RESEARCH ARTICLES

CHILDHOOD VISCERAL LEISHMANIASIS: A REVIEW OF 30 CASES

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SUMMARY

Purpose: *Visceral leishmaniasis (VL) is a chronic parasitic infection which is endemic in the Mediterranean region with a predilection to early childhood. The aim of this study was to investigate the clinical, laboratory and therapeutic results in patients with VL.* ***Methods:*** *We retrospectively analysed 30 cases with VL admitted to the Pediatric Infection Unit of Ondokuz Mayıs University Children's Hospital, between 1985 and 2001.* ***Results:*** *Median age at presentation was 3 years. Fever and splenomegaly were found in all patients. Anemia, leukopenia, thrombocytopenia, and pancytopenia were found in 100%, 53%, 40%, and 37% of the cases, respectively. Bone marrow smear examination and Formol-gel test were positive in 93% of the patients. All patients were treated with meglumine antimonite. No death occurred.* ***Conclusion:*** *We conclude that VL should be kept in mind in patients with fever and splenomegaly, especially in the Mediterranean region.*

Key Words: *Visceral Leishmaniasis, Childhood.*

INTRODUCTION

Visceral leishmaniasis (VL), also called kala-azar, is caused by species of leishmania (L. donovani, L. chagasi, L. infantum) that disseminate hematogenously, infecting macrophages in the spleen, liver, bone marrow, and lymph nodes (1, 2). The leishmanias are obligate intracellular parasites. The infection is zoonotic in most areas. Dogs and other carnivores are the most common reservoirs (3). The leishmanias are estimated to affect 10-50 million people in endemic tropical and subtropical regions on all continents except Australia and Antarctica. The different forms of the disease are distinct in their causes, epidemiological features, transmission, and geographical distribution (1, 4). Here we reviewed 30 cases with VL in childhood and analysed the clinical, laboratory and therapeutic results.

PATIENTS AND METHODS

Between 1985 and 2001, 30 cases of VL were admitted to the Pediatric Infection Unit of Ondokuz Mayıs University Children's Hospital. All patients were hospitalised for fever and splenomegaly. Hematological studies including complete blood and reticulocyte counts, direct Coombs test, peripheral blood and bone marrow smear examinations, biochemical studies including liver and renal function tests, serological tests including HbsAg, HIV, formol-gel test, rheumatoid factor, ANA, anti-DNA, Gruber-Widal test, monospot test and brucella agglutination test, radiological studies including chest x-ray and abdominal ultrasonography,

microbiological studies including blood and urine cultures, immunological studies including immunoglobulin A, M and G, and reaction to PPD were investigated. The diagnosis of VL was based on the clinical and laboratory features, mainly the bone marrow examination that revealed Donovan bodies in macrophages. In cases who were not diagnosed by bone marrow examination, splenic aspiration was performed to confirm the clinical suspicion of kala-azar.

RESULTS

There were 30 cases of VL, with the age range of 10 months to 11 years; the majority were 1 to 5 years old (mean±SD 4.2±1.2 years). Twenty (67%) of the 30 patients were females and 10 (33%) were males. It was difficult to establish the incubation period of kala-azar. The symptoms of the patients had begun 10 days to 3 months before admission (mean±SD 28.9±9.7 days). Fever and splenomegaly were observed in all patients. Hepatomegaly, and less frequently, lymphadenopathy were the most common features after fever and splenomegaly. The symptoms and physical findings of our cases are summarized in Table 1 and 2.

Table 1: The symptoms of patients at admission.

	Number of cases	%
Fever	30	100
Abdominal distension	24	80
Pallor	22	73
Lack of appetite	14	47
Fatigue	10	33
Abdominal pain	8	27
Nonproductive cough	5	17
Diarrhea	3	10
Vomiting	2	7

Table 2: Physical findings of 30 patients with visceral leishmaniasis.

Physical findings	Number of cases	%
Splenomegaly	30	100
Hepatomegaly	24	80
Tachycardia	20	67
Cardiac murmur	16	53
Petechia/echymose	10	33
Lymphadenopathy	6	20
Jaundice	4	13

All patients had anemia and hemoglobin levels ranging from 4.1 g/dl to 8.8 g/dl (mean±SD 5.9±1.4 g/dl). Leukopenia (< 4x109/L), thrombocytopenia (< 100x109/L), and pancytopenia were found in 53%, 40%, and 37% of our cases, respectively. Direct microscopic examination of the bone marrow smear identified leishmania in 93% of cases (28 of 30 cases). Formol-gel tests were positive in 93% of our cases (28 of 30 cases). In two cases who were not diagnosed by bone marrow examination, examination of the smear of splenic aspiration confirmed the diagnosis of VL. Laboratory findings of our cases are shown in Table 3. All patients were treated with meglumine antimonate (Glucantime) for an average of four weeks. Five patients (17%) had pneumonia. Cases who showed evidence of secondary infection received appropriate antibiotic combinations.

