

Plasmablastic Myeloma Presenting with Nodular Liver Lesions: Rare but Important to Recognize

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ABSTRACT

Nodular liver lesions commonly represent solid tumour metastases. However, haematological neoplasms should also be considered as primary cause. Extramedullary infiltration of multiple myeloma with hepatic invasion at diagnosis is uncommon. We describe an unusual case of a woman presenting with multiple liver lesions initially suggesting disseminated solid tumour disease. She appeared to have widespread plasmablastic myeloma, an aggressive subtype of multiple myeloma, instead.

Key words: Multiple myeloma, plasmablastic myeloma, extramedullary, liver metastases, liver lesions

Nodüler Karaciğer Lezyonları ile Seyreden Plazmablastik Myeloma

ÖZET

Nodüler karaciğer lezyonları genellikle solid tümör metastazını gösterir. Bununla birlikte, hematolojik neoplazmalar bunların ana nedeni olarak kabul edilmelidir. Tanıda hepatik invazyonlu multipl miyelomun ekstrapredüller infiltrasyonu oldukça nadirdir. Biz başlangıçta yaygın solid tümör hastalığı olan multipl karaciğer lezyonları ile başvuran bir kadın olgu sunulmaktadır. Olguda yaygın plazmablastik miyelom tutulumu mevcuttur.

Anahtar kelimeler: Multipl miyeloma, plazmablastik miyeloma, ekstrapredüller, karaciğer metastazı, karaciğer lezyonu

INTRODUCTION

Multiple myeloma is a malignant plasma cell proliferation mainly involving the bone marrow. It commonly affects the middle-aged and elderly population. With increasing incidence it is the second most common haematological neoplasm. The survival from diagnosis ranges from several months to (in a minority of patients) more than 10 years depending on, amongst other things, stage and morphology of the disease (1-4). Extramedullary myeloma represents a less common manifestation in newly diagnosed patients usually indicating extensive disease with poor prognosis (2,5-7). Hepatic involvement at diagnosis is also rare, usually presenting with diffuse plasma cell infiltration and less common as nodular disease (5-14). Initially, several findings suggested disseminated solid tumour disease with liver metastases. Diagnostic work-up, however, revealed extramedullary plasmablastic

myeloma, a subtype of multiple myeloma, with multiple nodular liver lesions.

CASE

A 54-year-old woman was admitted to our hospital with lower back pain and hypercalcaemia. She also reported fatigue, lack of appetite and eight kilogram weight loss within three months. Her medical history revealed euthyroid multinodular goiter and a lumbar vertebral fracture after minor trauma a few months before admission. Besides a known goiter and low-grade fever physical examination was unremarkable. Laboratory investigation demonstrated a normocytic anaemia (5.2 mmol/L), normal white blood cell and platelet count, raised erythrocyte sedimentation (45 mm/hr), severe hypercalcaemia (4.36 mmol/L), suppressed parathyroid hormone (0.9

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Received: 18.03.2012, Accepted: 21.03.2012

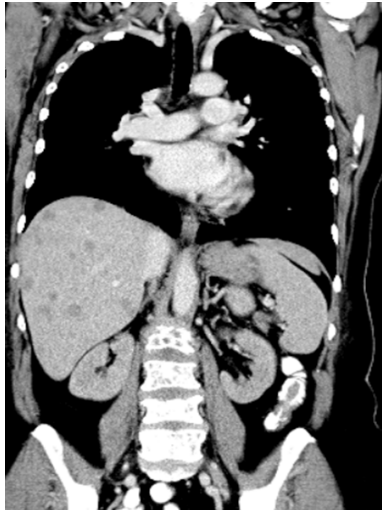


Figure 1. Abdominal computed tomography (coronal reconstruction) showing multiple liver lesions suspicious for metastases.

pmol/L), acute renal failure (creatinine 198 μ mol/L), abnormal liver biochemistry (alkaline phosphatase 121 U/L, gamma glutamyl transpeptidase 180 U/L, aspartate aminotransferase 149 U/L, alanine transaminase 150 U/L). Thoracic and abdominal computed tomography showed multiple bone and liver metastases (figure 1), mediastinal masses and several pathological vertebral fractures. Bone scintigraphy also revealed multiple hot spots (ribs and vertebrae) suspicious for bone metastases. Mammographic findings were normal. Since no primary tumour was identified with radiologic imaging and disseminated solid tumour disease was suspected, a percutaneous biopsy of a liver lesion was performed. The liver biopsy showed infiltration with plasmablastic cells (figure 2). Histopathological examination and flow cytometry of bone marrow matched with these findings, showing 80% infiltration with plasmablastic myeloma. Additional serum immunoelectrophoresis revealed the presence of an IgA kappa paraproteinemia (14.0 g/L), increased plasma B2 microglobulin level (4.9 mg/L) and absence of light chains in a urine sample. These results confirmed the diagnosis plasmablastic myeloma, a subtype of multiple myeloma, with widespread osseous as well as extramedullary involvement. Due to rehydration and infusion of pamidronate the patient became normocalcemic and her prerenal acute renal failure gradually improved. Induction chemotherapy (thalidomide, doxorubicin, dexamethasone) was started as soon as

