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Case Report and Review of the Literature

# Case Report: Pancreatic metastasis as the first presentation of disease recurrence in breast cancer after a 15-year interval

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ABSTRACT

Metastatic neoplastic lesions to the pancreas are extremely rare. In this article, we present the case of a 67-year-old woman who presented with a pancreatic mass as the first presenting following a 15-year disease-free interval from a Stage 1 breast cancer. EUS with FNA was suspicious for pancreatic adenocarcinoma. However, the final diagnosis of metastatic breast cancer was made following open biopsy and subsequent immunohistochemistry staining for GATA 3, GCDFP15, and mammaglobin.



## Introduction

Metastatic neoplastic lesions to the pancreas are rare and comprise an estimated 2% of all pancreatic malignancies [1]. In large autopsy series, the prevalence of pancreatic metastases falls within a wide range between 1.6 % to 11% [2-4]. Historically, the most common primary tumor to metastasize to the pancreas has been renal cell carcinoma, which has been well-described in the literature. We present an uncommon case of a metastasis to the pancreas as the first presenting lesion following a lengthy disease-free interval from breast ductal carcinoma.

## Case Presentation

A 67-year-old woman presented with a one-week history of progressive jaundice, pruritis and abdominal pain. She reported having nausea and diarrhea, but denied emesis, fevers and chills. She had a long-standing history of gastro-esophageal reflux disease (GERD) and irritable bowel syndrome (IBS), and specifically noted that the abdominal pain was atypical.

Her past medical and surgical history was significant for a T1 (1.1 cm) N0 ER-negative, PR-negative, HER2/*neu*-negative invasive ductal carcinoma of the right breast fifteen years prior for which she had undergone breast conservation therapy with lumpectomy with sentinel lymph node biopsy. Final pathology had negative margins and no evidence of cancer in two nodes. She receives adjuvant whole breast radiation and chemotherapy with 4 cycles of doxorubicin and cyclophosphamide. Within the past year, she had an elevation in her alkaline phosphatase from 130 to 270 units/liter and was subsequently diagnosed with Paget's disease of the skull.

On presentation her laboratory data revealed liver functions including: AST 154 U/L, ALT 144 U/L, alkaline phosphatase 781 U/L, total bilirubin 8.9 mg/dL and direct bilirubin 5.4 mg/dL; CA 19-9 was 23.2 U/mL.

Radiologic studies were obtained, which included an abdominal ultrasound and MRI/MRCP. The ultrasound revealed moderate intrahepatic and extrahepatic biliary ductal dilations. A focal echogenic

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area in the mid-common bile duct was noted. MRI/MRCP showed abrupt tapering of the common bile duct consistent with stricture, although no enhancing mass was seen (Figure 1A). The patient then underwent ERCP/EUS which demonstrated a 3.0 x 1.8 cm mass at the head of the pancreas (Figure 1B). Fine needle aspiration of the mass was suspicious for pancreatic adenocarcinoma. Following the results of the FNA, a PET/CT was ordered for pre-operative workup. Her PET/CT revealed extensive, widespread hypermetabolic osteolytic and osteosclerotic metastatic bone disease as well as the pancreatic mass, but no regional lymph node or liver metastases (Figure 1C). Subsequent bone biopsy confirmed metastatic carcinoma with breast origin. Of note, she had a bone scan three months prior, which was read as consistent with her history of Paget's disease and unchanged from previous scans.

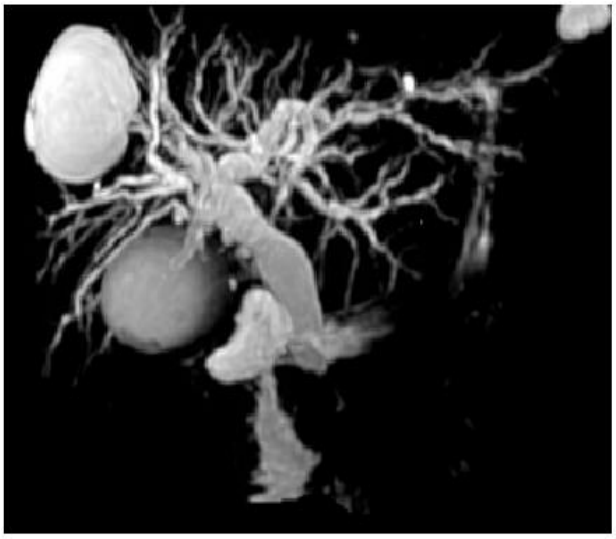

**Figure 1A:** MRI/MRCP showed abrupt tapering of the common bile duct consistent with stricture, although no enhancing mass was seen.

