

Review Article

Visceral Leishmaniasis in Children

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Abstract

Leishmaniasis is a protozoan parasitic disease. Leishmaniasis is divided into 3 categories, e.g. Visceral Leishmaniasis (VL), Cutaneous Leishmaniasis (CL) and Mucocutaneous Leishmaniasis (MCL). For VL, the estimated number of new cases per year may have decreased to <100,000, but previous estimates ranged up to 400,000 or more cases. Clinically, the Visceral leishmaniasis is characterized by fever (>14 days), loss of weight, anemia and splenomegaly. Children are affected and may die in two years if left untreated. Diagnosis is confirmed by demonstration of the parasite (*Leishmania donovani*) from bone marrow or splenic aspirate. A number of effective drugs are available to treat the disease including children. Oral drug Miltefosine is highly effective to treat VL in children.

INTRODUCTION

Leishmaniasis is a protozoan parasitic disease. Leishmaniasis is divided into 3 categories, e.g. Visceral Leishmaniasis (VL), Cutaneous Leishmaniasis (CL) and Mucocutaneous Leishmaniasis (MCL). For VL, the estimated number of new cases per year may have decreased to <100,000, but previous estimates ranged up to 400,000 or more cases. For cutaneous leishmaniasis, estimates of the number of new cases per year have ranged from approximately 700,000 to 1.2 million or more. In this communication only VL in children is discussed [1].

VISCERAL LEISHMANIASIS

Visceral Leishmaniasis is prevalent in India, Nepal, Bangladesh, Sudan, Brazil, Mexico, South America and Ethiopia. VL in an endemic area is suspected when a patient presents with fever of > 14 days (malaria excluded), weight loss and splenomegaly. Anaemia is usually present. Liver also becomes enlarged. Hair becomes sparse and fragile. Post Kala-azar Dermal Leishmaniasis (PKDL) is considered as a complication of VL. VL not only affects adults of both sexes but also infects children and produces full-blown disease (Figure 1). Untreated VL cases in children usually die with two years if not treated with effective drug [2,3]. Consequent to the effective Kala-azar Elimination Programme in India, Nepal and Bangladesh in collaboration with World Health organization the number of cases in the three countries have come down drastically.

North Bihar in India had the highest disease burden in the South-East Asia. In the Indian type of VL, children aged between 5 and 15 years are mostly affected. In areas with animal reservoirs, such as the Mediterranean Basin, VL mainly affects children of 1 to 4 years of age; it is caused by *L. infantum* and transmitted



Figure 1 Child with Visceral Leishmaniasis.

by phlebotomine sandflies. In this situation, dogs are the most common reservoir. The African type of VL is again caused by *L. infantum* affecting older children and young adults and rodents are the reservoir hosts. It has been demonstrated that children are at increased risk of getting leishmaniasis than adults in endemic areas [4].

Diagnosis is easy if the disease is suspected. Serological diagnosis is made by screening with rK39 strip test. However, for confirmation of the diagnosis, demonstration of the parasite is required. This can be done by bone marrow, iliac crest or splenic aspirate. *Leishmania donovani* is an intracellular parasite. The parasite invades the reticuloendothelial system. Thrombocytopenia and Leukopenia are observed. Worm

infestation is common particularly in children. Aldehyde test used extensively earlier is no longer recommended since it is highly non-specific [5].

TREATMENT

Supportive treatment

The children are anemic, often severely. Blood transfusion is required with usual precautions for blood transfusion in severe anemia. This is technically called building up of the patient for chemotherapy which is better tolerated when anemia is corrected. In summer months the patients are dehydrated which should be managed by Oral Rehydration Salt Solution (ORS) or Ringer's lactate depending upon the degree of dehydration. Worm infestation is common in children and deworming should be done. Albendazole is safe in children.

Specific treatment

Chemotherapy: It is effective and saves the life of the patient. Currently a number of drugs are available.

