Diffuse Liver Infiltration by Melanoma of Unknown Primary Origin: One Case Report and Literature Review

Guo-Dong Shan, Guo-Qiang Xu, Li-Hua Chen, Zhao-Ming Wang, En-Yun Jin, Feng-Ling Hu and You-Ming Li

Abstract

Diffuse liver infiltration by melanoma of unknown primary origin is rare. We encountered a unique case of diffuse liver infiltration by melanoma of unknown primary origin in our hospital. A 62-year-old woman was referred to our hospital for anorexia of 6 months duration and abdominal distension for 1 month. Ultrasonography (US), computerized tomography (CT) and magnetic resonance imaging (MRI) revealed an obvious enlarged liver without detectable nodules. She was diagnosed as liver metastasis by melanoma of unknown primary origin via percutaneous liver biopsy. The report demonstrates the difficulty of making a non-invasive diagnosis of diffuse hepatic infiltration on metastatic melanoma.

Key words: liver metastasis, melanoma, unknown primary origin

Introduction

Liver metastases are diagnosed in 10%-20% of patients with melanoma, and are associated with a bad prognosis and short survival time rates (1). Since masses in the liver have a previous history of melanoma, most liver metastases from melanoma are easy to diagnose.

We present here a case of melanoma of unknown primary origin which was diagnosed by percutaneous liver biopsy. In this case, US, CT and MRI showed a hepatomegaly without detectable nodules. To our knowledge, only two cases of diffuse liver infiltration by skin melanoma have been previously reported (2, 3). In order to facilitate a better understanding of melanoma, we report this case and review the literature.

Case Report

A 62-year-old woman was referred to our hospital for anorexia of 6 months duration and abdominal distension for 1 month. Abdominal ultrasound examination in a local hospital showed hepatomegaly and ascites. She had no fever or night sweats, and no contact with sick persons or animals.

Her past medical history revealed neck pain for over 1 year, which was treated occasionally with Chinese traditional medicine. She had no history of liver disease, alcohol abuse or pulmonary tuberculosis. Her family history was not significant. Physical examination showed that her vital signs were normal, and no pigmentation nor superficial nodular lesion was observed in her body. Her skin and sclera were slightly yellow colored. The liver was palpable 10 cm below the costal margin and the spleen was not palpable. Viral serological and autoimmune markers were all negative. Serum tumor markers of alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA) and cancer antigen 199 (CA199) were all normal except for elevated cancer antigen 125 (CA125) (49.87 U/mL, normal range <35 U/mL). PPD test was negative. The ascites was clear light yellow, and no malignant cells were detected. The serum-ascites albumin gradient (SAAG) was 11.9 g/L. Ziehl-Neelsen stain of the ascites was negative for TB. The remaining biochemical parameters were normal. An abdominal CT and MRI revealed hepatomegaly without focal lesions, a small amount of ascites and a slightly depressed inferior vena cava due to the enlarged liver (Figs.1 and 2). CT scan showed no tumors in the lung or head. No tumor was found by gastroscopy, colonoscopy, or video capsule endoscopy. No tumor was
found by urogenital, otolaryngologic, and ophthalmologic examinations. Because of uncertainty of her diagnosis, the patient was treated symptomatically with fluid restriction, Transmetil and Diammonium Glycyrrhizinate (JiangsuChia-Tai Tianqing Pharmaceutical Co., Ltd., China).

A percutaneous liver biopsy was performed which demonstrated hepatic intrasinusoidal infiltration by malignant melanoma cells (Fig. 3). Immunohistochemically, the tumor cells were immunostained positive for HMB-45 and MelanA proteins.

The patient’s clinical course continued to worsen after admission and he became markedly jaundiced and showed encephalopathy on the 23rd hospital day; the patient died of hepatic failure on the 31st hospital day. Her biochemical course is summarized in Table 1. After a definitive diagnosis, she received a herbal remedy and refused to receive any Western medication.

**Discussion**

Malignant melanoma is a cancer of melanocytes, usually in skin. It can be highly aggressive, with as many as 20% of patients developing metastases (4). Liver metastasis, in particular, has been shown to portend a grave prognosis, with a median survival time of approximately 4 months (5). Melanoma occasionally occurs as apparent metastasis to lymph nodes or viscera without a detectable or known primary lesion. Such melanomas of unknown primary site (MUP) are estimated to comprise between 3.7% and 6% of all incident melanomas (6-14). Diagnostic criteria for MUP initially were proposed in 1963 by Dasgupta et al (6). Contemporary criteria for the diagnosis include the following: 1) metastatic melanoma confirmed clinically, histologically, and immunohistochemically; 2) the absence of a previous cutaneous tumor, pigmented or not, destroyed or excised without his-
Inter Med 48: 2093-2096, 2009 DOI: 10.2169/internalmedicine.48.2542

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Figure 3A. Pathological result: the specimen was covered with a large number of melanoma cells (Hematoxylin and Eosin staining, original magnification ×400).

Figure 3B. Immunohistochemical staining of the liver biopsy specimen with MelanA.

Figure 3C. Immunohistochemical staining of the liver biopsy specimen with HMB-45.

tologic examination; and 3) exclusion of unusual primary sites, including urogenital, otolaryngologic, or ophthalmologic sites. A retrospective analysis of 40 patients diagnosed with melanoma as MUP revealed that 65% of the patients presented with lymph node metastasis only, 28% presented with visceral lesions, and 8% presented with subcutaneous nodules (15). In the present patient, only liver metastasis was found.

