

KALA-AZAR -A REVIEW PAPER

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ABSTRACT

Kala-azar, caused by the *Leishmania donovani* parasite and transmitted through sandfly bites, primarily affects impoverished areas in Asia, East Africa, and South America. The disease causes symptoms such as fever, weight loss, and organ enlargement, and can be fatal if left untreated. Diagnosis is made through laboratory testing, and treatment often involves medication such as Amphotericin B. Prevention methods include insecticide use and improved living conditions. While progress has been made in reducing the disease's incidence, drug resistance remains a concern and efforts to eliminate kala azar are ongoing.

Keywords: Leishmaniasis, kala-azar, Life cycle, parasite.

1. INTRODUCTION

Leishmaniasis occurs by protozoan parasites which are transmitted by female phlebotomine sandflies. It affects those people who are malnutrition and have a weak immune system. It is observed that 700000 to 1 million new cases occur every year.[1] Visceral leishmaniasis is sometimes known as systemic leishmaniasis or kala-azar. Black fever, or Kala-azar, is also known as Dum dum fever in Asia. It generally occurs 3 to 6 months after being stung by a sandfly. It infects the reticuloendothelial system and then It damages internal organs, like the spleen and liver and bone marrow, It's the most severe form of the complaint and, left undressed, is generally fatal. This disease is the second-largest parasitic killer in the world after malaria. [2]

There are 3 main types of the disease:

- **Visceral leishmaniasis (VL)**, it is also known as kala-azar, if left untreated then it is fatal in 95% of cases. The main symptoms are irregular bouts of fever, weight loss, enlargement of the spleen and liver, and anaemia. Most cases occur in Brazil, east Africa and India. It has outbreak and mortality potential.
- **Cutaneous leishmaniasis (CL)** is the most common form and causes skin lesions, mainly they are ulcers, These can leave life-long scars and cause serious disability or stigma. About 95% of CL cases occur in the Americas, the Mediterranean basin, the Middle East and central Asia.
- **Mucocutaneous leishmaniasis** leads to the partial or total destruction of mucous membranes of the nose, mouth and throat about 90% of mucocutaneous leishmaniasis cases occur in Bolivia, Brazil, Ethiopia and Peru.

Cutaneous and visceral leishmaniasis are amongst the most ruinous contagious conditions of our time, affecting millions of people worldwide. The treatment of these serious conditions calculate on a many chemotherapeutic agents, utmost of which are of parenteral use and induce severe side- effects. likewise, rates of treatment failure are high and have been linked to medicine resistance in some areas. Then, we reviewed data on current chemotherapy practice in leishmaniasis. medicine resistance and mechanisms of resistance are described as well as the prospects for applying medicine combinations for leishmaniasis chemotherapy. It's clear that efforts for discovering new medicines applicable to leishmaniasis chemotherapy are essential. The main aspects on the colorful way of medicine discovery in the field are bandied.[3]

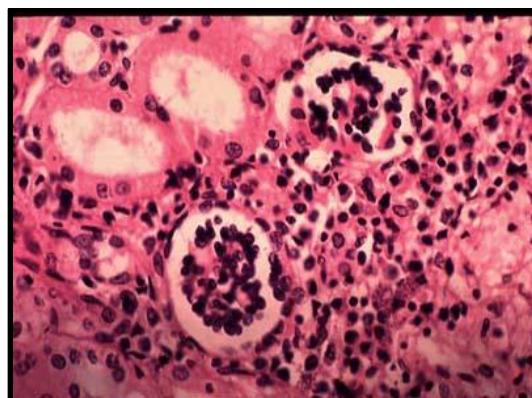


Fig-1 Visceral leishmaniasis

Early symptoms

Leishmania is a parasitic disease that can cause various symptoms, ranging from mild to severe. In the early stages of the disease, the symptoms may include weight loss, weakness, and fever that lasts for weeks or months. Patients may also experience an enlarged spleen, anaemia due to a decrease in the production of blood cells, bleeding, a peculiar darkening of the skin, swollen lymph nodes, loss of interest and desire for everything, and a pale appearance.

If left untreated, the disease can progress to its advanced stage, where the skin becomes dry, rough, and dark or pigmented. Hair may become brittle and fall out. This advanced stage of the disease can be fatal if treatment is not given on time. Therefore, it is essential to seek medical attention if any of these symptoms are experienced, especially if the symptoms persist for a prolonged period. Early diagnosis and treatment can help prevent the disease from progressing to a more severe stage.[4][5]

Cause

Originally, leishmania spongers beget skin blisters or ulcers at the point of the bite. However, it attacks the vulnerable system, If the complaint progresses.Kala-azar presents after two to eight months with further generalised symptoms including dragged fever and weakness.[6]

It's caused by Leishmania donovani(India and Eastern Africa),L. infantum(Mediterranean area), andL. chagasi, which is transmitted by the bite of small blood- stinking sandflies Phlebotomus, and Sergentomyia, common vectors of the Old World.[8][9]

Leishmania parasites which causes skin blisters or ulcers at the point of the bite, and Kala azar presents after two to eight months with further generalized symptoms. Two species of Leishmania are known to give rise to the visceral form of the complaintL. donovani andL. infantum. The nonentity vectors are species of sandfly of the rubric Phlebotomus in the Old World, and of Lutzomyia in the New World.

Sandflies are bitsy canvases , measuring 3- 6 mm long by1.5- 3 mm in periphery, and are set up in tropical or temperate regions throughout the world. The naiads grow in warm, wettish organic matter, making them hard to annihilate. Visceral Leishmaniasis/ kala- azar samples from India revealed the presence of not only the primary causative protozoan sponger, Leishmania donovani, but also co-infection with another protozoan member called Leptomonas seymouri(LS). The ultimate sponger(LS) farther contained a RNA contagion known as Lepsey NLV1[7][8][9][10]

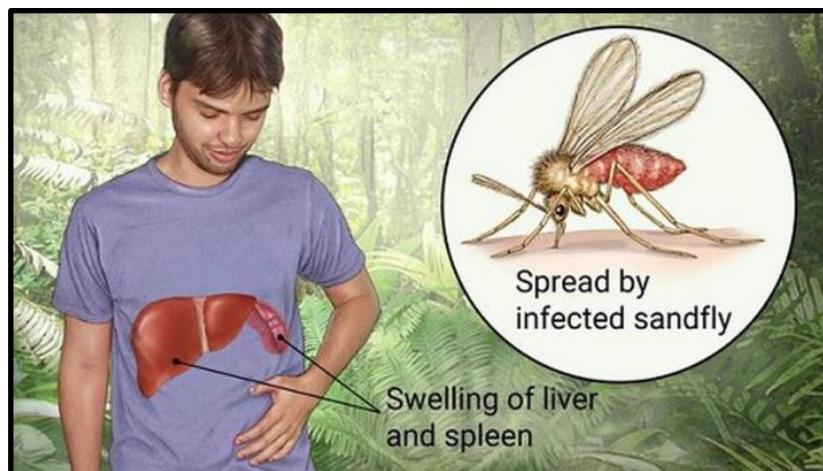


Fig-2 Spread of the disease a vector

Transmission

Leishmania parasites are transmitted through the bites of infected female phlebotomine sandflies, which feed on blood to produce eggs. Some 70 animal species, including humans, can be the source of Leishmania parasites.[1]

Life cycle

The life cycle of Leishmania is completed in two hosts, humans and sandflies. The adult womanish sandfly is a bloodsucker, generally feeding at night on sleeping prey. When the cover bites an individual infected with Leishmania, the pathogen is ingested along with the prey's blood. The protozoan is in the lower of its two forms, called an amastigote, which is round, non-motile, and only 3 – 7 micrometers in periphery. Inside the stomach of the sandfly, the amastigotes snappily transfigure into stretched 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 conduit, reproducing asexually, and also resettle to the proximal end of the gut where they come poised for a regurgitation transmission. As the cover mouthfuls, the promastigotes are released from the conk and introduced locally at the bite point. [12][13] Once inside the mortal host, promastigotes foray into macrophages. Inside the cells, they transfigure back into the lower amastigote form. The amastigotes replicate in the most hostile part of the macrophage cell, inside the phagolysosome, whose normal protective response they're suitable to help. After repeated addition, they break down their host cell by sheer pressure of mass, but there's some recent enterprise that they're suitable to leave the cell by driving the exocytosis response of the macrophage.[14] The son cells protozoans also resettle 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 supplemental apkins are also ingested by sandflies to enter another cycle.[15][16][17][18]

Major Threat factors

Socioeconomic conditions

Poverty increases the threat for leishmaniasis. Poor casing and domestic aseptic conditions(lack of waste operation or open sewerage) may increase sandfly breeding and resting spots, as well as their access to humans. Sandflies are attracted to crowded casing because it's easier to suck people and feed on their blood. mortal geste , similar as sleeping outdoors or on the ground, may increase threat.

Malnutrition Diets

lacking protein- energy, iron, vitamin A and zinc increase the threat that an infection will progress to a full-bloated complaint. Population mobility Pandemics of leishmaniasis frequently do when numerous people who aren't vulnerable move into areas where the transmission is high

Environmental and climate changes

The prevalence of leishmaniasis can be affected by changes in urbanization, deforestation or the mortal irruption into forested areas. Climate change is affecting the spread of leishmaniasis through changes in temperature and downfall, which affect the size and geographic distribution of sandfly populations. Drought, shortage and flood tide also beget migration of people into areas where the transmission of the sponger is high.[1]

Preventions

Visceral leishmaniasis, also known as kala azar, currently has no available vaccines or preventative medicines. However, vaccines are in development[1][20]. The most effective way to protect against infection is to avoid being bitten by infected sandflies. This can be achieved through preventative measures, such as staying indoors during peak sandfly activity hours and wearing protective clothing that covers as much skin as possible. In addition, insect repellents containing DEET can be applied to exposed skin and under the ends of sleeves and pant legs. When outdoors, staying in well-screened or air-conditioned areas can also help. Bed nets that have been treated with pyrethroid-containing insecticides can be used for sleeping, as well as for defences, curtains, waste, and clothing. These measures can help reduce the risk of infection and should be followed when possible. [19]

Diagnosis

The most effective individual tests for leishmaniasis are invasive and potentially dangerous, where towel samples are needed from the spleen, lymph bumps, or bone gist. These tests bear lab installations and specialists not readily available in resource-poor, aboriginal areas. The most common system of diagnosing kala azar is by dipstick testing. still, this system is largely problematic. In aboriginal areas, people can come infected with kala azar but it may not develop into the complaint. thus, no treatment will be needed. Unfortunately, dipstick testing only establishes whether a case is vulnerable to kala azar — so if the sponger is present it would appear that the case has the complaint. Because of this, dipstick testing cannot be used to see if the case is cured, isre-infected, or has regressed.[1] Early diagnosis and effective prompt treatment reduce the prevalence of leishmaniasis and prevent disabilities and death. Access to medicines has improved, and vector control helps to reduce or interrupt transmission. Control methods include insecticide spray, the use of insecticide-treated nets, environmental management and personal protection. Disease surveillance is important to monitor and act during epidemics and situations with high case fatality rates. Control of animal reservoir hosts is complex and should be tailored to the local situation. Social mobilization and strengthening partnerships are essential.[1]

Treatment

The lack of effective and affordable chemotherapy is a major issue for many diseases in developing nations, such as trypanosomiasis and malaria, and parasites or insect vectors are becoming increasingly resistant to existing anti-parasite drugs. Research into potential drug targets takes place in universities, funded by charitable organizations, and

the Product Development Partnership, Drugs for Neglected Diseases initiative is working to develop new treatments for visceral leishmaniasis.[21]

The traditional treatment for visceral leishmaniasis is pentavalent antimonials such as sodium stibogluconate and meglumine antimoniate, but resistance is now common, with rates of resistance as high as 60% in parts of Bihar, India.[22][23]. The treatment of choice in India is amphotericin B[24] in liposomal preparation[25][26], while in East Africa, the WHO recommended treatment is SSG&PM.[27]

Miltefosine is the first oral treatment for leishmaniasis, with a cure rate of 95%. Studies in Ethiopia and Africa have shown that it is effective in HIV immunosuppressed people. It has received approval by Indian regulatory authorities in 2002, in Germany in 2004 and in U.S.A. in 2014,[28] and is now registered in many countries. It is generally better tolerated than other drugs, with gastrointestinal disturbance in the first or second day of treatment. It is available as an oral formulation, avoiding hospitalization and outpatient distribution. However, there is evidence of reduced efficacy after a decade of use [29], and it is teratogenic and cannot be used in women of child-bearing age without anticonception.

