibit any symptoms, which is in line with what is commonly described in medical literature. However, if symptoms do persist, they can resemble those of primary pancreatic cancers, including abdominal pain, back pain, weight loss, nausea, melena, jaundice, gastrointestinal obstruction, upper gastrointestinal bleeding, and diabetic ketoacidosis. In such a scenario, regular patient follow-up and a combination of tumor markers can help improve the accuracy of ovarian cancer diagnosis and distinguish it from nonovarian causes.[12]

Primary as well as metastatic pancreatic lesions usually manifest as cystic in nature but can also appear as a relatively well-defined heterogeneously enhancing lesion like ovarian cancers. However, relying solely on endoscopic ultrasound and imaging features for differentiating between them is not diagnostic. While these radiological studies can assist in determining the size of a resectable metastasis, a tissue biopsy is mandatory to confirm the diagnosis and differentiate between primary and secondary pancreatic tumors as it also enables the reliable performance of ancillary studies.[13] Recently, it has been emphasized that endoscopic ultrasound-guided fine-needle aspiration can also aid in confirming the malignant origin of the cells, but to determine the origin of tumor the conjunction with IHC is essential.[14] In our case, the diagnosis of metastasis was made on tissue biopsy and was further confirmed by IHC.

Metastatic tumors to the pancreas are a rare indication for pancreatic resections, with most cases presenting with widespread metastasis and very poor outcomes.[2,3] In the case we encountered, a distal pancreatectomy was deemed necessary as the lesion was well-defined and confined to a solitary area on imaging. However, it is important to note that the role of surgery in improving the survival or quality of life of these patients is not clearly established and requires further exploration.[4] The average overall survival of advanced-stage, high-grade ovarian cancer patients in the studied series has been documented as 46.59 months, which highlights the need for more effective treatment options.[15] Nevertheless, overall, the prognosis of patients who develop distant metastasis is poor; however, in selected cases, integrated multi-modality treatment may result in palliation of the symptomatology and even in prolonged survival in such patients.

Conclusion

This case is a relevant valuable addition to the spectrum of metastasizing ovarian cancers and also underscores that pancreatic metastasis from an ovarian cancer should always be kept as differentials in those who present with a solitary pancreatic mass with a previous history of a nonpancreatic malignancy. Further, in such patients, a detailed clinical history and meticulous work up in form of cytological and radiological assessment can aid in its diagnosis, but it is histopathology along with IHC that is confirmative for timely intervention and suitable treatment. However, with the advancement in the fields of genomics and proteomics, the molecular profiling of ovarian cancer and its pancreatic metastasis can reveal the underlying molecular mechanisms and identify reliable diagnostic biomarkers in near future.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and that due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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