

Kala Azar in Utrakhand - A Clinical Study



Medical Science

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INTRODUCTION- Leishmaniasis is a group of protozoal disease which is caused by 20 species of Leishmania & transmitted through 30 species of sand fly¹. Most of Leishmania infections are zoonotic but in India it has a human-human cycle & the responsible species is *L. donovani* which causes Visceral Leishmaniasis (VL).

Leishmaniasis is endemic in many tropical & subtropical countries in Asian subcontinent. Around 2-4 lakh cases of Visceral Leishmaniasis (also popularly known as kala azar) are reported annually worldwide². Out of these 6 countries including India, Bangladesh, Brazil, Nepal, Ethiopia & Sudan account for 90% of global incidence. It is endemic in 52 districts of India which generally comprise of plains. It does not occur in altitude above 2000 feet (600 meters). However, recently there have been cases reported from various pockets of northern India including sub-Himalayan parts of Kumaun³, Garwal region⁴ of Utrakhand & sporadic cases from Himachal Pradesh⁵.

In this series of 12 patients which reported to our hospital from various areas of Utrakhand, we have highlighted that kala azar (VL) must now be considered as an important differential diagnosis of Pyrexia of Unknown Origin (PUO) among patients coming from sub Himalayan pockets of Kumaun who are otherwise not responding to other treatment. We have also discussed the clinical & biochemical profile of such patients.

MATERIAL & METHODS- We studied 12 patients of Pyrexia of Unknown Origin who were admitted in our hospital from 2010-2014. They underwent thorough clinical examination & investigations for fever. Blood investigations like Haemogram, Peripheral Smear (PS) for malaria, Malarial Parasite (MP) antigen, Blood culture, Urine routine examination & culture along with Widal test were performed in all the patients. Liver & kidney function test were also done along with viral markers. Chest X-ray & ultrasound abdomen were done in all the patients & CECT whole abdomen performed in 2 patients where it was indicated. They were subsequently subjected to bone marrow examination & sample sent for rapid K-39 antigen strip test. All the investigations were done in our Central lab & bone marrow examination was done by pathologist.

RESULTS- Out of 12 patients, 10 patients were male & 2 were females. The mean age was 30.41 year ranging between 14-53 year. They were all residents of Kumaun except two patients who were from Lakhimpur khiri close to Kumaun foot hills (Table 1). None of them gave history of travel to the endemic areas of kala azar except one from Lakhimpur khiri who gave history of travel to Shimla, Himachal Pradesh for job where he had resided for 3-4 months. Fever of more than 3 months duration was the chief complaint of all the patients along with other asso-

ciated symptoms like cough, chest pain & abdominal discomfort. Bleeding manifestation was noted in four subjects. All of them had taken treatment of malaria & typhoid from outside. Anaemia was noted in almost all the patients & thrombocytopenia was seen in 11 out of 12 patients. Leucopenia was present in 10 & lymphocytosis (L>45%) was seen among 8 patients whereas ESR was raised in all. Hyper-bilirubinemia of mild degree was observed in 7 patients along with raised transaminases in 9 patients (Table 2). Almost all patients had hypo-albuminemia. Bone marrow examination showed presence of LD body's among 8 patients (66.6%) & k-39 strip test done in 8 out of 12 patients was positive in all cases (100%) even if the LD bodies were not seen in bone marrow. Ultrasound abdomen showed splenomegaly in all the subjects with only 2 patients showing massive enlargement whereas in others the size documented was only mild to moderate degree. Ascites was noted in 3 subjects only.