Incomplete treatment is a major cause of death from visceral leishmaniasis (VL). The Institute for OneWorld Health has adopted the broad spectrum antibiotic paromomycin for use in treating VL. Paromomycin was first identified in the 1980s and costs US\$15. The Indian government approved it in 2006.[30][31][32]

Treatment responses to visceral leishmaniasis vary by region, and thus the recommended treatments also differ. Together with our mates, we've worked to ameliorate being treatments by developing bettered combination treatments for Africa and new treatments for Asia. We've also worked to make substantiation for safer treatment druthers in Latin America[33]

Management of kala azar

Amphotericin B

Amphotericin B is an antifungal drug that acts on amastigotes by inhibiting sterol synthesis, leading to increased membrane permeability. It was initially used in a dose of 0.5 mg/kg body weight IV on alternate days for a total of 14 infusions, but was associated with high relapse rate. The dose is now recommended for 15 infusions,[34] and is used in patients resistant to antimonials[35] and HIV positive cases[36]. Its major side effects are fever, chills, thrombophlebitis and nephrotoxicity.

Pentavalent antimonials

Pentavalent antimonials are compounds that inhibit glycolysis and fatty acid oxidation in the parasite. One of these compounds, ureastibamine, was first made in India by Brahmachari and was probably the most used of this class of compound earlier in this century[37]. Sodium stibogluconate and meglumine antimonate are now available and the dose recommended by WHO in 1984 was 20 mg/kg body weight per day with a maximum of 850 mg/day for 20 days and double the duration in relapse cases. The drug is now recommended to be used in the above dose for a minimum period of 30 consecutive days[38].

Pentamidine.

Pentamidine is a polyamine which acts by inhibition of kinetoplast DNA function. It is used in cases resistant to antimonials in a dose of 4 mg/kg body weight per day IM or slow IV on alternate days. In the earlier part of the present epidemic, 10-12 injections were shown to produce a cure rate of 98.8% with no relapses. Recent studies have shown that even 20-33 injections may be followed by relapse. Side effects include hypoglycemia, transient hyperglycaemia, permanent insulin dependant diabetes mellitus and cardiac arrhythmias.[39]

Other drugs

Allopurinol, a xanthine oxidase asset, is used in combination with antimonials in a cure of 50 mg/ kg body weight/ day for 4 weeks or further. A combination of sulphadiazine, trimethoprim and metronidazole given orally for 12- 25 weeks has also been set up to be effective in a recent study[40]. Roxithromycin is set up to be as effective as sodium stibogluconate,[41] and sodium aurothiomalate 10 mg originally followed by 20 mg IM on alternate days to a aggregate of 250 mg has also shown good clinical responses[42]. Aminosidine, an aminoglycoside, Ketoconazole acts by dismembering cell membrane of the sponger and has been used in kala azar with promising results[43]. INH, rifampicin, fluoroquinolones and clofazamine are also some of the medicines which have antileishmanial exertion. Levamisole is a immunomodulator and may be of salutary value.

Is there a vaccine for leishmaniasis?

A Leishmaniasis vaccine can prevent leishmaniasis, a Trypanosomatida parasite that spreads from sandflies to humans. As we have seen earlier, no vaccine for humans was available [44][45], but some effective vaccines for dogs

exist[46]. Scientists wish for a vaccine and there is vaccine research. Public health practices can control or eliminate the disease without a vaccine.[45]

2. CONCLUSION

kala-azar, also known as visceral leishmaniasis, is a parasitic disease that primarily affects impoverished areas in Asia, East Africa, and South America. The disease is transmitted through the bites of infected sandflies and can cause symptoms such as fever, weight loss, and organ enlargement. While there are effective treatments for kala-azar, drug resistance remains a growing concern. Prevention efforts such as controlling the sandfly population through insecticide use and improving living conditions have shown some success in reducing the disease's incidence. However, the development of vaccines and preventative medicines is still needed to eliminate this debilitating and potentially fatal illness. Continued efforts are necessary to achieve this goal and to ensure that those at risk for kala-azar have access to effective prevention and treatment options.

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