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Mini Review

Leishmaniasis- On the Verge of Elimination in SEA Region

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Abstract

Leishmaniasis or Kala-azar is characterized by prolonged fever, splenomegaly and anemia. Post-kala-azar Dermal Leishmaniasis (PKDL) is considered as a complication of the disease. Stibogluconate, a drug which once was the cornerstone of therapy, became ineffective with drug resistance of about 60% in Bihar, India. Miltefosine, Paromomycin, Amphotericin B and Lipid Amphotericin B are drugs which may be used to treat VL. VL elimination from India, Nepal and Bangladesh undertaken in 2005 is progressing well.

INTRODUCTION

Leishmaniasis is clinically seen in Visceral (VL), Cutaneous (CL) and Mucocutaneous forms (MCL), and Post-kala-azar Dermal Leishmaniasis (PKDL) is considered as a complication of the disease. VL is caused by *Leishmania donovani, a* protozoan parasite. VL is manifested by prolonged fever (> 14 days), anemia, loss of body weight and splenomegaly. Other features include hepatic enlargement, loss of hair, and skin changes (blackening). Infestation of intestinal parasites is common. Lung infection and tuberculosis of the lung are well known. In the present communication, briefly, the diagnosis, management and elimination of the disease are discussed. The VL patient may treated by Stibogluconate, Miltefosine, Amphotericin B, Lipid Amphotericin B and Paromomycin. VL elimination from India, Nepal and Bangladesh undertaken in 2005 is progressing well.

DIAGNOSIS

A case of VL is suspected in an endemic area by the occurrence of prolonged fever and splenomegaly (Malaria excluded). The suspect case is subjected to a serological test (rK39) and if the test is positive, it is considered as a case of VL. This is a programmatically accepted definition. Confirmation is done by demonstration of the intracellular parasite in specimens obtained by bone marrow or iliac crest puncture. Other laboratory parameters include leucopenia, anemia, thrombocytopenia, low serum albumin, rise of serum enzymes like SGOT and SGPT. Skin changes do occur in patients with Post-kala-azar Dermal Leishmaniasis (PKDL) [1] occurs in macular, papular, nodular and papulo-nodular forms. PKDL occurs, after a VL patient is cured, during the next 1 to 10 years. Rarely, the PKDL forms occur in the active phase of the disease. Demonstration of L.D bodies in tissue obtained by biopsy from the lesions confirms the diagnosis along with the clinical features. PKDL cases are considered to be a potential reservoir and continue to transmit the disease to others. Asymptomatic cases are likely to play a significant role

MANAGEMENT

In the history of drug development, there were ups and down in context of development of new drugs and emergence of drug resistance. For quite long time Sodium stibogluconate enjoyed the status of drug of choice for the treatment of VL and PKDL, although long courses were required for the latter. Initially the drug was given in a dose of 20 mg/kg body weight and after some years, large-scale resistance developed so much so that even after escalating the dose to 30 mg/kg, the response was not satisfactory. Simultaneous, a potential cardio-toxicity of the drug increased and often this was fatal. In India, Brahmachari developed an anti-leishmanial drug known as Urea Stibamine, which was effective and saved many lives of VL patients. There were no oral drugs available till recently when Miltefosine became available. The drug was developed in Bihar, the State of India, where in its northern part VL is hyper-endemic. The drug soon after its development was marketed in India, Germany, Bangladesh and Nepal. It is reported that in subsequent years the appearance of significant resistance of the parasite to the drug. In a phase 4 trial [2-4] of the drug in Bihar, it was revealed that the drug may manifest few serious toxic effects (renal failure, hepatotoxicity). Paromomycin [5], an amino-glycoside, was developed and was safe and effective.

An anti-fungal drug (amphotericin B) has been found to be effective and relatively safe for the treatment of VL and PKDL. Amphotericin B has nephrotoxicity. When resistance to stibogluconate became significant, amphotericin B became the First-nine treatment for VL. This was followed by development of lipid *amphotericin B* [6,7] which is perhaps the safest anti-leishmanial drug so far developed. The dose of the drug is 3 mg/kg/day for 5 days or 5 mg/kg/day for 3 days. Single dose of 10 mg/kg/day was found to be > 95% effective. The side -effects of the drug are minimal. Only drawback of the drug is that it has to be given by intravenous route and generator support is required in case of power failure. Sitamaquine has recently been subjected

to evaluation and found to be promising. Attempts are being made to develop a therapeutic or preventive vaccine.

Elimination of VL or Kala-azar

In the Indian sub-continent, VL is restricted to 4 states (Bihar, West Bengal, Utterpradesh, Jharkhand), in several districts in Bangladesh and Nepal. Recently, a small focus of VL has been detected in Bhutan. The availability of the oral drug (Miltefosine) and a user-friendly, field-tested diagnostic test (rK39) made the three countries (joined later by Bhutan, Thailand and Sri Lanka) to take up the initiative to eliminate the disease from their countries. This concept was reinforced by the finding that there were no extra human reservoirs of the parasite and vector control with an insecticide (DDT, Pyrithroids) was feasible [8-10]. WHO agreed to provide technical assistance and operational research. The programme is progressing well towards its target (< 1 case per 10000 populations) and Nepal has already eliminated the disease from the country. Bangladesh and India are moving steadily towards the elimination goal. In the post elimination phase surveillance, intensive search for case search, detection and treatment of asymptomatic infection (infected but no symptoms of the disease), but over a period of time may develop full-blown disease) and PKDL.

CONCLUSION

Since in the absence of a suitable vaccine, it may be difficult to eradicate the disease, but elimination may be feasible in places where it is localized and limited number of reservoirs. A safe rug and proper vector control method should be used. Finally, research is important to develop newer tools. Drug and vector resistances are problematic. Resource mobilization and collaboration are crucial to success. The most gratifying aspect is that donors recently have become interested in control of Kala-azar, a neglected disease of poverty (NTD).

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