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CONTINUING MEDICAL EDUCATION
ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Internal Medicine Quiz – Case 12

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2009, 26(1):139–140

J. Meletis,[1]
E. Papakostas,[1]
P. Kouzis,[1]
J.V. Asimakopoulos,[1]
T. Chatzileonida,[1]
A. Giakoumis,[1]
E. Bazani,[1]
C.S. Floudas,[1]
S. Masouridi,[1]
A. Sarantopoulos,[1]
M. Aspradaki,[1]
M. Tsironi,[1]
E. Variami,[1]
E. Terpos,[2]
N. Viniou[1]

[1]First Department of Internal Medicine, National and Kapodistrian University of Athens, School of Medicine, "Laiko" General Hospital, Athens
[2]Department of Medical Research, 251 General Air Force Hospital, Athens, Greece

A 66-year-old man from a rural area was admitted for evaluation of fever accompanied by abdominal discomfort, nausea, loss of appetite and weakness. The fever started a month ago and was of low-moderate grade (<40 °C), intermittent –often with two daily peaks, with alternating periods of apyrexia– and responded to antipyretics.

On physical examination, the patient was alert and orientated. His heart rate was 92 beats per minute, blood pressure 160/110 mmHg, respiratory rate 25 breaths per minute, and his temperature was 38.9 °C. Physical examination of the heart and the lungs did not reveal any abnormal findings. Palpation of the abdomen showed splenomegaly, with the spleen extending 8 cm below the left costal margin. There were no palpable nodes or hepatomegaly. Skin examination did not show any ulcers, rashes, pruritus, or jaundice. The patient had not noticed any change in urination or defecation. Also, he denied any recent travels abroad for himself and his close persons.

His medical history was significant for hyperuricemia, for which he was not receiving any medication. Nineteen years ago he had received a 9-month course of rifampin and isoniazid for pulmonary tuberculosis. Moreover, he had been treated with intermitted small doses of cortisone because of a dermatological disease for almost 22 years. His family history was unremarkable.

A complete blood count revealed hypochromic microcytic anemia (Ht 26.1%, Hb 8.9 g/dL, MCV 68.9 fL, MCH 23.5 pg, MCHC 34.2 pg/dL) with leukocytes 1,800/μL (neutrophils 900/μL, lymphocytes 800/μL and monocytes 100/μL), platelets 50,000/μL and reticulocytes 1.21%. Serum chemistries revealed hyperuricemia (uric acid 11.6 mg/dL), elevated urea 59 mg/dL (range: 17–50 mg/dL) and creatinine 1.9 mg/dL (range: 0.6–1.2 mg/dL), normal total bilirubin, normal total proteins with reduced albumin at 2.6 g/dL (range: 3.5–5.5 g/dL), low total cholesterol at 55 mg/dL (range: 140–200 mg/dL), an elevated AST at 48 U/L (range: 5–40 U/L) with normal ALT at 22 U/L and ALP at 172 U/L, mild elevation of the γ-GT at 53 U/L (range: 7–32 U/L), elevated lactate dehydrogenase at 807 U/L (range: 200–460 U/L) and normal creatine kinase at 27 U/L.

Serum iron levels were low (20 μg/dL) while the serum ferritin was markedly elevated (6,685 ng/mL). Serum haptoglobin levels were within normal range. C-reactive protein and ESR were increased at 112 mg/L (range: 0–5 mg/L) and 61 mm/h, respectively. The international normalized ratio was elevated at 1.77 and the activated partial thromboplastin time was prolonged at 43.2 sec, while fibrinogen levels were within the normal range.

A tuberculin skin reaction was negative. Serologies for HBV, HCV and HIV were negative. Coombs' test was positive (+++). Wrights' test was negative. Repeated blood, urine and stool cultures for common aerobes and anaerobes, *M. tuberculosis* and *Brucella* were negative.

A chest X-ray was normal, while a CT scan of the thorax showed pericardial effusion and emphysematous lungs. An MRI of the abdomen confirmed the splenomegaly.

Serum protein electrophoresis was performed revealing diffuse hypergammaglobulinemia (fig. 1). A bone marrow smear was performed and the diagnosis was established by the morphology of the bone marrow smear (figures 2, 3). Appropriate treatment resulted in an early fever improvement as well as progressive amelioration of anemia and rapid normalization of bone marrow findings.

