Leucopenia as Presentation of Sarcoidosis

Lawrence Akinsanya[1], Iftikhar Hussain[2], David Awoniyi[3] and Khalid Usman[4]
[1]Consultant Medicine, [2]Hematologist, [3]Consultant Surgeon, [4]Histopathologist,
Midnab General Hospital, Midnab, Qassim, Saudi Arabia

Abstract: A 20-year-old male Saudi national presented initially with leucopenia and splenomegaly. The absence of other signs of disease, progressive pancytopenia and normal bone marrow examination posed a diagnostic dilemma as to the cause of hypersplenism. Subsequently, the patient had splenectomy the histopathological appearance of which was non-caseating granuloma. A high level of angiotension converting enzyme (ACE) was found in this patient. Sarcoidosis is a recognized cause of hypersplenism, and though the disease is not yet widely described in this part of the world. It is the most probable diagnosis in this patient.

Keywords: Pancytopenia, Splennomegaly, Sarcoidosis.

Correspondence:
Dr. Iftikhar Hussain
Midnab Gerenal Hospital
Midnab (Qassim)
Saudi Arabia
E-mail: iftikharhusa38@hotmail.com

Sarcoidosis is a disorder of unknown etiology, with the pathological hallmark of non-caseating epithelioid granulomas, and the derangement of the normal tissue architecture. Any part of the body can be affected, but the organ most frequently affected in the lung. While hypersplenism is well recognized, it usually occurs with other features of sarcoidosis. We describe a patient with pancytopenia and splenomegaly, in which other features of sarcoidosis were absent. Splenectomy rapidly corrected the haematological abnormalities.

Scenario

A 20-year-old Saudi male was referred because of fatigue. A course of ranitidine and metronidazole for dyspepsia was taken about six weeks earlier, and three weeks before presentation, he experienced a short febrile illness which resolved spontaneously. There was no relevant travel or family history.

He was lean built. No clinical pallor and no palpable superficial lymphadenopathy. The spleen was 6 cm below the left costal margin. Further examination was unremarkable. Haemogram values, as shown in the Table 1, were the remarkable abnormality being marked leucopenia. Stool and urine analyses showed no significant finding. The chest radiograph and 12 lead electrocardiographs were normal.

A week later, haemogram profile was quite similar to the first analysis (Table 1). Serology for brucella, salmonella, HbsAg, HCV-ab, bilharzia, VDRL and infectious mononucleosis were non-reactive.

Three weeks after the initial presentation, hemoglobin had fallen (Table 1), with a microcytic and hypochromic picture. He was admitted for bone marrow aspiration, the result of which was normal. No evidence of LD bodies or malarial parasites (Fig. 1).

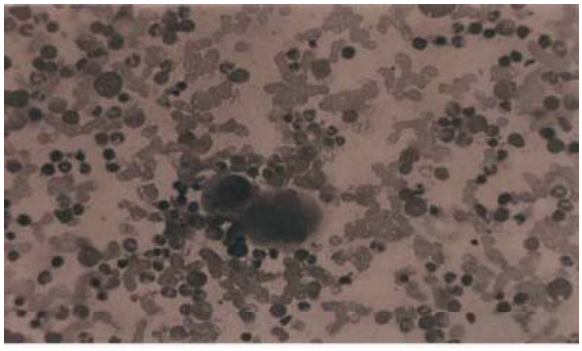

Fig. 1. Shows normal bone marrow aspirate (Leishmen x40).

Abdominal ultrasound revealed normal appearance of liver, splenomegaly of normal parenchymal architecture and normal kidneys. Tuberculin test was negative, and serum electrophoresis pattern was normal. The patient chose to continue the care at another hospital, where he was a medical laboratory technician trainee.

Subsequently, he turned up at the regional referral center. Bone marrow studies were once again found normal. Splenectomy was advised. The patient opted to return to this hospital for the surgery. Apart from splenomegaly which was then 15 cm below the left costal margin, he was very much the same clinically as before. The chest radiograph and electrocardiograph showed no abnormality. The operation and the post operative period were uneventful.

The size of the spleen was 30 x 18 x 8 cm, and weighed 1800 gms. Histology showed an infiltration of the red pulp by multiple discrete non-caseating epitheloid cell granulomas. The granulomas had no giant cells. There was a marked diminution of lymphoid follicles. Deeper tissue showed autolytic changes (Fig. 2 (x40) and Fig. 3 (x 200)).

Fig. 2. Spleen showing epitheloid cell granuloma (H and E x40).

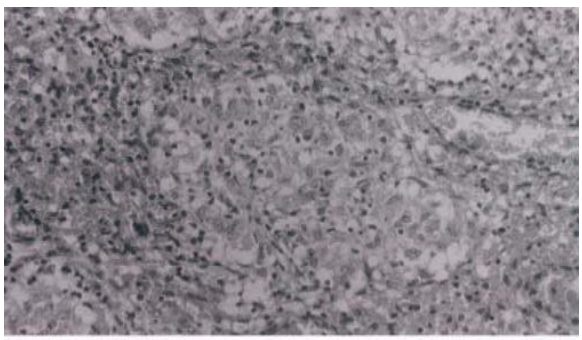

Fig. 3. Section highlighting non-cascous nature of granuloma (H and E x200).

