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Case study

Multiple myeloma relapse in the irradiated liver: involvement of hepatocyte growth factor akin to that after hepatocyte transplantation

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Abstract

We described a rare case of multiple myeloma in a 60-year-old man, in whom relapse limited to the irradiated area in the left lobe of the liver developed following radiotherapy for lesions in 11th and 12th thoracic spines. Immunohistochemical analysis revealed expression of hepatocyte growth factor (HGF) and hepatocyte growth factor receptor (c-Met) in the hepatocytes in the irradiated area of the liver. We speculate that the malignant plasma cells might have proliferated in response to local increase of HGF production in the irradiated liver. The role of HGF in the extraosseous spread of multiple myeloma and also under the experimental condition of hepatic transplantation is discussed.

Keywords

hepatic growth factor; hepatocyte transplantation; myeloma; radiation

INTRODUCTION

Multiple myeloma is a disorder of unknown origin that is characterised by clonal malignant plasma cell proliferation. It is associated with the production of monoclonal immunoglobulins, painful bone destruction, anemia, hypercalcemia, and renal dysfunction. Liver involvement in multiple myeloma has rarely been reported in living patients. We described a rare patient with multiple myeloma who developed relapse limited to the irradiated liver following radiotherapy for lesions in the 11th and 12th thoracic spines (Th11/12). The role of hepatocyte growth factor (HGF) in the extraskeletal spread of plasma cell neoplasms and also in hepatocyte proliferation under the experimental condition of hepatocyte transplantation is discussed.

Case report

A 60-year-old man visited our hospital in January 2007 with the chief complaint of lumbar back pain. His previous medical history

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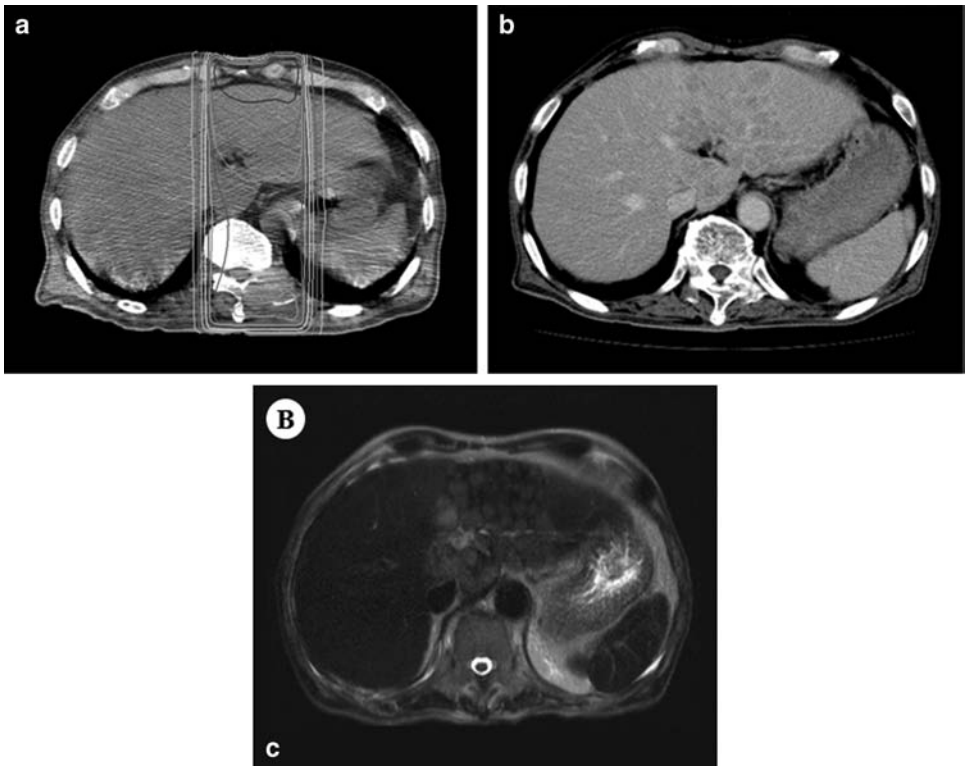

Figure 1. A CT slice showing isodose lines of irradiation (A). A well-defined, poorly enhanced lesion is visualised in the liver corresponding to the irradiated area (B). The lesion is visualised as an aggregation of nodules on MRI (C).

was unremarkable. In lumbar spine magnetic resonance imaging (MRI), obtained at presentation, all the vertebral bodies of the lumber spine were hypointense on T1-weighted images, and a compression fracture of the second lumber (L2) vertebral body was noted; this fracture was suspected to be a pathological fracture associated with metastatic spread from a malignant tumour. Whole-body CT revealed osteolytic areas with a mass lesion in Th11. No other findings suggestive of malignancy were observed. Bone scintigraphy showed abnormal accumulation at the site of compression fracture in L2, but not in the osteolytic lesions in Th11. Based on the above findings, multiple myeloma was suspected; bone marrow biopsy was performed, which confirmed the diagnosis of multiple myeloma (IgA ktype). Radiotherapy was initiated (30 Gy in 15 fractions) for pain control in February 2007, with radiation delivered to the Th10 to Th12 vertebral bodies in two opposing anterior-posterior fields (Figure 1A). Chemotherapy (vincristine, adriamycin, and dexamethasone) was started after the radiotherapy.

