CASE REPORT

Primary Granulomatous Inflammation of Liver – A Case Report

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ABSTRACT

Granulomas that consist of focal accumulations of macrophages are commonly found in the liver due to stimulation of the immune system by a number of pathophysiologic agents. Manifestations are variable depending on whether the underlying cause is a systemic disease or a primary hepatic granulomatous reaction. Here we report a case of a 30-year old female who presented with complaint of fever and vomiting. Liver biopsy from focal lesion was suggestive of granulomatous inflammation.

KEY WORDS: Granuloma, Liver, Tuberculosis.

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INTRODUCTION

Granulomatous inflammation are a group of lesions that are characterized by presence of granuloma ; a local circumscribed collection of epitheloid cells against chronic non-degradable agent or as a result of cell mediated hypersensitivity response.[1] Granuloma may be well marginated or confluent. Granuloma may be having necrosis and variation in cellular elements. Hepatic granuloma may be accompanied by characteristic inflammation in adjacent hepatic parenchyma or it may be a bland granuloma with no significant inflammation in surrounding tissue.[2]

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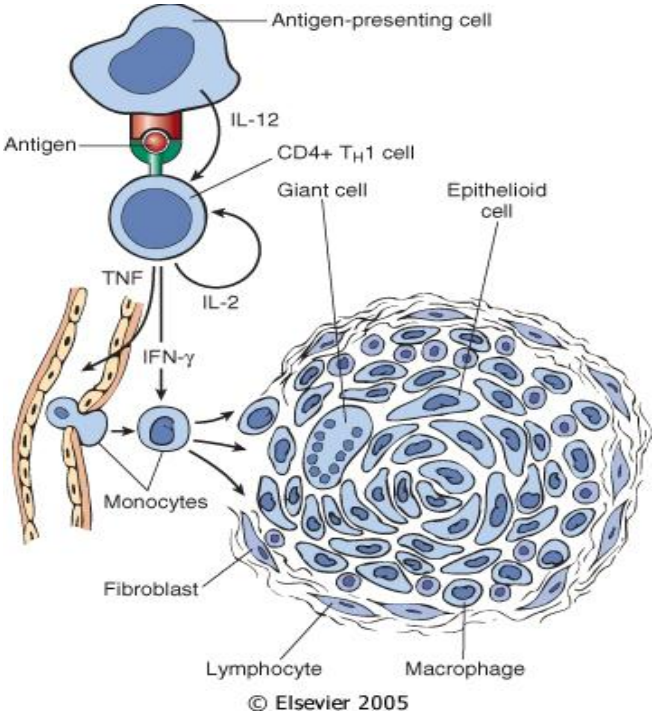

Fig.1: Pathogenesis scheme for granuloma formation.[2]

Majority of granulomatous diseases are caused by infections, immune mediated responses, hypersensitivity reactions, foreign agents and some neoplastic lesions.[1,2]

Among the liver biopsies the prevalence of granuloma is almost 2.4%–15%.[3] Marcy and colleagues reported that 66% of granulomatous diseases of liver were due to systemic infections. Other cases of granulomatous reaction in their study were secondary to a systemic disease, among those 28% cases had primary liver disease while 6% were idiopathic.[2] However the frequency is high in patients with long term infections and in immunodeficient individuals.[3] Here follows a case report of an exceedingly rare granulomatous disorder of liver. A relevant review of literature, encompassing both the clinical and pathological features of this lesion is also presented.

CASE PRESENTATION

The case study was approved by institutional Ethical Board for publication. A 30-year female presented to general practitioner with complaint of fever, vomiting and flatulence. On examination, patient was having hepatosplenomegaly. Patient also had diffuse shadows on X-ray so suspicion of lymphoma was present. In order to rule out the possibility of lymphoma, patient was sent for bone marrow examination to aid in diagnosis.

An abdominal-pelvic ultrasound revealed increase in size of liver but no focal lesion was present. Ultrasound also revealed splenomegaly and a 7mm calculus at lower pole of left ureter.

Pre-op serological tests revealed ESR of 65mm/1st hrs. Serum calcium was 9.1 mg/dl. Antinuclear antibody (ANA) and Rheumatoid A Factor (RA) were negative. Patient was also evaluated for the possibility of syphilis by Veneral Disease Research Laboratory Test (VDRL)//Rapid Plasma Reagin Test (RPR) which was negative. Urine examination revealed 2 – 4 pus cells. Serum iron and Total Iron Binding Capacity (TIBC) was normal. Serum alkaline phosphatase was markedly elevated (658 U/L).

