

Metastatic adenocarcinoma of the pancreas presents as metastases to the axillary/supraclavicular region as the first sign of the disease

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Mucinous tumors of the pancreas are rare and the diagnosis of invasive carcinoma can be a dilemma. While metastatic disease from mucinous cystadenocarcinoma (MCAC) and invasive intraductal papillary mucinous neoplasms (IPMN) have been reported, no extraperitoneal mucinous cystic metastatic disease has been described. When metastatic, the overall survival rates for invasive adenocarcinoma, mucinous cystadenocarcinoma (MCAC) and invasive intraductal papillary mucinous neoplasms (IPMN) are similar. The best improvement in the overall and progression free survival has been demonstrated with FOLFIRINOX (folinic acid – fluorouracil – irinotecan – oxaliplatin) for metastatic adenocarcinoma and Gemcitabine based regimens for MCAC. However, the variable responses of metastatic mucinous lesions have been observed and the overall prognosis remains poor. We describe a case of a patient who presented with metastatic adenocarcinoma of the pancreas as cystic masses in the supraclavicular and axillary regions. Additionally, this patient was initially treated with FOLFIRINOX and continues to have stable primary and metastatic disease after 18 months from the diagnosis. ([Ann Hepatobiliary Pancreat Surg 2017;21:247-251](#))

Key Words: Pancreatic cancer; Mucinous metastases; Mucinous pancreatic neoplasm

INTRODUCTION

Patients with unresectable pancreatic cancer continue to experience poor overall survival. While metastatic adenocarcinoma to various sites of the body is well documented, metastatic disease presenting as mucinous cystic lesions have primarily been reported as mucinous cystadenocarcinoma (MCAC) and invasive intraductal papillary mucinous neoplasms (IPMN) and include only intra-peritoneal locations.¹⁻⁶ Both metastatic adenocarcinoma as well as metastatic MCAC, when treated with systemic chemotherapy only, have an overall survival of approximately 11 months.^{7,8} Metastatic adenocarcinoma when compared to invasive metastatic IPMN have also been proven to have a similar overall survival.⁶ We report a case of a patient with metastatic adenocarcinoma of the pancreas that presented initially with metastatic mucinous cystic lesions to the axilla and supraclavicular region and found later to have a cystic lesion and primary ad-

enocarcinoma of the pancreas. Additionally, this patient was initially treated with FOLFIRINOX (folinic acid – fluorouracil – irinotecan – oxaliplatin) and continues to have stable primary and metastatic disease after 18 months from the diagnosis.

CASE

This is a 47 year-old female who presented to the surgical oncology office with a complaint of a left neck mass for about 2-3 months. She denied any significant past medical history and had only undergone a laparoscopic tubal ligation in 2000. She initially reported to her primary care physician with a lump on the left side of her neck for a few months. She was given antibiotics without any resulting change in the size. Ultrasound of the head and neck was then performed which displayed a mildly enlarged thyroid as well as a fluid-filled cyst cranial to the left clavicle without color flow. She was recommended to

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undergo magnetic resonance imaging (MRI) for further characterization, which exhibited several conglomerate cystic lesions in the left supraclavicular area, left axilla, and left paraspinal tissues adjacent to T2. The largest area

was the supraclavicular, which measured at 6.3×3.5×4.2 cm and possibly represented venolymphatic malformations and/or lymphangiomas (Fig. 1). Given the unclear diagnosis, she was recommended to undergo an open biopsy

