Case Report: Treatment of Kala-Azar by Amphotericin B Lipid Complex (ABELCET®)

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SUMMARY: A 45 year-old female was admitted to Department of Infectious Diseases of Social Security Hospital, Tepecik, İzmir. She was found to have hepatosplenomegaly; pancytopenia and hypergammaglobulinemia during physical and laboratory examinations. Leishmania amastigotes were seen in the bone marrow smears and serological and bacteriological tests were all found to be positive. The patient was given diagnoses of visceral leishmaniasis and salmonellosis. A dosage regimen of Amphotericin B lipid complex (Abelcet®) infusion was given intermittently and this was found to be effective in the treatment of visceral leishmaniasis.

Key Words: Leishmaniasis, visceral, Abelcet, case report

Olgu Sunumu: Kala-azar'ın Amphotericin B Lipid Komplex (Abelcet®) ile Tedavisi

ÖZET: SSK İzmir, Tepecik Eğitim Hastanesi İnfeksiyon Hastalıkları kliniğine başvuran 45 yaşındaki kadın hastanın fiziksel ve laboratuvar incelemelerinde; hepatosplenomegali, pansitopeni ve hipergammaglobulinemi saptanmıştır. Kemik iliği yayma preparatında Leishmania amastigotları görülen hastanın, serolojik ve bakteriyolojik testlerinin de pozitif olduğu görüldükten sonra hasta, leishmaniasis e salmonellosis tanısı almıştır. Amphotericin B Lipid Komplex (Abelcet®) infüzyon olarak aralıklı olarak uygulanmış ve visseral leishmaniasisin tedavisinde etkili olduğu görülmüştür.

Anahtar kelimeler: Leishmaniasis, visseral, Abelcet, olgu sunumu

INTRODUCTION

Visceral leishmaniasis (VL, Kala-azar) is a disseminated protozoal infection, transmitted by sand fly bite. The infection may result in a progressive disease, which is invariably fatal, if untreated. Visceral leishmaniasis is seen in 80 countries in Asia and Africa (*Leishmania donovani*), southern Europe (*L. infantum*), and South America (*L. chagasi*). *L. donovani* is the principal pathogen. In Europe, leishmaniasis is endemic in all Mediterranean countries, including Turkey.

The clinical features of VL in Turkey are consistent with the Mediterranean type, which is mostly seen in children younger than 11 years. In Turkey, diagnosis of VL usually depends on the identification of amastigotes in giemsa-stained bone-marrow aspirate smears and/or culture of the aspirates in NNN medium; detection of antibodies against *Leishmania* by IFAT and/or whole ELISA and/or rK39 ELISA was found to be sensitive in the diagnosis of VL in both humans and dogs (7).

Until the beginning of the 1990s, treatment of Kala-azar, in both children and adults, was essentially limited to pentavalent antimony (Sb^V) worldwide, which has been in use for 50 years. Sb^V therapy requires once-a-day injections, usually for 28 days. However, it is not necessarily well-tolerated and is now ineffective in the Indian region, called Bihar State, which houses the 90% of all cases of India and 40% of all cases of the world (11).

Fortunately, clinical trials, carried out during the past decade, have opened the door to a range of new treatments, including short-course (even single-dose) parenteral regimens and highly effective oral therapy (Table 1).

Here, we report a rare case of visceral leishmaniasis and salmonellosis co-infection, successfully treated with the intermittent application of amphotericin B lipid complex (Abelcet®).

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Table 1. Treatment alternatives in visceral leishmaniasis (6)

1950–1990	1990–2000
Pentavalent Sb^V	Pentavalent Sb^V
Pentamidine	Pentamidine
	Amphotericin B
	Lipid-associated amphotericin B, as amphotericin B cholesterol dispersion, amphotericin B lipid complex or liposomal amphotericin B
	Amphotericin B in fat emulsion
	Aminosidine
	Combination chemotherapy with aminosidine and Sb^V
	Immunochemotherapy with interferon-γ and Sb^V
	Oral chemotherapy with miltefosine

CASE REPORT

A 45 years old female, suffering from shoulder and back pain, fever, chilling and shaking for a month, have been admitted to a local hospital in Manisa city. Due to the detection of pancytopenia and elevated erythrocyte sedimentation rate (132/h), she was referred to the Outpatient's Infectious Diseases Clinic of Tepecik Social Security Association Hospital, Izmir, Turkey.

On the physical examination, general condition of the patient was fine, body temperature was 37.6 °C, pulse was 80/min and the blood pressure was 85/60 mmHg. There was paleness on the face and conjunctivas, liver and spleen were palpable 3-4 cm and 2-3 cm below the right costal margin and the left costal margin, respectively, and there was matity on the Traube region. There was no abnormality in the examination of other systems.

