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CASE REPORT | BILIARY

Primary Bile Duct Melanoma Causing Obstructive Jaundice

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ABSTRACT

Malignant melanoma is one of the few malignancies that are well known for unusual behavior. Primary malignant melanoma usually originates from squamous epithelium of skin, mucous membranes, retina, and uvea. Although melanoma can metastasize to any part of the body, including biliary tract, primary malignant melanoma of bile ducts is an extremely rare entity. We present a 52-year-old man who presented with 5-month epigastric pain and 15-pound weight loss, with 1-week duration of jaundice, nausea/vomiting, pale stools, and dark urine, blood work suggested cholestatic jaundice. Imaging revealed a large perihilar/peripancreatic mass involving the portal vein and hepatic artery, and intrahepatic biliary dilation. Biliary brushings revealed neoplastic cells strongly suggestive of malignant melanoma.

INTRODUCTION

Malignant melanoma is one of the few malignancies that are well known for unusual behavior. Primary malignant melanoma (PMM) usually originates from squamous epithelium of skin, mucous membranes, retina, and uvea. Although melanoma can metastasize to any part of the body, including the biliary tract, PMM of bile ducts (PMM-BD) is an extremely rare entity.

CASE PRESENTATION

A 52-year-old man with history of diabetes, multiinfarct dementia, and polysubstance abuse presented with 1-week history of jaundice, pale stools, nausea, and vomiting. He also reported associated 5-month history of abdominal pain radiating to the back, right side of chest, and shoulder, associated with decreased appetite and weight loss of over 15 pounds. Patient was thin and cachectic, with scleral icterus, mild epigastric tenderness without distension, and normal cardiopulmonary exam. Laboratory workup revealed mild anemia (hemoglobin, 10.1 g/dL), hepatic panel in cholestatic pattern (alkaline phosphatase, 711 IU/L; AST, 86 IU/L; ALT, 96 IU/L; and total bilirubin 20.9, mg/dL). Abdominal computed tomography with contrast revealed a perihilar mass involving portal vein and hepatic artery (Figure 1). Due to vascular involvement, he was deemed unsuitable candidate for surgical intervention by surgical oncology. He was referred to gastrointestinal (GI) service for tissue acquisition and palliative biliary management.

Endoscopic retrograde cholangiopancreatography suggested narrowing at the level of common hepatic duct (CHD) with intrahepatic biliary dilation but normal appearing distal common bile duct (Figure 2). Endoscopic ultrasound did not reveal the mass to be arising from pancreas but rather from the perihilar area. Biliary brushings, biopsy of CHD, and fine needle aspiration (FNA) of perihilar tissue were performed, and a 8-mm to 6-cm uncovered metal stent was placed to relieve biliary obstruction. Fine needle aspiration showed neoplastic biliary ductal cells with eccentric and pleomorphic nuclei, intracytoplasmic pigment deposition, and strongly positivity for S-100 and MART staining, thus confirming diagnosis of malignant melanoma (Figure 3).

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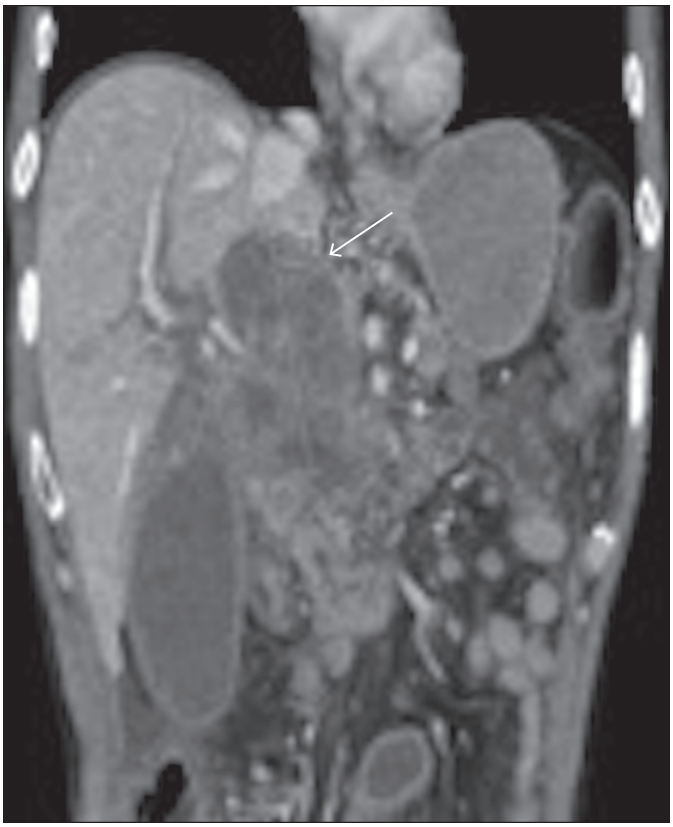

