Clinical Case Report

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Primary malignant melanoma of the gallbladder with multiple metastases

A case report

Jun-Ke Wang, MD[a], Fei Su, MD[b], Wen-Jie Ma, MD[a], Hai-Jie Hu, MD[a], Qin Yang, MD[a], Fei Liu, MD[a], Quan-Sheng Li, MD[a], Fu-Yu Li, MD, PhD[a,*]

Abstract

Rational: Primary malignant melanoma of the gallbladder is an extremely rare tumor, with fewer than 40 cases reported in the literature worldwide. The majority of patients presented as a solitary lesion in the gallbladder. To our knowledge, only one case of primary malignant melanoma of the gallbladder with multiple metastases has been reported, which involved the stomach, duodenum, pancreas, jejunum and a mesenteric lymph node.

Patient concerns: We report a case of primary malignant melanoma of the gallbladder with metastases to the duodenal bulb, right adrenal and a celiac lymph node.

Diagnoses: Primary malignant melanoma of the gallbladder with multiple metastases.

Interventions: Gastrojejunostomy, cholecystectomy, and biopsy of the three metastatic lesions were performed. Histopathologic examination revealed melanin pigments were within the tumor cells of the four lesions, however, junctional activity was noted only in the gallbladder, supporting that the gallbladder was the primary site. No pigmented lesions were detected on the skin or eyes. The postoperative recovery was uneventful, and subsequently, chemotherapy with paclitaxel and carboplatin was administered.

Outcomes: The patient survived for 16 months due to tumor. progression.

Lessons: The current case was unique due to the adrenal involvement. For patients with multiple metastases of malignant melanoma, gallbladder origin should be considered in the differential diagnosis from cutaneous origin.

Abbreviations: CA19-9 = carbohydrate antigen 19-9, CT = computed tomography, HMB-45 = human melanoma black 45.

Keywords: gallbladder, junctional activity, malignant melanoma, multiple metastases

1. Introduction

Malignant melanoma is generally characterized by cutaneous origin and wide metastases to soft tissues, lungs, brain, and liver, and only 2% to 4% of the patients metastases to the gastrointestinal system, commonly occurred in the intestines, colon, and in the stomach.[1–3] Malignant melanoma metastatic to the gallbladder is exceptionally rare and, when present, is usually part of a widespread metastases.[4–6] In 1907, Weiting and Hamdi reported the first case of malignant melanoma originated from the epithelium of the gallbladder.[7] Since then, fewer than 40 cases of primary gallbladder melanoma have been reported in the literature worldwide.[8] The overall prognosis is extremely poor, and few patients can survive >2 years.[9]

Here, we report a rare case of primary malignant melanoma of the gallbladder with multiple metastases involving the duodenal bulb, right adrenal, and a celiac lymph node, to help recognize the clinicopathological features of this disease. A brief review of the literature is also provided.

2. Case presentation

A 63-year-old female patient presented with a 5-day postprandial nausea and vomiting. She had a medical history of chronic cholecystitis for over 30 years, but no history of surgery. Mild tenderness on the right upper abdomen was detected during physical examination. Pertinent laboratory tests were within the reference range, except for a mildly elevated carbohydrate antigen19–9 level (41.5 U/mL, normal <22). Other relevant tests were as follows: serum bilirubin 11.2 μmol/L (normal 5.0–28); alanine aminotransferase 21 IU/L (normal <40); aspartate aminotransferase 23 IU/L (normal <35); alkaline phosphatase 98 IU/L (normal 50–135); glutamyl transpeptidase 34 IU/L (normal <45). The whole abdominal contrast-enhanced computed tomography (CT) scan revealed 3 major lesions located in the gallbladder, right adrenal, and a celiac lymph node adhesive to the pancreatic head (Fig. 1). Although advanced gallbladder carcinoma with multiple metastases was the provisional diagnosis, the patient was performed with laparotomy because of severe postprandial

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[a] Department of Biliary Surgery, [b] Department of Pathology, West China Hospital of Sichuan University, Chengdu, Sichuan Province, China.

[*] Correspondence: Fu-Yu Li, Department of Biliary Surgery, West China Hospital of Sichuan University, Chengdu 610041, Sichuan Province, China (e-mail: lfy_74@hotmail.com).

