Extraosseous myeloma of liver mimicking multifocal hepatocellular carcinoma where a distinction has to be made: two case reports

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Case reports

Case 1

A 67-year-old man with kappa light chain multiple myeloma (MM) had a baseline negative skeletal survey and had undergone dual-tracer positron emission tomography–computed tomography (CT) with fluorine-18 fluorodeoxyglucose and carbon-11 acetate. An initial biochemical response to combined chemotherapy with bortezomib, thalidomide and dexamethasone later plateaued; therefore, he was switched to second-line chemotherapy with ixazomib, lenalidomide and dexamethasone. He then developed progressively deranged liver function and new-onset pancytopenia with fever during the first cycle. Ultrasound revealed multiple bi-lobar hepatic hypoechoic lesions, some with a central echogenic focus surrounded by hypoechoic rim (target appearance), suggesting possible hepatic candidiasis. Nonetheless there was progressive worsening of liver function and recurrent fever despite intravenous antifungal therapy. Urgent multiphasic CT revealed a small arterial enhancing nodule in hepatic segment V with washout. A newly developed lytic sacral lesion was suspected to be myeloma involvement. The liver CT 3 weeks later showed an interval increase in size and number of these liver lesions with similar enhancement pattern.

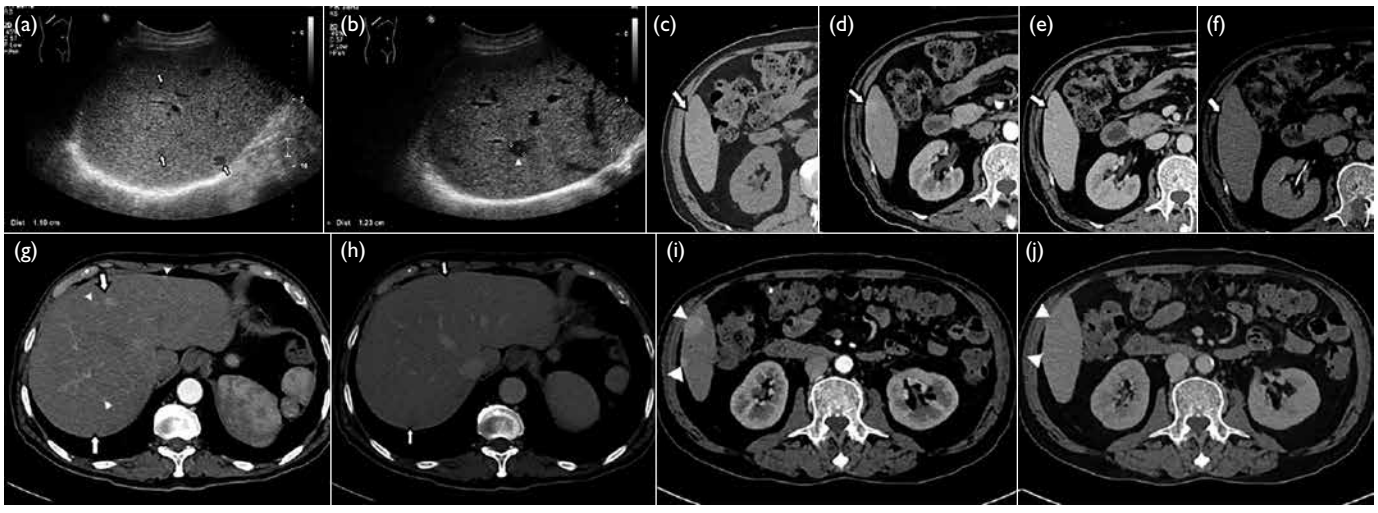

FIG 1. Case 1. Initial ultrasound scan revealed multiple well-circumscribed round hypoechoic hepatic lesions with central echogenic focus measuring up to 1.2 cm (white arrows and arrowhead in [a] & [b], respectively). Morphology resembles a 'bullseye' appearance and was thought to represent possible hepatic candidiasis. Subsequent multiphasic computed tomography (CT) [white arrows] revealed (c) a single hypoattenuating lesion at segment V (about 1.4 cm in diameter) demonstrating (d) arterial hyperenhancement, (e) portal venous washout and (f) delayed washout. Hepatocellular carcinoma is a possible differential for this radiological pattern. A developing left sacral lytic lesion with soft tissue component was noted on the same CT (not shown). Follow-up triphasic CT scan of the liver within 3 weeks showed multiple bi-lobar new arterial enhancing lesions (white arrows and arrowheads in [g]), (h) some with portal venous washout and delayed washout. The smaller ones (white arrowheads in [g]) were isoattenuating in portal venous and delayed phases and cannot be discretely identified. There was also rapid interval enlargement of segment V hepatic lesion, measuring up to 2.5 cm in diameter with (i) arterial enhancement, (j) portal venous washout and delayed washout (white arrowheads). Biopsy of this segment V lesion confirmed clonal plasma cells, consistent with the diagnosis of hepatic extraosseous myeloma

