INTRODUCTION

Visceral leishmaniasis (VL) or kala-azar, is most commonly caused by Leishmania donovani, L. infantum and L. chagasi, but on occasion other Leishmania species, such as L. amazonensis are isolated from patients with typical VL (Jeromino et al, 2005). A viscerotropic syndrome caused by L. tropica was identified among a small number of American military personnel who served in the Middle East (Magil et al, 1993). The first case of VL in Iran was reported from the northern part of the country in 1949. Increasing numbers of cases have been diagnosed from other parts of the country (Edrissian et al, 1998). Presently, the major foci of the disease are located in Meshkin-Shahr in the northwest and Farashband in the Fars Province. The Fars Province (site of study) is located in southwestern Iran and consists of two geographic regions (plain and mountainous). The epidemiological form of the disease in Iran is Mediterranean type, with a canine (dog, fox, jackal) reservoir, and the etiologic agent is L. infantum, which is transmitted by the bite of sandflies (Mohebali et al, 2001). We performed a retrospective study of epidemiological, clinical, therapeutic features and laboratory findings of VL in children.

MATERIALS AND METHODS

This study was conducted at hospitals affiliated with the Shiraz University of Medical Sciences in the southwestern part of Iran. Medical records of all children younger than 15 years with a final diagnosis of VL were reviewed from 1996 to 2006. Inclusion criteria were a positive serologic test result [indirect immunofluorescence antibody (IFA) test >1/128] and/or the presence of leishmania in the bone marrow smears or cultures for Leishmania donovani. Patients responded well to Glucantim therapy with a cure rate of 96.7%. Relapse was observed in 8.2%(30) of patients. Mortality in this series was 7.3%. Twenty-three patients died during therapy. Jaundice and grossly deranged liver function tests were bad prognostic signs.
bone marrow aspiration samples. Data recorded included age, sex, nationality, history of travel, fever, weight loss, anorexia, diarrhea, cough, abdominal distention, respiratory symptoms, and temperature at presentation, lymphadenopathy, hepatosplenomegaly, and skin changes. Laboratory records were reviewed for CBC, WBC with differential, ESR, reticulocytes, liver function tests, Widal test for typhoid and brucella, blood film for malaria, blood cultures for bacteria, urinalysis and urine culture, stool for ova and parasites, IFA and chest x-ray. Bone marrow aspirates were taken for Leishmania donovani bodies. Patients were treated with Glucantim 20 mg antimony/kg daily for 21 days. Response was assessed by defervescence, improvement in general condition, weight and anemia and regression of organomegaly. Drug side effects also were reviewed.

RESULTS

There were 62% males and 38% females. Their ages ranged from 3.5 months to 10 years. The disease was most common in those younger than 2 years of age (Table 1). The majority presented in late winter (March and April, 40.2%), followed by spring (23.5%) and a few were seen in the summer (11.3%) and autumn (18%) (Fig 1). About 80% of the children were from rural areas and nomads.

The majority of patients (98.4%) presented with a long history of fever (especially nocturnal type), usually for one month or more. Most patients were febrile on admission, a few (3.8%) were afebrile. Other symptoms included loss of appetite (64.3%), abdominal distention (50.1%), weight loss (40.6%), cough (38.7%), diarrhea (37.5%), abdominal pain (13.8%), jaundice (9.6%), and vomiting (5%). Joint pain, hemoptysis and hematemesis were less common (<0.5%). Ninety-six percent of patients had pallor on examination. Splenomegaly was found in the majority (91.2%), more than 6 cm below the costal margin in 78% of patients. Hepatomegaly was present in 86.6% of patients. Only 10.1% of patients had lymphadenopathy, mostly in the cervical area.

Table 2 shows the main clinical features. The majority of patients (95.3%) were anemic with a hemoglobin ≤ 9. The total WBC was less than 4,000/mm³ in 59.1% of patients, while polymorphonuclear cells were less than 1,500/mm³ in 72% of cases. The lymphocyte count was normal in the majority of patients, but 14% had an increased lymphocyte count (>4,000/mm³). The platelets were less than
Liver function tests were abnormal in 83.5% of patients. The serum aspartate aminotransferase (AST) was increased in 78.5% of cases and alanine aminotransferase (ALT) in 69%. Gross derangement of liver enzymes was a bad prognostic sign. Albumin was less than 3 g/dl in about 80.1%, and globulin was more than 3.5 g/dl in 91.7% of patients. The IFA test was positive in all patients with titers ranging from 1:64 to 1:1,024 (Table 4). A bone marrow smear for Leishmania donovani bodies was positive in 175 patients. All the children were treated with Glucantim. The mean dose was 20 mg antimony /kg/day and the mean duration of treatment was 21 days. Response to Glucantim therapy was excellent with a cure rate of 96.7%.

