Original Article

Children with Visceral Leishmaniasis Presented to Omdurman Emergency Hospital for Children

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ABSTRACT

We describe cases of visceral leishmaniasis (VL) from new endemic area in White Nile State on the west bank of the White Nile River in the central region of the Sudan. This area was not considered previously as endemic of visceral leishmaniasis apart from sporadic cases described in 1988. In total, 132 patients between 2- 14 years old from 5 villages presented with prolonged fever and/or spleenomegaly were diagnosed as visceral leishmaniasis based on finding the parasite from bone marrow aspirate (leishmania donovani (LD) bodies). Later direct agglutination test (DAT) and enzyme-linked immunosorbent assay (ELISA) performed to all patients. In 80 of the patients in whom lymphadenopathy is marked aspiration from lymph nodes also performed. The reported incidence rate was 17.6 % (n= 750). Of the 132 patients, 93.1% had splenomegaly, 91.6% suffer prolonged fever, 81.8% with hepatomegaly, 74.2% with generalized lymphoadenopathy, 27.2% suffer of bleeding tendency, 17.4% had jaundice, 1.5% reported with post kala-azar dermal leishmaniasis (PKDL) and only 0.7% showed eye complications and mucocutanous lesions. Median hemoglobin (Hb) for the studied patients was7.2 grams/dl and median weight was below normal (- 2.30 SD). DAT was positive in 91.6%, ELISA positive in 94.6% and only 16 (20%) patients (n=80) the parasite isolated from lymph nodes aspirate. Most of the patients 85.6% responded to sodium stibogluconate. In 6% sodium stibogluconate stopped due to toxic effects. In 8.3% of patients, there was resistance to sodium stibogluconate and was treated with liposomal amphotericin B. Four (3%) of the patients died, in 3 of them there was jaundice, bleeding and evidence of liver impairment. One death reported as sudden and may be due to toxic effect of the chemotherapy. More epidemiological implementations are discussed in this study.

Introduction

Since 1900s, visceral leishmaniasis (VL) has been among the most important health problems in Sudan, particularly in the mean endemic areas eastern, southern and central regions.

Several major epidemics have been occurred, the White Nile in the central region. This region was not known previously as endemic area apart from sporadic cases described in 1988, the event which triggered renewed interest of the disease.

Epidemiological and Entomological studies confirm phlebotomus orientalis as the vector in

several parts of the Sudan, typically associated with acacia seyal and balanites aegyptica vegetations.

The clinical presentation of VL in children in the most of the case is more severe than in adults, commonly with severe anemia.

Weight loss, hepatosplenomegaly, lymph adenopathy and prolonged fever were the most common clinical features. Post kala-azar dermal leishmaniasis (PKDL) is not rare in Sudanese VL.

Complications in eyes and mucous membranes were seen but rare.

Parasite diagnosis is the mainstay which can be isolated from lymph nodes, bone marrow or spleen aspirate with different sensitivity rates. Simple and cheap serological tests like direct agglutination test (DAT) also used in some remote centers in Sudan for diagnosis of VL. DAT as seen in previous studies is sensitive up to 72% and specific up o 94%, but DAT still cannot differentiate between active disease, subclinical infection or past infection.

Sophisticated serological tests are evaluated for research purposes and found to be more sensitive than DAT; these include an enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) using peripheral blood. PCR is seen to be more sensitive than lymph node aspirate or bone marrow.

The leishman skin test (LST) is typically negative during active disease and converted to be positive after 6 months of treatment in about 80% of cases.

In Sudan VL respond well to sodium stibogluconate and is the first line. In some cases with severe side effects and some rare case with resistance to sodium stibogluconate liposomal amphotericine B was very effective with fewer side effects and shorter duration of treatment than sodium stibogluconate.

The objective of this study is to describe clinical and some laboratory aspects of cases of VL in children in this new epidemic area and to study response to treatment and types of complications.

Materials and methods:

The study conducted in Omdurman Emergency Hospital for Children (OEHC). OEHC is a paediatrics hospital with 350 beds. In the hospital there is department of infectious diseases.

The hospital serves population of Omdurman city which is the western part of the Sudan capital to the western bank of the White Nile and the river Nile; also the hospital serves rural areas and villages along the western bank of the white Nile which lie south to Omdurman in the near state of White Nile.

The area of White Nile is covered by small subtropical forests with secondary foods. Along the banks of the White Nile primitive agricultural activities has been practiced by villagers, White Nile Living Schemes.

The cases of VL came mainly from 5 villages located in the west bank of the White Nile. The study carried in children aged 2 - 14 years presented to the OEHC with prolonged fever and/or splenomegaly. The duration of the study was 2 years from March 2006 to March 2008 in which 132 cases of VL were diagnosed.

For each case showing this criteria bone marrow aspirate examined for the presence of the parasite. Further investigations were done for those who were positive for the parasite. These investigations include DAT, ELISA, lymph node histopathology (n=80), complete blood count, liver function and renal function.

The study proposal was approved by ethical committee of the Federal Ministry of Health and patients informed regarding the purpose of the study and consent obtained before sampling.

Data were analyzed using a program of EPI-INFO (version 6.04). Incidence rate is estimated by dividing the number of confirmed cases of children

with VL divided by total number of children at risk multiplied by 100.

Results

In this study males (65%) are affected more than females (35%) with significant statistical difference. Older children more affected than younger age groups, 52% of the studied group are more than 10 years this shown in table (1).