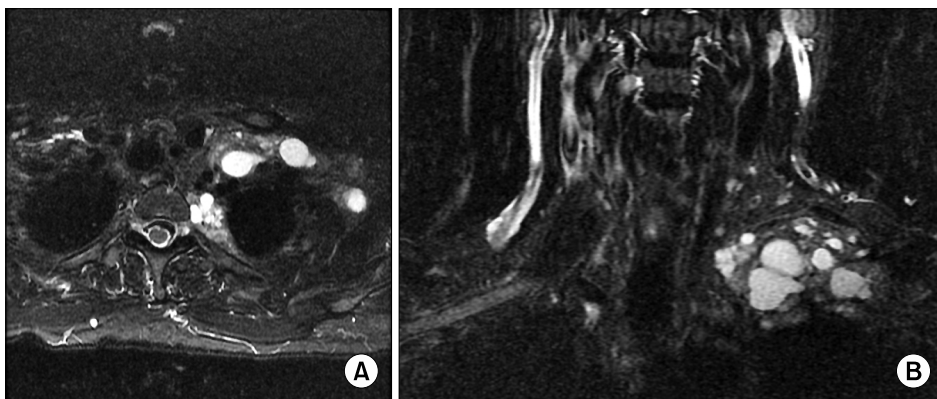


Fig. 1. Axial (A) and coronal (B) MRI images showing paraspinal, left supraclavicular and left axillary cystic lesions, the largest of which was 6.3×3.5×4.2 cm.

