



## Extrapulmonary Sarcoidosis Manifested as Cirrhosis with Portal Hypertension

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### ABSTRACT

Hepatic involvement has been reported in 20-30% of patients with systemic sarcoidosis. However, isolated liver involvement is rare. We report a case of cirrhosis with portal hypertension, diagnosed as hepatic sarcoidosis based on high angiotensin-converting enzyme level and presence of multiple non-caseating granulomas in liver histopathology. She improved clinically after treatment with steroid and ursodeoxycholic acid.

### KEYWORDS:

Sarcoidosis, Hepatic sarcoid, Cirrhosis, Portal hypertension

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### INTRODUCTION

Sarcoidosis is a chronic inflammatory granulomatous disease, primarily affecting the lungs. Multisystem involvement is not uncommon but isolated extrapulmonary disease is rare.<sup>1</sup> Hepatic involvement in sarcoidosis was reported in literature in 11-80% of cases. Lower rates were seen in studies conducted on symptomatic subjects and higher rates were reported in studies based on random liver biopsies.<sup>2</sup> Diagnosis of hepatic sarcoidosis is laborious in the absence of hilar lymphadenopathy and pulmonary involvement. Herein, we report a case of cirrhosis diagnosed as hepatic sarcoidosis based on high angiotensin-converting enzyme (ACE) levels and typical non-caseating granulomas in the histopathological study of liver tissue.

### CASE REPORT

A 56-year-old woman with diabetes (controlled well with oral hypoglycemic agents), presented with complaints of fatigue and loss of appetite for one year associated with a 10-kg weight loss. On clinical examination, she had hepatomegaly. Her hematological and biochemical work-up revealed thrombocytopenia (platelets: 1,19,000/cumm), rise in alkaline phosphatase (ALP: 270 IU/L) and gamma-glutamyl transpeptidase (GGT: 191 IU/L). Ultrasound (USG) of the abdomen showed gross



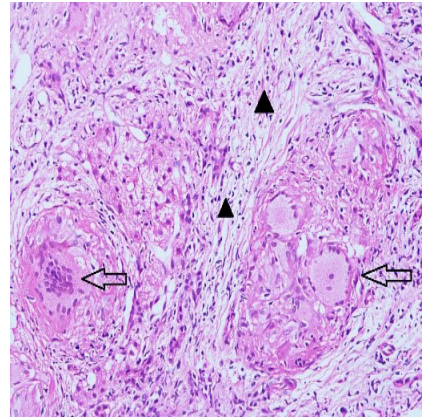
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**Fig.1:** Contrast enhanced CT showing gross hepatosplenomegaly with altered mottled pattern of architecture, studded with multiple nodules

hepatomegaly with coarse echotexture and splenomegaly with multiple ill-defined hypoechoic lesions in the liver and spleen. Portal vein diameter and flow velocity were increased. Upper GI endoscopy was performed and presence of small varices was noted. During further etiological workup of high enzymes (ALP and GGT) and portal hypertension, she was found to have high ACE level (173 U/L). Her autoimmune liver disease profile (antimitochondrial antibody [AMA], antineutrophil cytoplasmic antibody [ANCA], antinuclear antibody [ANA], liver kidney microsome antibody [LKM], and smooth-muscle antibody [SMA]), Hepatitis B, hepatitis C, HIV markers and biomarkers of defect in iron and copper metabolism were all negative. Chest radiograph was normal. With suspicion of sarcoidosis and to further characterize the liver and spleen lesions contrast enhanced computed tomography (CECT) of the thorax and abdomen was done. It showed gross hepatosplenomegaly with altered mottled pattern of architecture, studded with multiple nodules (figure 1) with no other abnormalities.