Most of the patients 123 (93.1 %) had splenomegaly this shown in table (2) together with other symptoms and signs. Prolonged fever was seen in 121 (91.6%). These two signs were the commonest followed by hepatomegaly in 108 (81.8%) and lymphadenpathy in 98 (74.2%) of the studied group. bleeding signs and jaundice were seen in 36 (27.2%) and 23 (17.4%) patients respectively. Other rare signs which appeared in this study were PKDL 2(1.5%) patients, uveitis and mucocutanous lesions only one patient (0.7%).

ELISA showed high sensitivity in the studied group 125 (94.6%) of the patients were positive. Also DAT was highly sensitive 121 (91.6%) showed positive results. Of the studied children in only 80 lymph nodes are significantly enlarged and aspiration or biopsied taken for histopathology, Leismania Donavani (LD) bodies found in 16 out of the 80 (20%). These results of the investigations were shown in table (3).

Table (1) Age and sex:

Age	Male	Female	Total
2 - 6	6	7	13
6 - 10	29	21	50
10 - 14	51	18	69
Total	86(65%)	46(35%)	132

Table (2) Common symptoms and signs:

Symptoms and signs	No	percentage
Splenomegaly	123	93.1%
Fever ≥ 3 weeks	121	91.6%
Hepatomegaly	108	81.8%
Lymphadenopathy	98	74.2%
Bleeding signs	36	27.2%
jaundice	23	17.4%
PKDL	2	1.5%
Mucocutanous lesions	1	0.7%
Eye complications	1	0.7%

Most of the patients 113 (85.6%) respond to sodium stibogluconate, in 8 patients (6%) sodium stibogluconate stopped due to toxic effects. Eleven (8.3%) of patients no response to sodium stibogluconate from the start . these patients and other patients with toxic effects who are a total of 19 (14.4%) are given libosomal amphotericin B and showed good response (table 4).

There are 4 deaths in the studied group 3 of them died due to bleeding and may be liver impairment; those 3 were showing good response to sodium stibogluconate. The fourth death was sudden after 8 days of treatment and was reported as a result of arrhythmias. All the deaths were in the group of sodium stibogluconate.

Table (3) showed the positivity of some investigations:

investigations	No	Percentage
ELISA	125	94.6%
DAT	121	916%
nodes	16	20%
(n=80)		

Table (4) Showed the response to treatment:

Medication	Responsive N (%)	Resistants N (%)	Stopped due to toxicity
Sodium Stibogluconate	113(85.6%)	11(8.3%)	8 (6.0%)
Liposomal Amphotericin B	19(14.4%)	None (00%)	None (00%)

Discussion:

Environmental changes have been associated with epidemiological profile of VL, with an increase number of reported cases or outbreaks in new areas usually periurban area. This suggesting an adaptation of the vector to these areas and its ability to change.

This study was conducted to describe cases of VL in children in a new focus with emphasis on differences in clinical presentation, diagnostic value and respond to chemotherapy from other foci of VL in Sudan. There were few differences in clinical presentation and laboratory findings in this new focus as compared with data from old endemic areas of VL.

As seen in this study males are affected almost twice as females, this may suggest that there may be association with working in farms as males do this more than females.

The male predominance in children with VL has been noted by Van Peenen and Reid in 1962; and again by Siddig et al in 1989. Many other studies especially the hospital based studies showed male predominance.

The severity of anemia in children with VL in this study also seen in other studies, Arlene J M et al 2006 and EL-hasan A M also mentioned in 2001 that children with VL suffer severe anemia than adults.

The clinical features of these cases from this new area is not much different from VL in old foci except for PKDL which appears as only 1.5% , where it mentioned as more 50% of patients developed PKDL in studies from other areas (Zijlstra & El-hasan 2001).

Fever, splenomegaly, hepatomegaly and lymphadenopathy seen in this study was similar to previous reports in old and recent studies, Henderson 1937, Vanpeenen and Reid 1962, Siddig et al 1990 and Hashim et al 1994 all report similar percentage to these constant signs.

Liver impairment and jaundice is a rare finding in VL in Sudan (EL-Hassan 2001), but in this study it was as high as 17.4%. This high number of cases with liver problem is not seen in any previous study. Liver impairment which reported in some studies (El-Hag et al 1994), was associated with the use of sodium stibogluconate and liver function return to normal one week after completion of treatment.

The sensitivity of lymph node aspirate in the diagnosis of VL in this study is much lower than been described in previous studies. In only 20% parasite was seen in aspirate from lymph nodes where it was ranging between 53%-58% in studies done by Siddig et al 1998 and Zijlstra 1992. No variations observed in other diagnostic tools.

In this study 85% respond to sodium stibogluconate (Pentostam) ® which is not different from studies in other areas, Kirk and Satti early in 1940 and Khalil et al late in 1998.

As in many other areas, liposomal amphotericin-B gave good results as second line for treatment of VL.

Conclusion and recommendations:

Due to environmental factors VL appeared in areas, and so every measures should carried out targeting prevention of this series infectious disease, measures should include ecological and medical

aspects.

Some serious complications like liver failure early in the disease, which was not a feature of VL in Sudan, seen in new cases and need more evaluation by researches.

Few diagnostic challenges in VL appeared and more efforts needed in the aspect of laboratory diagnosis.

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