After complete blood count and ruling out the possibility of any bleeding or clotting disorder, patient was taken for liver biopsy procedure. The specimen received in Pathology Laboratory consisted of three grey white needle core pieces of tissue. The largest core measured 1.2 cm in length and the smallest core was measuring 0.8 cm in length. The specimen was submitted totally in 2 blocks for tissue processing and histological examination. After tissue processing, the paraffin embedded tissue blocks were serially sectioned with the help of microtome and stained with Hematoxylin & Eosin, Periodic Acid Schiff (PAS) stain & Zheil Nelsen (ZN) stain.

Histological examination reveals hepatic tissue with preserved lobular architecture (Fig.2). The portal tracts reveal mild enlargement by focal mild fibrosis and chronic inflammatory cell infiltrate. The hepatic parenchyma is infiltrated by mild chronic inflammatory cell infiltrate with formation of variable sized mostly non-caseating granulomas (Fig.3) comprising of circumscribed collections of

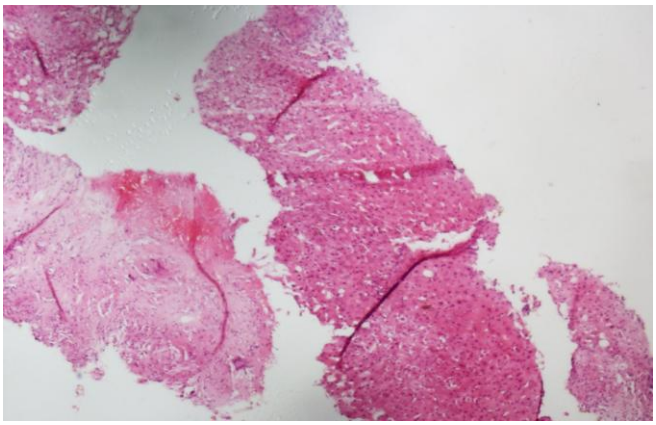

Fig.2: Needle core biopsy of hepatic tissue with preserved lobular architecture. (H/E stain; 400X)

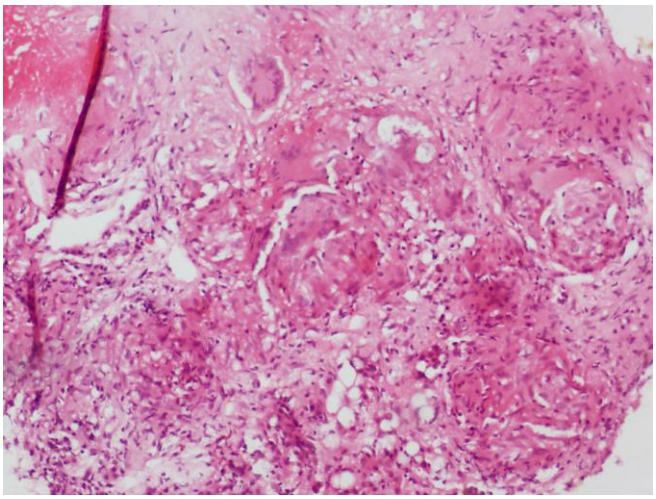

Fig.3: Granulomatous inflammation within the hepatic tissue. (H/E stain; 100X)

epithelioid cells along with foreign body and Langhan's type multinucleated giant cells (Fig.4). Occasional fragments reveal areas of necrosis (Fig.5). ZN stain for Acid Fast Bacilli (AFB) was negative. Mycobacteria are generally not seen in liver biopsy specimens taken from immunocompetent patients. PAS stain was negative for fungal infection and there was no evidence of any storage disease of liver.

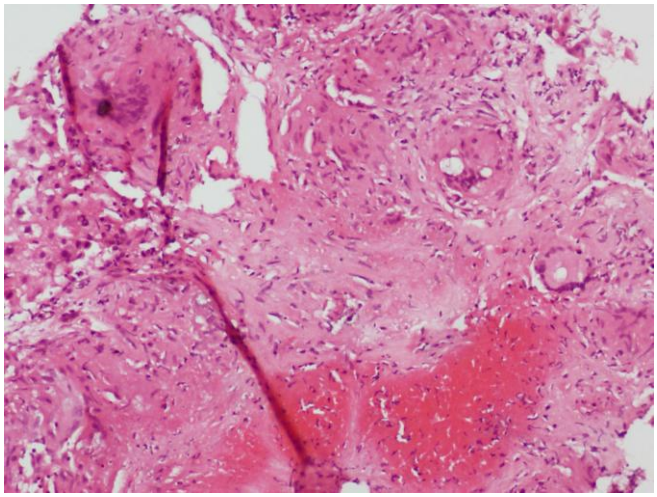

Fig.4: Presence of multinucleated giant cell reaction and necrosis within the granulomas. (H/E stain ; 100X)

