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Case Report
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A Case of Uveal Melanoma with Liver Metastasis 6 Years after Enucleation of the Left Eye Ball

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SUMMARY

In Europe and the United States, uveal melanoma involving the choroid membrane is the most commonly occurring intraocular malignancy in adults. Hepatic metastasis of uveal melanoma tends to have a poor prognosis. In the present study we describe the case of malignant melanoma of the choroid membrane, which was found to have developed from multiple hepatic metastases 6 years after the enucleation of the left eye ball. In metastatic hepatic tumor patients whose primary focus is unknown, it is important to conduct a detailed investigation of the patient's disease history, bearing the present findings on uveal melanoma in mind.

Key Words : Uveal melanoma, Malignant melanoma, Liver metastasis

INTRODUCTION

Hepatic metastasis of malignant melanoma tends to have a poor prognosis. It has been reported that the average survival period ranges from 4 to 8 months after a metastatic focus has been diagnosed^{1,2)}. When melanoma is classified by the site of metastasis, a hepatic metastasis has a poorer prognosis at a statistically significant level than a dermal or lymph node metastasis^{3,4)}. Up to now there have been 5 reported cases of deaths caused by fulminant liver failure^{5~9)}. In the present study we describe the case of malignant melanoma of the choroid membrane, which was found to have developed from multiple hepatic metastases 6 years after the enucleation of the left eye ball and for which we had difficulty making a diagnosis.

CASE REPORT

A 54-year-old male patient was hospitalized on March 1, 2005, with complaints of right hypochondralgia and anorexia. His elder brother underwent an operation for bladder carcinoma at the age of 57 years. There was no other noteworthy history of disease in his family. He had received surgical intervention to remove his left eye in December 1998. At the time of hospitalization, his disease was unidentified. He had no history of excessive consumption of alcoholic beverages, but had a continued habit of smoking 20 cigarettes a day for 34 years. Measured on admission, he was 173 cm in height, weighed 54 kg, remained clearly conscious, and had a blood pressure of 132/69 mmHg, a regular pulse beat of 65/min., and a body temperature of 37.3°C. There was no anemia in the eye conjunctiva and no icterus. There was no appreciable findings in the neck, the chest, and the four limbs. The pulmonary/hepatic boundary was between the 4th and 5th ribs. The abdomen was hard and swollen. The liver was palpable under the right hypochondriac region at the position of 8 lateral fingers. Laboratory studies on

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Fig. 1 Abdominal radiograph showing the movement of intestinal gases in the left, downward direction caused by the enlarged liver.

admission were as follows : hemoglobin 11.2 g/dl, white blood cell count 3830 cells/mm³, platlet count 429,000 cells/mm³, alanine aminotransferase (ALT) 126 U/l, aspartate aminotransferase (AST) 112 U/l, alkaline phosphatase (ALP) 221 U/l, gamma-glutamyl transpeptidase (GGT) 446 U/l, lactate dehydrogenase (LDH) 911 U/l, total bilirubin 0.5 mg/dl, albumin 3.5 g/dl. Viral serology screen was negative for hepatitis B surface antigen and anti-hepatitis C virus.

Chest radiograph showed a mild degree of pulmonary emphysema. Abdominal radiograph showed that the enlarged liver had brought pressure on the intestinal tract and excluded intestinal gases in the left downward direction (Fig. 1). Abdominal ultrasonography showed that the liver had enlarged markedly and that tumors had occurred in many places throughout the entire liver. The tumors exhibited bull's eye signs or cluster signs, which are findings that match those of metastatic liver tumors (Fig. 2). Contrast computed tomography (CT) showed liver tumors with a ring-shape contrast, thereby suggesting metastatic liver tumors, similar to the findings of the abdominal ultra-

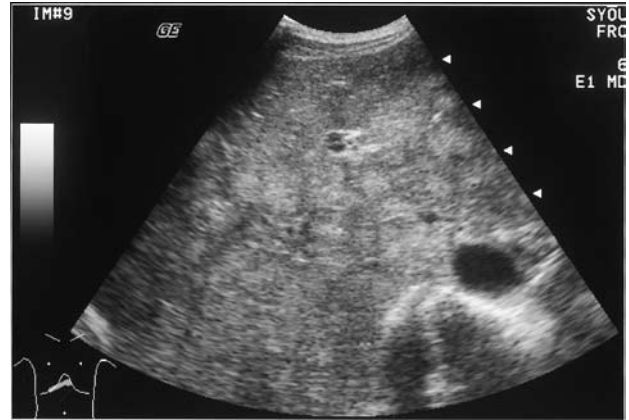


Fig. 2 Abdominal ultrasonography showing many recurring hyperechoic tumors in the liver. These tumors have a bull's eye sign or a cluster sign, which indicates metastatic liver tumors.