Sodium stibogluconate was the sheet anchor of anti-leishmanial therapy for the past 6-7 decades. It was a very effective and relatively safe drug. However, intramuscular injections were extremely painful. The development of drug resistance among the *L. donovani*, particularly in the Indian State of North Bihar with diminished effectiveness of the drug necessitated its discontinuation in the area. The drug resistance is to the tune of 60%. It is consensus and recommendation that in those areas where the *L. donovani* is sensitive to Sodium Stibogluconate, the drug may be used, since it is cheap and easily available. As the resistance increased, physicians escalated the dose with the intention to overcome the drug resistance. The result was that cardiotoxicity of the drug increased and some patients died [6].

Miltefosine is the first oral drug that was developed against leishmaniasis. Initial trial in adults was highly encouraging and efficacy exceeded 95%. Side-effects included those primarily related to gastrointestinal tract e.g. nausea, vomiting, abdominal cramps, diarrhoea etc. Efficacy and safety of the drug in adults prompted to undertake trial in children in several centres in Bihar. The drug was well tolerated in children and efficacy was ~95%. The dose in children was 2.5mg/kg/day in 2 divided doses after meals. The drug was given for a period of 28 days. A phase 4 study of Miltefosine demonstrated that the drug could be dispensed in an outpatient' setting with reasonably high compliance. In view of the encouraging results of this study, Miltefosine was taken up as the first-line drug of choice by the Regional Technical Advisory Group (RTAG) of the South-East Asia Regional office off World Health Organization, New Delhi, for the Kala-azar Elimination Programme of India, Nepal and Bangladesh. Meanwhile Bhutan also reported few indigenous cases of VL. Subsequently, Miltefosine was replaced by Liposomal Amphotericin B in the programme. There is no doubt that Lipid Amphotericin B was the best effective in single dose and safe drug for the treatment of VL, but the switch over required creation of fresh infrastructure including cold chain and training of health workers to administer lipid amphotericin B parenterally taking safe infection control measures. At that point of time arguments were made that the decision could have been delayed because

the programme was going well and we may lose the efficacy of the most effective drug (lipid amphotericin B) for the treatment of VL [7].

Liposomal Amphotericin B is a safe and highly effective anti-leishmanial drug even when used as a single dose of 10 mg/kg. The drug has to be given by slow intravenous injection. It was recommended as the drug of choice for the Kala-azar Elimination Programme from India, Nepal and Bangladesh. It is equally effective and safe in children [8, 9].

Amphotericin B is also highly effective in the treatment of VL and has to be given by intravenous infusions. The drug is nephro and ototoxic. Many physicians use this drug for the treatment of VL in children. Paromomycin was developed as an anti-leishmanial drug almost at the same time as Miltefosine. Paromomycin is also highly effective drug.

Combination therapy using single dose of Lipid amphotericin B plus short course of Miltefosine or Paromomycin or only single dose of Lipid Amphotericin B had undergone clinical trial. Combination therapy was found to be about 95% effective. It was also proposed that since it is a combination therapy development of drug resistance may be avoided or delayed. Combination therapy has been suggested as the first-line drug for VL.

Nutrition: Children with VL in VL-endemic areas are often malnourished. Improvement of nutrition of the individual patient as well as the community is of paramount importance. Vitamin and micronutrient supplementation is essential. Growth retardation occurs in children suffering from VL.

Vaccine: A preventive and a therapeutic vaccine are required as a long-term strategy. Although currently there is no such vaccine, efforts are underway to develop suitable vaccines.

HIV/VL co-infection in children: HIV can be transmitted from HIV infected mother to child. The HIV positive children in VL endemic areas can develop VL also. To treat such children, a large number of drugs are required which may cause drug-drug reaction and pose therapeutic challenge.

CONCLUSION

VL in children is an important cause of morbidity and mortality in VL-endemic areas. Untreated patients die in about 2 years. Effective treatment is available. No vaccine is available. Nutritional care is important for VL affected children. Blood transfusion and deworming are important supportive treatment. Kala-azar elimination programme has drastically reduced the incidence of V cases in children in Nepal, Bangladesh and India.

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