# *Visceral Leishmaniasis of Childhood*

## *Çocuklukta Visseral Leyşmanyazis*

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**Abstract**

Leishmaniasis is widespread in many countries, including Turkey. We present the clinical characteristics and the retrospective analysis of 22 children with visceral leishmaniasis, identified between 1995-2008.

The mean age at presentation was 3.3±1.96 years (range 0-8). All patients had splenomegaly. Fever was found in 19 (86.3%) cases. Anemia, thrombocytopenia, and leukopenia was observed in all, 19 (86.3%), and 13 (61%) cases respectively.

Diagnosis of visceral leishmaniasis was made with the identification of amastigotes in giemsa-stained bone-marrow aspirate smears.

Initial treatment consisted of meglumine antimoniate in 19 (86.3%) patients and liposomal amphotericin B in 3 (13.7%) patients. Three children who did not respond to meglumine antimoniate were cured with liposomal amphotericin B.

The findings highlight liposomal amphotericin B as an effective therapy for visceral leishmaniasis in children. Early detection and appropriate management of complications may reduce morbidity and mortality in childhood visceral leishmaniasis.

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**Key words:** Visceral leishmaniasis, childhood, liposomal amphotericin B

**Özet**

Leyşmanyazis, Türkiye'nin de içinde olduğu Akdeniz ülkelerinin birçoğunda yaygındır. 1995-2008 yıllarında tanı koyduğumuz 22 olgunun klinik özelliklerini sunmak istedik.

Hastaların ortalama yaşı 3,3±1,96 yıl (dağılım: 0-8). Dalak büyüklüğü 19 hastada (%86,3), anemi tüm hastalarda, trombositopeni 19 hastada (%86,3) ve lökopeni 13 hastada (%61) görüldü. Visseral leyşmanyazis tanısı, tüm olgularda kemik iliğinde parazitlerin görülmesi ile kondu.

Başlangıç tedavisi olarak 19 hastaya (%86,3) meglümin antimoniyat ve üç hastaya (%13,7) lipozomal amfoterisin B tedavisi başlandı. Meglümin antimoniyat tedavisine yanıt vermeyen 3 hastada lipozomal amfoterisin B ile tam kür sağlandı.

Sonuç olarak, amfoterisin B çocukluk dönemi visseral leyşmanyazisinde ilk seçenek olarak kullanılabilen, etkili bir tedavi ajanı olarak görünmektedir. Erken tanı ve komplikasyonların uygun yönetimi ile mortalite ve morbidite azaltılabilir.

*(Çocuk Enf Derg 2009; 3: 109-11)*

**Anahtar sözcükler:** Çocukluk dönemi, visseral leyşmanyazis, amfoterisin B

## Introduction

Visceral leishmaniasis (VL), known as kala-azar, is caused by Leishmania species and is endemic in tropical and subtropical regions. It is transmitted with sandfly bites (1,2). VL caused by Leishmania infantum is found throughout the Mediterranean region, especially in southern Italy, France, Greece, Malta, and Turkey (3-9).

Leishmaniasis, a disease that may cause considerable diagnostic difficulty in the setting of a hospital in the developed world, may be contracted on short visits to countries where it is endemic. Children with this disorder may be misdiagnosed as having a primary hematological disorder, such as leukemia. Leishmaniasis may present as an acute disorder with fever, hepatosplenomegaly or as a more chronic condition characterized by increasing hepatosplenomegaly, lymphadenopathy, and pancytopenia. Pentavalant antimonial drugs have been used for many decades as the standard treatment for VL. Pentavalent antimonials are safer than trivalent ones, but their adverse effects, such as life-threatening electro-

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cardiographic changes are frequent (10). During the last decade, the emergence of Leishmania strains that are resistant to pentavalent antimonials and the occurrence of side-effects have prompted the evaluation of other drugs, including lipid formulations of amphotericin B (8,9,11,12). Liposomal amphotericine B (L-AmB) was the first drug approved for the treatment of visceral leishmaniasis by the United States Food and Drug Administration (13). The purpose of this study was to investigate the epidemiological, clinical, laboratory and therapeutic features of 22 children affected by VL in southern Turkey retrospectively.

## Material and Methods

All children diagnosed as VL during the years 1995-2008 were included in study. All the data were taken from patient records. Demographic characteristics, clinical and laboratory findings, therapeutic interventions and clinical outcomes were noted. Diagnosis of VL was established with giemsa-stained bone marrow aspirate smears in all cases.

The patients who presented from 1995 up to 2000 were treated with meglumine antimoniate (MA) (Glucantim; Rhone-Poulenc, France) whereas those who presented thereafter were treated with L-AmB (AmBisome; Gilead, USA). MA was administered intramuscularly for 21 days at a dosage of 20 mg/kg/day. L-AmB was administered intravenously at a dosage of 3 mg/kg for 10 days. All patients were hospitalized during treatment. L-AmB was used for three patients for the initial treatment and for three patients that did not respond to antimonial treatment (4,5,8,9,11).

Clinical response was assessed at the completion of treatment. Most of the patients were followed up for at least six months after completion of treatment.

