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CASE REPORT

Primary malignant melanoma of the liver: One case report and literature review

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Abstract

Objective Primary malignant melanomas of the liver are exceedingly rare. Only 19 cases have been reported in the literature worldwide. In this report, we describe our pathological findings and review the literature in order to improve our understanding of the disease and prevent misdiagnosis, as well as provide evidence for its treatment and prognosis.

Methods We present a case of an isolated malignant melanoma of the liver in a 61-year-old male Chinese patient.

Results Comprehensive dermatological and ophthalmological examinations did not reveal any evidence of a primary cutaneous or ocular lesion. Similarly, serial physical examinations, auxiliary examinations, and bone scans did not demonstrate any other lesions in the brain, respiratory tract, and gastrointestinal tract. Microscopic examination of the resected specimen revealed malignant melanoma, which was confirmed by immunohistochemical staining for S-100 protein (+), ki67 (30%+), EMA (+), CD10 (+), and HMB-45 (++).

Conclusion Primary malignant melanoma may occur in the liver, and should be considered when the histopathological appearance is atypical of other hepatic neoplasms. The diagnostic criteria for hepatic malignant melanoma depend mainly on the clinical, radiographic, and histopathological findings. Pathomorphology and immumohistochemical staining can be utilized to confirm the diagnosis.

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Key words: malignant melanoma; liver; pathomorphology; immunohistochemistry

Malignant melanoma occurs most frequently in the skin, but may also manifest in many other organs and tissues. However, primary hepatic malignant melanoma is exceedingly rare. Only 19 cases have been reported thus far, comprising 8 cases from PubMed and 11 cases from the Chinese literature. Only 4 cases of definite primary melanoma have been reported in PubMed (mean patient age 42.2 years, range 27–60 years). Microscopically, it may be easily misdiagnosed because of the morphological heterogeneity and hypomelanotic appearance. We report the only case of primary hepatic malignant melanoma encountered in our department.

Case report

A 61-year-old man was admitted to the Department of Hepatopancreatobiliary Surgery, Huai'an No. 1 Hospital, the Nanjing Medical University (Huai'an, Jiangsu Province, China) with a 3-month history of right upper abdominal pain that had been worsening over the past 2 days. His past medical history included a 1-year history of neck year, a 20-year history of hepatitis A, a 10-month history of hypertension, and a 10-day history of diabetes, all of which were under treatment. His family history was not significant. His vital signs were normal apart from a slightly elevated blood pressure (145/75 mmHg, normal range 90–140/60–90 mmHg). His skin and sclera were not yellow, no superficial nodular lesions were observed on his body, and no palmar erythema and spider nevi were present. On auscultation, his breath sounds were rough bilaterally, and bronchial wheezing was occasionally heard. The liver was not palpable below the costal margin, and the spleen was not palpable as well. Light percussion elicited pain in the hepatic region. Routine clinical biochemistry tests showed normal levels of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), γ-glutamyltransferase (γ-GTP), total bilirubin (TB)，direct bilirubin

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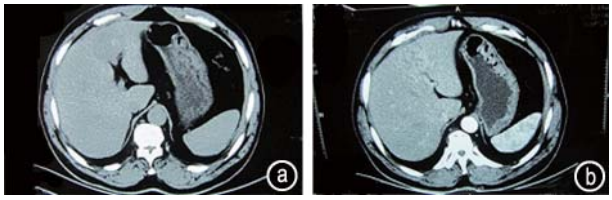

Fig. 1 (a) Computed tomography (CT) scan showing a 3.7 cm × 3.4 cm mass in the left lobe of the liver that appeared round in shape and uneven in density. (b) Contrast-enhanced CT scan displaying a 3.7 cm × 3.5 cm well-defined hepatic mass in the left internal lobe of the liver, which showed low-density enhancement

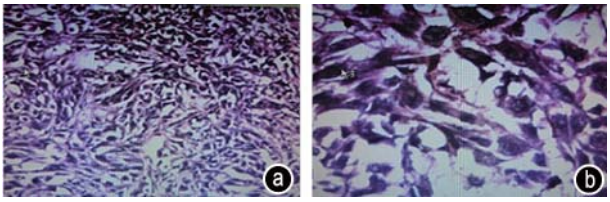

Fig. 2 Pathological findings. (a) The tumor cells were arranged diffusely or in nests, and mesenchymal fibrous tissue hyperplasia was observed. On deep dyeing with hematoxylin and eosin, spindle-shaped nuclei were observed in the tumor cells (original magnification, ×100). (b) Tumor cells were pleomorphic and eosinophilic, and had large volumes, abundant cytoplasm, large nucleus, and abundant nucleoli (original magnification, × 400)

