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CASE REPORT | BILIARY

Cholangicarcinoma Presenting as a Sister Mary Joseph Nodule

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Abstract

Sister Mary Joseph nodules represent metastatic cancer of the umbilicus. More than half of these cases are attributable to gastrointestinal malignancies including gastric, colonic, and pancreatic cancer. In addition, gynecologic (ovarian, uterine cancer), unknown primary tumors, and, rarely, bladder or respiratory malignancies may cause umbilical metastasis. We report the case of a Sister Mary Joseph nodule originating from a hilar cholangiocarcinoma. Umbilical nodules should prompt clinical evaluation, as these tumors are usually associated with poor prognosis.

Introduction

Umbilical tumors are relatively rare and can be classified as benign or malignant.[1] In turn, the malignant tumors can be further classified as primary or metastatic. Periumbilical metastases are an uncommon symptom of advanced cancer mostly of abdominal location (typically stomach, large bowel, and ovary).[2,3] This clinical finding was first described by Dr. William Mayo's surgical assistant, Mary Joseph Dempsey. Hence the eponym "Sister Mary Joseph's nodule" (MJN) was first used by Dr. Hamilton Bailey in his book, *Demonstrations of Physical Signs in Clinical Surgery* in 1949.[4] MJN arising from cholangiocarcinoma (CCA) has been previously reported only 4 times.[5-9]

Case Report

A 49-year-old woman presented with a 2-month history of mild periumbilical pain and progressive cholestatic jaundice. She reported 2 weeks of worsening right upper quadrant pain, abnormally dark urine, and light-colored stool. She had 2 episodes of small-volume bleeding per rectum mixed with stools. She denied pruritus, rash, nausea, vomiting, abdominal distention, altered mentation, or bleeding from any other site. Over this same period of time, she experienced anorexia and had lost nearly 8 kg. On physical exam, she was icteric and had an enlarged, nontender liver with a clinical span of 14 cm. She also had a 2 x 1-cm hard umbilical nodule with marked pigmentation (Figure 1). Hepatitis panel was negative for hepatitis B and C. Liver function tests were abnormally elevated and tumor markers demonstrated a markedly elevated CA 19-9 (43.4 U/mL), carcinoembryonic antigen (14.4 mcg/L), and normal alpha-fetoprotein. The clinical picture was consistent with obstructive jaundice.

Abdominal ultrasound showed that the liver was cirrhotic in architecture with an ill-defined heterogeneously hypoechoic space-occupying lesion (4 x 4.4 x 3 cm) in segment VII. While the main portal vein showed normal hepatopetal flow, there was an eccentric partial thrombosis of the right portal vein. The gallbladder and common bile duct (CBD) were normal. Contrast-enhanced computed tomography (CT) showed that the liver was shrunken and measured approximately 12 cm in craniocaudal span, and showed a cirrhotic architecture with lobulated margins, widened interlobar fissure, and relatively hypertrophied left and caudate lobes. No evidence of intrahepatic biliary radical dilation was seen. A 7 x 5-cm ill-defined mass lesion in liver segment-VI/VII showed mild peripheral hypervascularity with washout and peripheral retention on contrast, on dynamic study. There was an associated

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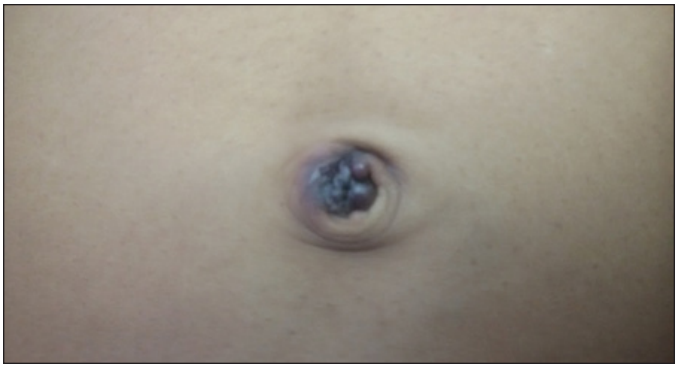

Figure 1. Sister Mary Joseph's umbilical nodule.

encasement and non-enhancing thrombosis of the posterior division of the right portal vein (Figure 2).

