



Fig. 3 Lung ultrasound, anterior longitudinal scan; the absence of lung sliding in B-mode (a) is expressed in M-mode (b) as the “seashore sign”, horizontal lines without the grainy pattern seen on the seashore sign

ration and absent in expiration. This sign expresses the spot where visceral pleura detaches from parietal pleura in the presence of pneumothorax, therefore the lung point cannot be found in cases of total lung collapse.

Discussion

Chest ultrasound is an emerging clinical application in the management of the ED patient. The literature supports its accuracy, as well as its role as a point-of-care modality. Differentiating pulmonary processes such as pneumothorax [6–10], pulmonary contusion [12], heart failure [13, 14] and ARDS [15] with chest ultrasound have shown high diagnostic effectiveness. Chest radiographs remain the standard of care for the diagnosis of pneumothorax [3], despite lower overall accuracy as compared to ultrasound. As our case illustrates, care must be taken with some rare, misleading artefacts. The emergency physician must maintain a high index of suspicion when the chest radiograph does not match the patient presentation. Point-of-care chest ultrasound is gaining support as a diagnostic tool which is easy to perform, readily available, safe and time-saving, and should be recognised as a necessary skill for the emergency physician [16].

Acknowledgement We are very grateful to Resa Lewiss and Heidi Ladner for revising the manuscript.

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Intern Emerg Med (2007) 2:238–242

DOI 10.1007/s11739-007-0069-z

A case of pancytopenia and splenomegaly: haematological disease?

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Received: 2 August 2006 / Accepted in revised form: 30 October 2006 / Published online: 28 September 2007

A 61-year-old man was admitted to our hospital for a febrile illness and asthenia. He had been in a state of health until August 2004, when dizziness developed. In September 2004, he was admitted to another hospital for persistent asthenia: he was afebrile and physical examination was normal except for moderate hepatomegaly and splenomegaly. The laboratory tests are shown in Table 1. The tests for hepatitis B and C viruses were negative. Abdominal ultrasonography confirmed hepatosplenomegaly. Bone marrow biopsy and aspira-

tion did not reveal granulomatosis and neoplastic lesions. On 26 September he was discharged home with a diagnosis of "pancytopenia, liver cirrhosis".

On 6 October he had fever with shaking chills and was admitted to our hospital. The patient was a native of Umbria, where he lived. There was no history of travel, exposure to animals or sick people, receipt of blood products, sexual promiscuity or other pathologies. He did not use alcohol or illicit drugs; he had smoked one pack of cigarettes daily from the age of 45 years and he had no eaten

Table 1 Haematologic laboratory and blood chemical values

Variable	Four weeks before admission	On admission	One week after discharge
Haemoglobin (g/dl)	7.9	6.3	11.7
Mean corpuscular volume (μm^3)	–	94.7	87.9
Reticulocyte count (%)	–	22	10
Erythrocyte sedimentation rate	–	120	17
White-cell count (per mm^3)	3400	1050	3030
Differential count (%)			
Neutrophils	52	44.9	53.2
Lymphocytes	43	38.1	34.3
Monocytes	–	8.7	7.4
Eosinophils	–	0.6	2.8
Basophils	–	1.6	0.8
Band forms	–	6	1.5
CD4 cell count (%) ^c	–	55	–
Prothrombin time	–	91	96
Partial-thromboplastin time	–	30	27.3
Platelet count (per mm^3)	126 000	36 000 ^b	31 000
Iron ($\mu\text{g}/\text{dl}^a$)	–	22	75
Ferritin (ng/dl)	–	461	289
Urea nitrogen (mg/dl)	–	14	16
Creatinine (md/dl)	–	0.8	0.8
Uric acid (mg/dl)	–	3.2	1.6
Protein (g/dl)	–	5.8	5.5
Albumin	–	2.26	4.20
Globulin	–	1.95	0.90
Glucose (mg/dl)	–	76	103
Sodium (mmol/l)	–	143	142
Potassium (mmol/l)	–	3.8	4.8
Chloride (mmol/l)	–	111	105
Calcium (mg/dl)	–	7.1	8.7
Bilirubin (mg/dl)			
Total	2.5	2.90	1.50
Conjugated	0.66	1	0.29
Alanine aminotransferase (ALT, U/l)	85	23	20
Aspartate aminotransferase (AST, U/l)	55	37	19
Lactate dehydrogenase (LDH, U/l)	510	502	178
Alkaline phosphatase (U/l)	–	861	804
GGT	340	213	326
Cholinesterase	–	2407	3956
Amylase (U/l)	–	23	32
Lipase (U/l)	–	7	13