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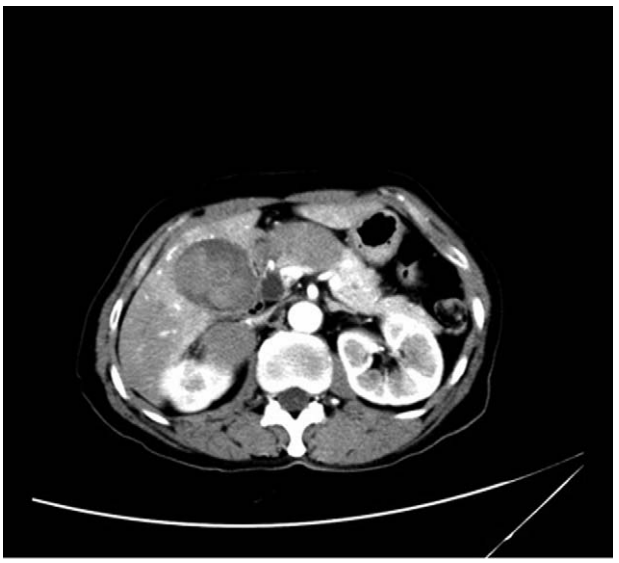

Figure 1. Abdominal contrast-enhanced CT imaging. Three major masses were found, respectively, located in the gallbladder, right adrenal, and a celiac lymph node. The gallbladder was enlarged with the mass almost totally filling the lumen. CT = computed tomography.

vomiting. The surgery was started with a detailed intra-abdominal exploration, which found that duodenal bulb area was also invaded. Finally, gastrojejunostomy was performed to relieve the intestinal obstruction, along with cholecystectomy and biopsy of the 3 other lesions to achieve a definite diagnosis.

Macroscopically, the resected gallbladder revealed a polypoid mass of dark-yellow color, 5 cm in diameter, arising from the mucosa of the gallbladder. Histopathologic examination of the gallbladder tumor revealed sheets of atypical cells with abundant melanin pigments in the cytoplasm (Fig. 2A). Junctional activity (the aggregation of malignant melanoma cells at the junction of the epithelium and lamina propria), which is considered the most indicative of the primary site of a melanoma, was noted in the fundus of the gallbladder (Fig. 2B, C). No tumor cells were seen in the submucosal layer. Immunohistochemically, the tumor cells were strongly positive for melanocytic marker of S-100 (Fig. 2D), vimentin, and Human Melanoma Black 45. In addition, melanin pigments were also found in the other 3 lesions and limited to the mucosal layer; however, no junctional activity was found. These findings were consistent with the diagnosis of primary gallbladder melanoma. Then, an elaborative re-examination (physical examination, anamnesis, fundoscopy, and so on) was performed for the patient. No pigmented lesions were found on the skin and eyes. The definitive diagnosis of primary malignant melanoma of the gallbladder with multiple metastases was eventually made. After surgery, the patient received regular chemotherapy with paclitaxel and carboplatin for 6 cycles. The dosage was paclitaxel 180 mg/dL and carboplatin 500 mg/dL, and it was well-tolerated without significant side effects. The patient died on the 16th month of follow-up due to tumor progression.

The Institutional Review Board was waived for this retrospective study. Informed consent was not obtained because the patient died due to progression of the disease before we wrote the case report.

3. Discussion

Melanoma is a very aggressive and highly metastatic malignancy, which arises from the melanocytes in the epidermis, uvea meninges, and intestinal tract. Since the first case of primary gallbladder melanoma was reported by Weiting and Hamdi in 1907, it is controversial whether this disease is really existing.