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Multifocal hepatocellular carcinoma (HCC) was one of the prime differential diagnoses (Fig 1). Hepatitis B and C tests were negative. Tumour markers including alpha-fetoprotein were normal. Due to the rapid interval lesion enlargement, absence of risk factor for HCC, and the need to exclude possible opportunistic fungal infection, ultrasound-guided liver biopsy was performed and confirmed myeloma involvement.

Case 2

A 51-year-old woman with lambda light chain MM diagnosed in 2011 was in remission following treatment with bortezomib, thalidomide and dexamethasone. Autologous peripheral blood stem cell transplantation was performed but she developed disease relapse 18 months later, salvaged by combined bortezomib-melphalan-prednisone. She presented within a year with a second relapse and a 1-week history of fever, increasing diffuse bone pain and abdominal distention. Mild hepatosplenomegaly was noted on physical examination. Pancytopenia was evident (haemoglobin 7.6 g/dL, platelet count 17×10^9/L, white blood cell count 1.7×10^9/L). Blood culture and hepatitis markers were negative. Ultrasound revealed a hypoechoic lesion at the right hepatic lobe, bi-lobar hepatic hyperechoic lesions with hypoechoic rim and mild ascites. In the presence of her high swinging fever, liver abscesses were suspected. Hepatosplenomegaly was confirmed on CT performed 1 day later. In addition, multiple hypodense liver lesions, most of which were subcapsular, were observed. They showed arterial contrast enhancement and became hypo-enhancing in the portovenous phase. No rim-enhancing lesions were present to suggest abscess formation. There were innumerable lytic lesions in bone, including partial collapse of T11 and L1 and a lytic lesion at the right transverse process of T10 with enhancing soft tissue mass (Fig 2). Overall features suggested progressive disease with presumably myelomatous involvement of liver and bone. She was prescribed two cycles of lenalidomide, bortezomib, and dexamethasone followed by four more cycles of lenalidomide and dexamethasone. Follow-up CT showed interval resolution of the previous noted bi-lobar liver lesions and sub-centimetre hypo-enhancing focus representing post-treatment change or residual disease, supporting the presumption of liver extraosseous myeloma (EM). Repeat bone marrow examination revealed hypercellular marrow with residual plasma cell myeloma. She then underwent hematopoietic stem cell transplantation.