The results of the laboratory examinations were as follows: Haemoglobine, 9.7 g/dL; hematocrit, 27.9%; erythrocyte count, 3.71x 10^6 cells/mm3; WBC count, 1300 cells/mm3 (53% PNL, 45.5% lymphocytes, 1% monocytes,); platelet count, 80,000 cells/mm3; erythrocyte sedimentation rate, 132 mm in the first hour and; C-reactive protein, 31.5 mg/dL (Normal: < 5 mg/dL); and lactate dehydrogenase 521 U/L; romatoid factor 82.3 IU/ml. AST 9 U/lt, ALT 29 U/lt, ALP 117 U/lt, GGT 35 U/lt, total bilirubine 0.7 mg/dL, globuline 5.9 g/dL (N: 1.5-3.5 g/dL), albumine 3.7 gr/L (N: 3.5- 4.7 g/dL), IgA: 542 mg/dL (N: 85- 453 mg/dL), IgG: 3320 mg/dL (N: 751- 1560 mg/dL) and IgE: > 1220 IU/mL (N: 0.01- 100 IU/mL).

Abdominal ultrasonography demonstrated enlarged liver and spleen (157 mm). Consultations to hematology, gastro-enterology and gynecology departments revealed no pathology related to malignity.

The patient reported eating fresh white cheese frequently, suffering from fever and waist pain. Considering *Brucella* infection, group agglutination (Vidal) and *Brucella* agglutination (Rose Bengal) tests were done and found to be negative. In addition, due to elevated serum IgE levels, *Toxocara* infection was sought by ELISA and Western blot methods, which were then found to be negative. Although *Salmonella typhi* was not isolated in neither blood nor bone marrow cultures, acute salmonellosis was diagnosed in consecutive serological tests, with 10-day interval, due to the four-fold increase in the O (from 1:200 to 1:800) and H (from 1:100 to 1:400) antibodies against *Salmonella*.

Examination of the bone marrow aspiration sample was revealed intracellular and extracellullar *Leishmania* amastigotes. However, no reproduction was detected in the culture of the aspiration sample in NNN medium. Serological test results demonstrated high levels of positivity (1/512) in Indirect Immunoflourescent Antibody (IFA) test, and in both *Leishmania* rK39 dipstick test and Western blot method.

In order to treat visceral leishmaniasis, Amphotericin B Lipid Complex (Abelcet®) was given in intermittent infusions as 100 mg (1st day), 100 mg (3rd day), 400 mg (5th day) and 400 mg (16th day and totally 1000 mg). In addition, 14-day treatment of levofloxacin in 1000 mg/day in two doses, was given to treat acute salmonellosis. Two IU fresh blood and 4 IU platelet suspension were transfused to elevate their blood levels.

After the therapy, clinical and parasitological evaluations of the patient, proved that the patient recovered completely from both infections.

DISCUSSION

Pentavalent antimonial compounds [sodium stibogluconate (Pentostam®) or meglumine antimonate (Glucantime®)] have been the mainstay in the treatment of Kala-azar, being used as first-line drugs. Although it has not been reported in Turkey yet, there is an increasing primary resistance to Sb^V in India (2).

Amphotericin B has selective toxicity for *L. infantum* and has been used for the treatment of Kala-azar cases in India. However, its use is limited owing to its serious side effects, poor tolerance, requirement for infusions, length of the therapy, and to some extent, cost (6). The new formulations of amphotericin B provided important opportunity to reduce the duration of therapy in Kala-azar, while preserving its efficacy (1, 9). Each of the three commercially available preparations, given once daily by infusion, is well-tolerated and their efficacy in Kala-azar has exceeded all clinical expectations

(5). Today, some authors suggest that the new formulations of amphotericin B should be used as the first-line treatment for visceral leishmaniasis in immunocompetent patients, particularly in children (4).

Several clinical trials have been conducted to test the utility of Abelcet® and AmBisome® in the treatment of VL. The results of the clinical trials with Abelcet revealed that; (*i*) it was safe, (*ii*) infusion reactions and other toxicities, associated with amphotericin B, were minimum and no organ-specific toxicity was observed. (*iii*) In addition, it was possible to infuse a cumulative dose of 10mg/kg of Abelcet® within 24 hours (*iv*), or a total dose of 10-15 mg/kg, which could cure 90-100% of patients, and (*v*) the duration of therapy could be reduced to 2-5 days (12).

Pagliano *et al*. (8) have compared the efficacies of meglumine antimonate and liposomal amphotericin B (L-AmB) on 64 VL-positive patients, and reported that, when given at 3 mg/kg/d on days 1, 5 and 10, L-AmB had a faster recovery, less treatment failures and no significant toxicity (8). Sundar *et al*. (10) investigated the efficacies of ultra-short courses of amphotericin-B-lipid complex on Indian patients, unresponsive to meglumine antimonate and found that, 89%, 100% and 92% of patients, given single infusion of 5 mg/kg, two infusions, each of 5 mg/kg, 5 days apart and two infusions, each of 5 mg/kg, on consecutive days, respectively, were treated successfully (10).

In recent years, there have been some obstacles in the availability of Pentavalent antimonial compounds in Turkey. This led to the search of alternative treatment regimens for VL in Turkey. Our patient was treated as intermittent dosage regimen with Amphotericin B Lipid Complex (Abelcet®) as 1st day 100 mg, 3rd day 100 mg, 5th day 400 mg and 16th day 400 mg (totally 1000 mg). The control studies have proved that the patient was effectively treated, without any side effect.

Only one case of renal transplantation, co-infected with VL and non-typhoid salmonellosis, was reported by Hussein et al. in the literature (3) but we should note that, fever is the predominant manifestation in both infections and thus may be conceal each other. Therefore, all such patients should be interrogated whether they live in an endemic area for VL.

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