

# Late Liver Metastases of Choroidal Melanoma Detected by Laparoscopy

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**Abstract.** Choroidal melanoma represents the primary intraocular malignancy in adults with a reported incidence of about 4000 cases per year. The liver is the sole site of metastases in more than 80% of cases and is affected in up to 90% of patients who develop metastatic disease. Patients with metastatic melanoma have usually a median survival of 6 months. In the present paper, the case of a 42-year-old woman with choroidal melanoma who underwent surgery and was followed up for 7 years with no evidence of relapse is reported. Eight months later she had a car accident and was admitted to the hospital complaining of abdominal pain, lack of appetite and asthenia. At physical examination, jaundice and hepatomegaly were found. Abdominal ultrasonography revealed the presence of several hypoechoic lesions, and liver function was compromised due to coagulation deficiency. Thus, the diagnosis of metastatic choroidal melanoma was obtained by video-assisted laparoscopy that showed disseminated darkly pigmented lesions on the surface of the liver. The patient died of liver failure three months later. At autopsy, histopathological examination of the liver confirmed the diagnosis, excluding local recurrence of the choroidal melanoma.

Choroidal melanoma (CM) represents the primary intraocular malignancy in adults and its mean age-adjusted incidence in the United States is 4.3 per million (1). This tumor arises from the melanocytes in the uveal layer of the choroid, which is a sponge-like membrane extending as far forwards as the *ora serrata* and firmly adherent to the sclerotic tissue (2). Most cases (>95%) occur in the Caucasian population, with a significant variation of incidence (males > females) between genders (1).

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At early stage, the CM is asymptomatic, however more than 90% of patients show visual symptoms, including visual field loss, blurred vision, metamorphopsia, photopsia or local pain (3). Most cases are detected during a routine eye examination and the ophthalmologist recognizes the tumor due to its degree of pigmentation. Ultrasonography (US) and fluorescein angiography are not usually required, neither is a biopsy (4, 5). The liver is the principal site of metastases of CM becoming involved in up to 90% of patients who develop metastatic disease (4, 6). This report describes an unusual case of a patient who developed multiple liver metastases of a CM removed 8 years previously.

## Case Report

*December 1999.* A 42-year-old woman with severe ocular pain, inflammation and edema of the right eye was admitted to Padua University Hospital. The ophthalmologist found vitreous hemorrhage, large retinal detachment and a large pigmented mass corresponding to a typical CM. The patient was also examined by the dermatologist in order to exclude the presence of additional cutaneous melanoma. The screening for excluding liver, pulmonary or bone metastases was achieved by either liver function test (including bilirubin, aspartate-aminotransferase [AST], alanine-aminotransferase [ALT], alkaline-phosphatase [ALP], gamma glutamyl transpeptidase [ $\gamma$ GT], lactate dehydrogenase [LDH]) or liver US and whole bone scintigraphy. Head, upper abdomen and thoracic helical computed tomography (CT) scanning were also performed.

*January 2000.* The patient underwent surgery and the final pathology confirmed the presence of a CM. No postoperative radiotherapy was performed. The patient was followed-up by physical examination, liver function tests, abdominal US and head CT scan every 6 months for the first 5 years, and yearly afterwards; she also underwent whole bone scintigraphy and thoracic CT scan each year. No signs of relapse or alterations of the liver function were observed until February 2006.