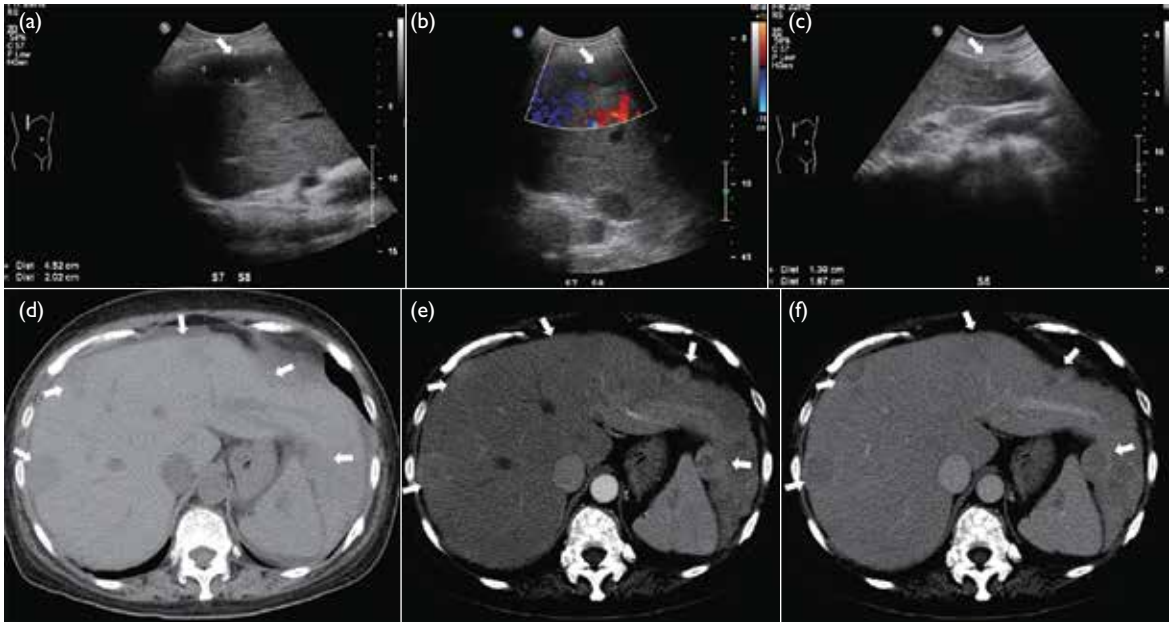

FIG 2. Case 2. (a) & (b) Ultrasound of upper abdomen revealed a hypoechoic lesion at the right hepatic lobe [white arrows], (c) multiple hyperechoic lesions with hypoechoic rim in both hepatic lobes (one in white arrow). These were non-specific. Multiphasic computed tomography performed a day later confirmed hepatomegaly. (d) Multiple hypodense liver lesions (white arrows), most being subcapsular, were also seen. They showed (e) arterial contrast enhancement (white arrows) and (f) became hypo-enhancing on portovenous phase (white arrows). There were no rim-enhancing lesions to suggest abscess formation. Mild ascites was noted. There were innumerable lytic lesions in bone, including partial collapse of T11 and L1 and a lytic lesion at the right transverse process of T10 with enhancing soft tissue mass (not shown). Overall features suggested progressive disease with myelomatous involvement of liver and bone

Discussion

Extraosseous myeloma is an uncommon form of MM associated with poorer prognosis and survival.[1,2] It is caused by migration of malignant plasma cells from the bone marrow microenvironment. The presence of extraosseous involvement of MM is not uncommon; it has been previously reported in more than 63% of patients in an autopsy series, with 28 to 30% having liver involvement.[1] The reticuloendothelial system (liver, spleen and lymph nodes) is the most commonly affected extraosseous site.[2] Although well documented in the pathology literature, this clinical entity remains under-recognised and underreported in radiology.

We report two cases of multifocal EM of the liver in two Chinese patients from a tertiary hospital in Hong Kong, mimicking multifocal HCC on multiphasic CT. To the best of our knowledge, this pattern has not been reported previously. First, we aim to increase radiologist awareness of the hypervascular multinodular pattern of liver EM. Second, HCC is common in Southeast Asia including Hong Kong and remains an imaging diagnosis with no histological confirmation required prior to treatment. There are overlapping imaging features of both extraosseous MM in liver and HCC. Hence, biopsy is needed for differentiation.