Esophagogastroduodenoscopy (EGD) to assess rectal bleeding cause was normal with no endoscopic evidence of portal hypertension, and a colonoscopy revealed multiple polyps in the sigmoid and the rectum. Biopsies confirmed that the rectal polyps were inflammatory. Ultrasound-guided fine-needle aspiration cytology from the liver space-occupying lesion showed moderately cellular smears, comprised of clusters and groups lined by atypical cells. These cells showed mild pleomorphism with round to eccentrically placed hyperchromatic nucleus with coarse chromatin, inconspicuous nucleoli, and small-to-moderate amount of cytoplasm. This was morphologically consistent with a well-to-moderately differentiated adenocarcinoma of pancreaticobiliary origin. On immunohistochemistry, the tumour cells were positive for CK7, CK19, and MUC-1, but were negative for Hepar-1 and synaptophysin, consistent with a diagnosis of cholangiocarcinoma (Figure 3).

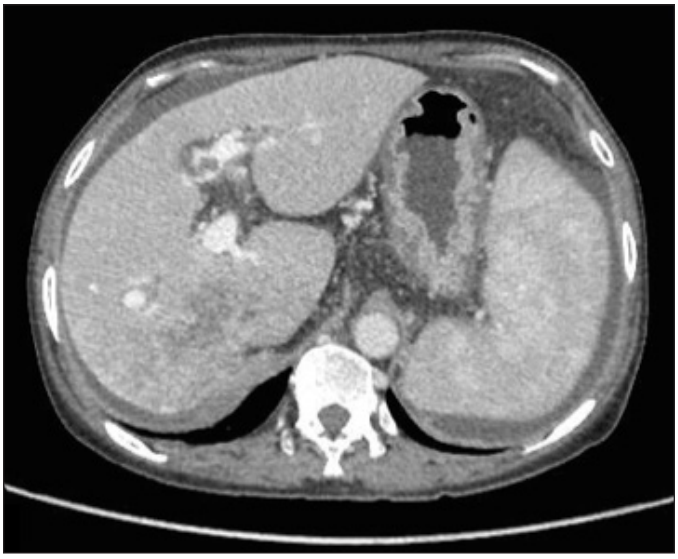

Figure 2. Contrast-enhanced CT showing a shrunken liver (12 cm craniocaudal span), cirrhotic architecture with lobulated margins, widened interlobar fissure, and relatively hypertrophied left and caudate lobes.

Subsequently, an endoscopic retrograde cholangiopancreatography revealed a tumor within the biliary tree consistent with a Klatskin tumor, an adenocarcinoma located at the bifurcation of the common hepatic duct. Once the diagnosis of metastatic cholangiocarcinoma was established, palliative stenting of the biliary tree and hepatic ducts was done to alleviate the obstruction.

Discussion

Umbilical nodules have been described in various cancers, but the association with cholangiocarcinoma is rare.[10] The most common histological type of MJN is adenocarcinoma (75%), more rarely squamous cell carcinoma, undifferentiated tumors, carcinoid, sarcoma, mesothelioma, melanoma, and lymphoma.[11-13] A number of hypotheses have been proposed for explaining the spread of these tumors, including direct transperitoneal spread via lymphatics passing along the obliterated umbilical vein, hematogenous spread, or along remnant involuted structures like the falciform ligament, median umbilical ligament, or by a remnant of the umbilical duct.[14] Direct implantation by laparoscopy is also possible. In most case series, a MJN is associated with multiple peritoneal metastases and signifies a poor prognosis.[2]

