A New Breakthrough in Treatment of Visceral Leishmaniasis in Children

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Abstract

Fifty cases of visceral leishmaniasis were admitted in Children's Hospital, Islamabad. Common clinical features were fever (100%), splenomegaly (100%), hepatomegaly (100%), anaemia (96%), abdominal distension (40%), bronchopneumonia (26%) and bleeding diathesis (22%). Hb was below 7.0 G/dl in 80%, white cell count below 4x109/cmm in 88% and platelet count below 100x109/c4mm in 86%. All the patients showed leislunania donovani bodies in the marrow smears. Fourteen patients were treated with aminosidme (15 mg/kg), intramuscularly daily for 4 weeks. All responded dramatically and none of them went into relapse in a year's follow-up. No side-effects were observed. Aininosidine can therefore, be recommended as a treatment of choice for visceral leishmaniasis in children (JPMA 45:155, 1995).

Introduction

Visceral leishmaniasis, also known as Kala-Azaroccurs in many sub-tropical and tropical areas, like Mediterranean, Central Asia, China, Middle East, India, Northern Pakistan, Africa and South as well as Central America. Leishmaniasis represents a major health hazard for children and should be specially emphasized since this age group is not only more vulnerable[1] ,but is also the group in which the risk of failure of diagnosis is the highest. If left untreated, it has a high mortality rate[2]. In Pakistan, visceral leishrnaniasis was first reported from the northern areas in the late fifties and early sixties[3]. The disease was thought to be restricted to foci in Gilgit and Skurdu, but since early eighties, cases of visceral leishmaniasis in children have been reported not only from different areas of AzadKashmir, but also in some extreme north-eastern areas of Punjab as well as nearby localities of NWFP[4,5].

Visceral leishnrnniasis in children is endemic in some areas of Azad Kashmir[6] and afew areas of northern Punjab and NWFP. In addition, tourists visiting the endemic areas are also at risk and the disease may be taken to other areas of Pakistan. In fact two cases of visceral leishmaniasis have already been reported from Karachi; one of them never left the city[5]. In Multan there was an epidemic of cutaneous leishmaniasis in 1971-1972[7]. As regards the vector of the disease, a sand fly-Phlebotomus? apatasii is responsible for spread of disease in Azad Kashmir[8]. In northern areas of the country, the sand fly identified is Phiebotomus burneyi[9]. dogs, foxes and jackals are important reservoirs of infection[10].Visceral leishmaniasis in Pakistan, has no uniform and clearly defined treatment protocol. However, cases have been treated with pentavalent antirnomals with good results. The major problem is not only of availability of these drugs, but also the cost is much bigger a problem. Furthermore, prolonged hospitalization of these patients adds another burden on already poorly existing health facilities.

At Children's Hospital, Islamabad, patients of visceral leishmaniasis were treated withPentostam (Sodium Stibogluconate) in recommended doses. This drug suddenly became unavailable in the market, therefore, we started looking for alternative and cheaper medication. Aminosidine (Gabromy-cin) has been used in Kenya with good results in adults[11]. This study reports the clinical pattern and the

results of a new and cheaper treatment (aminosidine) of visceral leishmaniasis in children.

Patients and Methods

Between 1987 and 1991, fifty cases of visceral leishmaniasis were admitted in Children's Hospital, Islamabad. In every case, detailed clinical notes were entered in a profonna, especially relating to age, sex, duration of illness, fever, pallor, abdominal distension, hepatomegaly, splenomegaly, bleeding diathesis, cough and nutritional status. A complete blood picture (including haemoglobin, total leucocyte count, platelet count and differential leucocyte count) was performed. In all the patients, bone marrow was aspirated, using Saleh's bone marrow aspiration needle: the smears were stained by May-Grunwald-Giemsa stain. In 34 cases immuno-fluorescent test for Leishmania denovanii (IFT) was also perfonned. Thirty-six cases were treated with pentostam (Sodium Stibo- gluconate) and 14 with aminosidine (Gabromycin) 15 mg/kg, intramuscularly. The effect and clinical response to aminosidine, especially in relation to fever, regression of spleen, peripheral blood picture and finally on bone marrow biopsy was evaluated. Since aminosidine is an aminoglycoside, so side effects were monitored. All the patients were closely watched for renal functions and hearing problems.

Results

Age and Sex Distribution

Of 50 cases of visceral leishmaniasis, 36 were male and 14 female with a male:female ratio of 2.3:1. Majority of patients (80%) were between 1 to 5 years of age; 10% were below one year and 10% more than 5 years. The mean age was 2.6 years. Majority of patients were from northern areas. Bagh, Rawalakot and Muzaffarabad had maximum number of cases. Three cases were from Muree, one each from GujarKhan and Karak (Table I).

Table I. Geographical distribution of 50 cases of visceral leishmaniasis.