Fever subsided within the first week and hepatosplenomegaly regressed gradually between the second and third weeks. Relapse was observed in 8.2% (30) of patients. These patients received a second course of Glucantim plus allopurinol or amphotericin B. The mortality rate in this series was 7.3%. Twenty-three patients died during therapy (after receiving 2 to 12 doses of Glucantim). They all had jaundice and markedly elevated liver enzymes (SGOT>1,000). The cause of death in these patients is likely to be secondary bacterial infection (9 cases) and severe bleeding (14 cases). Four patients had positive blood cultures and received appropriate antibiotics in addition to antileishmania therapy.

**DISCUSSION**

The results of the present study indicate...
VL is a relatively common disease in southwestern Iran. Visceral leishmaniasis in southern Iran affects predominantly infants and young children (Soleimanizadeh et al, 1993). Several studies in countries where the infantile form of VL is common (Saudi Arabia, Yemen) show similar results (Rageh, 1990). In Africa and India, the disease affects older children and adults (Pearson and Sousa, 1990).

About 70% of patients were males. Most were from rural areas or were nomads. Because of the age distribution of the cases, the disease in Fars Province (site of study) was thought to be similar to the Mediterranean variety, a zoonosis for which canines are the main reservoir (Shamsizadeh et al, 2006).

A study by Al-Zahrani et al (1989) identified the causative organism isolated from patients in southern Saudi Arabia as L. donovani SL. zymodeme LON-42. This was isolated also in Yemen (Rageh, 1990) and eastern Ethiopia (Maru, 1979). The clinical manifestations of VL exhibited by the children in this sample were similar to those published previously (Elnour et al, 2001).

Seasonal variation was observed in this study. The disease peaked in late winter and spring, then declined sharply in summer. This is similar to that seen in the Mediterranean variety (Manson-Bahr and Apted, 1982).

The predominant clinical features seen in our patients were fever, weight loss, anorexia, abdominal distention and hepatosplenomegaly. This is similar to the Saudi Arabian (Al-juraygan et al, 1992) and Indian experiences (Thakur, 1984). Lymphadenopathy was less common. Lymphadenopathy is commonly seen in the African type of the disease (Maru, 1979).

The main hematological findings were anemia, leukopenia and thrombocytopenia. Anemia is probably due to a combination of iron deficiency, hemolysis and bone marrow suppression (anemia of chronic disease). Neutropenia and thrombocytopenia were likely due to hypersplenism since they were absent in patients who had splenectomy (Maru, 1979). Although the liver was enlarged in most patients, liver enzymes and bilirubin levels showed minimal derangement. Serum albumin was low in the majority, probably as a result of chronic infection and malnutrition. The IFA test was positive in all patients. Cross-reactions occur with leprosy, malaria, schistosomiasis and cutaneous leishmaniasis (Badaro et al, 1983).

Definite diagnosis of visceral leishmaniasis depends on demonstration of amastigotes in the tissue. These results are comparable to those reported in the literature (Ho et al, 1948). Glucantim is the first-choice treatment and the side effects are few. The response to Glucantim in our series was excellent. This is similar to another Iranian (Shamsizadeh et al, 2006) and Saudi Arabian experience (Al-juraygan et al, 1992). The Indian variety of the disease also responds well to therapy (Thakur, 1984). Visceral leishmaniasis in Africa seems to be less responsive (Maru, 1979). The relapse rate after treatment in this study was 8.2%, but in Kenya ranged from 5-36.7%. Patients who do not respond to the initial course of antimony may respond to a second course (Thakur, 1984). The mortality in this series was 7.3%. The mortality rate was similar to that in published literature. Jaundice and markedly deranged liver function were found to be bad prognostic indicators. As death occurred early in the course of therapy, it is unlikely to be related to Glucantim toxicity. In summary, visceral leishmaniasis in Fars Province, Iran bears many clinical similarities to the Indian and Mediterranean types of this disease. All are known to have a good response to therapy.

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REFERENCES


