

VISCERAL LEISHMANIASIS IN MEDINA REGION

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SUMMARY:

Over a period of four months seven cases of Visceral Leishmaniasis were identified for the first time in our Hospital in Saudi Nationals in Al-Medina Health Region. The presentation was fever, anaemia, splenomegaly and general ill health.

The laboratory data showed evidence of anaemia and thrombocytopaenia in all the seven cases but leucopenia in only 2 cases. The diagnosis was confirmed by positive bone marrow aspirate for L – D bodies in 5 cases and Leishmania Anaemia, Titre of more than 1:64 in all the seven cases.

Six of the cases responded well to Sodium Stibogluconate at a dose of 20 mg. 1 kg body weight/day for 20 days intramuscularly.

Epidemiological survey isolated the specific vectors and fly (Phlebotomine sand fly) from the city of Al-Medina Al Manuara as well as the surrounding villages where the patients came from.

Since the preparation of this report, more cases of Visceral Leishmaniasis have been diagnosed in our hospital. We think that the Medina Region is endemic for this disease.

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INTRODUCTION:

Visceral Leishmaniasis was first describes in 1902 by Leishman in a British Soldier stationed at Dum Dum near Calcutta (India) so named Dum Dum Fever⁽¹⁾.

Donovan in the same year identified the organism is splenic tissue from a patient with what was named later as Visceral Leishmaniasis. Since then cases have been reported often in endemic forms from India, Africa, Mediterranean Areas and South America.

In Saudi Arabia Cutaneous Leishmaniasis is prevalent in many regions Visceral Leishmaniasis however is rare. The Leishmania centre at Riyadh have received few cases reported from Abaha, Al Baha and Gizan Health Regions⁽²⁾.

Therefore Medina Region is not recognized as an endemic area for this disease. We report seven cases of Visceral Leishmaniasis diagnosed in Saudi National residing in or around Medina. The cases were collected in a short period, about four months. Since the preparation of this reported more cases have been identified. It is very likely that the Medina region is endemic for Visceral Leishmaniasis.

GENERAL LOCATION:

Medina Region s situated on the North Eastern part of Saudi Arabia. It is 1000 kilometer from South East of Riyadh and 412 kilometer from North West of Jeddah.

The Holy City of Al Medina Al Munwarah, where Prophet Mohamed (SM.) Mosque and where he is buried is the capital of the Region. It is divided into 8 Health Sectors. The population is about 569,000

and most of them are living outside Madina city in rural areas. Those living in rural areas are mainly engaged in farming. The farms are irrigated by water wells. The rainfall is scarce.

Madina Maternity and Children Hospital situated in Al Madina Al Munawarah with the capacity of 500 beds. 250 beds for paediatric care is the main and only referral hospital for children needing secondary and sometimes tertiary care services.

Patients and methods:

Over a period of 4 months (June 1988 to October 1988) seven children were seen at the Madina Maternity and Children's Hospital who fulfilled the clinical and laboratory diagnostic criteria for Visceral Leishmaniasis (Table 1).

The Maternity and Children's Hospital is a regional referral hospital which serves the city of Madina and the neighbouring villages. Visceral Leishmaniasis was suspected in patients who had fever, hepatosplenomegaly, lymphadenopathy and anaemia with or without leucopenia. The diagnosis was confirmed by Indirect Haemiagglutination test (IHAT) for Leishmania Antibody Titre above 1:64 and proven by isolating Leishman-Donovani (L-D) bodies from bone marrow aspirate (Table II). Splenic puncture or lymph node aspirates were not done.

Case Description:

All our patients were younger than 5 years. 6 were females and one males. All were Saudi Nationals. All had prolonged fever of more than 3 weeks duration except one 6-month-old child, who presented with one week

duration of fever. All looked toxic on admission except one. One patient had clinical jaundice. One patient had cancrum oris which needed plastic surgery repair after completion of treatment. Six of the seven cases had hepato-splenomegaly. Three patients had significant generalized lymph gland enlargement and 5 had chest infection with radiological changes (Table I).