Area		No. of cases
Bagh	Azad Kashmir	11
Rawlakot	Azad Kashmir	10
Muzaffarabad	Azad Kashmir	8
Poonch	Azad Kashmir	5
Kotli	Azad Kashmir	4
Chakar	Azad Kashmir	3
Rangla	Azad Kashmir	2
Dhirkot	Azad Kashmir	2
Muree	Punjab	3
Gujar Khan	Punjab	1
Karak	NWFP	1
Total		50

Fever, splenomegaly and hepatomegaly were invariably present. Other common manifestations were anemia (96%), abdominal distension (40%), bronchopneumonia (26%), bleeding diathesis (22%) and lymphadenopathy (18%) as shown in Table II.

Table II. Clinical features in 50 cases of visceral leishmaniasis.

Clinical feature	No. of patients	Percentage
Fever	50	100
Splenomegaly	50	100
a. Massive (>10 cm)	12	
b. Marked (7-10 cm)	18	
c. Moderate (4-6 cm)	13	
d. Sight (1-3 cm)	5	
Hepatomegaly (Moderate)	50	100
Anaemia	48	96
Abdominal distension	20	40
Bronchopneumonia	13	26
Bleeding dialysis	11	22
Loose stool	11	22
Lymphadenopathy	9	18
Vomiting	8	16
Generalized werbus	6	12
Abdominal pain	5	10
Bruises/purpuric spots	5	10
Weight loss	4	8
Kwashiorkor	2	4
Generalized swelling	2	4

Since majority of the patients were from northern areas with prolonged fever and hepatosplenomegaly, it was presumedthatthis clinical triad (Azad Kashrnir+ Prolonged fever + Hepatosplenomegaly) indicated visceral leishmamasis unless proven otherwise. Leishmaniasis being chronic ailment was associated with loss of appetite and weight loss.

Table III. Visceral leishmaniasis in children: Nutritional status.

	(Gomez classification)	
	Number	Percentage
PCM I	24	48
PCM II	16	32
PCM III	8	16

*PCM= Protein calorie malnutrition

Table Ill shows the nutritional status of patients according to Gomez Classification. Laboratory investigations (Table IV)<

Table IV. Laboratory investigation in cases of visceral leishmaniasis.

Lab. Investigation	Number of cases	Percentage
TLC (Less than 5000/cmm.)	44	88
(Less than 4000/cmm)	40	80
Neutrophils (less than 25%)	33	66
(less than 30%)	38	76
Lymphocytes (more than 70%)	38	76
Platelets (less than 100,000 cmm)	43	86
Haemoglobin (less than 7 G/dl)	40	80
ESR (more than 50)	44	88
(more than 80)	38	76

showed leucopema and haemoglobin below 7.0 grams/dl in 80%, platelet count below 100x109/L in 86% and increase in erythrocyte sedimentation rate in 88% of cases. Ifl all the cases, Leishmaniadonovani bodies were diagnostically seen in bone marrow smears. Immunofluorescent test performed in 34 patients at National Institute of Health, Islamabad was positive in 85.2% of cases. Cases of visceral leishmaniasis were treated with Pentostam (Sodium Stibogluconate) in recommended doses, till it became unavailable. As a substitute Aminosidine (Gabromycin) used in Kenya with good results in adults was administered in 14 new cases, in a dosage of 15 mg/kg intramuscularly daily for four weeks and response was monitored regularly. Fever settled in 7-10 days and spleen started regressing to normal size by 3rd week. There were no relapses in a follow up for one year. Since Aminosidine is an Aminoglycoside, so side effects were monitored. Renal functions and hearing test revealed no damage.

Discussion

Leishmaniasis is endemic in Northern Areas of Pakistan[3,4]. There are few cases reported from Punjab and one from Karak (NWFP) in our study. Sodium Stibogluconate (Pentostam) has remained the treatment of choice[8]. The results of treatment with Aminosidine alone and in combination with Pentostam reported by Change et al[11] were encouraging though this was mainly in adults. It is an aminoglycoside which has been givenby 1/M injections i.e., 15 mg/kg perdose for 4 weeks. Results were very gratifying with fever settling down in 7 days and other symptoms improvedby 10th day. All the hematological changes reversed back to normal at the end of treatment. Enlarged spleen regressed to normal size by the end of 3rd week. There were no relapses in 1 year follow-up. Aminosidine has high affinity for ribosomal subunit 30 s, causing a mis-reading of messenger RNA, giving rise to production of anomalous proteins. This is potent antibacterial agent aganst both gram positive and gram negative organisms. Absence of serious side effects of nephrotoxicity or ototoxicity in our 14 patients were very encouraging.

The most important factor in our country is cost of treatment per course. A course of aminosidine was only Rs.400/-, as compared to Rs.2000/- in case of pentostam. Due to an excellent response in terms of clinical recovery and splemc regression, no side effects and easy affordability, we recommend aminosidine as treatment of choice for visceral leishmaniasis in children.

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