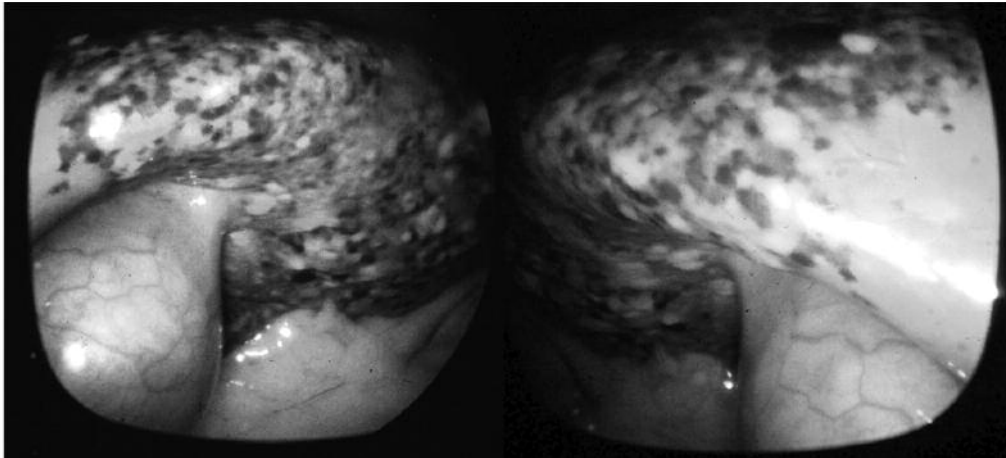


Figure 1. Video-assisted laparoscopy images showing disseminated darkly pigmented lesions on the surface of the liver, which are the typical macroscopic aspect of metastatic melanoma.

October 2006. The patient had a car accident and was admitted to the hospital complaining of abdominal pain, lack of appetite and asthenia. Physical examination revealed jaundice and hepatomegaly. Liver function test showed increased total bilirubin ( $36 \mu\text{mol/l}$ ), AST (62 U/l), ALT (71 U/l), ALP (178 U/l), LDH (1,256 U/l) and  $\gamma\text{GT}$  (124 U/l) serum levels, while alpha-fetoprotein and markers of hepatitis were normal. Abdominal US revealed the presence of several hypoechoic lesions in the right and left hepatic lobe, ranging from 8-12 mm in maximum diameter as confirmed by the CT scan. Since the standard coagulation screening tests (prothrombin time [PT], international normalized ratio [INR], partial thromboplastin time [PTT]) were abnormal (PT=52%, INR=1.42, PTT=46) a US-guided fine-needle aspiration biopsy was not performed. Thus, the diagnosis of metastatic CM was obtained by video-assisted laparoscopy that showed disseminated darkly pigmented lesions on the surface of the liver, presenting the typical macroscopic aspect of the disease (Figure 1). The patient was treated with sequential fotemustine, interferon- $\alpha$  and interleukin-2, as suggested by Becker *et al.* (7), but she died of liver failure three months later. At autopsy, histopathological examination of the liver confirmed the diagnosis but excluded local recurrence of the CM.

## Discussion

The incidence of CM is reported to be 3,500-4,000 cases per year and about 5-10% of all melanomas are primary ocular melanoma (1-3, 8). About 40% of patients with CM have hepatic metastases at the moment of initial diagnosis and the liver is the sole site of metastases in more than 80% of cases (7, 9-11). The 5-year survival for patients

with CM ranges from 50% to 70% and factors affecting results include lesion size, cell type, mitotic activity and local invasion (4, 12). Patients with metastatic melanoma have a median survival of 6 months and fewer than 10% survive after 1 year, although in selected cases, the patient may benefit from liver resection (13-15). Less common sites of metastasis from CM include the lungs, bones, skin and lymph nodes (4). LDH serum level is a useful biochemical parameter in patients with CM metastatic to the liver, but a multivariate analysis study showed that the metastasis-free interval and serum ALP are the main independent prognostic factors for survival (13, 16). A more recent study found that, based on likelihood ratios, ALP and LDH should be considered the best predictive biochemical test, although 50% of patients with metastasis had normal liver function (6).

Unfortunately, metastatic CM is difficult to treat. Systemic treatment strategies include immunotherapy (*i.e.* interleukin-2), chemotherapy (*i.e.* bleomycin, cisplatin, dacarbazine, lomustine) and antiangiogenic agents (*i.e.* thalidomide), alone or in combination (7, 17-20). Locoregional therapies, enclosed hepatic artery chemoembolization, chemotherapy or immunoembolization and isolated or percutaneous hepatic perfusion seem to be more effective, but at present they are still in clinical development (4). Finally, in carefully selected patients, resection of the liver metastases may increase survival, although the selection criteria remain unclear (14, 15). Due to multicentric liver metastases, the only possible therapy for the patient discussed here, was systemic chemo- and immunotherapy despite her 8-year disease-free interval.

In conclusion, metastatic CM remains an incurable disease, especially in patients who are not suitable for locoregional therapies or liver resection.

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