^aTo convert the value for iron to micromoles per litre, multiply by 0.1791

^bMicroscopical examination: presence of platelet aggregation

^cThe normal range is 38 to 55%

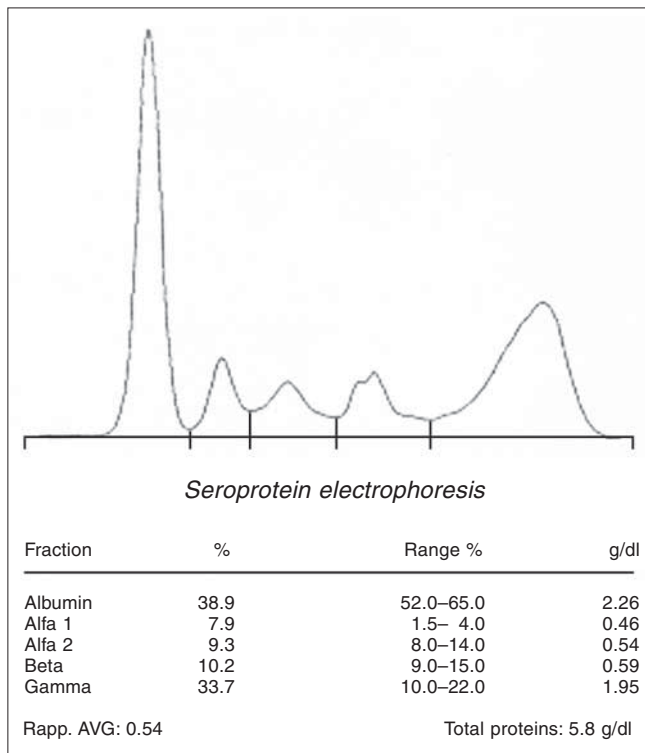


Fig. 1 Serum immunoelectrophoresis

uncooked seafood or meat. His temperature was 40.0°C, pulse was 110 beats/min and respirations were 18 breaths/min. Blood pressure was 80/50 mmHg.

On examination, the patient appeared fatigued; no rash, skin lesion or lymphadenopathy was found. The head and neck were normal, the lungs were clear and neurologic examination was normal. A grade 2 systolic murmur was present. Liver and spleen were palpated, respectively, 3 cm and 6 cm below the right and left costal margins.

The results of laboratory tests are presented in Table 1. Urine analysis was normal. Specimens of blood and urine were obtained for culture and no organisms grew. Radiographs of chest were normal. Transfusions were given and piperacillin and amikacin were administered intravenously, without relief of the fever.

The principal diagnostic hypotheses were: visceral leishmaniasis (VL), supported by the presence of fever and hypergammaglobulinaemia (Fig. 1), haematological diseases (haemolytic anaemia, leukaemia, myelofibrosis) and liver cirrhosis. In the differential diagnosis we consider also malaria, tuberculosis, cytomegalovirus and Epstein-Barr virus infection, systemic lupus erythematosus and rare diseases such as Gaucher's disease, amyloidosis and histiocytosis.

Serologic tests and diagnostic procedures were performed. The tuberculin skin test was negative at 48 h. The tests for HIV, EBV, CMV, brucella, hepatitis B and C and Coomb's and Ham's tests were negative. Abdominal

ultrasound revealed hepatomegaly (17.9 cm) and splenomegaly (20 cm) without focal lesion, portal, splenic and hepatic vein obstruction. A blood film and a bone marrow biopsy and aspiration were performed. The microscopic examination of peripheral blood revealed platelet aggregation. The bone marrow biopsy and aspiration revealed macrophages filled with amastigotes of *Leishmania*. The diagnosis was confirmed by serological tests (IgG 1:5120). The patient was treated with a lipid formulation of amphotericin B (AmB): 3mg/kg/day intravenously on days 1–5, 14 and 21.

His clinical condition improved, and the size of his spleen decreased. The serological tests, repeated after two years, showed a reduction of IgG (1:320) and normalisation of laboratory tests.

William Leishman and Charles Donovan, separately but simultaneously in 1903, demonstrated a protozoan parasite in the spleen of patients suffering from a malaria-like illness, which became known as visceral leishmaniasis (VL). The causative agent of VL was named as *Leishmania donovani* after its co-discoverers.

Actually, about 21 *Leishmania* species are known to infect humans and produce several, varied clinical syndromes, including visceral, cutaneous and mucosal leishmaniasis [1].

In Italy, human VL is caused by *Leishmania infantum*, which has different *Phlebotominae* species as the vector. The most prevalent sandfly species were *Phlebotomus perniciosus* and *P. papatasi* [2]. Their seasonal presence extends from the second half of May to September.

Dogs are the main reservoir of infection, but the results of a study carried out in Calabria and Sicily has revealed the presence of *Leishmania* spp. antibodies in murine serum. This indicates the presence of rodents as new reservoirs (*Rattus rattus* and *Rattus norvegicum*) in rural areas.

