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Review Article

A Review on Kala Azar

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Introduction

Kala-azar first noticed by western Doctors in 1824 in Jessore, India (now Bangladesh) where it was initially thought to be a form of malaria. Kala-Azar is derived from 'KALA' which means black in Sanskrit and Urdu word AZAR means disease. The disease is named for the darkening of the skin on extremities and abdomen that is a symptom of the Indian form of the disease. The agent of the disease was also first isolated in India by Scottish doctor William Leishman who observed the parasite in spleen smears of soldier who died of the disease in Dumdum, Calcutta, India and hence the name Dumdum fever and Irish Physician Charles Donovan, they working independently and published simultaneously hence the species was named Leishmania Donovani.

Geographic Distribution

Leishmaniasis is endemic in large areas of the tropics, subtropical regions including Africa, Central and South Asia and the Mediterranean region. More than 90% of cases occur in five countries namely India, Bangladesh, Brazil, Nepal and Sudan. Among the South East Asian Region, 200 million people in Bangladesh, India and Nepal are at risk of Kala azar; largely in rural communities with an estimated 100,000 new cases each year. This is 20% of global incidence. The disease is endemic in 52 districts in India, 12 districts in Nepal and 45 districts in Bangladesh. The situation is worsening due to the occurrence of asymptomatic cases Post Kala-azar dermal leishmaniasis (PKDL), under nutrition, and Kala azar / HIV infection. This is the second largest parasitic killer in the World after malaria responsible for estimated 2-4 lakhs infections each year worldwide. The parasite migrates to the internal organs such as liver, spleen and bone marrow and if left untreated, always results in the death.

Epidemiology of Visceral Leishmaniasis (VL)

Agents

Leishmania donovani is the causative agent of Kala azar. Leishmania tropica is the causative agent of Cutaneous leishmaniasis (oriental sore) and L.braziliensis is the causative agent of mucocutaneous lesions. The life cycle is completed in two different hosts- humans and sand flies, in the former, it occurs in an amastigote form which is round, non-motile form called "leishmania bodies" and in the latter as a,spindle-shaped, flagellated motile form called promastigote. Dogs, jackals, foxes, rodents and other mammals are the animal reservoirs. In India kala Azar is considered to be non-zoonotic infection and man is the only reservoir.

Host Factors

There are an estimated 500,000 new cases of VL and more than 50,000 deaths from the disease each year. Migration, lack of control measures and HIV-VL co infection are the three main factors driving the increased incidence of VL.

Age: Children are mostly affected particularly infants below the age of one year and the peak age is 5-9 years.

Sex: Males are affected twice than females

Population: Migrants, labourers and tourists between endemic and non-endemic areas can result in the spread of infection.

Socio-economic status: It usually affects the poorest of the poor.

Occupation: The disease is strongly associated with occupation.Those who are working in farms, forestry, mining and fishing have a great risk of being bitten by sand-flies.

Immunity: HIV Positive, immunocompromised patients are at risk.During recovery phase of Kala-azar there is impairment of cell mediated immunity. Recovery from Kala-azar and oriental sores gives a lasting immunity. High prevalence during and after rains and generally confined to rural areas where breeding of sand flies exist compared to urban areas .It breeds in cracks and crevices in the soil and buildings, tree holes etc. Overcrowding, ill-ventilation and accumulation of organic matter in the environment facilitate transmission. Kala-azar is transmitted from person to person by the bite of sand fly. It may also take place by contamination of the bite wound or by contact when the insect is crushed during the act of feeding. After infective blood meal it becomes infective in 6-9 days(extrinsic incubation period). Transmission has also occur through blood transfusion, contaminated syringes and needles.

Clinical Presentation of VL

Incubation period is generally 2-6 months; range is 10 days to 2 years. Following this, VL patients present signs and symptom of persistent systemic infection including fever, fatigue, weakness, loss of appetite and weight loss and parasitic invasion of the blood and reticuloendothelial system such as enlarged liver, spleen and lymph nodes. Fever is usually associated with rigor and can be intermittent. Fatigue and weakness are worsened by anemia, which is caused by persistent inflammatory state, hypersplenism and sometimes by bleeding.There may be nausea,vomiting and sometimes diarrhoea. Darkening of skin of the face, hands, feet and abdomen is common in India (kala-azar usually mentioned as black sickness). PKDL appears several years after cure of Kala azar. The lesions consist of multiple nodular infiltrations of the skin usually without ulceration. As the disease advances splenomegaly can increase, causing abdominal distension, and pain which is sometimes increased by concomitant hepatomegaly. Signs and symptoms of bacterial co- infection such as pneumonia, diarrhoea or tuberculosis can confuse the clinical picture at the time of initial diagnosis. Symptoms often persist for several weeks to months before patients either seek medical care or die from bacterial co-infections, massive bleeding or severe anemia. Cutaneous leishmaniasis is characterised by painful ulcers in the parts of the body exposed to sand fly bites such as legs, arms or face. More cases are reported last year from Kerala.

