Unusual association of diseases/symptoms

Hepatic nodule: a case of primary myelofibrosis

Filipe Sousa Cardoso, João Veríssimo Pires, José Simão Miranda, João Mascarenhas Araújo

Department of Medicine, Hospital Professor Doutor Fernando Fonseca, Amadora, Portugal

Correspondence to Dr Filipe Sousa Cardoso, filipe_sousacardoso@hotmail.com**Summary**

Primary myelofibrosis is one of the entities that may manifest with lesions of extramedullary haematopoiesis, especially in spleen and liver. The authors report a case of primary myelofibrosis presenting incidentally as an intrahepatic focal lesion of extramedullary haematopoiesis, a rare occurrence that highlights the challenge of hepatic nodule differential diagnosis, and allows reflection about the diagnostic criteria and prognostic factors of this myeloproliferative disease.

BACKGROUND

Primary myelofibrosis (PMF), the least common of the myeloproliferative neoplasms with an incidence rate of 0.2 per 100 000 per year, is characterised by bone marrow hypercellularity, megakaryocytic atipia and fibrosis, not due to underlying inflammatory or other neoplastic diseases.^{1 2}

Approximately 15 to 30 percent of patients are asymptomatic, with the diagnosis being made during investigation of splenomegaly (at least 90 percent), hepatomegaly (40 to 70 percent) or abnormal blood findings.³ Due to bone marrow failure, foci of extramedullary haematopoiesis (EMH) may occur in almost any organ, being spleen and liver common sites.⁴ In the liver, both diffuse microscopic infiltration and focal lesions of EMH have been described.⁵ Although unusual, focal intrahepatic EMH can mimic other solid lesions of the liver leading to a troublesome differential

diagnosis, especially with haemangioma, hepatocellular carcinoma (HCC) and metastatic cancer.

In PMF general median survival was reported to be between 3.5 and 5 years.⁶ Several adverse prognostic factors were described, such as the presence of constitutional symptoms (ie, fever, night sweats or weight loss greater than 10 percent), age greater than 65 years, haemoglobin less than 10 g/dl, leucocyte count greater than 25 000/ μ l and circulating blast cells one percent or greater, but those that would facilitate individual patient selection during follow-up for allogeneic hematopoietic cell transplantation (allo-HCT) or pharmacological therapy are not yet established.^{7 8}

The authors present a case report regarding a patient diagnosed with PMF after complete investigation of an incidental hepatic nodule.

Figure 1 Abdominal ultrasound: hepatic nodule, left lobe, 5.5 cm.

Figure 2 Abdominal CT: hepatic nodule, segments 6 to 7, 5.5 cm.

CASE PRESENTATION

A 63-year-old man was admitted to our clinic after he was found to have a hepatic nodule on occasional ultrasound examination (figure 1). He denied symptoms such as fatigue, fever, night sweats or weight loss. There was no palpable splenomegaly, hepatomegaly or enlarged lymph nodes. Laboratory tests revealed haemoglobin level of 12.4 g/dl, leucocyte count of 10 900/ μ l, platelet count of 361 000/ μ l, polychromasia, alanine aminotransferase 48IU/l, bilirubin 0.6 mg/dl, lactate dehydrogenase level of 362IU/l, natural immunisation for hepatitis B virus infection, negative serologic test for hepatitis C virus infection and α -fetoprotein (AFP) level of 2.74IU/ml. CT and magnetic resonance scans showed liver size within normal limits, with a nodular lesion located in the transition between segments 6 and 7, 5.5 cm in largest dimension, not suggesting haemangioma, and homogeneous spleen enlargement, 14 cm in largest dimension (figures 2 and 3). Ultrasound-guided liver biopsy within the nodule revealed islands of haematopoietic elements (figure 4). Bone marrow biopsy showed hypercellularity, megakaryocytic atypia and fibrosis (figure 5). Fluorescence in situ hybridisation testing for the fusion gene BCR-ABL was negative. These findings were all consistent with the diagnosis of PMF.

OUTCOME AND FOLLOW-UP

After 1 year follow-up, the patient still had no symptoms, laboratory tests were similar to the initial ones and hepatic lesion size had not progressed significantly.

DISCUSSION

The most common presenting complaints in PMF are fatigue (50 to 70 percent), symptoms related to splenomegaly (20 to 50 percent), like left upper abdomen discomfort or early satiety, and constitutional symptoms (5 to 20 percent), such as fever, night sweats or weight loss.³ No similar complaints were experienced by the patient.

In the laboratorial tests haemoglobin is less than 10 g/dl in 50 percent of patients with PMF, most of them having also anisocytosis, poikilocytosis and polychromasia, being the leucocyte and platelet counts variable.³ Our patient presented with anaemia, polychromasia, leukocytosis and thrombocytosis. Lactate dehydrogenase is usually elevated in PMF, as it happened with the patient.

An incidental hepatic nodule always poses a challenge in the differential diagnosis. Malignant hepatic tumours are the most common cause of focal hepatic lesion. Metastatic cancer represents the majority of cases within this group of diseases, followed by HCC. Between benign hepatic

Figure 3 Abdominal magnetic resonance (T1): hepatic nodule, segments 6 to 7, 5.5 cm.

