A rare case of fever of unknown origin. *Idiopathic granulomatous hepatitis*

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Granulomatous hepatitis is a rare cause of fever of unknown origin (FUO), which can accompany infections such as tuberculosis, histoplasmosis, or coccidiomycosis; or be seen along with non-infectious disorders like sarcoidosis, vasculitis, and hematologic malignancies.[1] Idiopathic granulomatous hepatitis is an even rarer entity.[2] Here, we report a case of FUO, presenting with constitutional symptoms and isolated rise in cholestatic enzymes.

A 41-year-old male, attended with a fever of 39 degrees Celsius, prominent at nights and rising with chills. His history did not reveal any disorders, and he denied smoking or consuming alcohol. On physical examination, both the liver and spleen were palpable one cm below the costal margins. Laboratory studies showed: hematocrit 28.7%, hemoglobin 9.1 gr/dl, mean corpuscular volume 63.6 fl, erythrocyte sedimentation rate 139 mm/hr, C-reactive protein 7.65 mg/dl (normal range [NR] 0-0.8), gamma glutamyl transferase 203 mg/dl (NR 0-55), and alkaline phosphatase 263 mg/dl (NR 30-120). Other biochemical parameters were within normal limits. Tuberculin skin test, Rose-Bengal, and Gruber-Widal tests were all negative besides Brucella agglutination with Coombs. Cultures of blood and urine drawn twice during the febrile period were negative. Serologic markers for hepatitis B, hepatitis C, human immunodeficiency viruses, syphilis, and markers for autoimmune and collagen vascular disorders were all negative. Angiotensin converting enzyme (ACE) levels carried out to rule out sarcoidosis were normal. Quantitative immunoglobulin levels, hemoglobin, serum protein, serum, and urine immunofixation electrophoreses were within normal limits. A CT of the thorax did not show any lymphadenopathy, whereas abdominal CT showed hepatosplenomegaly (craniocaudal axes for liver was 180 mm, and 135 mm for spleen). His echocardiography did not reveal any signs of endocarditis. Both upper and lower gastrointestinal system endoscopy was normal. A liver and bone marrow biopsy was performed. Liver biopsy showed non-necrotizing granulomas in portal and lobular areas with minimal sinusoidal dilatation. His bone marrow biopsy revealed hypercellularity with non-necrotizing granulomas consisting of multiple epithelioid histiocytes and Langhans-type cells. He was diagnosed as 'idiopathic granulomatous hepatitis,' and his fever declined gradually without any medications. He was discharged with outpatient follow-up.

Hepatic granulomas are common and are found in up to 30% of routine liver biopsy specimens arising from a number of infective and non-infective conditions.[3,4] Granulomatous lesions can be found in the liver secondary to antimicrobials, antineoplastic agents, and antiepileptic drugs.[2] Non-necrotizing granulomas in bone marrow can accompany hepatic granulomas with no known cause.[5] Idiopathic granulomatous hepatitis should be considered as a rare cause of FUO (**Table 1**).

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Table 1- Less common causes of fever of unknown origin.

Infections	Malignancies	Systemic diseases	Miscellaneous
Amebic liver abscess	Atrial myxoma	Allergic granulomatous angiitis	Behçet's disease
Brucellosis	Aleukemic leukemia	Granulomatous hepatitis	Chronic fatigue syndrome
Chronic active hepatitis	Kaposi's sarcoma	Hypersensitivity vasculitis	Disorders of temperature regulation
Dental abscess	Lung cancer	Inflammatory bowel disease	Drug fever
Diskitis	Malignant melanoma	Panaortitis	Environmental
Epididymitis	Sarcoma	Reiter's syndrome	Factitious fever
Fascioliasis		Sarcoidosis	Familial Mediterranean fever
Gonococcal arthritis			Periodic fever
Herpes simplex encephalitis			Pulmonary emboli
Infectious mononucleosis			Retroperitoneal hematomas
Kala azar			Thyroiditis
Kikuchi's disease			
Lyme disease			
Pyelonephritis			
Pyometra			
Rheumatic fever			
Sinusitis			
Typhoid fever			
Whipple's disease			

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ERRATA

In manuscript "The effects of diethylstilbestrol administration on rat kidney. Ultrastructural study" Saudi Med J 2013; 34: 1114-1124. The name of the authors should have appeared as: Adel M. Hussein, Mohamed H. Badawoud, Hesham N. Mustafa.

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