Abdominal contrast-enhanced computed tomography (CT) obtained 3 months later revealed a well-defined, poorly enhanced area in the liver corresponding to the irradiated area (Figure 1B). This area was visualised as an aggregation of nodular lesions on MRI (Figure 1C). Thus, needle biopsy of the liver was performed in July 2007, with specimens obtained both from the irradiated area and surrounding area of the liver. The biopsy specimens showed a large number of myeloma cells in the irradiated area (Figure 2A), while the non-irradiated area showed regenerative changes only, and no tumour cells were found (Figure 2D). Based on the known involvement of HGF in the growth of myeloma, we measured the plasma concentration of HGF, which was 1.6 ng/mL (normal, $<$ .0.39 ng/mL). Immunohistochemical analysis revealed expression of both HGF and its receptor c-Met in

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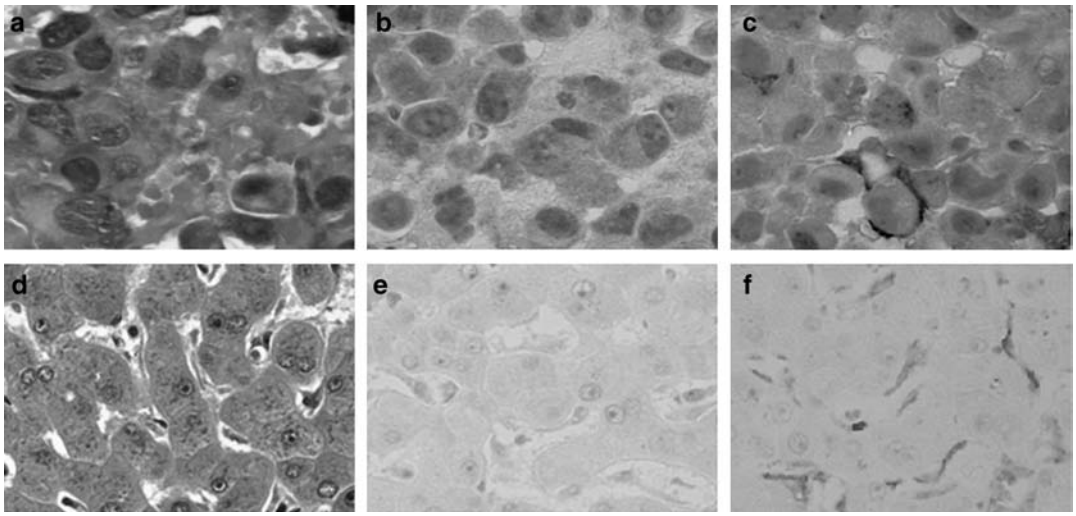

Figure 2. Histological findings (H-E) (A,D) and results of bimmunohistochemical analysis for HGF (B,E) and c-Met (C,F) in both the irradiated and surrounding non-irradiated areas of the liver: proliferation of myeloma cells and expression of both HGF and c-Met in the proliferating hepatocytes are observed.

the myeloma cells from the irradiated area of the liver (Figures 2B and 2C), but not in the cells from the surrounding non-irradiated area (Figures 2E and 2F). Unfortunately, one month later, the patient subsequently developed disseminated intravascular coagulation and expired (August, 2007).

DISCUSSION

Multiple myeloma cells often produce HGF, and the plasma concentrations of HGF are significantly elevated in patients with clinically active multiple myeloma[1] HGF acts in both a paracrine and autocrine manner to stimulate the proliferation of the myeloma cells.[2] In a mouse experiment conducted by Landis et al.,[3] partial liver irradiation in combination with systemic HGF expression using a recombinant adenoviral vector, resulted in selective replacement of the host hepatocytes in the irradiated part of the liver with progeny of transplanted hepatocytes. They suggested that the partial liver irradiation caused inhibition of host hepatocyte proliferation and that the HGF provided a strong mitotic stimulus to the hepatocytes transplanted into the irradiated area of the liver. In our patient, radiation was delivered to the left hepatic lobe, the serum HGF was elevated to 1.6 ng/mL, and the hepatocytes obtained from the irradiated area of the liver showed expression of HGF and c-Met. These findings suggest coincidental occurrence of the same pathophysiological condition in the liver in this patient as in the experiment conducted by Landis et al.[3] Accordingly, multiple myeloma relapse occurred solely within the irradiated liver in this case, although liver involvement in multiple myeloma is rare.[4]

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