Fig. 3 Contrasted computed tomography showing multiple liver tumors enhanced in a ring shape. The left branch of the portal vein was patent, but the right branch was occluded by the tumors.

sonography (Fig. 3). The left branch of the portal vein was patent, but the right branch was occluded due to pressure from the tumors. There was no dilatation of the intra- and extrahepatic bile duct. No tumor was observed in the gall bladder, the pancreas, other organs inside the abdominal cavity, and in the peritoneum. The chest CT showed an old inflammatory change in the upper lung fields of both lungs and a pulmonary emphysema image, but did not reveal any tumor. Esophago-gastroduodenoscopy detected erosive gastritis in the antrum and colonoscopy did not reveal any appreciably abnormal findings. Systemic galium scin-

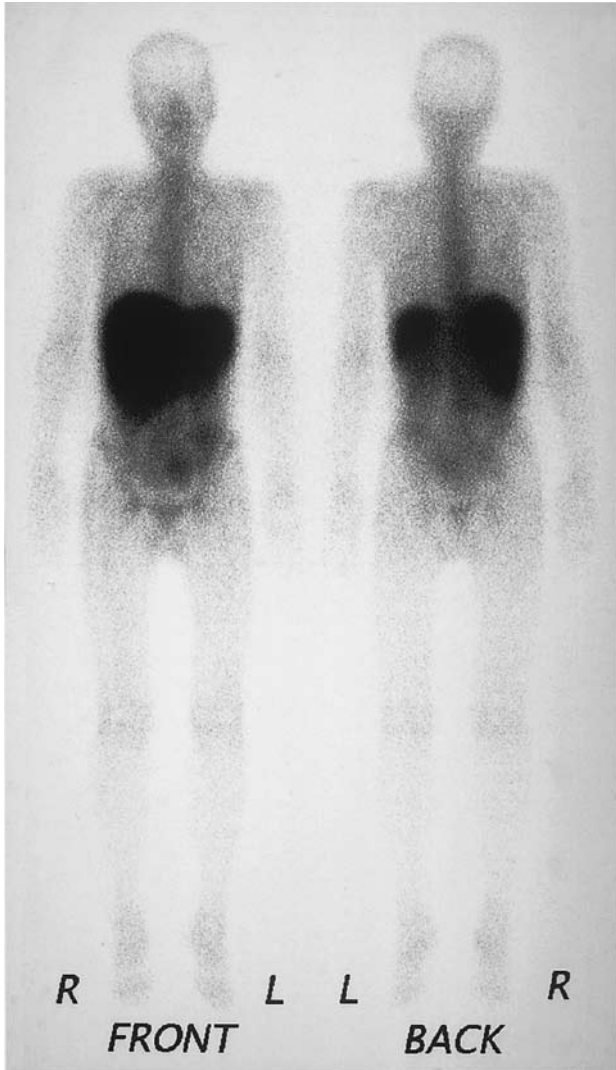


Fig. 4 Systemic galium scintigraphy showed abnormal accumulation only in the enlarged liver, but no accumulation in other organs.

