

Idiopathic Granulomatous Venulitis of the Liver: An unusual condition

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Abstract

Liver is a common site for granulomas in view of its extensive blood supply and presence of reticulo-endothelial cells. Hepatic granulomas usually have an underlying aetiology which can be variable. We report an interesting case of idiopathic granulomatous venulitis of the liver which presented with a diagnostic challenge needing the input of consultants from different specialties. We also discuss about the aetiology of hepatic granulomas and the management of idiopathic granulomatous venulitis.

CASE REPORT

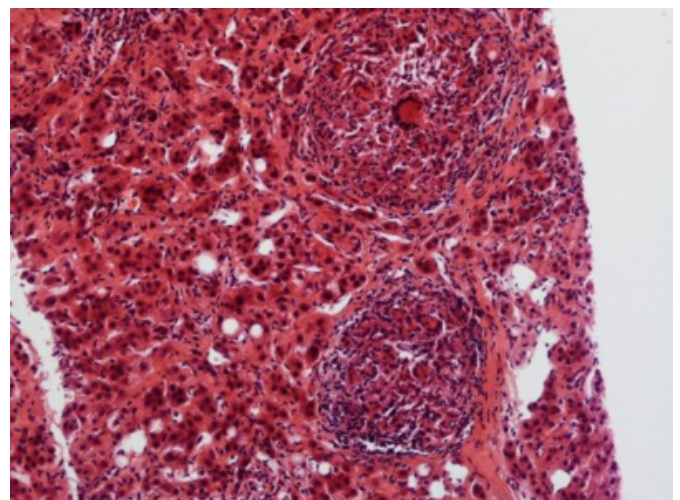
A 74-year old lady was evaluated by the hematology service for macrocytic anaemia and leucopenia in May 2005 (Haemoglobin 10.9 g/dl, mean corpuscular volume 102 fl white blood cell count $2.9 \times 10^9 / l$). Further tests showed splenomegaly and raised IgM microglobulins. Her platelets, renal function tests, liver function tests (LFTs) and haematinics were normal. Lymphoma was ruled out. Six months later, she presented with weight loss and pruritus. Blood tests showed pancytopenia, macrocytosis, bilirubin 65 $\mu\text{mol/l}$, alanine transaminase 97 iu/l, and alkaline phosphatase 226 iu/l. There was no biochemical evidence of multiple myeloma or haemolysis. A Chest X-ray was normal.

She was referred to the Gastroenterology service. A liver screen was negative apart from positive antinuclear factor at 1:160 dilutions and negative double-stranded DNA antibody. Liver biopsy revealed non-caseating granulomas, portal and parenchymal fibrosis, and negative staining for iron, copper bound protein and hepatitis B antigen. Sarcoidosis, primary biliary cirrhosis and drugs as a cause for the granulomatous disease were ruled out. A second opinion was sought from tertiary hepatology centre. A diagnosis of 'granulomatous venulitis of the liver' (figure 1) associated with outflow obstruction was made based on features of extensive sinusoidal fibrosis with narrowing of hepatic venules. Portal tracts were unaffected and bile ducts were normal. Several non-caseating granulomas were also evident. She was started on steroids and her liver function normalised. The patient

refused further investigations and she remains well.

Figure 1

Figure 1: Liver containing two non-caseating granulomata with sinusoidal fibrosis and hepatocyte atrophy. A van Geison stain shows hepatic venule narrowing.



DISCUSSION

Epithelioid granulomas have been reported in 2-15% of unselected liver biopsies. They can be associated with wide variety of diseases (Table 1). The main pathologic abnormality in our case is the destruction of hepatic venules by an idiopathic granulomatous venulitis. There were however no signs of systemic vasculitis or a generalised granulomatous disorder such as sarcoidosis. Our patient was thoroughly investigated and no cause for granulomas was identified. Classic sarcoidosis was unlikely in our patient in

view of absence of lymphadenopathy, rash, iritis, arthritis or pulmonary involvement.

Veno-occlusive disease involving the small hepatic veins and terminal hepatic venules presents with portal hypertension and hepatic congestion. ² It is therefore possible that splenomegaly found in our case may be related to granulomatous involvement of the small hepatic veins and terminal hepatic venules

There is no specific biochemical, haematological or immunological abnormality associated with this condition. Most of the investigations are done to rule out any underlying disorder. Infectious causes should be ruled out before initiating treatment with steroids, which are the first line medication. There have also been reports of good response to other immunosuppressants such as methotrexate and cyclophosphamide. ³⁴ Young et al. reported a unique case of Budd-Chiari syndrome caused by idiopathic granulomatous hepatic venulitis that resolved with steroid therapy. ⁵ The unique feature of this case is the good response to steroids clinically and biochemically, but we couldn't evaluate the response in any other way as patient refused further investigations.

CONCLUSION

Recognition of this rare condition is important as it can have long term sequelae on liver function. Of course the common causes of hepatic granuloma should be ruled out before this diagnosis is made.

Figure 2

Table 1: Aetiology of hepatic granulomas

Infections	Systemic disorders
- <i>Bacteria</i>	Sarcoidosis
Actinomycosis	Wegener's granulomatosis
Brucellosis	Crohn's disease
Cat-scratch fever	Ulcerative colitis
Tuberculosis	Polymyalgia rheumatica
Syphilis	
Lyme disease	Drugs
Listeriosis	Allopurinol
Q fever	Phenylbutazone
Psittacosis	Sulphonamides
Leprosy	Quinidine
- <i>Viruses</i>	Malignant diseases
Ebstein -Barr virus	Hodgkin's disease
Cytomegalovirus	Non-Hodgkin's disease
Coxsackie viruses	Carcinoma
AIDS	
Hepatitis viruses	
- <i>Parasitic</i>	Liver diseases
Leishmaniasis	Primary biliary cirrhosis
Toxoplasmosis	Sclerosing cholangitis
Amoebiasis	Hypersensitivity cholangitis
Malaria	Steatosis
Schistomiasis	Extrahepatic biliary obstruction
Toxocariasis	
Strongyloidiasis	
- <i>Fungal</i>	Idiopathic/Cryptogenic
Balstomycosis	
Histoplasmosis	
Cryptococcosis	
Candidiasis	
Aspergillosis	

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