

Metastatic Mucinous Cystic Adenocarcinoma of the Pancreas Presenting as Sister Mary Joseph's Nodule

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ABSTRACT

Context Sister Mary Joseph's nodule usually represents metastatic cancers from gastrointestinal malignancy including adenocarcinoma of the pancreas. Mucinous cystadenocarcinoma is a rare malignancy of the pancreas. However, pancreatic mucinous cystadenocarcinoma metastasized to Sister Mary Joseph's nodule is much rarer and has never been reported before.

Case report A 73-year-old Thai woman presented with progressive epigastric discomfort, severe back pain and significant weight loss over a 3 month period. Physical examination revealed right supraclavicular lymphadenopathy and Sister Mary Joseph's nodule at the umbilicus. A CT scan showed a large cystic lesion with internal septation at the pancreatic tail. Cyst fluid analysis revealed a brown mucoid fluid having high carcinoembryonic antigen and carbohydrate antigen 19-9 levels. Skin biopsy from the nodule confirmed the presence of metastatic mucinous cystadenocarcinoma.

Conclusion To our knowledge, this is the first report of pancreatic mucinous cystadenocarcinoma metastasized as Sister Mary Joseph's nodule.

INTRODUCTION

A pancreatic mucinous cystic neoplasm is a rare neoplasm with malignant potential. Therefore it should be managed aggressively by pancreatic resection. The prognosis is generally excellent in the absence of invasive disease. However, a patient with a metastatic lesion has a poor prognosis. Generally, Sister Mary Joseph's nodule is known as an umbilical metastasis of gynecological and gastrointestinal malignancy. The pancreas has been reported as the site of origin in less than 10% of all umbilical metastatic lesions [1]. We herein report the case of a patient with advanced pancreatic mucinous cystadenocarcinoma who presented with an umbilical metastasis. This case illustrates an unusual manifestation of this potentially low malignant tumor.

CASE REPORT

A 73-year-old Thai woman without any previous significant underlying conditions came to our hospital with progressive epigastric discomfort and an 8 kg weight loss over a 3 month period. Most recently, she complained of severe back pain when she lay down. Over the last 2 weeks, she had noticed the presence of weeping serosanguinous fluid from the umbilicus.

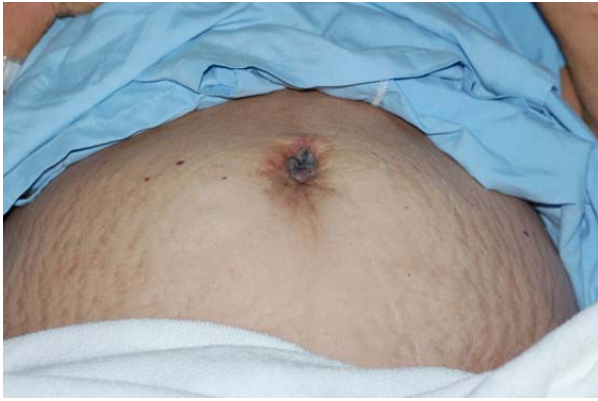


Image 1.

Physical examinations revealed a 1.5 cm fixed right supraclavicular lymph node of hard consistency. She was not jaundiced. She had a normal liver span without any sign of chronic liver disease. There was a brownish-black infiltrative plaque surrounded by an indurated and erythematous border at the umbilicus. Image 1 shows the distended abdomen with abdominal striae and an umbilical nodule. A close-up view of the ill-defined infiltrative umbilical plaque (Sister Mary Joseph's nodule) is shown in Image 2. The plaque was hard in consistency. With deep palpation, a firm 15 cm mass was detected underneath the umbilicus.

Serum amylase was 52 IU/L (reference range: 0-160 IU/L). Serum carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA 19-9) and standard blood profiles were unremarkable. A CT scan of the abdomen showed a 9.3x5.2 cm well-defined cystic lesion with internal septation at the tail of the pancreas (Image 3a). After contrast



Image 2.