In the first half of the 20th century, VL, caused by *Leishmania infantum*, was a typical infantile syndrome in Italy, with high incidence in southern regions and islands. Stable endemic foci of both human and canine VL were present only in southern, central and insular regions in Italy. Recently, new foci of canine and human leishmaniasis and the presence of sandfly vectors are reported also in northern regions [3]. However, in the last 10 years, the geographic distribution of canine and human leishmaniasis in Italy has spread and these diseases are expanding into northwestern continental climate areas, because of global warming and increased movement of infected animals and sandfly vectors from Mediterranean coastal areas.

Another important factor that can explain the increased incidence of VL is the increase of this infection in immunosuppressed patients. Recent evidence has shown that *Leishmania*–HIV coinfection is becoming a major health problem in affected areas [4]. It is unclear whether HIV infection increases the probability of a new

leishmanial infection becoming symptomatic or allows the re-activation of a previous asymptomatic latent infection or both.

The hosts immune system plays an important role in establishing the course of this infectious disease. Early studies largely defined the Th1/Th2 paradigm of resistance/susceptibility to infection and the role of IL-12 and IL-4 respectively in driving Th1 and Th2 cell development [5]. Milano et al. [6] suggested endogenous IL-15 as having a role in increasing the T-cell response to human intracellular pathogens.

The clinical presentation and evolution of VL is the result of the complex interplay between the parasite and the hosts immune system. The infection can remain asymptomatic or subclinical in many cases, or can follow an acute, subacute or chronic course. Unrecognised and untreated acute VL is usually associated with a fatal outcome. Complications include secondary bacterial infections and haemorrhage, both salient contributors to mortality.

VL has a classic symptomatology, characterised by fever, cachexia, moderate hepatomegaly, usually massive splenomegaly, pancytopenia and hypergammaglobulinaemia with hypoalbuminaemia, but it can have also atypical clinical presentations. An unusual symptomatology is present mainly in immunosuppressed patients, in which dry cough, diarrhoea and concomitant cutaneous lesions are described, reflecting the failure of the hosts immune system to prevent the spread of the parasites into unusual sites, such as the respiratory and gastrointestinal tracts. However, atypical clinical presentations of VL are described also in immunocompetent patients. In fact, two cases of VL presenting as an adrenal cystic mass [7, 8] and a case as an axillary lymphadenopathy and splenic infarct [9] has been reported in immunocompetent patients.

In the last years some serologic tests have been tested in the diagnosis of leishmaniasis. Enzyme-linked immunosorbent assay (ELISA), indirect immunofluorescence assay (IFA) and direct agglutination tests (DAT) are used by investigators in various endemic regions. The sensitivity and specificity of each assay varies with the species of *Leishmania* used as a source of antigen, with the species of parasites causing the infection and with the humoral immune response of the host [10]. The ELISA appears to be the most sensitive (>90%) and specific of these methods in VL [11]. However the antibody search can be used as supportive data in the diagnosis of leishmaniasis.

A definitive diagnosis requires demonstration of the *Leishmania* organism by histology. VL can be diagnosed by aspirate or biopsy of any involved organ. Bone marrow biopsy with examination for amastigotes on Giemsa-stained or Wright-Giemsa-stained smears is reported to have approximately 80% sensitivity [12, 13] and is second only to examination of splenic aspirates, in which the sen-

sitivity is 96–98% [14], but there are major complications such as the risk of splenic rupture. Therefore, microscopy is reported to be highly sensitive and specific in the diagnosis of VL. Nevertheless, it may yield false negative results when examined in laboratories without good expertise [13]. Alternative diagnostic methods include liver biopsy and lymph node aspiration, but they are less sensitive than bone marrow specimens.

The arsenal of drugs available for treating VL is limited. Pentavalent antimonials have long been the cornerstone of anti-*Leishmania* chemotherapy and are still the mainstay of therapy for leishmaniasis in most of the world, but long admission to hospital, toxicity and possible unresponsiveness to treatment have limited the use of these drugs. AmB is the new current alternative treatment of choice. Liposomal preparation of AmB (lip AmB) is preferable to the conventional AmB deoxycholate, which has some disadvantages (high cost, limited availability in some areas, and toxicity – notably infusion-related side-effects, hypokalaemia, renal impairment and anaemia). Lip AmB has been reported to have greater efficacy and less toxicity *in vivo* [15] and at present is the most active antileishmanial agent in use. Although the resistance to Lip AmB is rare, relapses are sometimes found after treatment, especially in HIV-positive patients.

In conclusion, VL must always be taken into consideration in the differential diagnosis in patients presenting with splenomegaly and pancytopenia. Diagnosis can be difficult because the demonstration of *Leishmania* spp. in bone marrow biopsy does not have a very high sensitivity.

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