



PULMONARY PUZZLE

Fever, splenomegaly and lymphopenia in sarcoidosis

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CLINICAL PRESENTATION

A 42-year-old woman was referred to our department with a 5 months history of intermittent fever and fatigue. Her past medical history included a consolidated diagnosis of sarcoidosis (obtained 7 years before with a sub-carinal lymph node biopsy) and in the previous years she had been treated with steroids, hydroxychloroquine, methotrexate and azathioprine with persistent and progressive enlargement of mediastino-hilar adenopathies and bilateral nodular infiltrates. Her symptoms progressed despite a course of antibiotics prescribed for presumed community-acquired pneumonia and a course of corticosteroids. The patient lived in Italy and there was no history of travels or other additional risk factors for infections.

At the time of admission, the patient had a temperature of 38.5°C and the physical examination was only notable for hepatomegaly and splenomegaly. A white blood cell count showed lymphopenia ($0.39 \times 10^9/l$, $CD4+ 0.22 \times 10^9/l$) and anaemia (Hb 10.4 g/dl, MCV 78.7 fl).

CT images of the thorax revealed bilateral nodules of variable sizes predominantly in the upper lung fields and a positron emission tomography showed several areas of increased metabolism in the liver, spleen, lymph nodes (above and under the diaphragm), D3 vertebra and bilateral nodular infiltrates (figure 1).

Fibre-optic bronchoscopy was normal and all investigations for infections (blood, bronchoalveolar lavage, urine and serological tests) were negative. ECG was normal.

A bone marrow biopsy was performed: the perivascular region was characterised by a concrete number of polyclonal mature plasma cells (for κ and λ light chains of immunoglobulins) and a diffuse interstitial infiltration of foamy macrophages with intracellular inclusions was noted as showed in figure 2.

QUESTION

What is the diagnosis?

See page 498 for the answer



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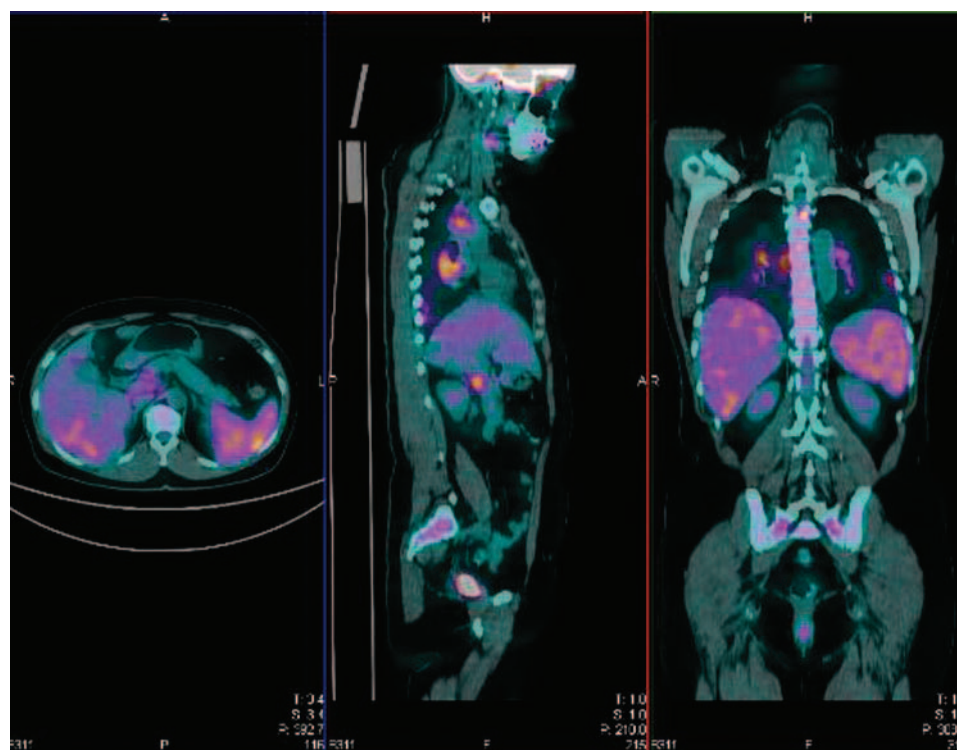


Figure 1 CT/PET showed numerous areas of increased metabolism in the liver, splenic parenchyma, thoracic and abdominal lymph nodes.

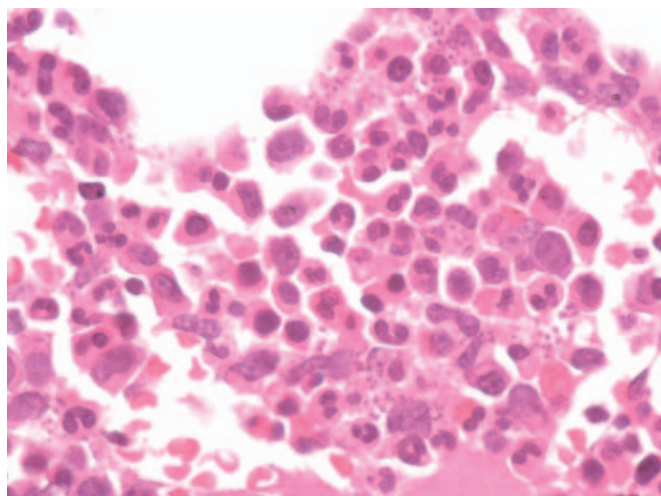


Figure 2 Bone marrow biopsy showing diffuse interstitial infiltration of foamy macrophages containing *Leishmania* protozoa.

ANSWER

From the question on page 497

The pathological analysis of the bone marrow revealed diffuse interstitial infiltration of foamy macrophages containing *Leishmania* protozoa. The conclusive diagnosis was visceral leishmaniasis in immunocompromised patient. The patient was treated with liposomal amphotericin (3.5 mg/kg for 5 days and then with a maintenance dose); treatment was well tolerated and resulted in immediate regression of the fever and improvement in general state of health; C-reactive protein decreased from 87 mg/l to 24 mg/l and lymphocytes increased from 0.39 mg/l to 0.95 mg/l.

Fever, splenomegaly and lymphopenia may arise from a large range of infectious, haematological or systemic diseases and therefore represent a difficult diagnostic challenge.¹ In this case, the previous history of sarcoidosis was an apparent clue; however, we know from literature that sarcoidosis and lymphoma, mainly non-Hodgkin's lymphoma, may occur together,

with sarcoidosis usually preceding lymphoma² and the coexistence of sarcoidosis and opportunistic infection, even in the absence of any immunosuppressive therapy, has previously been documented.³ A possible infectious cause of fever, splenomegaly and lymphopenia is visceral leishmaniasis (VL, kala-azar), a systemic infection of the reticuloendothelial system caused by protozoa of the genus *Leishmania*. The definitive diagnosis of kala-azar requires demonstration or isolation of parasites from samples collected by invasive organ aspiration.⁴ VL is endemic in areas bordering the Mediterranean Sea; even though leishmaniasis is seen relatively infrequently in connection with sarcoidosis, our case presentation demonstrates that VL must be taken into consideration in the differential diagnosis of febrile splenomegaly in patients living in areas endemic for such protozoa.⁵

Contributors All authors have made important contributions in the discussion of the clinical case and drafting the article.

Competing interests None.

Patient consent Obtained.

Ethics approval Ethics approval was provided by Area Vasta Romagna Review Board.

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