The gastrointestinal tract is the most common location of the primary neoplasm (35–65%), followed by a gynecological origin (12–35%). Common sites in decreasing order of frequency are: stomach (25%), colorectal (10%), and pancreas (7%).[3] Primary tumors have also led to MJN, including gallbladder, liver, breast, lung, prostate, penis, peritoneum, lymphoma, bladder, kidney, endometrium, cervix, and fallopian tubes.[12,13,15,16] A number of benign conditions may also present with umbilical nodules, including endometriosis, melanocytic nevi, fibroma, epithelial inclusion cysts, pilonidal sinus, granuloma, polyp, abscess, and hernia. Primary malignant umbilical tumors account for 17% of cases, and include melanomas, basal cell carcinomas, squamous cell carcinomas, myosarcomas, and adenocarcinomas.[17]

The clinical appearance varies; commonly, it is a firm nodule with irregular margins and hard consistency. The surface may be pigmented or ulcerated. The size of the nodule varies from 0.5–2 cm, although some nodules may reach up to 10 cm in size.[4] Our patient had a pigmented nodule; this has been described once before in a similar case of MJN with cholangiocarcinoma, and is due to marked melanocyte infiltration of the nodule.[9]

The diagnostic algorithm to identify the primary cancer rests on establishing a tissue diagnosis and locating the site of the primary tumor.[18,19] Imaging techniques include ultrasound, CT, magnetic resonance imaging, and positron emission tomography. A fine-needle aspiration cytology is invaluable in

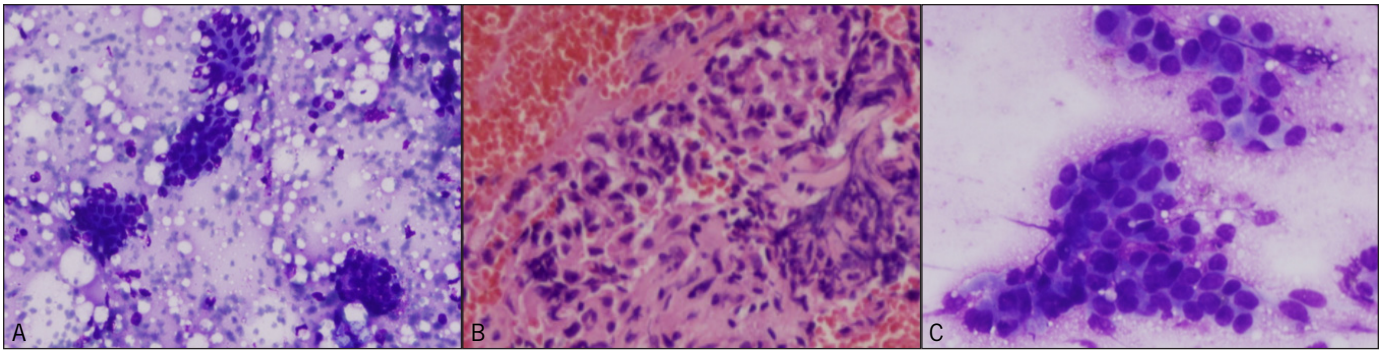

Figure 3. (A) Fine-needle aspiration (FNA) cytology from umbilical nodule showing discohesive groups and occasional acini lined by atypical epithelial cells, which showed enlarged, pleomorphic nuclei, irregular nuclear membrane, coarse chromatin, and small amount of cytoplasm. (B) FNA cytology from liver space-occupying lesion showing moderately cellular smears comprised of clusters and groups lined by atypical cells, which showed mild pleomorphism with round to eccentrically placed hyperchromatic nucleus with coarse chromatin, inconspicuous nucleoli, and small to moderate amount of cytoplasm. (C) Cell block of liver space-occupying lesion showing few clusters and groups lined by atypical cells embedded in blood clot. These cells showed mild pleomorphism with round to eccentrically placed hyperchromatic nucleus with coarse chromatin, inconspicuous nucleoli, and small to moderate amount of cytoplasm.

establishing the type of tumor, and immunohistochemistry can further characterize the specific diagnosis.[20] Careful scrutiny combined with fine-needle aspiration or biopsy should be used to diagnose MJN. Although the prognosis is not regarding peritoneal metastasis, palliative treatment can be offered to such patients.

Disclosures

Author contributions: All authors wrote, edited, and approved the manuscript. S. Grover and C. Sharma provided pathology information. YK Joshi is the article guarantor.

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