Special stains for fungus, mycobacterium and malaria were negative. Three days post operatively, WBC had risen to normal level (Table 1).

The angiotensin-converting enzyme (ACE) level was high at 224 u/liter (reference range 8-52 u/l). Sarcoidosis was by exclusion, presumed to be the diagnosis in this case. He had further consultation at another hospital where liver biopsy was reported as showing granulomatous disease, consistent with a diagnosis of sarcoidosis. Apart from an episode of acute bronchitis, and one of varicella, he remains in reasonably good health, and has gained two kilograms in weight since splenectomy. Slit lamp examination of the eyes is normal. Serum calcium concentration and renal function indices have remained within normal limits, but the levels of serum alkaline phosphatase remained high, up to 10 times of normal values.

Discussion

Sarcoidosis is recognized throughout the world. It affects people of all racial and ethnic groups and occurs at all ages although it usually develops before the age of 50, with the incidence peaking at 20 to 39 years [1]. Sarcoidosis is recognized throughout the world, but there are marked differences in reported incidences from one country to another. The prevalence in the Kingdom of Saudi Arabia is not known, but a few recent publications suggest that it is not rare. One such study gave an incidence of 19/100,000 in a hospital population [2].

The typical features of sarcoidosis are well described [3], and when present, they pose a little difficulty in including the disease in the differential diagnoses. Presentation may be acute, over a period of a few weeks, and these individuals usually have constitutional symptoms such as fever, fatigue, malaise, anorexia, or weight loss. The chronic form usually presents predominantly with respiratory symptoms. About 10% of these individuals have symptoms referable to organs other than the lung, and may go on to develop permanent damage to these [4].

Hypersplenism is a recognized feature of sarcoidosis, though presentation solely as this is rare [5] and in an area where the disease is not frequently seen, diagnosis would depend on a high index of suspicion. In one study, the patient's most prominent clinical feature was pancytopenia, autoimmune haemolytic anaemia and hypersplenism. Clinical signs compatible with sarcoidosis and common variable immunodeficiency (CVID) did not develop until 10-11 years later [6]. There is no laboratory test or histological appearance that is pathognomomic, and diagnosis is largely one of exclusion. Tests such as angiotension converting enzyme (ACE) activity, and gallium–67 scanning, recommended as corroborative evidence are not readily available in the typical general hospital. In the patient with classic presentation, anergy to tuberculin would be supportive. The test was negative in our patient, but in the absence of typical features of sarcoidosis, it did not help very much, except to make the diagnosis of tuberculosis less likely. The elevation of serum angiotension I converting enzymes in patients with sarcoidosis was reported in literature. It is not specific for sarcoidosis. Its value increases in many granulomatous diseases such as berylliosis hypersensitivity pneumonitis, leprosy, lymphoma, and tuberculosis. It represents granulomatous "load" of the body [7]. Alkaline phosphatase may be elevated as a consequence of hepatic involvement [8]. In our patient, the diagnosis of sarcoidosis was considered only after splenectomy. The decision to go on with splenectomy was based on increasing fatigue, abdominal discomfort on the account of splenomegaly, and progressive pancytopenia. (It is now not clear whether a pre-operative spleen biopsy would have altered the management plan). The use of steroid is generally an option in chronic symptomatic sarcoidosis. Perhaps the employment of steroid therapy in this patient could have improved the haematological deficit, and if so, for how long, is subject to speculation. A patient with extensive abdominal sarcoidosis, including giant splenomegaly, was described who presented with recalcitrant hypercalcemia and pancytopenia. Hypercalcemia, and presumably the pancytopenia, resolved completely after splenomegaly without the need for other therapy [9]. Similarly, this patient has enjoyed improved health status since splenectomy without the need for intervention. Though the overall prognosis for sarcoidosis is said to be good, the involvement of the liver in this case does not give room for complacency. He needs follow up to determine the need for steroid therapy, if and when required.

During the past 15 years in this hospital, this has been the first case of sarcoidosis presenting

Table 1. Effects of plenectomy on hematological parameters

	WBCs X 109/L	Hb gm/dl	PlateletsX109/L
At presentation	1.5	13	125
3 weeks later	0.8	11.6	-
Immediate pre-splenectomy (9 months later)	1.1	10.6	81
Post-splenectomy			
(3 days)	6.8	11.6	390
Post-splenectomy			
(12 months)	9.9	13.6	466

as leucopenia initially supported by non-casuseating granuloma and raised angiotension I converting enzymes.

Acknowledgement

The authors thank Dr. Vishwesh Rajawat (Histopathology, King Fahad Specialist Hospital, Buraydah Qassim) for his useful advice. We thank Dr. Imran-ul-Haque (Histopathology, King Fahad Specialist Hospital, Buraydah Qassim) for his opinion and getting the microphotograph. We thank Awni Hassan (Chief of Technicians) for his technical assistance, and Ms. Suja Isac for her secretarial assistance.

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