Visceral Leishmaniasis.

***Professor Dr.Dawood Al-Aazzawi**

VL (kala-azar) typically affects children <5 yr of age in the New World (L. chagasi) and Mediterranean region (L. infantum) and older children and young adults in Africa and Asia (L. donovani).

After inoculation of the organism into the skin by the sandfly, the child may have a completely asymptomatic infection or an oligosymptomatic illness that either resolves spontaneously or evolves into active kala-azar.

Children who are oligosymptomatic have mild constitutional symptoms (malaise, intermittent diarrhea, poor activity tolerance) and intermittent fever; most will have a mildly enlarged liver. In most of these children the illness will resolve without therapy, but in approximately ¼ it will evolve to active kala-azar within 2–8 mo.

Extreme incubation periods of several years have rarely been described. During the 1st few weeks to months of disease evolution the fever is intermittent, there is weakness and loss of energy, and the spleen begins to enlarge.

The classic clinical features of high fever, marked splenomegaly, hepatomegaly, and severe cachexia typically develop approximately 6 mo after the onset of the illness, but a rapid clinical course over 1 mo has been noted in up to 20% of patients in some series. At the terminal stages of kala-azar the hepatosplenomegaly is massive, there is gross wasting, the pancytopenia is profound, and jaundice, edema, and ascites may be present.

Anemia may be severe enough to precipitate heart failure. Bleeding episodes, especially epistaxis, are frequent. The late stage of the illness is often complicated by secondary bacterial infections, which frequently are a cause of death. A younger age at the time of infection and underlying malnutrition may be risk factors for the development and more rapid evolution of active VL. Death occurs in >90% of patients without specific antileishmanial treatment.

A small percentage of patients previously treated for VL develop diffuse skin lesions, a condition known as **post-kala-azar dermal leishmaniasis (PKDL).** These lesions may appear during or shortly after therapy (Africa) or up to several years later (India). The lesions of PKDL are hypopigmented, erythematous, or nodular and commonly involve the face and torso. They may persist for several months or for many years.

***Consultant Pediatrician CABP DCH MB ChB**
Diyala Medical College

Laboratory finding.

Laboratory findings associated with classic kala-azar include anemia (hemoglobin 5–8 mg/dL), thrombocytopenia, leukopenia (2,000–3,000 cells/μL), elevated hepatic transaminase levels, and hyperglobulinemia (>5 g/dL) that is mostly immunoglobulin G (IgG).

Differential diagnosis;

VL should be strongly suspected in the patient with prolonged fever, weakness, cachexia, marked splenomegaly, hepatomegaly, cytopenias, and hypergammaglobulinemia who has had potential exposure in an endemic area. The clinical picture may also be consistent with that of malaria, typhoid fever, miliary tuberculosis, schistosomiasis, brucellosis, amebic liver abscess, infectious mononucleosis, lymphoma, and leukemia.

Diagnosis;

Serologic testing by enzyme immunoassay, indirect fluorescence assay, or direct agglutination is very useful in VL because of the very high level of antileishmanial antibodies. An enzyme-linked immunosorbent assay using a recombinant antigen (K39) has a sensitivity and specificity for VL that is close to 100%. A negative serologic test result in an immunocompetent individual is strong evidence against a diagnosis of VL. Serodiagnostic tests have positive findings in only about half of the patients who are co-infected with HIV.

Definitive diagnosis of leishmaniasis is established by the demonstration of amastigotes in tissue specimens or isolation of the organism by culture.. In patients with VL, smears or cultures of material from **splenic, bone marrow, or lymph node aspirations** are usually diagnostic. In experienced hands, **splenic aspiration** has a higher diagnostic sensitivity, but it is rarely performed in the USA because of the risk for bleeding complications.

Treatment;.

The pentavalent antimony compounds (sodium stibogluconate [**Pentostam**,] and meglumine antimoniate [**Glucantime**] have been the mainstay of antileishmanial chemotherapy for >40 yr. These drugs have similar efficacies, toxicities, and treatment regimens. Currently, for sodium stibogluconate the recommended regimen is 20 mg/kg/day intravenously or intramuscularly for 28 days. Repeated courses of therapy may be necessary in patients with severe VL. An initial clinical response to therapy usually occurs in the 1st week of therapy, but regression of splenomegaly and normalization of cytopenias for VL is usually not evident for weeks to a few months after completion of therapy. When clinical relapses occur, they are usually evident within 2 mo after completion of therapy. Adverse effects of antimony therapy are dose and duration dependent and commonly include fatigue, arthralgias and myalgias (50%), abdominal

discomfort (30%), elevated hepatic transaminase level (30–80%), elevated amylase and lipase levels (almost 100%), mild hematologic changes (slightly decreased leukocyte count, hemoglobin level, and platelet count) (10–30%), and nonspecific T-wave changes on electrocardiography (30%). Sudden death due to cardiac toxicity is extremely rare and usually associated with use of very high doses of pentavalent antimony.

Several other therapies have been used increasingly in the treatment of the leishmaniases. Amphotericin B desoxycholate and the amphotericin lipid formulations are very useful in the treatment of VL . Liposomal amphotericin B (Ambisome, Gilead Sciences, Foster City, California) is approved by the Food and Drug Administration for treatment of VL and should be considered for 1st line therapy in the United States.

Parenteral treatment of VL with the aminoglycoside paromomycin (aminosidine) has efficacy (–95%) similar to that of amphotericin B in India.

Miltefosine, a membrane-activating alkylphospholipid, has been recently developed as the **1st oral treatment** for VL and has a cure rate of 95% in Indian patients with VL when administered orally at 50–100 mg/day for 28 days. Gastrointestinal adverse effects were frequent but did not require discontinuation of the drug. Treatment of LCL with oral drugs has had only modest success.

Prevention;

Personal protective measures should include avoidance of exposure to the nocturnal sandflies and, when necessary, the use of insect repellent and permethrin-impregnated mosquito netting.

Where peridomiciliary transmission is present, community-based residual insecticide spraying has had some success in reducing the prevalence of leishmaniasis, but long-term effects are difficult to maintain.

Control or elimination of infected reservoir hosts (e.g., seropositive domestic dogs) has had limited success.

Several vaccines have been demonstrated to have efficacy in experimental models, and vaccination of humans or domestic dogs may have a role in the control of the leishmaniases in the future.