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Case Report

Amphotericin -B in the Management of Resistant Kala-azar

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Abstract

Kala-azar is a re-emerging global problem. Recent years have shown a notable improvement in both morbidity and mortality in patients with Kala-azar. Much of this benefit is derived from the use of the newer therapeutic agents. Among these Amphotericin-B deoxycholate for the treatment of resistant Kala-azar is very effective and offer many advantages. We report a case of resistant Kala-azar where we used Amphotericin-B deoxycholate and it showed a very good clinical and parasitological response.

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Introduction

Kala-azar or visceral leishmaniasis is a chronic febrile disease caused by protozoal parasite *Leishmania donovani* which is transmitted by bite of female phlebotomine sand fly that usually bite at dusk. In Bangladesh *L. donovani* has no animal reservoir; human serves as both host and reservoir[1]. Now it is a re-emerging public health problem, which affect rural poor living in mud house and having cattle, sheds around them and juvenile ages are more vulnerable. Kala-azar was first noticed in epidemic form in our country in the Garo hills areas of Bangladesh and adjacent Brahmaputra Valley of Asam in 1880[2]. It has significant morbidity and mortality, which can cause secondary infection (Pneumonia, TB), anaemia, bleeding gastroenteritis, bacillary dysentery, and liver disease. Rarely cancrum oris and case fatality 19% in women and 6-8% in men[3].

To reduce this morbidity and mortality some drugs are used in appropriate dose and duration e.g. sodium stibogluconate, meglumine antimoniate, pentamidine isothionate, Amphotericin-B deoxycholate, Liposomal amphotericin (less toxic), Miltefosine, Ketoconazole, Itraconazole, Dapsone, Allupurinol etc. But it is not possible to make universal recommendations of a single treatment regimen that would be optimal in all cases. Many treatment regimens are associated with significant failure rate and toxicity and drug resistance is a big burden especially for Indian subcontinent and HIV coninfection[4]. Throughout the world, pentavalent antimonial compound (Sb) have been the mainstay of antileishmanial therapy for more then 50 years

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and has been highly effective. But in the early 1980s reports of ineffectiveness emerged and dose increased to 20mg/kg for 30-40 days. This regimen was effective for some years and further a proportion of patients unresponsive to (Sb) have steadily increased[5]. Resistant Kala-azar is a newly emerging problem in the Indian subcontinent. Important reasons for drug resistance are rampant use of sub therapeutic dose, incomplete duration of treatment and substandard drugs Pentamidine was the first drug to be used and cured 99% of these refractory patients, but over time even with double the amount of initial doses, it cures only 69-78% patients now and its use has largely been abandoned in India. Amphotericin-B deoxycholate is very good and relatively a bit expensive but less toxic drug being used it has the highest cure rate (99%)[9]. Recent study shows that amphotericin-B is the first line of drug in the treatment of visceral leishmaniasis, not for resistant cases only[6]. Patients who respond to therapy usually become afebrile and begin to feel much better within a week of commencing therapy, although reduction in spleen size can be delayed by months[7].

Case report

Miss S, a 16 years old young girl hailing from Godagari, Rajshahi was admitted into Rajshahi Medical College Hospital in MU-III on 10 March 2005 with the complaints of fever for the last 4 months and epistaxis for several times. On examination, she was febrile, anaemic with huge enlargement of the spleen measuring about 17 cm from the Lt. costal margin along its long axis. She gave history of treatment with 2 courses of Inj. Sodium Stibogluconate for 20 days apart. On the first occasion Inj. Stibatin was given at a dose of 15 mg/kg body wt/dose for 21 days. In the 2nd course 20 mg/kg body wt/dose of Inj. Stibatin was given I/V for 30 days. But unfortunately L D bodies in the splenic aspirate were persistently positive after completion of these two courses and she developed epistaxis. After admission, investigations showed that her haemoglobin was 6.8 mg/dl, ESR-115 mm in 1st hour; total white cell count was 1500/mm^3 with relative Lymphocytosis. Platelet count was 2,40,000/mm^3. Her prothrombin time was 17 sec (control 12 sec) but other liver function tests, renal function tests were within normal limits. Sonography of the abdomen showed gross splenomegaly and echocardiogram revealed mild pericardial effusion.

Subsequently patient was transfused fresh human blood to correct anaemia and Inj. Amphotericin-B (Fungizone) was started. On the 1st day Inj. Fungizone (50 mg/vial) 0.2 ml (1 mg) diluted with 10 c.c. 5% Dextrose aqua (DA) was given I/V slowly in 100 c.c. 5% DA over 20 minutes. Then on 2nd day 2 ml (10 mg) Inj. Fungizone diluted with 250 ml 5% DA was given I/V 100 ml/hr. The dose of Inj. Fungizone was gradually increased (10 mg/day) over four days and full dose was given on 5th day as 10 ml (50 mg) in 250 cc of 5% DA I/V 100 ml/hr. After starting the full dose she developed high fever and shivering which was managed by reducing the rate of infusion and by giving for a total period 14 days with higher dilution (500 c.c. of 5% DA) I/V over a period of 4 hours. The whole course of treatment was uneventful except febrile reaction, nausea, and anorexia. Gum bleeding stopped and the spleen gradually decreased in size. After completing the course the girl was in good health without any fever, shivering, epistaxis, and her spleen size was about 1 cm from the left costal margin in its long axis at the end the treatment. Splenic aspiration was done but LD body was absent.

Discussion

Kala-azar is a re-emerging global problem but yet not a threat for Bangladesh. Recent years have shown a notable improvement in both morbidity and mortality in patients with Kala-azar. Much of this benefit is derived from the use of the newer therapeutic agents [6]. Among these Amphotericin-B deoxycholate for the treatment of resistant Kala-azar is very effective and offer many advantages[8]. Despite higher treatment cost (8,000-10,000 Taka), the advantages of this drug are more than any other drugs used in resistant Kala-azar, high cure rate (99%), less side effects, less hospital stay. Our patient stayed in hospital for 17 days, but studies show 10 days treatment also have complete cure[9]. As regards the patient, the economic status of the patient must be taken into good

consideration in the treatment of resistant Kala-azar in our socio-economic condition. So this may partially explain the benefits of Amphotericin-B deoxycholate over other drugs on mortality and morbidity in the patients with resistant Kala-azar.

Conclusion

Number of cases of resistant Kala-azar is increasing day by day. Though this is our first experience with Inj. Amphotericin-B in resistant Kala-azar but the management of this patient was uneventful with good recovery. So we can use it in resistant cases of visceral leishmaniasis.

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