Table: 1- Case description and presenting symptoms.

Case	Age	Sex	Saudi / Non Saudi	Fever	Pallor	Hepato- megaly	Lymph node
1	16 months	F	5	+	+	+	-
2	21 months	F	5	+	+	+	+
3	17 months	F	5	+	+	+	+
4	18 months	M	5	+	+	+	-
5	2 years	F	5	+	+	+	+
6	5 years	F	5	+	+	-	-
7	12 months	F	5	+	+	-	-
Total	100%		100%	100%	100%	85.7%	42.85%

All the patients were anaemic. Only 2 had E.B.C. less than 4000, all had thrombocytopenia, platelets, less than 100×10^9 . I.L. Four had platelets count less than $50 \times 10^9/L$. Five out of seven had positive bone marrow aspirate for L-D, bodies. All the seven cases has positive leishmania antibody titre (IHTAT) of 1:64, or above. In 2 patients bone marrow failed to show positive Leishman-Donovan bodies Table 2.

Table: 2- Haematological features, antibody titres and the outcome.

Cases	Hb. GM %	WBC X $10^9/l$	Platelets X $10^9/L$	Leishmania A/B titre	Bone marrow (L.D Bodies)	Outcome
1	4.2	6.5	72	1:512	+	Improved
2	9.9	12	51.7	1:256	-	"
3	3.2	2.1	50	1:64	+	"
4	5.7	8.2	74	1:56	+	"
5	4.1	4.7	48	1:128	+	Diet
6	7.6	2.4	88	1:156	+	Improved
7	8.0	5.6	32	1:128	-	"

Routine cultures of urine, blood, stools and chest x-ray done, and other causes of fever such as malaria, typhoid, brucellosis were excluded by appropriate tests.

All patients received initial supportive treatment including blood transfusion, fresh frozen plasma or platelets concentrates when indicated. Specific treatment was initiated with Pentostam (Sodium Stibogluconate) according to WHO recommendation on chemotherapy of Visceral Leishmaniasis. The dose used was 20 mg/kg body weight per day for 20 days intramuscularly. One of our patient received 10 mg/kg 1 day for seven days which was later changed to intramuscularly for total of 20 days in the same dose. ECG was done on diagnosis during treatment and after discharge. No side effects particularly arrhythmia was seen. One patient had diarrhoea on day 15 of treatment lasting for 3 days and required no specific treatment.

One of our patients was admitted to the Intensive Care Unit because his condition was critical on admission. He had marked thrombocytopenia, severe chest infection and marked ulcerations of the mouth and naso-pharynx. He was ventilated for 7 days but eventually died. His repeated bone marrow 2 days before death showed multiple L-D bodies although less in number than his initial bone marrow aspirate. He had received frequent fresh frozen plasma, platelets concentrates, fresh blood transfusions and antibiotics as well, and pentostam for 7 days, in a dose of 20 mg/kg day but he had repeated cardiac arrests and died on day 7. The other six patients made an uneventful recovery with average hospital stay of 23 days.

Epidemiological Survey:

All the cases were reported to the Leishmania centre of Madina Health Region. Details of the possible sites of contracting the infection indicated that one patient had traveled to Gizan (which is a known endemic area for Visceral Leishmaniasis) during school vacation. She could have contracted the disease while there. The other six cases had not left the Madina region since birth. One patient was from Madina City itself, while the other came from the villages surrounding the city.

Epidemiological survey for the sand fly was conducted using the night catch method as well as trapping. The insects (flies) caught were identified by the entomologist of the department of communicable diseases. Specific sand flies (*Phlebotomus*) were identified in all the areas where the 7 patients came from including the city of Al-Madina Al-Munawarah.

DISCUSSION:

Visceral Leishmaniasis (VL) is known to be endemic in many areas in the world. It has been reported in every continent except 'Australia (3).

In Saudi Arabia (VL) has been reported in several occasions in the published literature the first case was reported in 1955 at Dahrhan Hospital ARAMCO in eastern province by Tarrizoo et al (4).