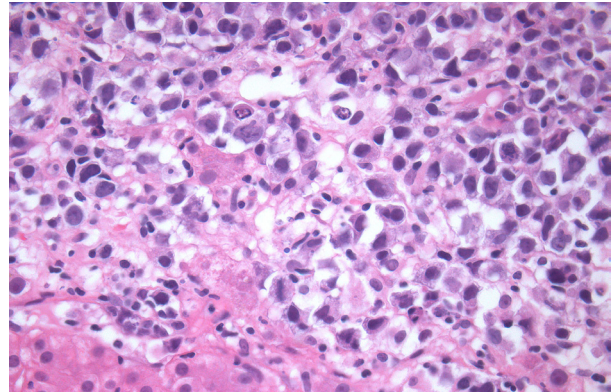


Figure 2. Liver biopsy with preexistent hepatocytes (lower right) and blasts with high nuclear-to-cytoplasmic ratio and with an immunophenotype (CD138, Mum1, CD79a and kappa light chain positive, CD20 negative) showing plasmablastic differentiation.

the patients' condition stabilized. Complete remission was achieved after 3 cycles. Subsequently, stem cell mobilisation and administration of high-dose melphalan was followed by autologous stem cell reinfusion. Shortly after bone marrow regeneration the patient died of sudden cardiac arrest. The family refused to conduct autopsy.

DISCUSSION

Extramedullary involvement of multiple myeloma is uncommon at diagnosis and is caused by haematogenous spread. Lymph nodes, pleura, endocrine glands, gastrointestinal tract, kidneys, meninges and reticuloendothelial organs such as liver and spleen can be affected in the course of disease (5-7,11). Hepatic invasion is rarely diagnosed at initial presentation because symptoms, physical examination and laboratory findings are nonspecific (7-9,13,15). However, at autopsy extramedullary involvement in general as well as hepatic invasion are found in up to two-thirds and almost fifty percent (28-50%) of patients respectively (5-7,10,11). Plasmablastic myeloma represents a small morphological subtype of multiple myeloma, characterized by blasts with high nuclear-cytoplasmic ratio, small nucleoli and occasional eccentrically located nuclei and is associated with a poor prognosis (3,16,17). Liver involvement is also rare in patients with newly diagnosed plasmablastic myeloma. Patients with hepatic invasion of multiple myeloma can

be either asymptomatic or present with clinical signs of hepatomegaly, splenomegaly, ascites and jaundice. Laboratory analysis may reveal abnormal liver biochemistry (7,8,10,13,14). Involvement of the liver can either appear as diffuse plasma cell infiltration, which can only be seen on microscopic examination, or scarce as space-occupying liver lesions with circumscribed tumour nodules like in our patient (6-15). Ultrasound as well as computed tomography can be used to identify mass lesions. However, imaging features are non-specific and based on few published case reports. Moreover they cannot be used to distinguish between liver metastases from multiple myeloma or solid tumours (7,9,13,15).

The clinical relevance and prognostic implications of liver involvement in multiple myeloma remains uncertain (8,10,14,15). Plasmablastic myeloma, regardless its extensiveness or localisation, should be treated as any high-risk multiple myeloma (17). High-dose melphalan followed by autologous stem cell transplantation (SCT) remains the first-line therapy for young high-risk multiple myeloma patients who are responsive to conventional induction chemotherapy (vincristine or thalidomide, doxorubicin, and dexamethasone) (1,2,17). Compared to other multiple myeloma subtypes, plasmablastic morphology is reported as predictor of poor prognosis with high risk of complications, relapse or refractory disease, despite these aggressive treatment approaches (3,16,17). In general, nodular liver lesions suggest a differential diagnosis that would include metastases from various solid malignancies and lymphoma (9,10,13). Our report points out that multiple myeloma should also be considered as a potential cause of nodular liver lesions. Easy accessible and low-risk diagnostic tests like detection of monoclonal proteins (M-proteins) and bone marrow aspirate/biopsy should be considered, in absence of reasonable suspicion of a synchronous primary cancer, and thus avoiding a more invasive and hazardous liver biopsy. It should be noticed that accurate diagnosis is crucial regardless the clinical and radiological appearance, since specific treatment options exist for haematological and solid malignancies.

Nodular liver lesions suggesting metastatic disease are usually caused by primary solid malignancies. However, this case illustrates that haematological neoplasms such as multiple myeloma should also be considered as uncommon cause. Accurate diagnostic work-up of metastatic liver disease is crucial since specific treatment options for haematological malignancies differ from

solid tumours, leading to more favourable long term outcome.

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