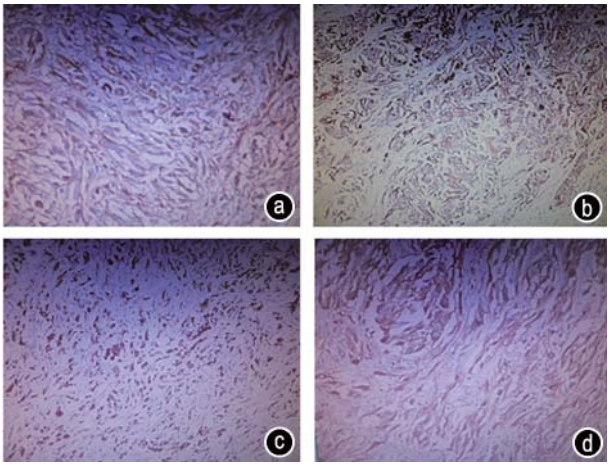

Fig. 3 Immunohistochemistry: revealing tumor cells positive for CD10 (× 100) (a); HMB-45 (× 100) (b); Ki67 (× 100) (c); and S-100 protein (× 100) (d)

(DB), indirect bilirubin (IB), and pre-albumin; however, his blood glucose level (GLU) was elevated (7.89 mmol/L, normal range 3.60–6.20 mmol/L). Levels of serum tumor markers including alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), and cancer antigen 50 (CA50) were within the normal range. Laboratory tests demonstrated negative hepatitis B surface antigen (HBsAg). An abdominal computed tomography (CT) scan showed a 3.7 cm × 3.4 cm mass in the left lobe of the liver, which appeared round in shape and uneven in density (Fig. 1a). A contrast-enhanced CT scan displayed a 3.7 cm × 3.5 cm well-defined hepatic mass in the left internal lobe of the liver, and revealed low-density enhancement without evidence of spread to the neighboring lymph nodes (Fig. 1b). A chest radiograph confirmed chronic bronchitis in both lungs. The working diagnosis was liver cancer on a background of chronic bronchopneumonia, hypertension, and diabetes.

Macroscopically, the resected mass had an intact capsule, and measured 4 cm × 4 cm × 3.5 cm at the junction of the left lateral lobe and left internal lobe. The mass was clearly differentiated from the normal surrounding tissue, and its cut surface was ash-black in color. Microscopically, the tumor cells showed diffuse infiltration, and fibrous tissue was observed between the lesion and the normal hepatocytes. Microscopically, the tumor cells were arranged diffusely or in nests, and mesenchymal fibrous tissue hyperplasia was observed. On deep dyeing with hematoxylin and eosin (HE × 100), spindle-shaped nuclei were observed in the tumor cells (Fig. 2a). The tumor cells were pleomorphic and eosinophilic, with large volumes, abundant cytoplasm, large nucleus, and abundant nucleoli (HE × 400) (Fig. 2b).

Immunohistochemically, the tumor cells were positive for S-100 protein (+), ki67 (30% +), EMA (+), CD10 (+), HMB-45 (++) (HE × 100) (Fig. 3). The complete absence of any cutaneous, ocular, or mucosal lesions in all organs on serial physical examinations, auxiliary examinations, and bone scans supported the final diagnosis of primary hepatic malignant melanoma. After local surgical resection, the patient was started on a comprehensive treatment regime of cisplatin, fluorouracil, interferon, epirubicin, and thymosin. He showed good recovery. However, recurrent foci were found 5 months postoperatively. The patient underwent 8 months of regular follow-ups in total, and no disease recurrence was observed.