Imaging findings of EM are highly variable and non-specific. The two most common presentations are the more common diffuse form with hepatomegaly in the absence of a focal lesion due to diffuse liver parenchymal infiltration and the focal nodular form with hypodense non-calcified nodule and minimal enhancement. On ultrasound, focal patterns of involvement can be hypoechoic, hyperechoic, mixed or target (isoechoic nodule with hypoechoic rim). On CT, focal lesions are generally described as hypoattenuating with minimal enhancement and no calcification. On magnetic resonance imaging, focal lesions may be hyper- or hypo-intense on T1-weighted images and hyperintense on T2-weighted images with minimal gadolinium enhancement.[2,3] Scarce literature has documented hypervascular enhancement patterns with washout on multiphasic CT or magnetic resonance imaging, and only few case reports have reported only a solitary focal mass.[4-6] The multinodular form with hypervascular enhancement pattern has not been reported before. Currently there remains a lack of knowledge about distinction of EM of liver from other hypervascular liver tumours due to its rarity. Arterial phase imaging is vital for lesion detection since some of the lesions may be too small and too vaguely hypo-enhancing to be detected during portovenous or delayed phases. The differential diagnoses with multiple hypervascular liver masses commonly include multifocal HCC and hypervascular metastases. Its significance is underestimated, especially in areas where HCC is endemic, such as Southeast Asia. Clinicians and even radiologists may misdiagnose these lesions as HCC, which is an imaging diagnosis, and specific oncological treatment will be given without histological confirmation of the lesion leading to mismanagement. It is important to bear in mind the possibility of myeloma of liver in patients with known myeloma who present with hypervascular mass on CT. We advocate a diagnostic approach with emphasis on the use of multiphasic cross-sectional studies including CT for detection, and risk stratification (by alpha-foetal protein, and hepatitis status). If these appear atypical of HCC or EM involvement of liver, a timely biopsy to confirm the diagnosis is recommended to avoid misdiagnosis and subsequent mismanagement.

There are other points in the diagnostic challenge posed by EM of the liver that influence clinical management.

First, the variable sonographic appearance of multinodular hepatic lesions, including target appearance mimicking hepatic candidiasis, and hypoechoic lesions raising a suspicion of pyogenic abscesses, may lead to unnecessary antifungal or antibacterial treatment.

Second, only one single large lesion was initially seen in our first case on multiphasic CT. This was in concordance with multiple previous studies that reported cases of EM of liver where lesions are more conspicuous on ultrasound than on CT.[3] Regarding the hepatic lesions on CT from our cases, they were most conspicuous on the arterial phase, while the smaller ones may be isoattenuating or minimally hypo-enhancing on portovenous or delayed phases. In addition, most lesions had a subcapsular location in the liver, an important area to review. Knowing that this entity may be underdiagnosed, further studies are needed to determine the most sensitive initial staging modality to look for liver involvement. Based on our cases, both ultrasound and multiphasic CT (including arterial, portovenous, and 5-minute delayed) phases play an important role in initial screening, subsequent characterisation, and in guiding biopsy.

Conclusion

Extraosseous myeloma of the liver is a rare and under-recognised entity associated with poorer prognosis and survival. Imaging features are non-specific but can mimic multifocal HCC on multiphase CT. We advocate the use of multiphasic CT (including arterial phase) for detection. The presence of hypervascular liver masses in patients with known MM should alert radiologists to this diagnosis. Definitive diagnosis should be by tissue biopsy if there is a mismatch between clinical risk factors and imaging, especially in areas endemic for HCC.

Author contributions

Concept or design: HM Kwok, ES Lo.
Acquisition of data: HM Kwok, ES Lo.
Analysis or interpretation of data: All authors.
Drafting of the manuscript: HM Kwok, ES Lo.
Critical revision of the manuscript for important intellectual content: HM Kwok, ES Lo.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

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Declaration

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Ethics approval

This study was approved by the Kowloon West Cluster Research Ethics Committee [Ref No.: KW/EX-21-054 (157-19)]. Patients were treated in accordance with the Declaration of Helsinki, with informed consent provided for treatment, procedures, and publication.

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