

# Pediatric visceral leishmaniasis in Tartous, Syria

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## ABSTRACT

**Background:** Visceral leishmaniasis (VL) type in Syria is *Lishmania infantum*, a fatal incapacitating disease, which is mostly seen in infants. **Subjects and Methods:** Hospital records of 19 children with VL were retrospectively reviewed. The period of the study was from June 2016 to July 2019. **Results:** The median age of the patients was 45.5 months. None was coinfecting with human immunodeficiency virus or known to be immunocompromised. Pallor and anemia were observed in all cases, fever in 13 (68.42%), splenomegaly in 18 (94.7%), hepatomegaly in 11 (57.9%), thrombocytopenia in 15 (78.95%), and leukopenia in nine (47.4%). A bone marrow aspirate was obtained and *Leishmania* amastigotes were detected in all patients. All patients were initially treated with meglumine antimonate; one child did not respond and was treated with lipid formulations of amphotericin B. **Conclusions:** Presentation of VL in the pediatric age group is characterized by pallor, fever, splenomegaly, and hepatomegaly. Hematological and biochemical indices are typical with cytopenias. In all cases, microscopic examination provided a positive diagnosis. Despite recent reports on decreased responses to antimonial drugs of patients with Mediterranean VL, meglumine antimonate treatment appears to be still highly effective in Syria.

**Key words:** Children, *Leishmania infantum*, meglumine antimonate, pediatric, visceral leishmaniasis

## INTRODUCTION

Leishmaniasis consists of a complex of vector-borne diseases caused by more than 20 species of the protozoan genus *Leishmania* and is transmitted by sand fly vectors. Visceral leishmaniasis (VL) is caused primarily by the two related species *Lishmania donovani* and *L. infantum* (synonym *L. chagasi*).<sup>[1]</sup>

*Lishmania infantum* occurs in the Mediterranean (including Spain, France, and Greece), the Middle East, Afghanistan, Iran, Pakistan, and Brazil. In addition, sporadic cases have been reported in Central Asia, China, Mexico, and Central and Latin America outside of Brazil.<sup>[2]</sup>

We present the epidemiological, clinical, hematological, biochemical, and therapeutic characteristics of VL in 19

children, who were admitted to Children's Hospital, between 2016 and 2019.

## SUBJECTS AND METHODS

The details recorded included the patient and family history, area of residence, physical examination, ultrasonography, and laboratory tests included complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, Widal test and Wright test to exclude the typhoid fever, and Brucellosis, respectively. Polymerase chain reactions (PCRs) were carried out in two patients

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to avoid the risks of bone marrow aspiration such as tibial plateau displacement. Diagnosis of VL was established according to the following criteria: (1) clinical picture, (2) laboratory tests, and (3) demonstration of *Leishmania* parasites in Giemsa-stained bone marrow aspirates.

Bone marrow aspirates were obtained from patients for direct examination by microscopy after staining with Giemsa.

Patients were treated with meglumine antimonate (Glucantim) and liposomal amphotericin B.

Meglumine antimonate was administered intramuscular for 28 days at a dosage of 20 mg/kg/day.

Liposomal amphotericin B was administered intravenously at a dosage of 3 mg/kg on days 1, 2, 3, 4, 5, 10, and 21 to the patients who did not respond to the antimonial treatment.

Clinical response was assessed after treatment and was defined as cure (defervescence, normalization of laboratory results, and reduction of spleen and liver size) or failure (persistence of clinical and laboratory findings).

## RESULTS

The patients' age ranged from 10 months to 13 years. All of the patients were human immunodeficiency virus-negative and not immunosuppressed. The cases are listed with the categories of age, sex, local origin, symptoms, clinical findings, methods of diagnosis used, and treatment in Table 1. Hematological and biochemical data of the patients are given in Table 2.

The symptoms of the patients began 5–77 days before diagnosis (median = 29.5, SD = 18.74). Two patients had a concurrent urinary tract infection. Hypersplenism was observed in two patients and they had a transfusion. Detection of *Leishmania* antibodies by the (PCR) antibody test had been carried out in two patients, one of them had a positive result and the other had a negative one. Only one patient needed an additional course of treatment with Glucantim for 15 days without any improvements therefore the treatment was switched to liposomal amphotericin B. No adverse effects were reported. No splenectomy was performed. All children were recovered.

## DISCUSSION

In Syria, two types of Leishmaniasis are observed: *L. infantum* is responsible for infantile Mediterranean VL, whereas *L. tropica* causes cutaneous leishmaniasis (CL).<sup>[3,4]</sup>

Until 1960 cutaneous leishmaniasis prevalence in Syria was restricted to two areas to which it is endemic (Aleppo and Damascus).<sup>[5]</sup> However, in early 2013 41,000 cutaneous leishmaniasis were reported.<sup>[5,6]</sup>

Our data showed that there was an increase in VL cases in Syria.<sup>[7,8]</sup> In our study of VL, the cases originated in north, east, south Tartous due to the randomized population expanding in the last 10 years which increased the contiguity between humans and wild animals which is considered a natural reservoir of leishmaniasis such as dogs and jackals.