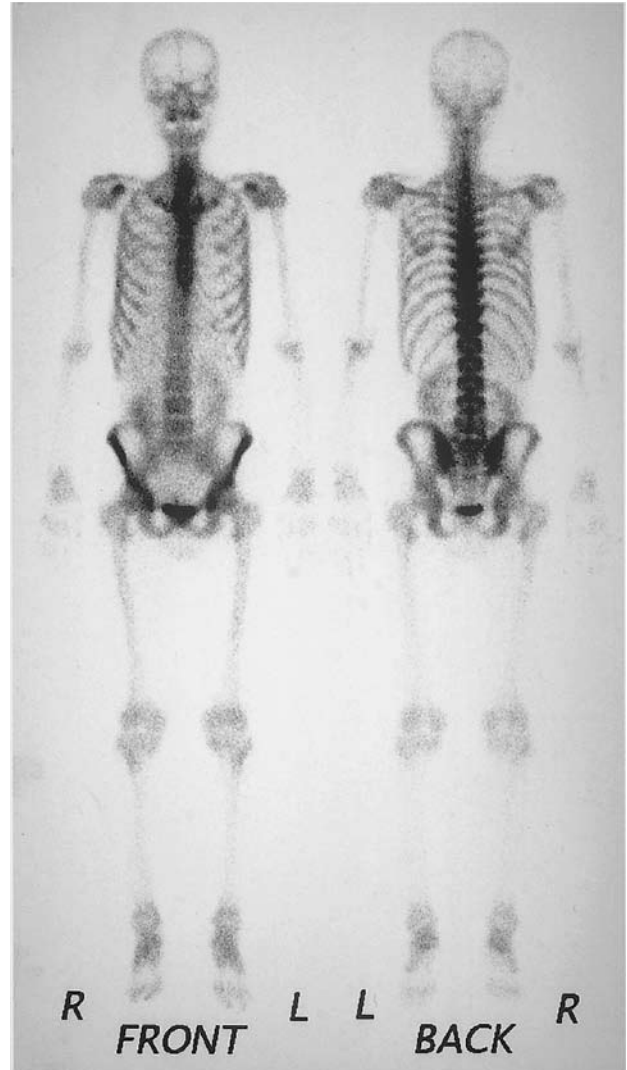


Fig. 5 Systemic bone scintigraphy gave no result of abnormal accumulation.

tigraphy showed abnormal accumulation only in the enlarged liver (Fig. 4). but systemic bone scintillation did not yield results suggestive of abnormal accumulation (Fig. 5). Magnetic resonance imaging (MRI) was not performed because of his claustrophobia. A tumor biopsy under ultrasonic guidance was carried out on March 14 for the purpose of histological diagnosis because it was not possible to diagnose any primary focus from imaging tests and tumor markers. Moreover, there were no abnormal findings in the fields of otorhinolaryngology and urology. Macroscopic observation revealed that the collected specimens had a black color. Hematoxylin and eosin staining showed solid growth of atypical cells associated with a brown pig-

ment (Fig. 6). When this pigment was bleached by a melanin-bleaching method, the disease was diagnosed as hepatic metastasis of a histopathologically malignant melanoma (Fig. 7). On admission of this patient, we attempted to contact the hospital where he had received the operation for his eye lesion in 1998. After we conducted a tumor biopsy, that hospital sent a report, which indicated that the eye lesion had been diagnosed as a malignant melanoma of the left choroid membrane. Recurrence and distant metastasis had not been clearly observed in the systemic examination conducted in July 2003. After the established diagnosis, serum 5-S-cysteinyl-dopa (5-S-CD) revealed a markedly increased level of 293.3 nmol/l (normal 1.5 to 8.0 nmol/l).

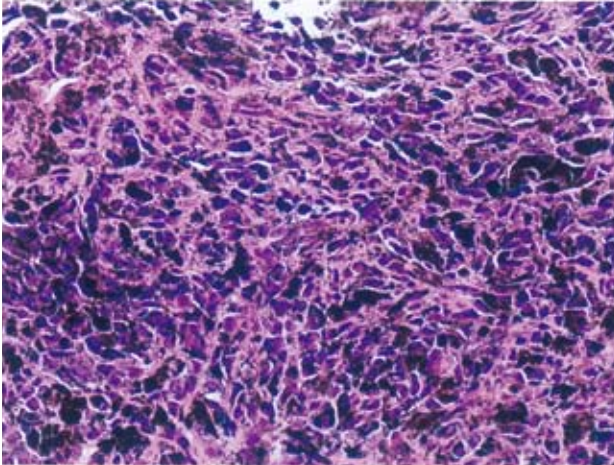


Fig. 6 Hematoxylin and eosin staining showed solid growth of atypical cells with a brown pigment.

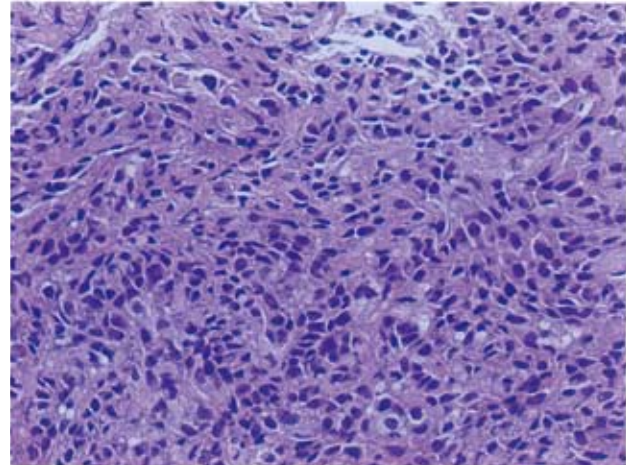


Fig. 7 The pigment was bleached by a melanin-bleaching method, the disease was diagnosed as hepatic metastasis of a histopathologically malignant melanoma.