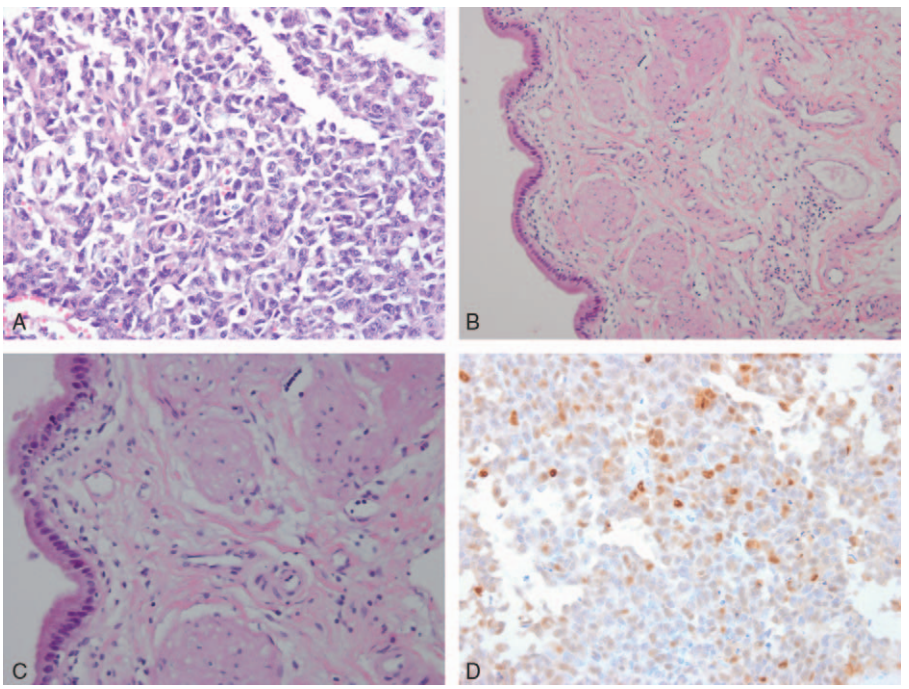

Figure 2. Pathological findings. (A) Dense melanin pigments were found within the cytoplasm of the tumor cells (HE ×200). (B, C) Malignant melanoma did not infiltrate the muscular layer of the gallbladder, supporting a junctional activity (HE ×200, ×400). (D) Tumor cells immunostained with anti-S-100 antibodies were positive (×400). HE = hematoxylin and eosin.

Some scholars argued that all gallbladder malignant melanomas are metastatic disease.[10,11] However, there is the fact that cases of primary malignant melanoma of the gallbladder have been reported in the literature.

Theoretically, primary malignant melanoma of the gallbladder is possible because of the following 2 reasons: firstly, melanocytes have been demonstrated in both normal and malignant gallbladder,[12] and melanocytes may come from an ectopic migration of the neural crest or originate from precursor cells originally resident in the gallbladder[13]; secondly, junctional activity, a prerequisite for the diagnosis of primary melanoma,[14] was seen in some previous cases, including ours.

The male-to-female ratio is approximately equal, and the peak age is between 40 and 60 years.[8] Clinical presentations are nonspecific, and patients with this disease are usually asymptomatic when diagnosed.[15] However, involvement of the cystic duct may present with obstructive jaundice or acute cholecystitis. Different from gallbladder adenocarcinoma, gallbladder melanoma does not seem to be related to cholelithiasis.

Preoperative diagnosis is substantially impossible to achieve, because pathological examination is the gold standard for a definite diagnosis. Ultrasonography, the cheapest method, is important to help distinguish between benign and malignant polyps; 94% of the former are less than 1 cm in diameter, whereas 88% of the latter are more than 1 cm.[16] In 2011, Gligorijevic et al[17] reviewed previous 31 cases of primary gallbladder melanoma, and found that the size of the tumor ranges from 1.5 to 7.5 cm in diameter. CT or magnetic resonance imaging is valuable, especially in detecting metastatic disease like our case.

It is difficult to distinguish primary from metastatic lesions based on the histopathology alone. For gallbladder malignant melanoma, which cannot be differentiated as primary or metastatic, certain criteria have been established for supporting a gallbladder melanoma as primary by Allen and Spitz,[14] and then revised by Heath and Womack,[18] that is, the gallbladder tumor must be: solitary and arise from the mucosal surface; papillary or polypoid; either displaying junctional activity or excluding other possible primary sites such as skin and eyes. Junctional activity is the most important diagnostic criterion for primary melanoma; however, the absence of junctional activity in a lesion cannot exclude the possibility of primary tumor because it may be destroyed owing to the rapid growth of the tumor cells.[19] Based on the above criteria, we were convinced that our case was a primary gallbladder melanoma, with metastases to the duodenal bulb, right adrenal, and a celiac lymph node. Junctional activity was found in the fundus of the gallbladder in the present case. To our knowledge, only 1 prior case has been reported with a similar multiple metastasis, which involved the stomach, duodenum, pancreas, jejunum, and a mesenteric lymph node.[20] Our case was unique due to the right adrenal involvement. Apart from this, a case was also reported to have metastasized to the common bile duct at operation,[21] and 2 cases metastasized to the jejunum.[18,22]

The prognosis of primary gallbladder melanoma is extremely poor, and few patients can survive >2 years. Because of small number of patients, there exists no consensus on standardized treatment strategy. Cholecystectomy seems to be the most effective treatment for the nonmetastatic primary gallbladder melanoma[8]; however, using conventional or laparoscopic technique is controversial. The effectiveness of adjuvant chemotherapy has not yet been established. The patient in our case survived for 16 months, which is longer than the majority of the previous reported cases, and we think that the chemotherapy of paclitaxel and carboplatin may have played a vital role.

4. Conclusions

We report a rare case of primary malignant melanoma of the gallbladder with multiple metastases involving the duodenal bulb, right adrenal, and a celiac lymph node. Our case is consistent with the diagnostic criteria for a primary gallbladder melanoma; however, it is still difficult to distinguish between the primary and metastatic tumors. For patients with multiple metastases of malignant melanoma, gallbladder origin should be considered in the differential diagnosis from cutaneous origin.

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