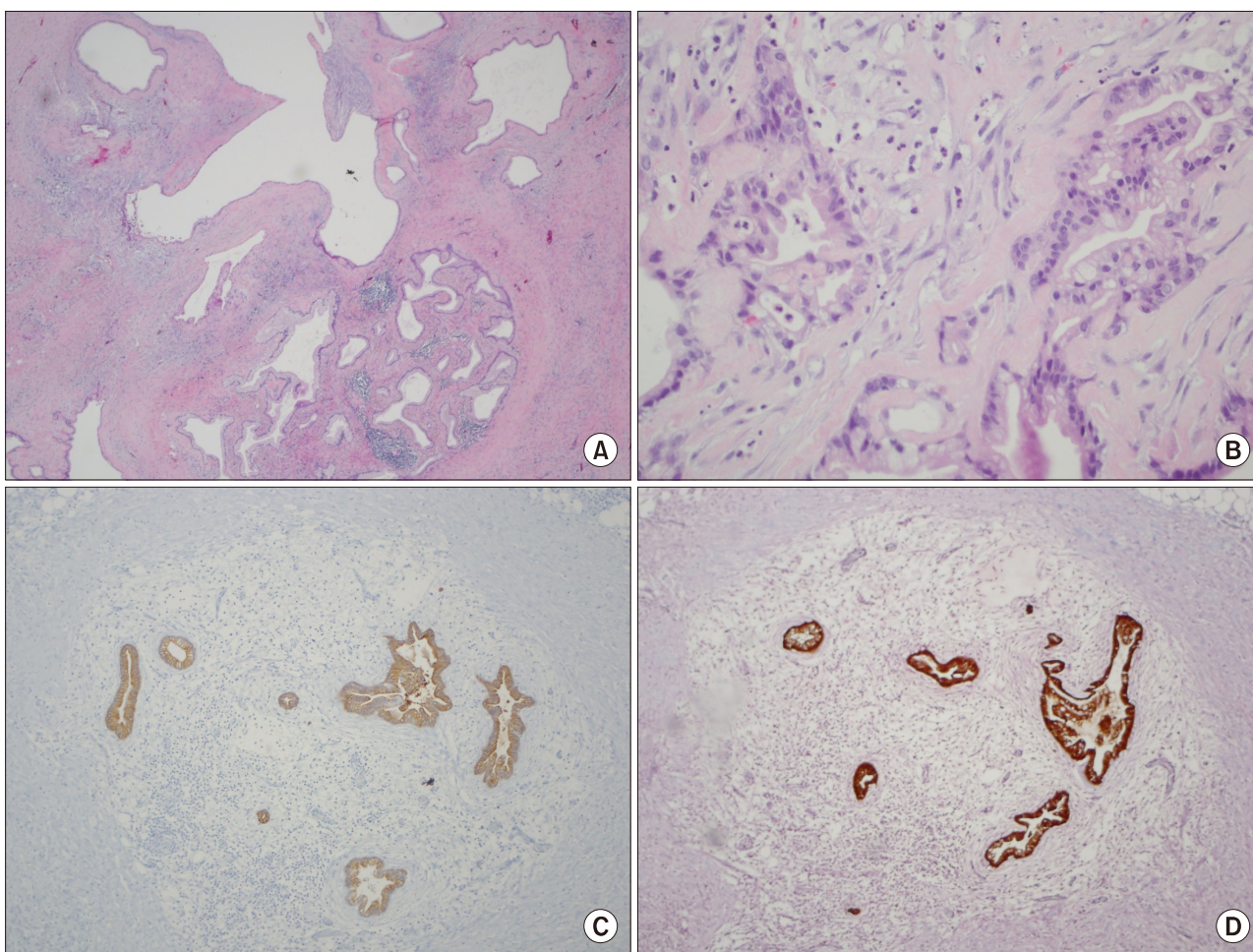


Fig. 2. (A) Excisional biopsy specimen from the left axillary mass showed a multiple cystic lesion in a background fibrosis and focal mature lymphocytes, with an original magnification ×40. (B) The cysts were lined by atypical glandular cells with focal mucinous cells. The glands showed complexity with focal angulated gland, with an original magnification ×400. (C and D) Immunohistochemical studies showed that the glands/cysts were positive for CK7 (C), and positive for Masp1/VHL in a dual staining (D), with an original magnification ×100.

of the area.

She underwent an excision of a portion of the left axillary cystic mass as well as the adjacent lymph node, and the final pathology displayed a benign lymph node and multiple cysts with atypical mucinous glands that were concerns for metastatic disease of pancreaticobiliary origin. Immunohistochemistry stains revealed the cells to be positive for CK7, Maspin, CDX2 (few cells), calponin (focal) and negative for CK20, Napsin, TTF-1, PAX-8, GATA-3, p63, estrogen receptor (ER), and smooth muscle myosin heavy chain (SMMHC) with loss of DPC4 (Fig. 2). A second opinion was obtained from a tertiary care center who agreed with the diagnosis. Computed tomography (CT) scans of the chest, abdomen and pelvis displayed nonspecific bilateral ill-defined pulmonary nodules, nonspecific peripancreatic and retroperitoneal adenopathy as well as a moderate-sized fluid collection within the lesser sac that was concerning for a pancreatic cystic lesion with adjacent adenopathy (Fig. 3). An endoscopic ultrasound was performed that showed a round, cystic mass in the pancreatic body that measured at 46 mm with a hypoechoic small solid/cystic component that was 15×20 mm in size (Fig. 4). The mass measured at 5×4.6 cm and had one large cavity with a few smaller cavities and solid adjacent area. The pancreatic duct appeared normal. Cyst aspiration was performed and displayed an amylase <3 U/L and CEA of 618.13 ng/ml. The fine needle aspiration (FNA) of the portahepatic lymph node was consistent with metastatic adenocarcinoma of the

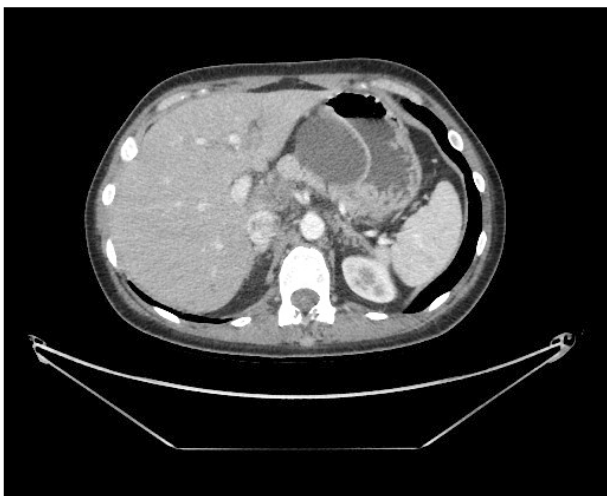


Fig. 3. Axial CT image showing a large 4.8×6.3×5.1 cm cystic lesion at the body of the pancreas.

pancreas. Immunohistochemical staining proved the lesion to be the primary. A positron emission tomography (PET)-CT scan was then performed and exhibited multiple lung nodules, upper abdominal and mesenteric lymph nodes and scattered fluorodeoxyglucose (FDG) uptake around the uterus and ovaries. The areas within the lung, upper abdominal and mesenteric lymph nodes had a max SUV of 3.83. No FDG uptake within or surrounding the pancreatic cystic mass was observed. A transvaginal ultrasound displayed a normal left ovarian cyst. The serum CA19-9 was 4.0 U/ml (normal <35 U/ml) and serum CEA was 1.5 ng/ml (normal <5.2 Ng/ml).

