Fulminant hepatic failure secondary to diffuse liver infiltration by melanoma

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Although metastatic liver disease is common, it is unusual for even substantial replacement of liver by tumour to cause clinically significant impairment of liver function. Hepatic failure secondary to metastatic liver disease appears to be rare and has been the subject of occasional reports[1-3]. In the following unusual case, the principal clinical manifestation of a metastatic melanoma was fulminant hepatic failure. At autopsy, diffuse infiltration of the liver parenchyma by melanoma was found.

Case report

Mr RM, aged 59, first presented in February 1983 with a pigmented, fleshy lesion (1 × 3 cm) on the right scapula and a second, similar lesion (1.5 × 0.5 cm) with pigmented satellites at its apex in the left sacral region. These had been present for many years but had recently enlarged and were bleeding and itching. Excision biopsy of the scapular lesion revealed a nodular Clark 4 malignant melanoma with a tumour depth of 5 mm, and an intradermal naevus with a superficial spreading melanoma *in situ* in the sacral lesion. An elective wide excision and split-skin grafting of both lesions was undertaken. Histology of the excised skin showed no residual melanoma.

The patient remained well until November 1984 when he re-presented with a non-tender 4 × 3 cm right axillary lymph node. Histology of the excised lesion showed large deposits of metastatic malignant melanoma.

In January 1985, he developed right hypochondrial pain with nausea and vomiting over a 10-day period and a 4 kg weight loss. On examination (21.1.85), he was a well-looking man with no lymphadenopathy. The liver was 5 cm enlarged, firm and tender; the spleen was enlarged 3 cm beyond the left costal margin. Chest X-ray was normal but abdominal ultrasound examination revealed a markedly enlarged liver, but no focal abnormalities. The common bile duct and intrahepatic bile ducts were of normal calibre. The pancreas was normal.

Over the ensuing days, he became progressively jaundiced, and nausea and vomiting intensified. He became pyrexial (38.3°C) and the hepatic tenderness

Table 1. Haematological and biochemical course

	21.1.85	*23.1.85*	*26.1.85*	*28.1.85*	*29.1.85*	*31.1.85*
Haemoglobin (g/dl) (NR 14–18)	16.0	16.8	17.4	16.3	15.2	12.0
WCC ($\times 10^9$/l) (NR 4–11)	9.7	10.9	15.9	14.6	19.8	13.0
Platelets ($\times 10^9$/l) (NR 250–450)	130	101	77	68	60	39
Sodium (mmol/l) (NR 135–146)	137	132	127	125	122	125
Potassium (mmol/l) (NR 3.5–5.0)	4.2	4.3	4.6	4.1	4.0	3.5
Chloride (mmol/l) (NR 94–105)	100	93	87	85	83	87
Bicarbonate (mmol/l) (NR 22–30)	23	20	15	15	16	14
Urea (mmol/l) (NR 2.5–6.7)	10.5	14.7	25.5	28.7	31.3	31.1
Creatinine (mmol/l) (NR 0.05–0.10)	0.13	0.14	0.16	0.20	0.24	0.32
Bilirubin (μmol/l) (NR 2–17)	22	31	78	138	168	188
Alkaline phosphatase (iu/l) (NR 25–100)	166	182	288	448	418	455
SGOT (IU/l) (NR 10–40)	78	69	430	1086	1134	1146
Total protein (g/l) (NR 62–80)	60	56	56	54	47	44
Albumin (g/l) (NR 36–47)	34	32	30	28	25	22
PT (sec) (NR 12)	16	16	22	22	19	26
PTTK (sec) (NR 35)	36	37	49	51	49	64
TT (sec) (NR 10)	10	10	10	10	10	11
Glucose (mmol/l) (NR 4.5–5.8)	6.3		2.2		3.7	

NR = Normal range

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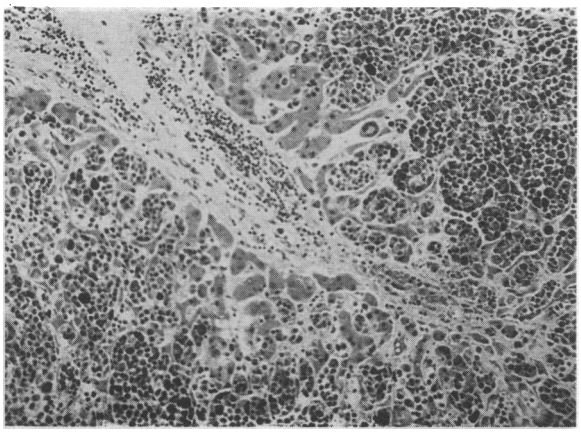