## Results

Twenty two children were diagnosed with VL. The median age of the patients was 3.3±1.9 years (range: 1-8 years). No patient had an underlying disease on admission. Splenomegaly, hepatomegaly, and fever were found in all (100%), 20 (91%), and 19 (86.3%) patients on initial physical examination (Table 1). All patients had anemia. Thrombocytopenia (<150x109/L), leukopenia (<4x109/L), and pancytopenia were found in 86.3%, 67%, and 48% of patients, respectively (Table 2).

**Table 1.** Clinical features of children at admission

| Clinical features | no. of cases | % |
|---|---|---|
| Fever | 19 | 86.3 |
| Abdominal distention | 14 | 63.6 |
| Pallor | 14 | 63.6 |
| Fatigue | 5 | 22.7 |
| Lack of appetite | 4 | 18 |
| Splenomegaly | 22 | 100 |
| Hepatomegaly | 20 | 91 |

Initial treatment was meglumine antimoniate in 19 (86.3%) patients who were diagnosed in 1995-2000, and L-AmB in 3 (13.7%) patients who were diagnosed after 2000. Treatment failure with MA, which was evident by the persistence of enlarged spleen and hematologic abnormalities, occurred in three children. All were subsequently cured with L-AmB. According to the results of the therapies, L-AmB was better than meglumine antimoniate, so that 16 (79%) patients who received meglumine antimoniate were cured, and 6 (100%) patients who received L-AmB were cured (Table 3). After six months of follow-up, no relapses were seen.

## Discussion

Leishmaniasis is widespread in most countries in the Mediterranean region, including Turkey. *L. infantum* is responsible for VL, which is sporadically seen mainly in the Aegean, Mediterranean, Central Anatolia, and Black Sea regions (3,9,14).

Typically, patients with VS present with unexplained fever lasting longer than two weeks, abdominal pain, fatigue, splenomegaly, hepatomegaly, cachexia, pancytopenia and history of exposure in an endemic area (2,5-7). Splenomegaly, hepatomegaly and fever were found in 100%, 91%, and 86.3% of patients respectively on admission in our series.

Laboratory data usually show severe and progressive hypochromic anemia, leukopenia with a predominance of lymphocytes and macrocytes, thrombocytopenia, hypoalbuminemia with polyclonal hypergamaglobulinemia and, at times, even an increase in liver function tests. All patients had pancytopenia and some had abnormal liver function tests.

Diagnosis of VL is made by means of visualizing the organism in giemsa-stained smears of splenic aspirate, liver biopsy, or bone marrow. Examination of bone marrow smears is an easy method to establish the diagnosis of VL and is positive in 22-95% of cases (2,5,7). Specific serology and genomic amplification using polymerase chain reaction are also useful for diagnosis. Confirmation of the diagnoses of our patients were made with the examination of bone marrow.

An ideal drug for VL will lead to a clinical and parasitological cure and avoid adverse effects and relapses. VL usually responds to treatment with a pentavalent antimonial, such as sodium stibogluconate or meglumine antimonate. Side-effects of therapy are dosage and duration dependent and may include painful injection, arthralgia, fever, rash, elevation of hepatic enzymes, gastrointestinal irritation, pancreatitis, renal failure, and particularly cardiac toxicity.

**Table 2.** Hematological and biochemical features of children at admission

| Variable | Median value (SD) | Range |
|---|---|---|
| Hemoglobin (g/dL) | 6.7±2.03 | 3.4-9 |
| Hematocrit (%) | 20.1±7.75 | 9.5-25.7 |
| Leukocyte count ($X10^9$ cells/L) | 4.0±2.18 | 1.2-10.4 |
| Platelets ($X10^9$ cells/L) | 83.52±61.23 | 2-218 |
| Erythrocyte sedimentation rate (mm/h) | 68.5±40.5 | 20-140 |
| Fibrinogen (mg/dL) | 281.15±93.23 | 110-473 |
| Albumin (gr/dL) | 3.06±3.2 | 1.8-4.5 |
| Total protein (g/dL) | 7.53±6.5 | 4.6-10.7 |

**Table 3.** Treatment and outcome of 22 children with visceral leishmaniasis

| Drug | Dosage | Duration of therapy | No. of cases | Clinical response | Treatment failure |
|---|---|---|---|---|---|
| Meglumine antimoniate | 20 mg/kg/day | 20 days | 19 | 16/19 | 21% |
| Liposomal AmB | 3 mg/kg/day | 10 days | 3 | 6/6 | 0% |
| | | | patients, initially 3 more patients added thereafter | | |

When compared with other drugs used in the treatment of VL, treatment with pentavalent antimonial compounds is cheaper as the agent is readily supplied free of charge by the Ministry of Health in Turkey and the clinical response is also much better; hence it is still the antimicrobial of choice for VL. The resistance to this class of drugs is usually seen in India and Africa (1). In our series, the resistance was noted in 21% of patients.

Amphotericin B has good antiprotozoan activity, but-has limitations because of its dosage dependent side-effects, including nephrotoxicity and thrombophlebitis. L-AmB is especially suitable for the treatment of leishmaniasis, because the drug is concentrated in the reticuloendothelial system; however, the cost precludes its wider use in developing countries (8,11,12). All our patients who used L-AmB were cured. After six months of follow up, no relapses were seen.

In conclusion, L-AmB appears to be an effective therapy for VL in children and could be used as a first line treatment. Early detection and appropriate management of complications may reduce morbidity and mortality in childhood VL.

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