Discussion

Melanomas were first described by Pilliet in 1887 [1]. They originate from epidermal melanocytes or neural cells, both of which derive from neural crest precursors. Chamaejasme extract is thought to inhibit proliferation and induce apoptosis of malignant melanoma B16 cells by down-regulating the expression of Akt and up-regulating the expression of PTEN [2]. Only 10%–30% of malignant melanomas are radio- or chemo-sensitive [3]. Malignant melanomas may present as single or multiple lesions, and are characterized by a coated appearance, easy hemorrhage, necrosis, cystic degeneration, tumor cells rich in melanin granules, a high degree of malignancy, rapid metastasis, and a poor prognosis. In particular, liver metas-

tasis portends a grave prognosis, with a median survival time of approximately 4 months. Malignant melanomas are most prevalent in Caucasian patients over the age of 30 years [4]. They mainly manifest in the skin (accounting for 79% of cases) [5], and usually originate from border hemorrhoids. Hepatic metastases occur in 20% of patients with malignant melanoma. In the early stages of the disease, metastasis occurs via the lymphatic route. However, in the advanced stages, the tumor cells spread to the lungs, liver (14%–20% of cases), bone, and brain via blood flow. Therefore, primary malignant melanoma of the liver is extremely rare and very few cases have been reported. Hepatic metastasis is more common in intraocular melanomas, which makes up 50% of such cases [6]. Melanomas of unknown primary sites (MUP) are estimated to account for 3.7% to 6% of all incident melanomas [7]. Previous studies have reported that hepatic malignant melanomas tend to present as single or multiple lesions, grow expansively, may have false capsules (mean diameter 8.8 cm, range 1.8–16 cm), and usually develop in the right lobe of the liver. Their origin and pathogenesis remain unclear, but interleukin (IL)-8 is thought to play a crucial role in disease progression. A relationship between Hepatitis B virus (HBV) and malignant melanoma has not been established. The HbsAg test result was negative for our patient. Genetic analyses have shown that abnormalities in chromosomes 1, 6, 7, 9, and 10 may be present.

The diagnosis of hepatic malignant melanoma depends mainly on the clinical, radiographic, and histopathological findings, and may be confirmed by pathomorphology and immumohistochemical staining. The clinical manifestations of hepatic malignant melanoma are non-specific, comprising symptoms such as epigastric discomfort, paroxysmal abdominal pain, and abnormal liver function. Indeed, our patient conformed to this pattern of presentation. Abdominal CT scans generally display single or multiple slightly high-density nodules with calcification. Contrast-enhanced CT scans may enhance the foci slightly. The garland manifestations of metastatic malignant melanoma can usually be identified on CT images [8]. Discoidin domain receptor (DDR)-2 promotes A375 melanoma metastasis to the liver [9]. As compared to CT scans, magnetic resonance imaging (MRI) scans can provide more detailed information for hepatic malignant melanomas. Wang *et al* has suggested that the most characteristic finding on imaging is a T2-weighted low-signal lesion with abundant hemosiderin from remote hemorrhages [10]. In our case, the CT scan showed a mass in the left internal lobe of the liver, which appeared round in shape and uneven in density. The focus showed mild strengthening on contrast-enhanced CT. Due to insufficient experience in diagnosing and treating hepatic malignant melanoma at that time, we did not request an MRI scan to be performed.

Pathologically, the tumor cells were pleomorphic, with a large nucleolus, and with or without melanin pigment deposition. Immunohistochemically, the tumor cells tended to express HMB-45, S-100 protein, vimentin, and Melan-A strongly [11]. Gong *et al* suggested that once the pathologic diagnosis is established, it is important to consider whether the tumor is a primary or secondary lesion. If an extensive investigation of potential primary sites demonstrates no evidence of primary melanomas, the hepatic tumor is likely to be a primary melanoma of the liver [12]. Our experience was in complete accord with this report.

A standard treatment approach for hepatic primary malignant melanoma and single metastatic malignant melanoma has yet to be established. While partial liver resection may be effective, the prognosis is poorer for cases with multiple or metastatic lesions. Surgical treatment is always palliative. Adjuvant measures such as chemotherapy, immunotherapy, and radiotherapy are extremely important in prolonging survival and improving quality of life postoperatively. Molecular targeting therapies have been used to manage Stage III melanomas effectively. Previous studies have reported that ipilimumab can prolong the median and 5-year survival rates [13], and that IL-18 can effectively prevent the inflammation associated with malignant melanoma [14].

Long-term follow-up is necessary for melanomas with a diameter of 2 cm or larger. Imaging examinations such as X-rays, positron emission tomography (PET)-CT, and MRI are commonly used to monitor patients. Serum LDH may also be used to monitor disease progression – higher LDH levels tend to indicate more aggressive tumors and poorer prognoses. Serum LDH may also be used to assess treatment effect [15].

No large randomized controlled studies have been conducted thus far. As such, we need to constantly summarize our experiences of diagnosing and treating malignant melanomas of the liver.

Acknowledgments

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Conflicts of interest

The authors indicated no potential conflicts of interest.

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