Figure 1. Abdominal computed tomography showing a perihilar mass.

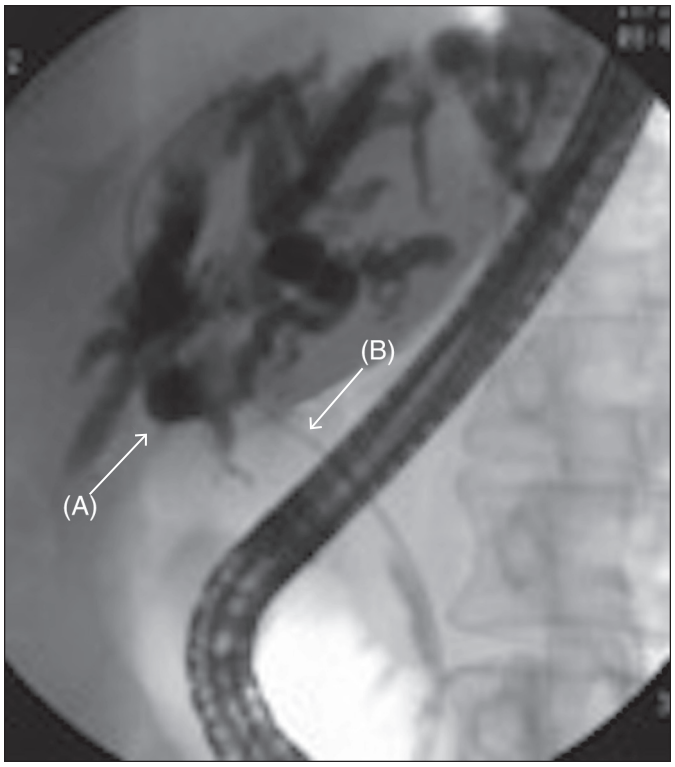

Figure 2. Cholangiogram showing intrahepatic biliary dilation (A) and narrowing at the level of CHD (B) with normal appearing distal common bile duct.

Extensive physical examination did not reveal any cutaneous, scalp, or mucosal lesions suggestive of melanoma. Fundoscopy did not show any intraocular, retinal, or uvea lesions suggestive of melanoma. Patient denied having any prior sunburns, prolonged exposure to the sun, atypical moles, or excised skin cancer. He did not have family history of any skin cancers. Colonoscopy also failed to show any mucosal lesions suggestive of melanoma. A whole-body positron emission tomography was performed 2 months later that showed spread of melanoma to sub- and supradiaphragmatic lymph nodes, liver, and mesentery. Patient was not deemed a candidate for ipilimumab due to poor performance status, and he declined chemotherapy. Few weeks later, he was diagnosed with brain metastases and was offered whole-brain radiation, but he chose to be comfort care and passed away.

DISCUSSION

Melanocytes are derived from the neural crest, which is part of ectoderm, and migrate throughout the body.[1] Malignant melanoma originates from tissues/organs derived from squamous epithelium, most commonly from skin, but also less commonly from uvea, retina, mucous membranes, and leptomeninges. Very recently, melanocytes have been understood to be present in normal human gallbladder, hence theoretically making it possible for melanomas to arise from endodermal regions of the GI tract, including mucous membranes of mouth, esophagus, lower colon, and anus.[2] Primary malignant melanoma of GI tract is a rather rare entity, only 24 cases of PMM-gallbladder and 12 cases of PMM-BD were reported thus far, and is hence very poorly understood by practicing gastroenterologists. In addition, a handful of primary ampullary melanoma cases are reported. It is observed that the majority of melanomas of the bile duct represent metastases from a cutaneous source and tend to present as multiple, flat pigmented lesions, whereas primary lesion manifests as a single pedunculated polypoid mass in the lumen of duct.[3-5] Our case was novel, because it manifested as perihilar mass with CHD narrowing, which is not reported in literature thus far.