Figure 4 Hepatic nodule histology: islands of hematopoietic elements (EMH).

neoplasms, haemangioma is the most frequent, followed by adenoma, focal nodular hyperplasia and hepatic cysts.⁹

The absence of both constitutional symptoms and specific organ-disease manifestations was not in favour of metastatic cancer. The lack of underlying liver disease manifestations associated with an AFP level within normal

limits helped to rule out HCC as the likely diagnosis. Radiological findings were not suggestive of haemangioma or other benign hepatic neoplasms.

The nature of our patient's hepatic lesion was revealed after ultrasound-guided liver biopsy, being that of EMH. In 12 case reports of focal intrahepatic EMH with imaging

Figure 5 Bone marrow histology: hypercellularity, megakaryocytic atypia and fibrosis.

features described, there was a solitary lesion in five of them and extra-hepatic foci were not detected in three of them.¹⁰ The patient had a sole hepatic lesion of EMH, and splenomegaly, although homogeneous and marginal, could in fact be due to diffuse microscopic infiltration of EMH.

Bone marrow biopsy characteristics were suggestive of PMF. The final diagnosis was made after fulfilment of the WHO criteria for PMF, which demand exclusion of other myeloproliferative neoplasms.²

The absence of adverse prognostic factors at presentation gave the patient an expected median survival of 135 months, and for the time being no indication for treatment.^{7 8}

At present, allo-HCT constitutes the only treatment modality with a curative potential in PMF, however it has been limited to patients below the age of 60 years and to those who have a human leucocyte antigen-identical sibling donor. Other treatment modalities are, at best, palliative and include drugs such as androgen preparations or thalidomide with prednisone for anaemia, lenalidomide in the presence of del(5q), hydroxyurea for splenomegaly, splenectomy or radiation therapy for symptomatic foci of non-hepatosplenic EMH.^{11 12}

This case report emphasises that, even in the absence of a suggestive clinical context, EMH might need to be taken into consideration in the differential diagnosis of a hepatic nodule.

PMF has a large spectrum of clinical and laboratory manifestations, making the diagnosis difficult. Its prognosis is highly variable and treatment options are limited.

Learning points

- EMH can be part of the differential diagnosis of a hepatic nodule.
- PMF can present with a large spectrum of clinical and laboratory manifestations.
- PMF expected median survival depends on the number of adverse prognostic factors at presentation.
- PMF treatment resides between curative transplant and palliative pharmacological therapy.

Acknowledgements Department of Radiology, Hospital Professor Doutor Fernando Fonseca, Amadora

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Stein BL**, Moliterno AR. Primary myelofibrosis and the myeloproliferative neoplasms: the role of individual variation. *JAMA* 2010;**303**:2513–8.
2. **Tefferi A**, Thiele J, Orazi A, *et al*. Proposals and rationale for revision of the World Health Organization diagnostic criteria for polycythemia vera, essential thrombocythemia, and primary myelofibrosis: recommendations from an ad hoc international expert panel. *Blood* 2007;**110**:1092–7.
3. **Tefferi A**. Clinical Manifestations and diagnosis of primary myelofibrosis. Uptodate 2010. <http://www.uptodate.com/contents/clinicalmanifestations-and-diagnosis-of-primary-myelofibrosis>
4. **Georgiades CS**, Neyman EG, Francis IR, *et al*. Typical and atypical presentations of extramedullary hemopoiesis. *AJR Am J Roentgenol* 2002;**179**:1239–43.
5. **Jelali MA**, Luciani A, Kobeiter H, *et al*. MRI features of intrahepatic extramedullary haematopoiesis in sickle cell anaemia. *Cancer Imaging* 2006;**6**:182–5.

6. **Abdel-Wahab OI**, Levine RL. Primary myelofibrosis: update on definition, pathogenesis, and treatment. *Annu Rev Med* 2009;**60**:233–45.
7. **Cervantes F**, Dupriez B, Pereira A, *et al.* New prognostic scoring system for primary myelofibrosis based on a study of the International Working Group for Myelofibrosis Research and Treatment. *Blood* 2009;**113**:2895–901.
8. **Morel P**, Duhamel A, Hivert B, *et al.* Identification during the follow-up of time-dependent prognostic factors for the competing risks of death and blast phase in primary myelofibrosis: a study of 172 patients. *Blood* 2010;**115**:4350–5.
9. **Schwartz J**, Kruskal J. Approach to the patients with a focal liver lesion. Uptodate 2011. <http://www.uptodate.com/contents/approach-to-the-patient-with-a-focal-liver-lesion>
10. **Gupta P**, Naran A, Auh YH, *et al.* Focal intrahepatic extramedullary hematopoiesis presenting as fatty lesions. *AJR Am J Roentgenol* 2004;**182**:1031–2.
11. **Cervantes F**. Modern management of myelofibrosis. *Br J Haematol* 2005;**128**:583–92.
12. **Arana-Yi C**, Quintás-Cardama A, Giles F, *et al.* Advances in the therapy of chronic idiopathic myelofibrosis. *Oncologist* 2006;**11**:929–43.

This pdf has been created automatically from the final edited text and images.

Copyright 2011 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Cardoso FS, Pires JV, Miranda JS, Araújo JM. Hepatic nodule: a case of primary myelofibrosis. *BMJ Case Reports* 2011;10.1136/bcr.05.2011.4220, date of publication

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow