



Kala-azar/ Leishmaniasis :

objectives : the objectives of this lecture are to know :

1. Symptoms, Causes, Diagnosis, Management& Prevention of kala-azar.

Visceral leishmaniasis (VL), also known as **kala-azar**^[1] **black fever**, and **Dumdum fever**,^[2] is the most severe form of leishmaniasis and, without proper diagnosis and treatment, is associated with high fatality.^[3] Leishmaniasis is a disease caused by protozoan parasites of the genus *Leishmania*.

Post Kala-Azar Dermal Leishmaniasis (PKDL)

Post Kala-Azar Dermal Leishmaniasis is a condition in which *Leishmania donovani* parasites invade skin cells. The parasite

resides and develops there and manifests as dermal lesions. Recently it is believed that PKDL may appear without passing through visceral stage. However, adequate data is yet to be generated on course of PKDL manifestation.

Life cycle[edit]

The life cycle of *Leishmania* is completed in two hosts, humans and sandflies. The adult female sandfly is a bloodsucker, usually feeding at night on sleeping prey. When the fly bites an individual infected with *Leishmania*, the pathogen is ingested along with the prey's blood. The protozoan is in the smaller of its two forms, called an amastigote, which is round, non-motile, and only 3–7 micrometers in diameter. Inside the stomach of the sandfly, the amastigotes quickly transform into elongated and motile forms called the promastigotes. Promastigote is spindle-shaped, triple the size of the amastigote, and has a single flagellum that allows mobility. The promastigotes live extracellularly in the alimentary canal, reproducing asexually, then migrate to the proximal end of the gut where they become poised for a regurgitational transmission. As the fly bites, the promastigotes are released from the proboscis and introduced locally at the bite site.

Once inside the human host, promastigotes invade macrophages. Inside the cells they transform back into the smaller amastigote form. The amastigotes replicate in the most hostile part of the macrophage cell, inside the phagolysosome, whose normal defensive response they are able to prevent. After repeated multiplication, they break down their host cell by sheer pressure of mass, but there is some recent speculation that they are able to

leave the cell by triggering the exocytosis response of the macrophage. The daughter cells protozoans then migrate to fresh cells or through the bloodstream to find new hosts. In this way the infection is progressive, spreading to the host's mononuclear phagocyte system, particularly the spleen and liver. The free amastigotes in peripheral tissues are then ingested by sandfly to enter another cycle.

Symptoms

Recurrent fever intermittent or remittent with often double rise of temperature.

- Loss of appetite, pallor and weight loss with progressive emaciation
- Weakness
- Skin – Dry, thin and scaly and hair may be lost. Light colored person show grayish discoloration of the skin of hands, feet, abdomen and face which gives the Indian name Kala-Azar meaning “Black fever”.
- Anemia – develops rapidly
- Splenomegaly – spleen enlarges rapidly to massive enlargement, usually soft and non-tender.
- Liver – enlargement not to the extent of spleen, soft, smooth surface, sharp edge.

Diagnosis : A case of fever of more than two weeks duration not responding to anti-malarials and antibiotics. Clinical laboratory findings may include anemia, progressive leucopenia thrombocytopenia and hypergammaglobulinemia.

Laboratory:

- Serology tests: A variety of tests are available for diagnosis of Kala-azar. The most commonly used tests based on relative sensitivity; specificity and operational feasibility include Direct Agglutination Test (DAT), rk39 dipstick and ELISA. However all these tests detect IgG antibodies that are relatively long lasting. Aldehyde Test is commonly used but it is a non-specific test. IgM detecting tests are under development and not available for field use.
- Parasite demonstration in bone marrow/spleen/lymph node aspiration or in culture medium is the confirmatory diagnosis. However, sensitivity varies with the organ selected for aspiration. Though spleen aspiration has the highest sensitivity and specificity (considered gold standard) but a skilled professional with appropriate precautions can perform it only at a good hospital facility.

Management

The traditional treatment is with pentavalent antimonials such as sodium stibogluconate and meglumine antimoniate. the WHO recommended treatment is SSG&PM (sodium stibogluconate and paromomycin) developed by Drugs for Neglected Diseases *initiative* (DNDi) in 2010.

Miltefosine is the first oral treatment for this disease. The cure rate of miltefosine in Phase III clinical trials is 95%; Studies in Ethiopia show that it is also effective in Africa. In HIV immunosuppressed people which are coinfecting with leishmaniasis it has shown that

even in resistant cases 2/3 of the people responded to this new treatment. Miltefosine has received approval by the Indian regulatory authorities in 2002, in Germany in 2004 and in U.S.A. in 2014.^[68] It is now registered in many countries.

Prevention

.The most effective method to prevent infection is to protect from sand fly bites. To decrease the risk of being bitten following precautions are suggested:

Outdoors:

-Avoid outdoor activities, especially from dusk to dawn, when sand flies generally are the most active. When outdoors (or in unprotected quarters): Minimize the amount of exposed (uncovered) skin. To the extent that is tolerable in the climate, wear long-sleeved shirts, long pants, and socks; and tuck your shirt into your pants.

-Apply insect repellent to exposed skin and under the ends of sleeves and pant legs. Follow the instructions on the label of the repellent. The most effective repellents generally are those that contain the chemical DEET (N,N–diethylmetatoluamide)

Indoors:

-Stay in well-screened or air-conditioned areas.

-Keep in mind that sand flies are much smaller than mosquitoes and therefore can get through smaller holes.

-Spray living/sleeping areas with an insecticide to kill insects. If you are not sleeping in a well-screened or air-conditioned area, use a bed net and tuck it under your mattress.

-If possible, use a bed net that has been soaked in or sprayed with a pyrethroid-containing insecticide. The same treatment can be applied to screens, curtains, sheets, and clothing (clothing should be retreated after five washings).”

On February 2012, the nonprofit Infectious Disease Research Institute launched the world’s first clinical trial of the visceral leishmaniasis vaccine. The vaccine is a recombinant form of two fused Leishmania parasite proteins with an adjuvant.