Different publications have focused on potential criteria to differentiate between primary and secondary melanomas, including exclusion of previous history of primary melanoma, absence of synchronous involvement of sites other than the considered one, unicity of the lesion, polypoid or papillary shape, and presence of a junctional activity at the tumor site, as proposed by Ricci et al in 2001.[1-5,18] However, these criteria are very weak if each is considered singularly. Hence, a thorough physical examination is essential to exclude alternative sites of melanoma origin, including dermatology evaluation for naevi (both skin and scalp), mucosal exam (buccal, upper

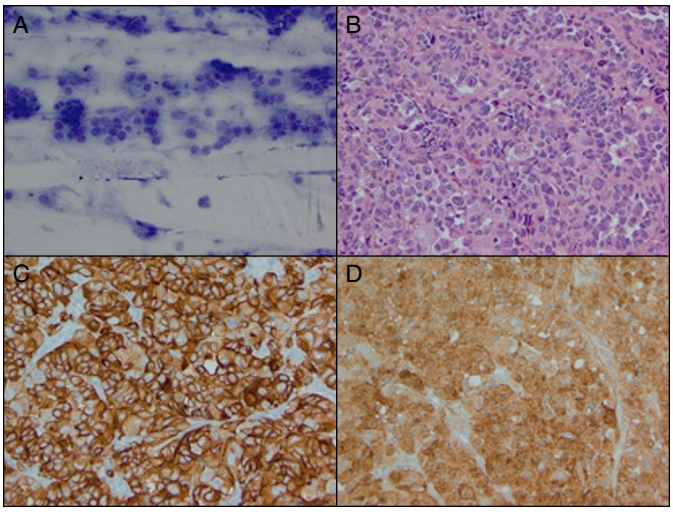

Figure 3. (A) Smear of FNA specimen from bile duct showing pleomorphic malignant cells with enlarged nuclei and multiple nucleoli. (B) H&E stain 200x magnification showing pleomorphic malignant cells, some with pigmentation and atypical mitotic figures. These tumor cells are strongly and diffusely positive for S-100 and MART-1 stains as below. (C) Tumor cells showing positive staining for S-100. (D) Tumor cells showing positive stain for MART stain.

GI and colon), ophthalmologic exam (retina and uvea lesions), and neuroradiology to exclude lepto-meningeal origin. Inquiry into prior skin lesions, which may have regressed or resected, is equally important, for it is quite possible to have them as the source of future metastases.[6]

There is a dearth of understanding on the presentation, behavior, and prognosis of PMM-BD due to rarity of this tumor. Review of all 12 published case reports suggests it be more common in males than females, common age of diagnosis being 40-50 years, and variable survival rates. The youngest case reported was a 26-year-old man, but had the best disease-free survival of 6 years.[19] The most common presentation is cholestatic jaundice (in 7/12 patients), as was the case with our patient, followed by abdominal pain/discomfort,[9,13,19] diffuse pruritus,[15] and acute cholecystitis.[11] Diagnosis of PMM-BD needs a high index of suspicion and may employ several diagnostic modalities, including ultrasonogram, computed tomography, or MRI/MRCP to demonstrate biliary obstruction and exclude pancreatic/ampullary pathologies. Presence of melanosomes in the tumor can occasionally provide high-intensity signal on MRI.[12] Ultimately, tissue acquisition is the key, with endoscopic retrograde cholangiopancreatography brush or biopsy or endoscopic ultrasound-FNA, or rarely resected specimen, for histochemical staining and precise diagnosis. Treatment options are guided by presence or absence of metastases. Patients with nonmetastatic PMM-BD lesions are surgically managed (with Whipple procedure or cholecystectomy with bile duct resection, hepatic lobectomy, with or without en-bloc lymph node resection), whereas metastatic cases may require more palliative approach.

DISCLOSURES

Author contributions: NS Addepally and JS Klair searched literature and prepared the manuscript. K. Lai provided pathology pictures. M. Girotra and F. Aduli supervised the manuscript preparation and are the article guarantors.

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