The clinical manifestations of VL in Syria suggest that it is the Mediterranean type, which is mostly seen in pediatric age.<sup>[9]</sup> Presentation of VL in this age group is characterized

**Table 1: Clinical manifestations, the amastigotes presence on bone marrow, and treatment of patients**

Cases	Age (months)	Sex	Local origin	Symptoms	SM	HM	LAP	BM	Treatment
1	42	M	North Tartous	Fever, pallor, fatigue	+	+	-	+	Glucantim
2	108	F	East Tartous	Fever, pallor; night sweats, weight loss	+	+	-	+	Glucantim
3	10	M	North Tartous	Fever, pallor	-	-	-	+	Glucantim
4	48	F	North Tartous	Fever	+	-	-	+	Glucantim
5	156	M	South Tartous	Pallor; night sweats, weight loss	+	+	+	+	Glucantim
6	26	F	North Tartous	Pallor; fatigue	+	+	-	+	Glucantim
7	60	M	North Tartous	Fever, pallor	+	+	-	+	Glucantim
8	48	F	East Tartous	Fever, pallor; night sweats	+	+	-	+	Glucantim
9	19	M	North Tartous	Fever, pallor	+	-	-	+	Glucantim
10	36	M	North Tartous	Fever, pallor; fatigue, weight loss	+	+	-	+	Glucantim
11	21	F	East Tartous	Fever, pallor; fatigue	+	+	-	+	Glucantim
12	38	M	South Tartous	Fever, pallor; fatigue	+	+	-	+	Glucantim
13	46	F	East Tartous	Fever, pallor; fatigue, weight loss, night sweats	+	-	-	+	Glucantim
14	84	M	North Tartous	Fever, pallor; fatigue, weight loss	+	-	-	+	Glucantim
15	48	M	South Tartous	Pallor; fatigue, weight loss, night sweats	+	-	+	+	Liposomal amphotericin B
16	19	F	North Tartous	Pallor	+	-	-	+	Glucantim
17	24	M	East Tartous	Fever, pallor; fatigue, weight loss, night sweats	+	+	-	+	Glucantim
18	19	M	North Tartous	Pallor; fatigue	+	-	-	+	Glucantim
19	14	F	North Tartous	Fever, pallor; fatigue, weight loss,	+	+	-	+	Glucantim

M = male, F = female, SM = splenomegaly, HM = hepatomegaly, LAP = lymphadenopathy, BM = bone marrow, + = present, - = absent

**Table 2: Hematological and biochemical features of the patients with visceral leishmaniasis**

Cases	RBC ( $\times 10^6/\mu\text{L}$ )	Hb (g/dl)	Hct %	WBC ( $\times 10^3/\mu\text{L}$ )	Platelet ( $\times 10^3/\mu\text{L}$ )	ESR (mm/h)	CRP (mg/l)	Widal test	Wright test
1	3.7	6.1	19.7	3.7	80		95.5	-	-
2	5.36	11.4	34.7	4.19	250			-	-
3	3.1	5.8	19	4	29		132	-	-
4	3.38	8.4	25.6	5.4	109		101	-	-
5	3.99	8.4	29.4	4.1	137		29.5	-	-
6	2.25	5.1	14.8	3.1	11			-	-
7	3.45	9.5	27.6	10.8	448		0.1	-	-
8	2.85	7.8	23	4.7	200	92	45.9	-	-
9	2.8	5.2	17	3.2	75	85	112	-	-
10	4.72	11.5	33.3	3.52	53	98	37.3	-	-
11	2.3	4.7	15	4.9	39			-	-
12	3.41	8	25	2.3	100	51	52	+	-
13	3.78	8.6	27	3.6	73	120	148	-	-
14	5.8	8.5	28.5	2.9	226	78	107	-	-
15	3.5	5.4	17	6.2	134	90	102.4	-	-
16	3.19	5.9	18.5	4.1	77		2.6	-	-
17	2.75	5.8	18	3.3	78			-	-
18	2.2	5	16	2.9	26			-	-
19	2.65	5.3	20	4.2	49	140	138.3	-	-

RBC = red blood cells, Hb = hemoglobin, Hct = hematocrit, WBC = white blood cells

by pallor, fever, splenomegaly, and hepatomegaly.<sup>[7-9]</sup> These features were observed in the majority of the present infants. None of the current patients presented with dermal aspects such as hyperpigmentation, which is typical of the disease acquired in countries other than India and Bangladesh.<sup>[10,11]</sup>

No therapeutic complications were reported. Hematological and biochemical indices are typical with cytopenias and increased ESR,<sup>[7-9]</sup> all of the patients had anemia, 78.95% of them had thrombocytopenia, 47.46% had leukopenia, and 13 patients out of 14 had increased CRP levels. These hematological abnormalities, observed in this study, are similar to the data reported by other workers.<sup>[7-9]</sup>

Examination of bone marrow smears was positive in 100% of present cases. Thirty-six point 84% of the patients were initially misdiagnosed. The clinical picture of VL may also be the same as that of malaria, typhoid fever, miliary tuberculosis, brucellosis, syphilis, amoebic liver abscess, infectious mononucleosis, lymphoma, and leukemia.<sup>[12,13]</sup>

Leukopenia is predisposing factor to development of secondary infections in patients with VL.<sup>[14]</sup> We also observed that two patients experienced urinary tract infection which presented with fever ( $>39^\circ\text{C}$ ), poor feeding, vomiting, and irritability more than 2 days.<sup>[15]</sup> The treatment included IV fluid replacement and parenteral antibiotics (cephalosporin, amoxicillin-clavulanic acid, and trimethoprim-sulfamethoxazole).<sup>[16]</sup>

The main treatment used in Syria is meglumine antimonate.<sup>[17]</sup>

Another study from Turkey reported that of 40 patients treated with meglumine antimonate, 38 responded well without significant side effects.<sup>[18]</sup>

All of the present patients were treated initially with meglumine antimonate. One child, whose condition did not improve with two courses of meglumine antimonate, recovered when treated with liposomal amphotericin-B<sup>[19]</sup>

Our results show that treatment of VL with antimonials in pediatric patients is a relatively inexpensive, safe, and effective treatment, as reported by other authors.<sup>[18]</sup>

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#### Conflicts of interest

There are no conflicts of interest.

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