DISCUSSION- As already discussed Visceral Leishmaniasis (VL) is a disease of low altitude, endemic in Bihar, West Bengal, Jharkhand & eastern state of Uttar Pradesh. Occurrence of kala azar in sub Himalayan region of Himachal Pradesh (2300-3000m above sea level)⁶, Garwal (1500-2500m above sea level) & Kumaun (350-900m) areas of Utrakhand has now been well documented. First mention of VL from Kumaun area of North India was made by Singh S et al⁷ when several cases of PUO were being treated at AIIMS, non-responsive to anti tubercular treatment & various antibiotics, some of which were detected to have LD bodies on bone marrow examination. A series of 24 patients of VL found from low endemic zone of North West India was reported by Naik et al⁸ in 1978. Our series also reports cases of kala azar from hilly areas of Kumaun who were being treated as cases of PUO elsewhere not showing any improvement with anti-malarial & anti-tubercular treatment. They were all referred to our tertiary care hospital for further management & treatment. Point to highlight is that, our first differential diagnosis was not kala azar in any of the mentioned cases & only after thorough investigations & prophylactic treatment for other common causes of fever; we arrived at a diagnosis of kala azar.

None of the patients had history of travel to areas where kala azar is endemic except one boy who had a short history of visit to Shimla in search of job where he stayed for 3 months. Fever of more than 3 months duration was the chief complaint of all the patients along with associated features which were mostly non-specific. Few had bleeding tendencies either due to thrombocytopenia or coagulation disorder. In our study, almost all patients had pancytopenia which was similar to findings in studies by Ashok Kumar et al³ & Harish et al⁴ with pancytopenia in 96.2% of patients. This finding was in contrast to another study by Danesbodh et al⁹ where pancytopenia & thrombocytopenia were noted in 10% & 30% of patients respectively. Lym-

phocytosis was observed in 8 out of 12 (66.6%) subjects in our study whereas Raina et al¹⁰ noted lymphocytosis in 8 out of 18 patients.

Liver involvement in the form of jaundice was of mild degree among 7 patients in contrast to study by Raina et al¹⁰ where none of the patients had jaundice but raised transaminases were found. According to literature, liver involvement is seen less commonly in VL (17%)¹¹ & is usually of mild degree & self-limiting. Liver involvement in kala azar involves a mononuclear cell dominated granulomatous inflammation mediated by cytokines, chemokines & reactive oxygen & nitrogen particles¹². Ultrasound documented splenomegaly in all the patients but massive spleen was noted in only 2 patients who were in contrast to Raina et al¹⁰ where massive spleen was observed in 14 patients. In all other patients liver was mild to moderately enlarged & none of the patient had lymphadenopathy which is unusual in Indian kala azar.

Bone marrow examination performed in all patients & was positive in 8(66.6%) whereas K-39 antigen strip test done in 8 subjects was positive in all (100%) (Table 3). K-39 Leishmania antigen is a member of kinin in family of proteins. Detection of IgG antibody to this antigen has been found to very useful non-invasive method for diagnosis of VL¹³. There have been studies from Sudan¹⁴ using recombinant K-39 strip tests as an ideal tool for use in the field. In India, Sunder et al¹⁵ & Goswami et al¹⁶ found 100% sensitivity & 98% specificity in their 2 separate independent studies. Only drawback is that it can remain positive for as long as 3 years even after the treatment. In our study there has been 100% sensitivity.

We treated our patients with amphotericin-B, 8 patients showed recovery as they became afebrile, jaundice & liver enzymes improved & spleen size regressed on follow-up. 2 patients left against medical advice & 2 died due to delay in starting the treatment. Sensitivity of Sodium stibogluconate in treating patients from these non-endemic areas has been studied well by SK Verma et al¹⁷. Current concern is that a steadily increasing number of patients are now being diagnosed as VL coming from non-endemic areas. The disease is contracted by a local vector & probably a zoonotic reservoir. Six species of Phlebotomus & 15 species of Sergentomyia have been found in northern ranges of Himalayas including Kumaun region¹⁸. It has also been suggested that there is intrusion into the sylvatic cycle due to the construction activities, horticulture development leading to destruction of forests. Migration of labourers from endemic area of Bihar, Jharkhand, Eastern UP & Nepal³ is also of great concern.