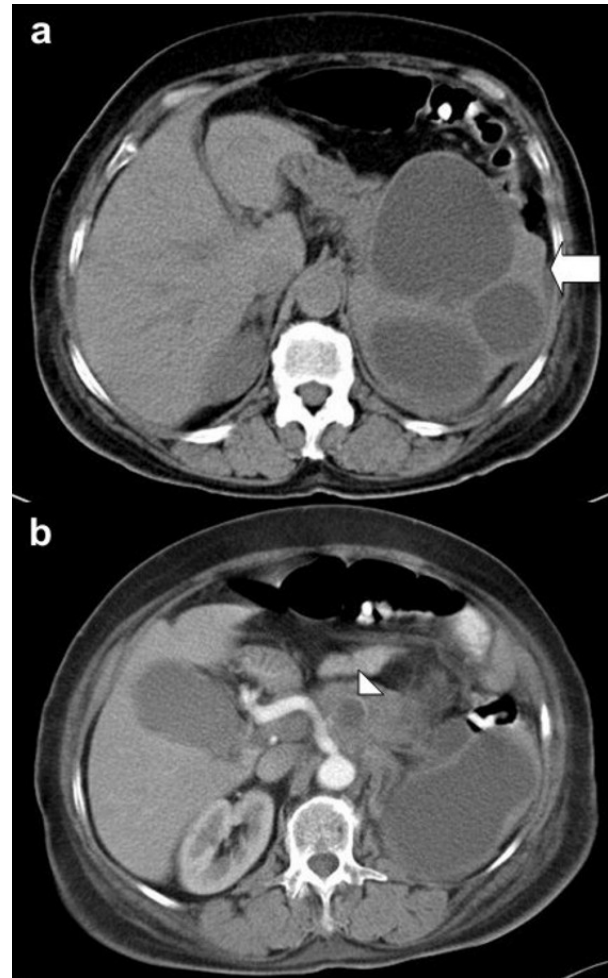


Image 3.

enhancement, a necrotic node at the pancreatic body was also seen (Image 3b). Cyst aspiration under ultrasonographic guidance revealed 50 mL of yellowish mucoid brown fluid. The cytology analysis was negative for malignancy. Cystic fluid presented CEA concentration greater than 2,000 ng/mL (reference range: 0-5 ng/mL), CA 19-9 concentration greater than 1,000 IU/L (reference range: 0-37 IU/L) and an amylase activity of 39 IU/L (reference range: 0-160 IU/L). The skin biopsy from the umbilical nodule demonstrated metastatic well differentiated adenocarcinoma with mucin lakes. The section from the periumbilical nodule (Image 4; x10, H&E stain) demonstrated multiple intradermal cystic spaces lined by atypical columnar cells with pleomorphic nuclei. The dermis showed atypical mononuclear cell infiltrates which are arranged in a glandular pattern. Higher

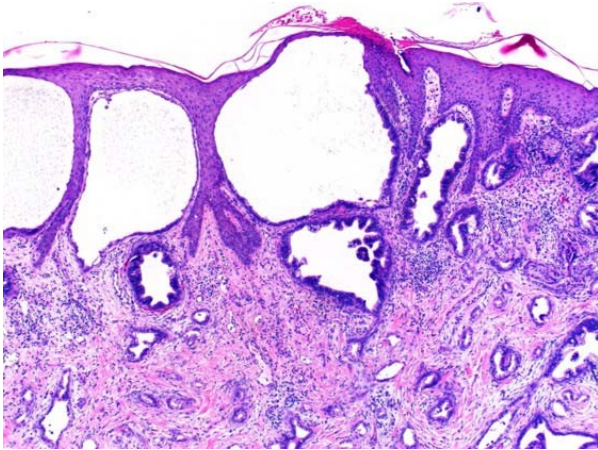


Image 4.

magnification (Image 5; x40, H&E stain) showed cystic spaces lined by atypical columnar cell. Alcian blue stain (Image 6) revealed the deposition of mucin in the cytoplasm of many atypical cells in the stroma of the tumor. The diagnosis of advanced mucinous cystadenocarcinoma presented as Sister Mary Joseph's nodule was considered.

She is still alive after six-month therapy with gemcitabine based chemotherapy.