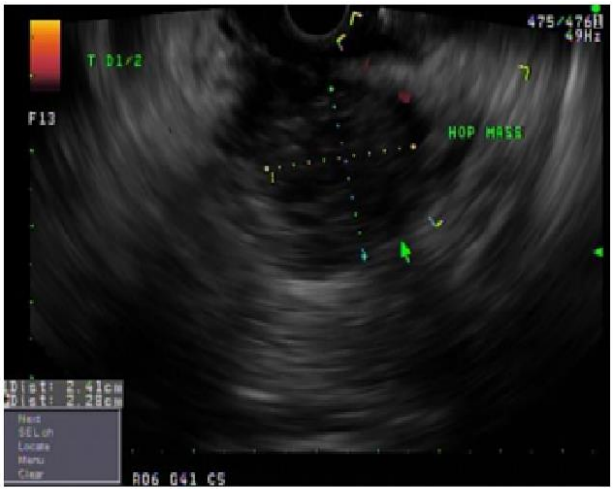


**Figure 1B:** ERCP/EUS which demonstrated a 3.0 x 1.8 cm mass at the head of the pancreas ("HOP mass").

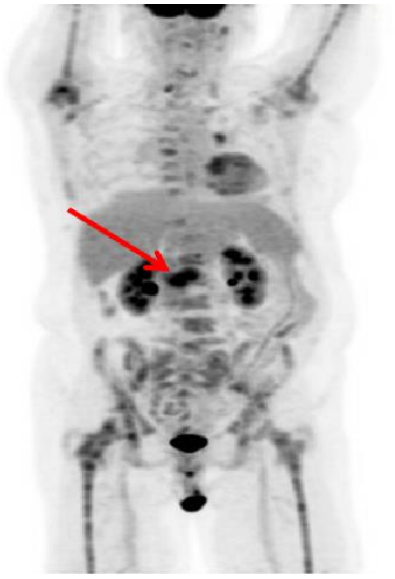

**Figure 1C:** PET/CT scan demonstrating osteolytic bony metastases as well as the pancreatic mass (red arrow) without regional nodal or liver metastasis.

In the context of a primary pancreatic neoplasm and metastatic breast cancer, an in-depth conversation about available treatment and surgical therapy was had with the patient, her family and her medical oncologist. Given the expected survival from her breast cancer and the presumed pancreatic adenocarcinoma, as well as the additional chemotherapeutic options available for her breast cancer, the risks and benefits of a pancreaticoduodenectomy were discussed, and the patient elected to proceed with surgery. At exploration, gross peritoneal disease was noted. Peritoneal and pancreatic biopsies were obtained with intra-operative frozen section demonstrating metastatic cancer consistent with her breast cancer. In the setting of this diagnosis, a palliative hepaticojejunostomy and cholecystectomy were performed. Final pathology of the pancreatic mass confirmed metastatic breast cancer confirmed by immunohistochemistry for GATA3, GCDFP15 and Mammaglobin (-D). The patient began palliative weekly regimen of carboplatin and paclitaxel, which was initiated three weeks post-operatively.

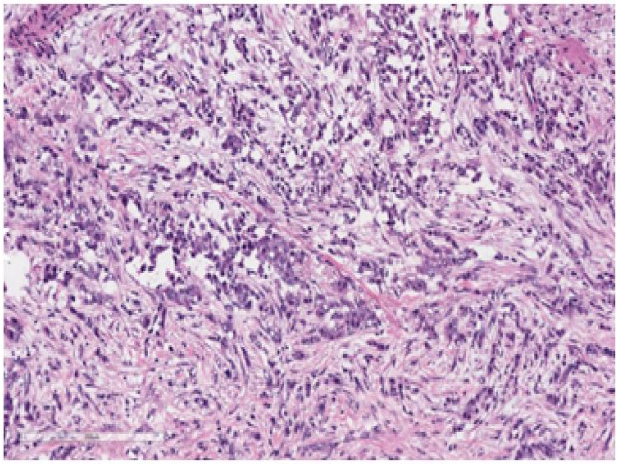

**Figure 2A:** Pancreatic mass (Frozen section, H&E stain, 200x): minimally pleomorphic malignant cells in a linear pattern and irregularly-sized nests, dispersed in a fibrotic matrix.

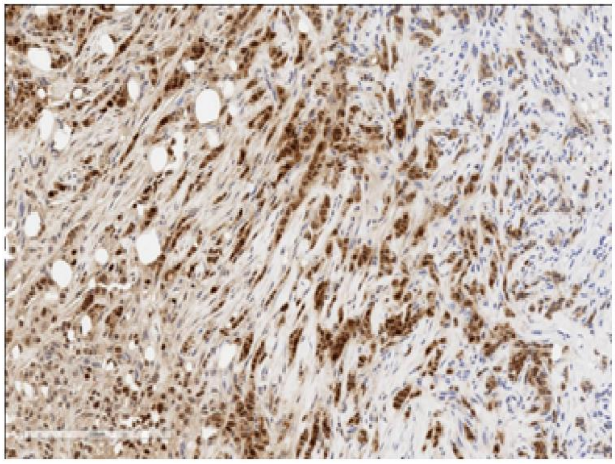

**Figure 2B:** Immunohistochemistry for GATA 3 of the pancreatic mass (strong, diffuse stain, immunohistochemistry, 200x).