Other reports in the published literature had included 13 cases from Jeddah (5) 45 cases from Khamis Mushiyat in Asir (6) and several cases were seen in Abha but not reported in the literature (7).

Reports from Riyadh had included 1 case of a boy age 4 years with a positive bone marrow smear for leishmania Donovan bodies (8)

and by Al Sebbah et al 8 cases of (VL) (9). Ginedan Yousef and other have pointed out that (VL) is less documented in Saudi Arabia. The only endemic area is in and around Gizan. The majority of cases are children (10). It has been also pointed out by Al Zahrani, who reviewed visceral leishmaniasis in man and dog in South east of Saudi Arabia that isolated *L. infantum* were obtained from bone marrow biopsies of both infants and dogs in the same area which suggests a Zonotic reservoir (11). Up to 1987 a total of 188 cases of visceral leishmaniasis have been reported to the Ministry of Health in Saudi Arabia and none of these was from Al Madina Region. 1216 cases of cutaneous leishmaniasis from Madina were reported by Ikram but none has contracted (VL) (12). So no cases have been reported from Madina region with (VL) and to the best of our knowledge we think these are the 1st 7 cases diagnosed and reported from this region. Our 7 cases have shown typical clinical presentation of (VL) with prolonged fever, hepatosplenogaly and lymphadenopathy (13) Lymphadenopathy was seen in only 42.8% of our cases. Siddique et al, reporting from Sudan have pointed out that (14) lymph node enlargement is significant finding in Sudanese patients. Patel reported from Khamis Mushiyat has pointed as well that lymph node enlargement is not a significant finding in their Saudi Patients (6).

One case from our reported cases had jaundice with a serum bilirubin of 204 $\mu\text{mol/litre}$. In our series jaundice has been a presenting symptom in at least one case.

The laboratory data are consistent with reports from other countries, particularly anaemia and thrombocytopenia. However, leucopenia was seen in only 2 of our cases. Because of the high incidence

of infection which might lead to leucocytosis absence of leucopenia should not distract one from the diagnosis of (VL).

Chest infection was seen in every case and superficial abscesses in two cases. One abscess was seen at the local anesthesia site given for bone marrow aspiration although routine strict antiseptic techniques were used but this might show that these children are particularly vulnerable to infections because of the depressed immunity. Because of the vulnerability to infection our cases have been on protective isolation.

P.T. and P.T.T. were raised more than p-5 seconds in 2 of our 7 cases they have responded well to vit K. and fresh frozen plasma at a dose of 10 ml/kg.

Abnormal liver function tests were seen in 3 cases but there was no significant liver problem. None of our cases has shown manifestations of liver cell failure.

Our diagnosis was confirmed by positive bone marrow biopsy in 5 cases out of 7 (71%) which is very similar to king Faisal Specialist Hospital and Research Centre (positive 7 out of 8 in bone marrow aspiration) (9) and highest than 45% reported by Patel from Khamis Mushiyat and 50% by Rageh from Yemen (15).

However, we found that indirect Haemogglutination test (IHAT) is extremely useful test and was positive in all our 7 cases, positivity taken when titre is above 1:64 as recommended by the manufacturers.

The sero-diagnosis of (VL) from the direct haemagglutination titre. Gel diffusion and counter current immunoelectrophoresis Elisa and complement fixation test is quoted from the literature as 95%, 64%, 95%, 90% and 60% respectively (see table 4) (16).

Table: 3- Sero-diagnosis of (VL) positivity

Indirect haemiagglutination test (IHAT)	95%
Gel Diffusion Test	64%
Counter current immunoelectrophoresis	95%
ELISA	> 90%
Complement fixation	60%

By Courtesy: Richard Mulgal and Anthanl Brycesson

The frequency of parasite yield from different aspiration sites was quoted as 95% from spleen, 75-85% from the liver and 64-85% from bone marrow and 64% from the lymph node biopsy if enlarged (Table 3)(16).

