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PRV: Where does the truth lie?

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Question:

A 62-year-old female presented with haematological abnormalities of leukocytosis 17.2x10^9/L (4 -11x10^9/L), specifically a persistent neutrophilia and monocytosis, with a bone marrow biopsy suggesting possible early chronic myeloid monocytic leukemia type I (hypercellular, 1% myeloblasts and 13% monocytes). Philadelphia chromosome and Bcr-abl were negative. The haemoglobin was 140-150g/L (R 115-155g/L) with a positive JAK2 mutation suggesting a diagnosis of Polycythemia Rubra Vera (PRV). She subsequently developed lethargy and non-specific bilateral costal margin discomfort. She was obese but no stigmata of chronic liver disease. Her liver edge was palpable 4cm below the costal margin but no splenomegaly was detected. CT was performed (Fig A) showing at least 6 focal hepatic lesions, largest 62mm in segments 2 and 4 and splenomegaly of 16cm. Capsular retraction was seen in association with subcapsular lesions. The liver was not obviously cirrhotic. Her liver test showed Albumin 39 g/L, Bilirubin 10 µmol/L, ALP 110 U/L, GGT 61 U/L, AST 48 U/L, ALT 27 U/L, LDH 604 U/L. Percutaneous targeted liver biopsies were indeterminate showing benign hepatocytes, fibrous bands and areas with proliferating ductules and inflammation.

The largest lesion was biopsied at laparoscopy. The nodular lesion showed a circumscribed but non-encapsulated area of marked atrophy of the hepatic parenchyma with replacement by fibrosis (Fig B). Radiological follow-up over 15 months showed no progression.

What is the diagnosis?

Answer :

Histopathology revealed preserved portal tracts within the fibrosis, a prominent mononuclear inflammatory cell infiltrate and enlarged multinucleated bizarre cells. Islands of atrophic hepatocytes were present. Sinusoids and portal vein were focally lined by large atypical mononuclear and multinucleated cells (Fig B), with focal obliteration of portal vein branches by cells and fibrosis. Abnormal cells were Factor VIII positive and some of the atypical cells were myeloperoxidase positive; with some small nucleated cells, positive for glycophorin, an erythroid marker. There were extensive bone marrow cells including megakaryocytes and round cells in the non-lesional liver interpreted as either haemopoietic or neoplastic chronic myeloid monocytic leukaemic cells suggestive of myeloid metaplasia. A final diagnosis of PRV associated Sclerosing Extramedullary Hematopoietic Tumour (SEMHT) of the liver was made.

Extramedullary haematopoiesis (EMH) is a compensatory mechanism recognised in chronic myeloproliferative disorders including myelofibrosis, chronic myeloid leukemia and PRV. Most common sites are liver, spleen, and lymph nodes. Rarely, they are termed “sclerosing extramedullary haematopoietic tumour” (SEMHT) when fibroblastic proliferation accompanies a solid mass. The stroma of these tumours is usually loose connective tissue with variable degree of fibrosis, however when there is a predominant fibrosis, they have been referred as “fibrous haematopoietic tumours”. Remstein et al, used the term SEHMT to describe the extramedullary trilineage haematopoiesis and the predominant sclerotic background. Although rare, SEMHT have previously been described in spleen, on serosal surfaces and skin, lung, breast and orbit [1,2,3]; and can histologically mimic other neoplasms including haemangioendothelioma. History of a haematological disorder and a high index of suspicion are important in making the

diagnosis. The clinical course of these tumours is relatively benign, and aggressive local therapy is not mandatory unless there is presence of mass effect symptoms.

Fig. A

Fig.B

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