DISCUSSION

Sister Mary Joseph (1856-1939) was a surgical assistant to Dr. William Mayo at St. Mary's Hospital in Rochester, MN, U.S.A.. She was able to predict malignant findings at laparotomy if she felt an umbilical mass while scrubbing the abdomen. Dr. Mayo first reported the condition as "pants-button

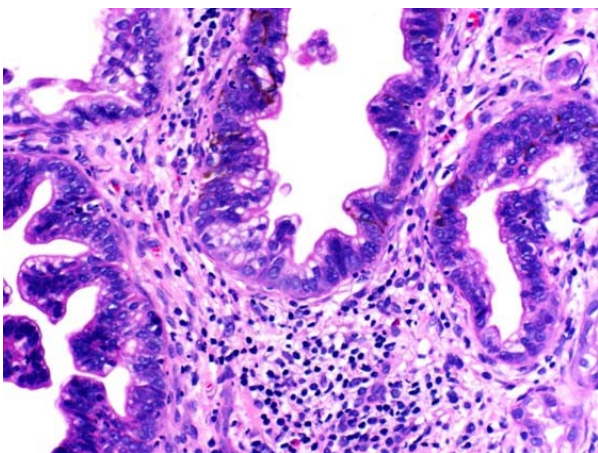


Image 5.

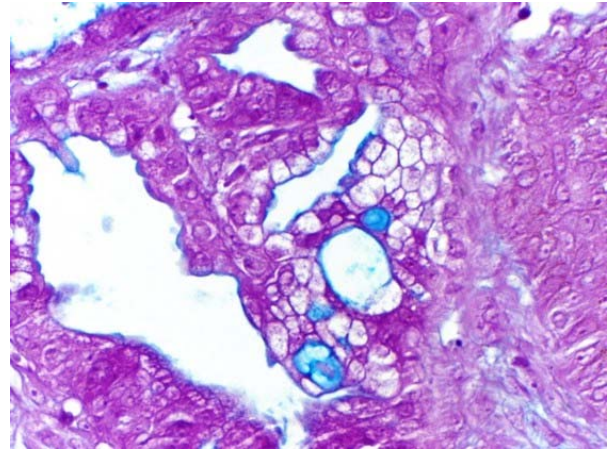


Image 6.

umbilicus" (without credit to Sister Mary Joseph) in a lecture to the Cincinnati Academy of Medicine in 1928, [2]. The term "Sister Mary Joseph's nodule" was proposed by Sir Hamilton Bailey in 1949 to accredit Dr. Mayo's brilliant assistant [3, 4].

Sister Mary Joseph's nodule usually presents as a painful lump with fibrotic consistency and irregular margins. Differential diagnoses should include umbilical hernia, cutaneous endometriosis, benign tumors such as foreign body granuloma, melanocytic nevi, papilloma, fibroma and primary umbilical carcinoma including melanoma, squamous and basal cell carcinoma. Since many benign conditions can mimic this umbilical metastasis, histological confirmation is always requisite before labeling these findings as umbilical metastasis.

Metastasis to the umbilicus is uncommon and represents only 10% of tumors which metastasize to the skin [5]. Gastrointestinal organs (35-65%), such as the stomach and the pancreas, are the most common sources of primary tumor which metastasize to the umbilicus (30%) [6, 7, 8, 9]. The most common primary site is the stomach in men and is the ovary in women. Initially, it was speculated that embryologic remnants which connect to the umbilicus play an important role in the genesis of Sister Mary Joseph's nodule. However, neoplastic cell propagation through lymph ducts and venous networks are also other important routes of umbilical metastasis [10]. In addition, the contiguous extension of the malignant cells which form

the primary site to the peritoneum and umbilicus were observed [11, 12, 13].

Yendluri *et al.* did a recent review of pancreatic adenocarcinoma in which the initial presenting sign was Sister Mary Joseph's nodule; they found that there were only 57 cases in this 100 year review. In addition, the majority of these cases originated from the tail and the body of the pancreas rather than the head of the pancreas [9]. Patients with tumors at the tail of the pancreas tend to remain asymptomatic until abdominal distension from tumor expansion or metastasis occurs. Our patient was not a classic case of pancreatic adenocarcinoma, however, this metastatic mucinous cystadenocarcinoma originated in the pancreatic tail. She presented with abdominal distension from the bulging mass.