Serum alfa fetoprotein (AFP) and CA 19-9 were normal. Ultrasound guided liver biopsy was done and histopathological examination showed multiple non-caseating granulomas consisted of epithelioid cells and multi-nucleated giant cells. Granulomas were predominantly confined to portal areas with fibrosis and lymphocytic infiltration (figure 2). Acid fast



**Fig.2:** Histopathological study (H&E stain) of liver tissue showing non-caseating granulomas (arrows) composed of epithelioid cells and multi-nucleated giant cells along with areas of fibrosis (arrow head).

bacilli and fungal stains were negative.

Final diagnosis of sarcoidosis causing cirrhosis and portal hypertension was made and prednisolone (initiated with 20 mg/day and over 8 weeks tapered to 10 mg/day in view of hyperglycaemia), ursodeoxycholic acid (UDCA: 600 mg/day) and carvedilol (6.25 mg/day) was started for the patient. After three months of treatment her symptoms were improved and liver enzymes (ALP and GGT) attained a declining trend.

## DISCUSSION

Spectrum of liver involvement in sarcoidosis varies from asymptomatic incidental granulomas to portal hypertension or chronic cholestasis.<sup>3</sup> Most patients with hepatic sarcoid remain asymptomatic, so in a diagnosed case of sarcoidosis, monitoring of liver enzymes (ALP) at regular intervals is recommended to diagnose hepatic involvement at an early stage.<sup>4</sup> Cirrhosis or portal hypertension was reported only in  $\leq 1\%$  of all sarcoidosis cases.<sup>5</sup> While 13% of the patients with hepatic sarcoidosis exhibit liver involvement without pulmonary disease, 35–40% have abnormal liver enzymes.<sup>6</sup> Our case presented with anorexia, significant weight loss and in the presence of high ALP and GGT, a malignant etiology was initially suspected. However, normal tumour markers (AFP, CA 19-9) and high ACE level made us suspect sarcoidosis at early stages of work-up. In sarcoidosis elevated ACE levels can be seen in up to 70% of patients.<sup>7</sup> In the presence of bilateral hilar lymphadenopathy, diagnosis of sarcoidosis

can be made with ease. Amarapurkar and colleagues reported six cases of hepatic sarcoidosis where all cases had pulmonary involvement.<sup>8</sup> However as in our case, when only extrapulmonary involvement exists, evaluation for other etiologies of granulomatous diseases need to be done. Differential diagnoses for granulomas in the liver are infective causes such as tuberculosis, histoplasmosis, schistosomiasis, chronic viral hepatitis, etc., and non-infective causes such as primary biliary cholangitis, drug induced hepatitis, very rarely carcinoma or Hodgkin's disease, etc.<sup>9</sup> We ruled out major causes in our case by performing necessary serology, autoimmune workup and special stains on liver biopsy. Long-term use of corticosteroids is the baseline treatment in symptomatic sarcoidosis,<sup>4,9</sup> Many patients require daily low dose of 10-15 mg prednisolone, often continued for several years. Higher doses may be needed in severe cases where patients develop cholestasis with jaundice and pruritus. Clinical and biochemical improvement is often observed but pathological changes ultimately progressed to development of portal hypertension. Hence, after bile duct depletion and fibrosis develops, corticosteroids may not show any benefit.<sup>10</sup> UDCA is useful in hepatic sarcoid at a dose of 10-15 mg/kg/day.<sup>2,4,10</sup> In the literature, cyclosporine, chlorambucil, and methotrexate were also reported as steroid sparing agents in treating hepatic sarcoidosis with varying efficacy.<sup>10</sup> Our patient's condition was improved with low-dose prednisolone and UDCA. Long-term follow-up is necessary to prevent complications such as variceal bleeding or hepatocellular carcinoma.<sup>11,12</sup>

### CONCLUSION

Hepatic sarcoidosis in the absence of pulmonary involvement is rare. Early diagnosis and treatment improved the clinical profile of the patient; however, long-term follow-up is needed since the histological progression may persist.

### ETHICAL APPROVAL

There is nothing to be declared.

### CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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