Table 3: Laboratory findings of 30 patients with visceral leishmaniasis.

Laboratory findings	Number of cases	%
Anemia	30	100
Formol-gel positivity	28	93
Leukopenia	16	53
Thrombocytopenia	12	40
Pancytopenia	11	37
Hyperglobulinemia (IgG)	12	40
Elevated AST	6	20
Indirect hyperbilirubinemia	4	13
Elevated ALT	4	13

DISCUSSION

Visceral leishmaniasis should be strongly suspected in the patient with prolonged fever, weakness, cachexia, splenomegaly, hepatomegaly, lymphadenopathy, cytopenias, and hypergammaglobulinemia who has had potential exposure in an endemic area. Petechiae, echymoses, and mild edema may appear; jaundice and ascites are rare. The clinical picture may also be consistent with that of malaria, typhoid fever, miliary tuberculosis, schistosomiasis, brucellosis, amebic liver abscess, infectious mononucleosis, lymphoma, and leukaemia (1,5). Fever and splenomegaly were observed in all patients.

When kala-azar is suspected, the diagnosis should be confirmed by biopsy or aspiration of an involved site. Splenic aspiration provides the highest yield (positive in 80% of cases) but may be risky if attempted by an inexperienced physician. It should not be performed in patients with severe thrombocytopenia (platelets < 40x109/L) or coagulopathy. Bone marrow aspiration is the second most useful procedure

(positive in 55-88% of cases), and liver biopsy may also be helpful (positive in 70% of cases). Aspiration of lymph nodes has provided the diagnosis in patients with kala-azar who have lymphadenopathy (1, 6). Bone marrow smears are stained with Wright and Giemsa and it is important to seek the parasites patiently for the early diagnosis of the disease in where kala-azar is suspected. We made the diagnosis in 93% of our cases at the initial examination of the bone marrow smear and the remaining two patients were diagnosed by examination of the aspiration smear of the spleen.

Serologic tests for the diagnosis of kala-azar include complement-fixation, fluorescent antibody, indirect hemagglutination, direct agglutination, and enzyme-linked immunosorbant assay tests. Serologic tests should not be used to the exclusion of other diagnostic tests, since routine tests are not species-specific and may be falsely positive in patients infected with Trypanosoma cruzi. The Montenegro skin test is negative in active kala-azar, only becoming positive after 6-8 weeks of successful therapy. The formol-gel test, a non-specific laboratory finding of the disease, may help the diagnosis and it becomes negative six months after complete recovery (1). The formol-gel test was positive in 93% of our cases.

The major complications leading to death, including hemorrhage and bacterial super infection, result from a decrease in blood elements due to leishmanial infection of the bone marrow and hypersplenism. Anemia, thrombocytopenia, and leukopenia are very common. Hypoalbuminemia, a marked polyclonal hypergammaglobulinemia (mostly IgG), circulating immune complexes and rheumatoid factor are associated with laboratory findings. Without treatment, death usually ensues within two years as a result of infectious complications including pneumonia, tuberculosis, dysentery, septicemia, anemia or hemorrhage (1, 7, 8). Anemia, leukopenia, thrombocytopenia, and pancytopenia were found in 100%, 53%, 40%, and 37% of our cases, respectively. In addition there was pneumonia in five patients who responded well to antibiotic therapy.

The pentavalent antimonial compounds sodium stibogluconate (Pentostam) and meglumine antimonate have been the mainstay of antileishmanial chemotherapy for more than 40 years. Both can be given intravenously or intramuscularly, and these drugs have similar efficacies, toxicities and treatment regimens. For treatment failure or recurrence, repeated courses are recommended. Side effects of therapy occur relatively infrequently. They include fever, rash, cough, and gastrointestinal irritation. Renal insufficiency may develop, and renal function should be controlled; adjustment of dose or interval in patients with renal insufficiency may be recommended (1, 9). Resistant disease can be treated with amphotericin B or pentamidine (10). In the series of Hicsonmez et al., there were two resistant patients who required additional treatment with amphotericin B (11). A variety of other agents such as rifampin, trimethoprim-sulfamethoxazole, allopurinol, and ketoconazole have been employed successfully in isolated cases or in small series of patients (1). All our patients were cured with meglumine antimonate for an average of four weeks and additional treatment was not necessary.

In conclusion, visceral leishmaniasis should be suspected in patients with fever, hepatosplenomegaly and cytopenia, especially in the Mediterranean region.

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