Variceal Upper Gastrointestinal Bleeding with Long Standing Fever and Anorexia: Sarcoidosis of the Liver

Liver histopathology revealed the findings depicted in Figures 1–4.

The differential diagnosis of granuloma of the liver includes sarcoidosis, primary biliary cirrhosis, various types of lymphomas, drugs like allopurinol, sulfonamides, phenylbutazone, phenothiazines and carbamazepine, Crohn's disease and infections like mycobacteria, brucellosis, nocardiosis, fungi, syphilis and schistosomiasis to name a few. In view of the presence of compact, non-caseating, naked granulomas which are negative for AFB and other organisms, a histological diagnosis of sarcoidosis of the liver with advanced fibrosis (Stage V) was made in this case. The granulomata of primary biliary cirrhosis are seen within the portal tracts in relation normal intra-lobular bile ducts (upto 40 microns). Multiple special stains should be used to exclude any infectious cause. A history of drug intake is also mandatory in this situation. Ten percent of the granuloma remain undiagnosed even after an extensive work-up and are then labeled as idiopathic.

Sarcoidosis is a multi-system disorder characterized by infiltration of organs with non-caseating granulomas. Most common involvement is of the lung and lymph nodes. Although the liver is involved commonly, hepatomegaly is found in only about 19% of patients of sarcoidosis.¹ Symptoms due to liver involvement are rare and liver involvement is usually detected on abnormal liver function tests and subsequent liver biopsy in a patient with active sarcoidosis of other organs. The characteristic liver function abnormality of elevated serum alkaline phosphate with only minor elevations of serum aminotransferase is seen in about one third of patients^{2,3} whereas liver biopsy shows granulomas in as many as 80–95% of cases of sarcoidosis.^{4,5} Hepatic sarcoidosis can occur without pulmonary involvement in a quarter of cases.⁶ The commonest clinical manifestations of hepatic sarcoidosis include systemic symptoms like fever and weight loss with markedly abnormal serum alkaline phosphatase levels with or without evidence of extrahepatic disease. Only rarely do patients with hepatic sarcoidosis have cholestatic symptoms^{7,8} or portal hypertension⁹ as was seen in this patient. Portal hypertension was seen in only 1.2% in an Indian series of 164 patients and in 3% in a Western

series of 100 patients.^{1,10} Portal hypertension may be either due to development of cirrhosis (25%) or more commonly due to extensive granulomas or nodular regenerative hyperplasia which cause presinusoidal portal hypertension (75%).^{9–11} Cirrhosis can be seen on biopsy in upto 6% and significant fibrosis in another 15% of patients with clinical liver disease.¹⁰ Of the patients with

Figure 1 A linear core of liver tissue with multiple compact epithelioid cell granulomata, both in the parenchyma (arrow) and in the fibrous septa (arrowhead) (H&E stain).

Figure 2 Details of the granuloma, showing collection of epithelioid cells (arrowhead) with occasional giant cells, without any necrosis or significant lymphocytic cuffing (naked granulomas). Often two three small granulomas are seen in a cluster with a common fibrous wall (granuloma in granuloma pattern) (arrows) (H&E stain).

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Figure 3 The granulomata are surrounded by fibrous tissue with extension into the granuloma (arrow). There was no loss of reticulin fibers inside this granuloma (Reticulin stain).

Figure 4 Extensive portal fibrosis with porto-portal and porto-central bridging (arrowhead) with occasional nodule formation (arrow) suggesting F5 fibrosis according to Ishak fibrosis score (Reticulin stain).

portal hypertension 75% have esophageal varices which can bleed on follow-up.^{12,13} However, initial presentation with variceal bleeding has not been previously described to the best of our knowledge.

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