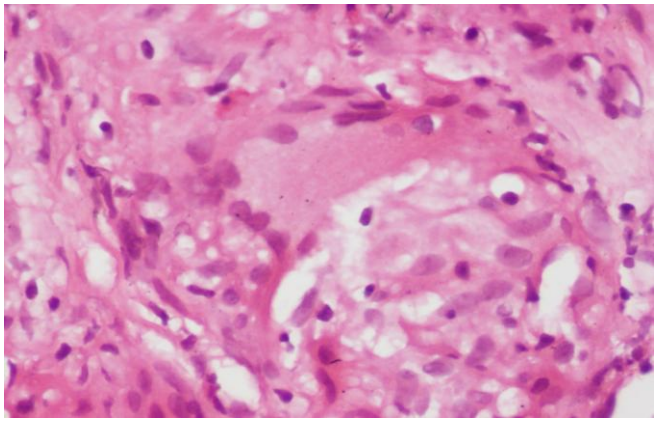

Fig.5: High power view of granuloma comprising of epithelioid cells along with multinucleated giant cells. (H/E stain; 40X)

Granulomatous Inflammation of Liver

Epithelioid granulomas are found in 3 to 15% of liver biopsies, the incidence varying according to geographic location and method of selection of patients for biopsy.[3] There are diverse etiologies of granulomatous inflammation of liver. The cause of hepatic granulomas may remain unknown in almost half of the cases.[4]

A full diagnosis of hepatic granulomatous lesions requires careful histologic evaluation of the granulomas themselves and of the associated changes. Serial deep levels are often helpful when granulomatous disease is suspected. Special histochemical stains like PAS & ZN stain may be helpful for the identification of etiological microorganisms.

The etiological diagnosis is made with clinical context in mind. Hepatic granulomas fall into one of the four groups. [5]

1. The etiology is clear on microscopic examination because the cause can be seen. Example include lesion with demonstrable Mycobacteria after appropriate ZN staining.
2. Knowledge of clinical data helps in correct interpretation, for example in primary biliary cirrhosis, diagnosis can be made based on histological findings in a middle-aged female patient with pruritus, raised serum alkaline phosphatase and positive testing for anti-mitochondrial antibodies.[6]
3. Cause may be unknown. Histology remains helpful as it narrows the diagnostic field and as the Tuberculosis is a worldwide problem the diagnosis should always be considered among the possibilities.[6]
4. The incidence of granuloma in patients with established sarcoid is reported in literature from 21-79%.[7] The epithelioid granulomas of sarcoidosis typically occur with great frequency in portal and periportal areas. These granulomas are of various ages.[1] Etiologically hepatic granulomas are categorized as autoimmune, infectious, drugs/chemical induced granulomas & those associated with malignancy.[5]

On histologic examination, circumscribed collection of epitheloid like cells along with few multinucleated giant cells are seen. These are surrounded by rims of lymphocytes. The latter are, however, not always universal findings on liver biopsy. In majority of hepatic granulomas, acid-fast bacilli are seen.[8] The diagnosis of tuberculosis in patients with hepatic granulomas may be difficult due to the lack of caseation necrosis on biopsy or

lack of a positive ZN stain or culture.[9] Polymerase chain reaction (PCR) assay has been reported to detect M. tuberculosis with a sensitivity of 88% and specificity of 100%.[10]

CONCLUSION

Despite the possibility of presence of numerous etiologic factors, the most common cause of hepatic granuloma is sarcoidosis & tuberculosis. Liver biopsy is gold standard. Specific diagnosis helps in treatment and prevention of complications.

LIMITAIONS OF CASE STUDY

PCR could not be done to confirm the possibility of M. tuberculosis.

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CONFLICT OF INTEREST

None to declare.

GRANT SUPPORT & FINANCIAL DISCLOSURE

None to disclose.

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Author's Contribution

SA, SA: Acquisition and analysis of data, Drafting of manuscript.

SH: Conception and design of study, contribution to intellectual content of manuscript.

ALL AUTHORS: Approval of the final version of the manuscript to be published.