She started FOLFIRINOX per the diagnosis of metastatic adenocarcinoma of pancreatic origin. Oxaliplatin was discontinued 7 months later, secondary to neuropathy. The most recent restaging CT scans of the chest, abdomen and pelvis were performed approximately 18 months after the initiation of treatment and exhibited overall stable primary and metastatic disease.

DISCUSSION

Cystic neoplasms of the pancreas are the second most common exocrine tumor, with ductal adenocarcinoma being the most common. The diagnosis of invasive mucinous lesions remains controversial and difficult. While our patient was thought to have metastatic adenocarcinoma,



Fig. 4. Endoscopic ultrasound showed a round, cystic mass in the pancreatic body that measured at 46 mm with a hypoechoic small solid/cystic component that was 15×20 mm in size.

only MCAC and IPMN have been reported as cystic metastatic lesions. The 2012 International Consensus Guidelines for the management of mucinous neoplasms of the pancreas states that mucinous cystic neoplasms (MCN) should be resected secondary to the progression of malignancy into MCAC.⁹ A review from our own institution explained that ovarian-type stroma and ER positivity typically separate mucinous cystic neoplasms from intraductal papillary mucinous neoplasms, which are both characteristics that are not observed in pathological metastasis. MCN with an invasive component have displayed loss of DPC4 expression, which is a feature that was observed in our patient.¹⁰ However, given the endoscopic, pathological and radiographic findings, this patient was also thought to not have a metastatic IPMN or mucinous cystadenocarcinoma, but rather metastatic adenocarcinoma of the pancreas, despite the presentation as metastatic mucinous cystic lesions.

While distant metastatic disease has been described for pancreatic adenocarcinoma, reports of metastatic disease as mucinous cystic lesions is limited. Detailed reports of the specific locations of metastatic disease for MCAC include the liver,^{4,5} peritoneum and ovaries^{1,2} and a Sister Mary Joseph node.³ For IPMN, metastatic disease has been reported in the peritoneum and liver.⁶ Therefore, this case report of a patient presenting with pancreatic adenocarcinoma or any pancreatic mucinous cystic lesion with extraperitoneal distant metastatic disease is the first of its kind.

Surgical resection for exocrine tumors of the pancreas results in the best prognosis. However, most patients presenting with pancreatic cancer are not resectable. Currently, FOLFIRINOX has been most effective for metastatic pancreatic cancer with a median overall survival of 11 months.⁸ When invasive MCAC were found to be metastatic, overall survival is comparable to metastatic adenocarcinoma.⁶ Patients with resectable MCAC have reported 5-year overall survival rates as high as 62-63%.^{11,12} For patients treated neoadjuvantly or non-operatively, systemic chemotherapy regimens included Gemcitabine alone or in combination with Oxaliplatin with variable responses. Favorable responses were observed, however, with 5FU and radiation, but primarily in the neoadjuvant setting.^{13,14} MCAC patients that were treated with systemic chemotherapy alone had a survival rate of 12% at 2 years, which

ranged from 4-37 months and had a median of 10.5-11 months.^{7,12,15,16} Given the poor prognosis for both metastatic adenocarcinoma as well as MCAC/IPMN, the decision was made to treat our patient with FOLFIRINOX.⁸ Our patient continues to have a stable disease (at the primary and metastatic sites) at approximately 18 months from her initial diagnosis.

In conclusion, this is the first report of a pancreatic adenocarcinoma that presented as a metastatic cystic lesion to the axillary and supraclavicular regions. She was originally treated with FOLFIRINOX and continues to have stable primary and metastatic disease.

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