Figure 1. Microscopic section of liver showing diffuse infiltrate of melanoma with islands of surviving hepatic tissue. (× 180; reduced 55%)

increased; left lower rib pleuritic type chest pain developed over the splenic area and ascites was present clinically. Biochemistry suggested fulminant hepatic necrosis with massively raised SGOT (1134 iu/l), falling albumin (34 to 22 g/dl), hypoglycaemia (glucose 2.2 mmol/l) and a rise in prothrombin time (14 to 22 sec) despite vitamin K therapy. Blood cultures were repeatedly negative.

An acute Budd–Chiari syndrome was suspected, secondary to tumour deposits within the hepatic vein. A radioisotope technetium scan, however, showed diminished but homogenous tracer uptake within the liver substance. Despite neomycin and lactulose treatment, a protein-free, low-salt and high-carbohydrate diet, he became profoundly jaundiced and encephalopathic, developed hepatorenal syndrome and died 10 days after his admission. His biochemical course is summarized in Table 1.

At post-mortem examination there was no sign of local recurrence of the tumour on the skin, but deposits of metastatic melanoma were found to be widespread. Nodules of tumour were seen in the atrial septum and in the mucosa of the small intestine. The liver and spleen were of a uniform black colour, but with no visible focal lesions. There were foci of tumour in the vertebral bodies. On microscopy, small groups of tumour cells were seen in interstitial tissue of the lung and in the renal glomeruli. The spleen, which contained an infarct, was also the site of deposits, as were lymph nodes and the pancreas. The liver itself was almost completely replaced by a diffuse infiltrate of melanoma cells, leaving only a few islands of surviving hepatic tissue (Figure 1).

Discussion

Hepatic metastases are not generally included in lists of causes of fulminant hepatic failure[4]. Metastases generally result in mild biochemical abnormalities with moderate elevations of SGOT and alkaline phosphatase and bilirubin[5,6]. Harrison *et al.*[2] reported a small series of patients with extensive liver metastases in whom the clinical course was characterized by rapid onset of abdominal pain, jaundice, rapidly deteriorating mental status and death within 1–12 days of admission. Biochemically the picture was dominated by striking elevations of SGOT, serum LDH, serum alkaline phosphatase and prothrombin time. At autopsy, in each case, a similar histological picture was present: extensive infiltration and replacement of liver by tumour and widespread coagulation necrosis of the remaining parenchyma, suggesting hepatic infarction. Eras and Sherlock[7] described a series of 21 patients with metastatic liver disease who developed coma, although no specific correlation was made between clinical courses, elevations of transaminases and histological findings at autopsy. It is unclear, therefore, whether true hepatic failure accounted for the encephalopathy in these patients.

The patient reported here is clearly unusual. Metastatic liver disease was suspected during life by the hardness of the liver, but because of the diffuse invasion of liver by melanoma, both ultrasound examination and radioisotope liver scans failed to reveal classical metastatic deposits. The rapid deterioration of liver function from near-normal at presentation to one characteristic of acute liver failure in the space of a few days, together with the rapid onset of hepatic coma, suggested massive hepatocellular necrosis. Clinically a Budd–Chiari syndrome seemed the most likely cause. The increasing size of the liver was against fulminant hepatitis as a cause, since the liver would be expected to shrink under these circumstances[8]. The mechanism of rapid liver failure here seemed more related to simple replacement of liver by melanoma rather than by a process of parenchymal infarction and necrosis as described by Harrison and colleagues[2].

The report demonstrates the difficulty of making a noninvasive diagnosis of diffuse hepatic infiltration from metastatic melanoma. Fulminant hepatic failure appears to be a rare presenting feature of metastatic hepatic involvement in this aggressive tumour.

Acknowledgment: We are grateful to Professor C J Dickinson for permission to report this case.

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(Accepted 20 November 1985)