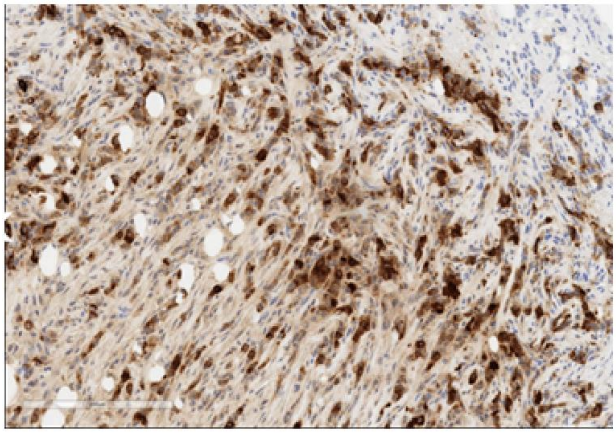

**Figure 2C:** Immunohistochemistry for GCDFP15 of the pancreatic mass (strong, diffuse stain, immunohistochemistry, 200x).

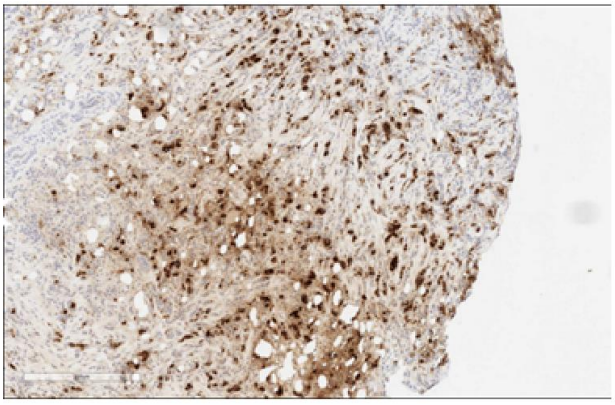

**Figure 2D:** Immunohistochemistry for mammaglobin of the pancreatic mass (strong, diffuse stain, immunohistochemistry, 200x).

## Discussion

The risk of distant metastases after breast cancer treatment has been well studied. A large retrospective study recently reported the 15-year incidence of cancer outcomes. In patients with Stage I disease, primary cancer risk is that of a second breast cancer (10.3%) or second primary malignancy (6.2%) and not metastatic disease [5]. Furthermore, at seventeen years following breast conservation therapy, non-breast cancer death is noted to surpass breast cancer death [5]. Thus, the presumption of a primary pancreatic cancer was reasonable in our patient who had been disease free for 15 years after her Stage I breast cancer.

However, breast cancer is a heterogeneous disease with the potential to metastasize known to persist for lengthy disease-free intervals. A review of 2147 autopsy results revealed the five leading sites of involvement at autopsy are lung, bone, lymph nodes, liver and pleura. Of the seventeen sites studied, the uterus, heart, pancreas and spleen harbored the fewest frequency of metastases [6]. A recent literature review cited 220 patients with pancreatic metastases found breast cancer as the primary malignancy in just 6.8% of cases; in contrast, renal cell carcinoma comprised 70.5% [7]. As of 2014, 23 cases of solitary pancreatic metastases arising from breast cancer have been reported in the literature, which is an incidence of less than 3% [8]. Interestingly, when further analyzed by subtype, lobular carcinoma is more likely to metastasize to the pancreas than ductal carcinoma, which is consistent with the lobular carcinoma's predilection for the gastrointestinal tract.

Our patient had undergone an endoscopic ultrasound with fine needle aspiration prior to surgery which had suggested a diagnosis of pancreatic adenocarcinoma. EUS is particularly useful for the evaluation of small pancreatic masses or equivocal cross-sectional imaging. It is also useful to evaluate mesenteric vascular invasion and facilitate treatment selection [9]. A single-center retrospective study of 54 patients evaluated the clinical impact of EUS-FNA in patients with pancreatic metastasis. In this study, cytomorphology was used to diagnose metastatic renal cell carcinoma, small cell lung cancer, and hepatocellular carcinoma. Morphology is generally sufficient but sometimes recommended in conjunction with immunohistochemistry for metastatic melanoma, breast cancer and colon cancer. Metastases from esophageal, gastric and non-small cell lung cancer require IHC for diagnosis [10]. IHC was not feasible for our patient given the scant cellularity but was used to confirm the diagnosis from intraoperative biopsies.

## Conclusion

We described a rare case of a breast cancer metastasis to the pancreas arising as the first symptom of metastatic breast cancer following a 15-year disease free interval. Preoperative workup and statistical probability strongly favored the diagnosis of a second primary malignancy. Clinically, pancreatic metastases are indistinguishable from a primary pancreatic malignancy. Thus, the clinician should maintain some suspicion for metastases and recurrence of disease when confronted with any patient with a prior history of cancer, including breast cancer.

## Disclosures and Funding Sources

None

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