CONCLUSION- In this short series of 12 patients, we have tried to highlight that VL must now be considered as a cause of PUO, if any patient from these non-endemic areas presents with history of fever of more than 3 months duration along with pancytopenia. It has been seen that spleen may not have been enlarged massively in such patients whereas in classic Indian kala azar spleen is massively enlarged. It is important to note that if the clinical suspicion for VL is high & bone marrow is not showing presence of LD bodies, simultaneous K-39 antigen strip test may be of help. From community point of view, it is important to be aware of the spread of VL from non-hilly to hilly areas as it poses a serious public health concern & appropriate measures should be taken to control further spread.

Table 1: Demographic and Clinical Profile of patients

S No	Age	Sex	Residence	Occupation	H/O Alcohol	Clinical Presentation
1.	15 yr	M	Bageshwar	Student	No	Fever ,vomiting, loose stool
2.	46 yr	M	Rudrapur	Labourer	Yes	Fever, epigastric pain
3.	14 yr	M	Khatima	Student	No	Fever, abdominal distension
4.	24 yr	M	Champawat	Teacher	No	Fever, cough, hemoptysis
5.	35 yr	F	Nainital	Housewife	No	Fever, cough
6.	53 yr	M	Champawat	Clerk	Yes	Fever, cough, vomiting
7.	35 yr	M	Lalkuan	Driver	No	Fever, headache, hiccups
8.	50 yr	M	Champawat	Pradhan	Yes	Fever, cough, loose motion
9.	22 yr	M	Lakhimpur khiri	Labourer	Yes	Fever, hematemesis, malena
10.	30 yr	F	Almora	Housewife	No	Fever, vomiting,
11.	21 yr	M	Almora	Student	No	Fever, vomiting, epistaxis
12.	20yr	M	Lakhimpur khiri	Labourer	No	Fever, epistaxis

Table 2: Biochemical Profile of patients

S no	Hb gm/dl	TLC/DLC	Platelet L/mm ³	ESR mm/1h	Bilirubin mg/dl	SGOT/SGPT IU	Protein / Alb gm/dl	USG abdomen
1.	6.6	2900/P51L47	84,000	40	1.2	29/39	5.4/2.2	Splenomegaly-mild
2.	10.1	1700/P59,L37	41,000	54	3.8	36/39	6.1/2.2	Hepatosplenomegaly-mild to moderate
3.	8.2	5100/ P31 L65	1.6 lakh	21	0.6	40/56	6.4/1.2	Mild hepatosplenomegaly
4.	5.4	700/P31 L17	51,000	42	1.9	92/74	6.1/1.1	Hepatosplenomegaly, mild ascites
5.	7.9	600/P35 L63	22,000	69	2.1	116/69	8.1/1.3	Mild hepatomegaly. massive splenomegaly
6.	6.1	970/P53 L47	1.1 lakh	72	0.8	34/12	7.4/3.2	Mild splenomegaly
7.	9.0	2200/P50 L45	52,000	40	1.0	187/166	5.6/2.9	Mild hepatosplenomegaly
8.	11.0	19000/P50 L48	1.1 lakh	29	6.8	1021/599	5.3/1.5	Mild hepatosplenomegaly
9.	5.1	2400/P31 L66	20,000	52	2.3	455/260	6.5/1.3	Massive splenomegaly, mild hepatomegaly
10.	6.1	1100/P29 L20	63,000	73	0.4	91/48	6.8/2.3	Moderate splenomegaly,
11.	9.9	2100/P61 L39	46,000	22	3.4	1780/1039	6.3/3.1	Mild hepato- splenomegaly, ascites moderate
12	6.1	1100/P10L40	15,000	56	6.4	113/204	5.80/1.60	Hepatosplenomegaly with ascites

Table 3: Sensitivity comparison –BM vs. k39

	Bone Marrow (n=12)	K39 (n=8)
Positive	8	8
Negative	4	0
Sensitivity	66.6%	100%

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