Table: 4- Frequency of Parasites yield from different aspiration sites in (VL)

ASPIRATE	% POSITIVE
Spleen	> 95%
Liver	> 75.85%
Bone Marrow	64.85%
Lymph-node if enlarged	64%

By Courtesy: Richard Mulgal and Anthanl Brycesson

Siddique et al from Sudan have advocated that lymph node biopsy should be the first step for confirmation of diagnosis (14) but because of the low incidence of lymph node enlargement of (2.8%) in our patients we don't think lymph gland enlargement is a common feature of (VL) in Saudi Arabia. We agree with Patel who reported the same low incidence in their series of 62 patients and suggested that recommendations must be tailored to suit the characteristics of the disease. Patel has further suggested that where limited facilities are available to establish the diagnosis with certainty, but where the diagnosis is strongly supported on clinical grounds, simple laboratory data and a history of being in an endemic area a trial with Pentostam stibogluconate is justified and that it is their policy to treat such cases (6). We have done this in at least one case of our series with a good response. However we think endemic areas are not fully known in Saudi Arabia like our area which was not considered as one.

For treating (VL) we have used Pentostam in the dose of 20 mg/kg for 20 days. None of our patients has shown any complications particularly arrhythmias or drug induced pneumonia (17), except the one who presented in a moribund shape and died in the ICU. The dose of 10 mg/kg/day which was used by many before is accompanied by higher incidence of relapse (3). Indian workers in their field or (VL) have reduced the relapse rate from 15% to 0.3% by using the above dose of 20 mg/kg/ for 20 days.

Higher dose of 30 mg/kg which was tried by Kenyan workers has shown higher incidence of complications and at least one of their patients has died from cardiac arrhythmias (18).

Supportive measures like antibiotics were also used to treat

the existing infections. Patients with Hb 6 mg% or less received blood transfusion initially. However the blood indices improved remarkably once specific treatment is started.

Fresh frozen plasma in a dose of 10 ml/kg was given in 3 of our patients who showed platelets count of less than 5×10^9 /dL or bleeding tendency.

Since the discovery of this seven cases more cases have been seen in our hospital not included in this report and our diagnostic approach to children with prolonged fever, anaemia hepatosplenomegaly and lymphadenopathy has included (VL) in the differential diagnosis, especially if haemological feature has shown anaemia, leucopenia and thrombocytopenia.

We don't think liver biopsy and splenic punctures are necessary for confirmation of diagnosis if (IHAT) facilities and the services of good haematologist with experience in bone marrow aspiration microscopy are available as one should not be discouraged if they cannot be done.

Although Kenyan workers have reported that splenic puncture is a safe procedure in their department and that their patients prefer it to bone marrow aspiration (3). In a series of 392 patients they had no complications except bleeding in three patients who respond well to conservative measures.

Splenic puncture should not be attempted if platelets are below 50×10^9 dl or P.T. and P.T.T. are prolonged with more than 2 seconds. The risk of bleeding is definitely higher.

Resistance to Pentostam is known but we have not encountered any. Other alternative drugs are Pentamidine and Amphotericin-B.

In our case which died with bleeding disorder and overwhelming infection resistance was not documented. We have done a repeated bone marrow aspiration 5 days after treatment and our haematologist has definitely demonstrated that L-D bodies are less than the previous bone marrow aspirate.

It should be emphasized that (VL) is a serious disease in children if not diagnosed and treated early, patients might die from its complications, such as bleeding disorders and overwhelming infection.

Peter Wallace and Al-Zahrani M.A. had suggested since 1987 that an intensive research programme is proposed by the National Leishmania Research Programme (NLRP) to investigate the presence of parasites in other parts of the country and epidemiological factors for their transmission to Asir, Baha and Gizan. They further pointed out that the launching of such programme will justify a major commitment on finances and personnel. It will also provide a good example of national disease control (19).

We think that a controlled epidemiological clinical survey is needed in Madina region because it is most likely that the cases are more than what our figures have suggested.

CONCLUSION:

We like to conclude that Visceral Leishmaniasis exists in Madina Region. We draw attention of Practitioners and Paediatricians practicing in this region that the diagnosis should be suspected in a child who presents with prolonged fever, hepatosplenomegaly and lymphadenopathy.

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