In the present case, imaging studies revealed hepatomegaly and slight ascites accumulation. Liver function test was slightly abnormal. Serum tumor markers of AFP, CEA, and CA199 were normal. Hepatic tumor was initially considered to be impossible. Gynura root is widely used in Chinese traditional medicine and it can lead to hepatic venoocclusive disease (HVOD) in some patients (16). The present patient had in the past taken a lot of traditional medicine to treat neck pain, however, she was not sure whether she had ingested Gynura root. Because of her long-term use of traditional medicine, gradually ascending bilirubin, hepatomegaly and ascites, a clinical diagnosis of HVOD was not excluded. The main clinical signs and symptoms of HVOD were caused by portal hypertension. However, in this patient, esophageal varices was not indicated by endoscopy, and B-ultrasonography, CT and MRI scan did not show a widened main portal vein (PV) and hepatic vein (HV) stenosis. So this case was not diagnosed as HVOD.

The liver is one of the most frequently involved organs in disseminated non-Hodgkin’s lymphomas, and may be detected in up to 40% of patients at the time of initial staging (17). Few patients with lymphoma have diffuse liver infiltration and present with hepatomegaly. The diagnosis of lymphoma should be considered. However, in the present patient, imaging studies and physical examination showed no enlarged lymph nodes in the body and bone marrow biopsy presented no sign of lymphoma. All of these findings ruled out lymphoma.

At last, liver biopsy was performed which demonstrated hepatic intrasinusoidal infiltration by malignant melanoma cells. But this patient had no previous history of melanoma. In order to find the primary site, the patient was underwent a series of examination including physical examination, imaging studies and endoscopy. However, various examinations verified that the disease was confined to the liver. According to the criteria for MUP, this patient was diagnosed as a melanoma of unknown primary site.

Anbari et al reported that in 40 patients of MUP, 20% had a history of regressed skin lesions. In none of those cases was there a clinically apparent area of regression suggestive of regressed melanoma. Dysplastic nevi were noted in 22.5% of the patients in series. The prevalence of dysplastic nevi and regressed skin lesion in the MUP patients suggested the likelihood of a primary cutaneous origin for the metastatic melanoma (15).

Twenty days after the diagnosis, the present patient died of fulminant hepatic failure. To our knowledge, only four cases of fulminant hepatic failure secondary to malignant melanoma were previously reported. Autopsy revealed that the liver was almost completely occupied by melanoma cells in these patients (2, 3, 18, 19). The increasing size of the liver ruled out fulminant hepatitis as a cause, since the liver would be expected to shrink in a patient with fulminant hepatitis (20). The mechanisms of rapid liver failure here
an individual nodular lesion, it is difficult to differentiate metastatic melanoma rather than by a process of parenchymal infarction and necrosis. When imaging indicates diffuse liver enlargement without an individual nodular lesion, it is difficult to differentiate diffuse intrasinusoidal liver metastasis from other diseases, such as fatty infiltration, hepatitis, lymphoma and HVOD. The present case report demonstrates the difficulty of making a noninvasive diagnosis of diffuse hepatic infiltration by metastatic melanoma.

References


Table 1. Serum Biochemical Parameters after Admission

<table>
<thead>
<tr>
<th>Biochemical parameters (Normal values)</th>
<th>day2</th>
<th>day9</th>
<th>day16</th>
<th>day23</th>
<th>day30</th>
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<tbody>
<tr>
<td>ALB (35-55g/L)</td>
<td>33.5</td>
<td>32.2</td>
<td>31.</td>
<td>28</td>
<td>27</td>
</tr>
<tr>
<td>ALT (1-50U/L)</td>
<td>17</td>
<td>117</td>
<td>286</td>
<td>578</td>
<td>1652</td>
</tr>
<tr>
<td>AST (1-40U/L)</td>
<td>53</td>
<td>120</td>
<td>473</td>
<td>942</td>
<td>2103</td>
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<tr>
<td>TB (0.2-22µmol/L)</td>
<td>80</td>
<td>88</td>
<td>99</td>
<td>153</td>
<td>306</td>
</tr>
<tr>
<td>DB (1-7µmol/L)</td>
<td>52</td>
<td>56</td>
<td>63</td>
<td>115</td>
<td>213</td>
</tr>
<tr>
<td>AP (30-115U/L)</td>
<td>134</td>
<td>171</td>
<td>221</td>
<td>493</td>
<td>1021</td>
</tr>
<tr>
<td>GGTP (0-54U/L)</td>
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<td>192</td>
<td>354</td>
<td>702</td>
<td>1902</td>
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<tr>
<td>PT (10.5-14.0s)</td>
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<td>14.2</td>
<td>15.1</td>
<td>28</td>
<td>120</td>
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<tr>
<td>LDH (150-450U/L)</td>
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<td>349</td>
<td>562</td>
<td>1282</td>
<td>4365</td>
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<tr>
<td>Ammonia (10-47µmol/L)</td>
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<td>44</td>
<td>71</td>
<td>98</td>
<td>134</td>
</tr>
</tbody>
</table>

ALB = albumin; ALT = alanine aminotransferase; AST = aspartate aminotransferase; TB = total bilirubin; DB = direct bilirubin; AP = alkaline phosphatase; GGTP = gamma-glutamyl transpeptidase; PT = prothrombin time. LDH = lactate dehydrogenase.