Comment

Leishmaniasis is a group of diseases caused by different types of

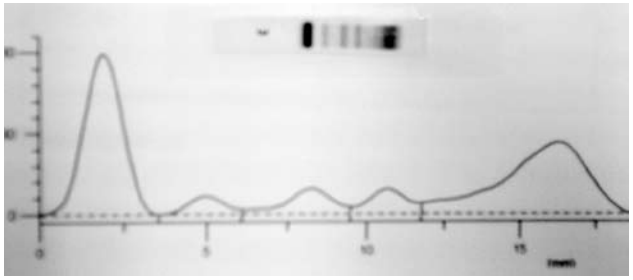

Figure 1

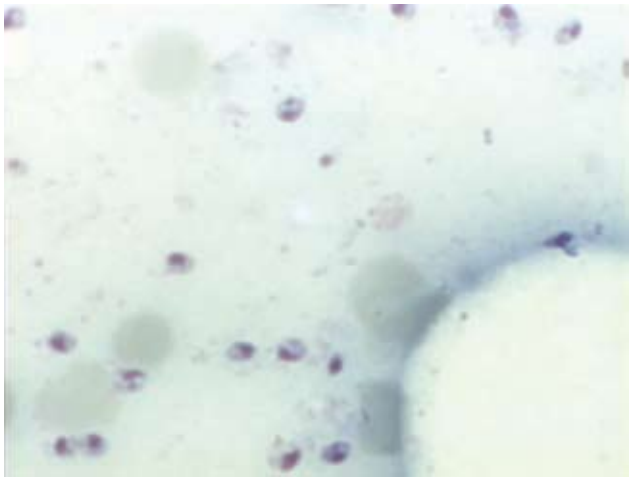

Figure 2

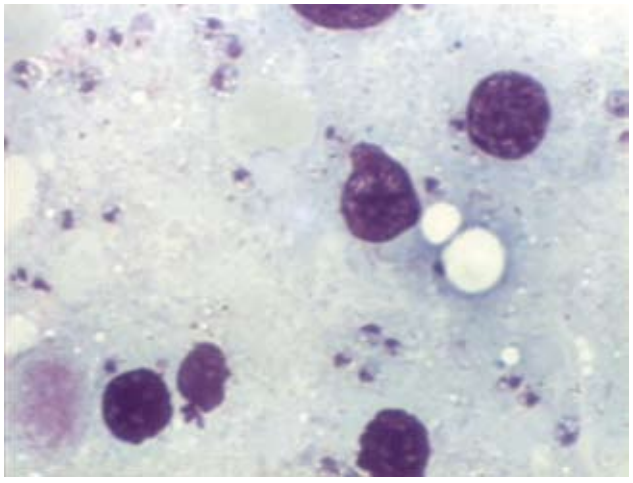

Figure 3

obligate intra-macrophage protozoan parasites, of Leishmania sp, transmitted to humans by approximately 30 different phlebotomine tiny sand flies. Vector flies are infected by biting humans or animals, while animal reservoirs include canines, rodents and humans, depending on the area. Infection by blood transfusion, shared needles, congenitally, or sexually is extremely rare. There are three forms of leishmaniasis; visceral (or Kala-azar, meaning black death), cutaneous and mucocutaneous. Visceral leishmaniasis results from infection with Leishmania donovani or Leishmania infantum/L. chagasi and is endemic in some parts of South and Central America, Africa (especially the Sudan), India, infrequently China and the Mediterranean basin. Irregular fevers (in some cases the fever is characterized by twice-daily temperature peaks), hepatosplenomegaly, pancytopenia and polyclonal hypergammaglobulinemia occur, as parasites disseminate from the skin to the lymph nodes, spleen, liver and bone marrow. The clinical manifestations usually develop gradually over weeks to months, even years, after inoculation of the parasite; nevertheless, only a minority of infected persons develops progressive visceral disease. Diagnosis is established by demonstrating parasites in Giemsa-stained smears or cultures of aspirates from spleen, bone marrow, liver or lymph nodes. Emaciation and finally death occur within 1 to 2 years in 80–90% of untreated symptomatic patients.

However, splenomegaly may be absent in immunocompromised patients, such as HIV-positive individuals, renal transplant recipients, patients with hematological malignancies and those on long-term steroids. Cases without splenomegaly have been reported in the past. Treatment options for visceral leishmaniasis include amphotericin B (liposomal and conventional) and pentavalent antimonials (meglumine antimonate and sodium stibogluconate). Treatment with amphotericin resulted in an improvement in the anemia and clearing of bone marrow from Leishmania donovani bodies in our patient. Anemia in leishmaniasis may be due to splenic sequestration and hemolysis, immune hemolysis, or bone marrow dyserythropoiesis. The reduction in the antibody titer to the rK 39 antigen of Leishmania donovani by 50% after treatment supports previous observations that this antigen can be used as a good marker to assess the response to treatment in the absence of significant clinical symptoms. Amphotericin is considered to-date the first choice of treatment.

Corresponding author:

J. Meletis, First Department of Internal Medicine, National and Kapodistrian University of Athens, School of Medicine, "Laiko" General Hospital, Athens, Greece, Tel.: +30 210 74 66 206, Fax: +30 210 77 88 830,
e-mail: imeletis@cc.uoa.gr