Diagnosis

The gold standard for diagnosis is visualisation of the amastigotes in splenic aspirate or bone marrow aspirate. The presence of the parasite LD bodies in the aspirates of liver, spleen, bone marrow, lymph nodes or in the skin is the classical confirmatory test for Visceral Leishmaniasis or Cutaneous Leishmaniasis. Bone marrow biopsy is also recommended. Aldehyde test of Napier is a simple test widely used in India for the diagnosis of Kala-azar. The test usually becomes positive 2-3 months after onset of the disease and reverts to negative 6 months after cure. This test is good for surveillance but not for diagnosis. Serological testing is much more frequently used in areas where leishmaniasis is endemic. Of the numerous serological test available, Direct Agglutination Test (DAT), rk39 dip stick test, ELISA and the Indirect fluorescent antibody test are considered most suitable. The rkd 39 –rapid diagnostic test is based on the recombinant k39 protein. The test is simple to perform and yields result within five minutes. The test should not be used in Kala azar relapse, reinfection and HIV co infection cases. In highly endemic areas, not everyone who becomes infected will actually develop clinical disease. Indeed, up to 32% of the healthy population may test positive, but not require treatment. Likewise,Patients with abnormal immune systems (HIV infection) will have false-negative results. Blood and urine examination is also carried out. In blood ,there will be reduction in the number of WBC and Platelets (Pancytopenia) anemia, and reversed albumin-globulin ratio with grately increased IgG. There will be increased ESR values and urine of VL patient shows the presence of low- molecular- weight carbohydrate antigen which is promising for initial results.

Treatment Strategies

It relies on specific anti leishmanial drugs and management of any concomitant bacterial or parasitic infections, anemia, hypovolemia and malnutrition. The pentavalent antimonials like sodium stibogluconate and meglumine antimoniate were used for the treatment of VL for many years. Conventional Amphotericin B has replaced antimonial as the first line of treatment because it is having side effects like cardiac arrhythmias and pancreatitis.

Treatment Guidelines

First Line Drug

SSG (Sodium stibogluconate) 20 mg/kg body weight daily IM/IV for 20 days. Maximum 850 mg per day.

Miltefosine 100 mg daily in two divided doses for 4 weeks (2.5 mg/kg body wt/day in two divided doses) forage above 12 years and 50 mg for below 12 years.

Second Line Drug

Amphotericin-B 1 mg/kg body weight, intravenous infusion daily or alternate days for 15-20 infusions. SSG and Miltefosine failure, then Liposomal Amphotericine B is considered as the best existing drug against VL and is used as a first-line treatment in Europe and United states.

Kala azar Control Strategies

The current control strategies for VL rely on reservoir and vector control, the use of insecticide-impregnated materials and active case detection and treatment.

Reservoir Control

Since man is the only reservoir of kala azar in India, active and passive case detection and treatment of those found to be infected may be sufficient to abolish the human reservoir and control the disease. House to house surveys and mass surveys may be undertaken in endemic areas for early detection of cases.

Vector Control

Sand flies are the vectors which is responsible for the transmission of cases. It lays eggs on moisture sand. Hence, indoor residual spraying with DDT is considered to be more effective. Residual IRS of houses and animal shelters and all other resting places up to a height of 6feet (2metres) from floor level was shown to be efficacious in India where the vector is restricted to areas in and around the home. DDT (two rounds per year) at the rate of 1-2 per sq metre is considered sufficient to control transmission. Spraying should be preceeded by an assessment of susceptibility. Any sign of resistance in vector should lead to an immediate change in insecticide. BHC should be kept as a second line of defence. Spraying should be repeated at regular intervals to keep down the density of sand flies. For long lasting results, insecticidal spraying should be combined with sanitation measures, viz., elimination of breeding places(eg.Cracks in mud stone walls, rodent burrows, removal of firewood, bricks or rubbish around the houses), location of cattle sheds and poultry at a fair distance from human dwellings and improvement of housing and general sanitation. Insecticide-impregnated bed nets could concomitantly prevent VL and other vector borne diseases such as malaria and Japanese encephalitis.Early diagnosis and treatment This is essential for both individual andfor the community. Adult patients with severe anemia, malnutrition and long duration of illness are at an increased risk for death. Untreated patients act as a reservoir for parasites and contribute to disease transmission in anthraoponotic VL areas. So it is considered an essential component of VL control.

Prevention

There are no vaccines or preventive drugs for VL. The most effective method is to protect from sand flies to decrease the risk of being bitten. These precautionary measures are suggested. Outdoors: Avoid outdoor activities especially from dusk to dawn, when sand flies generally are the most active. Minimize the amount of exposed skin by wearing long-sleeved shirts, long pants and socks. Apply insect repellents especially those containing chemical DEET(N, N-diethylmetatolumide) Indoors: Sand flies are much smaller than mosquitoes and therefore can get through smaller holes. So staying in well-screened areas and insecticide spraying in living areas are preferred. Insecticide repellants in the form of lotions, creams for temporary protection and keeping the environment clean.

Kala azar Elimination Program

A centrally sponsored programme was launched in 1990-91. This has brought down the incidence and death rate of the disease by 75% by the year 2002. In 2002 National health policy was revised and this envisages Kala azar elimination by the year 2010. For attaining this goal programs were carried out for improving the health status of vulnerable groups and risk population living in kala azar endemic areas of India. It also aims to reduce the annual incidence of kala-azar to less than one per 10,000 population at the sub district level preferably by 2010, towards elimination of Kala-azar in South and East Asia Region by 2015.

The strategies for kala-azar elimination includes enhanced case detection and complete treatment using PK39 rapid diagnostic kits and oral Miltefosine for treatment, interruption of transmission through vector control, Capacity building, monitoring, supervision and evaluation of ongoing programs, communication for behavioural impact and IEC activities. Moreover formulate research guidelines on prevention and control of kala-azar.

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