One of the differential diagnoses of cystic lesions of the pancreas is cystic pancreatic neoplasm. Patients with cystic tumors of the pancreas generally have no prior history of severe abdominal pain or acute pancreatitis. The cyst usually has internal septation without surrounding tissue inflammation [14]. The main etiologies of primary cystic pancreatic neoplasms are serous cystic neoplasms (SCNs), mucinous cystic neoplasms (MCNs), and intraductal papillary ductal neoplasms (IPMNs). Cysts in SCNs are microcystic with a honeycomb appearance, and some of them contain central calcification which is the unique character of SCNs [14]. In contrast, IPMNs cause only cystic dilatation of the main pancreatic duct and its branches due to intraductal mucin production, and 50% of the lesions are located in the pancreatic head region [15, 16]. MCNs represent about half of the primary cystic neoplasms of the pancreas. Mucinous cystic neoplasms predominantly affect woman (95%), with an average age of 53 years (range: 19-82 years) [14]. In addition, the majority of MCNs are located in the body and the tail of the pancreas. SCNs never turn into cancer. However, IPMNs and MCNs may contain invasive components.

There are no symptoms and signs which can be used to distinguish between mucinous

cystadenocarcinoma and benign MCNs. However, cyst calcification may be a helpful clue, even it is very rare but, when eggshell calcifications are present, the possibility of cystadenocarcinoma increases [17]. In our case, besides a large internal septated cyst at the tail with lymph node necrosis, there was no calcification detected by the CT scan.

The gold standard for the diagnosis of MCN and mucinous cystadenocarcinoma is tissue histology. However, in some circumstances, the tumor tissue is not obtainable. Thus, there are many alternative ways to aid in the diagnosis, such as cytological analysis of the cyst fluid and cyst fluid tumor marker analysis.

Fine needle aspiration (FNA) for the analysis of intracystic fluid for cytology and tumor markers can help to differentiate the various forms of cystic lesions of the pancreas. Cytology is reliable with a high specificity (83%) if malignant cells are detected [14]. Endosonography is a recent tool used in evaluating the details of many gastrointestinal masses. Due to the limitation of transcutaneous ultrasonography, endosonography can provide a closer look and more detail of the retroperitoneal organs, including the pancreas. Moreover, the accessory channel of the linear echoendoscope can be used to insert the needle for FNA. Nowadays, endosonographic-guided FNA has become standard practice for evaluating cystic lesions of the pancreas [14, 16]. Due to the generous size of the lesion and a location near the abdominal wall in the present case, percutaneous access was also possible and not too difficult. The present case had a negative cytological analysis which is correspondent with the low sensitivity of the test [14].

Cyst fluid for tumor markers such as CEA and CA 19-9 also help to differentiate the type of cystic tumors. For instance, if the CEA level in the cyst fluid is higher than 192 ng/mL, it will have 73% sensitivity and 84% specificity for the diagnosis of mucinous neoplasm [16]. Moreover, if the CA 19-9 level in the cyst is higher than 2,900 U/mL, it will have a 68% sensitivity and a 62% specificity for the diagnosis of mucinous

neoplasm [14]. Moreover, MCNs do not have a high level of amylase in the cyst fluid as do IPMNs since there is no communication between the cyst and the pancreatic duct [14]. In our case, the cyst amylase level was low and the levels of CEA and CA 19-9 were in the range of MCNs and mucinous cystadenocarcinoma.

Distinguishing MCNs from an early stage of mucinous cystadenocarcinoma is important but it is very difficult without tissue histology. The prognosis of a resectable MCN is excellent whereas the prognosis of mucinous cystadenocarcinoma is grave. In their series, Sarr *et al.* reported that, after pancreatic resection, seven mucinous cystadenocarcinoma patients had a dismal prognosis [18]. The prognosis of this tumor was reported as being similar to typical ductal adenocarcinoma of the pancreas [18]. Unfortunately, our patient was diagnosed with distant metastasis at a very late stage; thus, the aim of her treatment was only that of palliative chemotherapy.

To our knowledge, we report the first case of pancreatic mucinous cystadenocarcinoma presented with Sister Mary Joseph's nodule. This malignancy is very rare and the presentation for this patient is unusual. This case illustrates the possibility of this rare neoplasm as a primary source of umbilical metastasis.

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Keywords Cystadenocarcinoma, Mucinous; Neoplasm Metastasis; Pancreas; Umbilicus

Abbreviations MCN: mucinous cystic neoplasm; SCN: serous cystic neoplasm; IPMN: intraductal papillary ductal neoplasm

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