Arterial injection therapies were conducted three times, utilizing 100 mg of cisplatin. After the first injection, serum 5-S-CD decreased slightly to 159.6 nmol/l, but after the second treatment, the patient's general condition worsened. The patient died on June 25 from the complication of disseminated intravascular coagulation syndrome that developed on June 14. A pathological autopsy could not be conducted because family consent was not given.

DISCUSSION

In Europe and the United States, uveal melanoma involving the choroid membrane is the most commonly occurring intraocular malignancy in adults. It arises from uveal melanocytes residing in the uveal stroma, and accounts for 70 % of all primary ocular cancers. It occurs at the frequency of 0.7 persons per 100,000 people of the population in Europe¹⁰⁾. In Asia, it occurs at the frequency of 0.02 persons per 100,000 people of the population of India¹¹⁾. Uveal melanoma is reported to have a better prognosis than other types of melanoma, but there have been few reports in which the long-term prognosis has been investigated. Kujala et al. reported that the uveal melanoma death rate is 31 % in 5 years, 45 % in 15 years, 49 % in 25 years, and 52 % in 35 years, and concluded that distant metastasis exaggerates prognosis¹²⁾. Because the distant metastasis of uveal melanoma is hematogenous, the liver is the frequent destination of distant metastasis¹³⁾. Gragoudas et al. reported that hepatic metastases accounted for 136

cases (93.8 %) among 145 cases of metastatic uveal melanoma¹⁴⁾.

5-S-cysteinyldopa (5-S-CD) is an index for melanogenesis¹⁵⁾. There are reports that 5-S-CD is useful for the diagnosis of melanoma and for the prognostic calculation of those cases involving distant metastasis^{16~18)}. In our case, the level of 5-S-CD was substantially elevated to 293.3 nmol/l at the time of diagnosis. Although this level tended to decrease due to treatment with anticancer drug injections, the patient died on the 117th day after the first medical examination.

There is no established therapy for melanoma involving hepatic metastasis. In cases of melanoma that has spread to organs within the abdominal cavity, it has been reported that patients from whom the metastatic focus has been radically resected should have a prolonged survival period¹⁹⁾. Rivoire et al.²⁰⁾ investigated 63 cases of therapeutic results from uveal melanoma involving hepatic metastasis, and reported that cases who had undergone a radical resection yielded good prognostic results. The authors of this report followed up 602 cases of post-operative uveal melanoma by conducting abdominal ultrasonic tests at 6-month intervals, and detected 63 cases of hepatic metastasis in 14 years. Even though ultrasonography was conducted every 6 months, there were only 14 cases of hepatic metastasis in whom radical resection had been possible. Accordingly, surgical treatment is generally considered to be difficult. In 1998, Carrasco et al. re-

ported that transcatheter arterial embolization (TAE) combined with cisplatin was effective for treating uveal melanoma involving hepatic metastasis²¹⁾. Subsequently, the same group applied this therapy to 30 cases of hepatic metastasis, and reported efficacy in 46 % of the cases²²⁾. Ever since, there have been many reports in which TAE combined with cisplatin has been the first choice of treatment for uveal melanoma involving hepatic metastasis²⁾. In the past, these patients had an average prognostic period of about 5 months. Owing to this therapy, the 50 % survival period appears to have been extended to 14 months²³⁾.

The poorer prognosis of our case relative to other reported cases may be attributable to the fact that the tumor already occupied a majority of the liver when the patient received the first medical examination. Since the right branch of the portal vein had occluded, it was impossible to embolize the hepatic artery. Therefore, the treatment of last resort was via arterial injections of an anticancer drug.

Late recurrence cases are detected by distant metastasis that occurs within a period of 10 or more years after the first diagnosis of a primary focus. In melanoma, late recurrence is observed at a rate of 2.4 %, but reports suggest that there is no difference in the site of the primary focus²⁴⁾. The average period elapsing from the time of resection of a primary focus to the time of diagnosis of hepatic metastasis ranges from 2.4 years¹⁴⁾ to 4.3 years²⁵⁾. However, there are reports of hepatic metastasis being diagnosed at 30 years or more after the operation^{26,27)}. Therefore, it is necessary to follow up melanoma cases for a long period after the extirpation of uveal melanoma. Moreover, in metastatic hepatic tumor patients whose primary focus is unknown, it is important to conduct a detailed investigation of the patient's disease history, bearing the present findings on uveal melanoma in mind.

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