J Vector Borne Dis 46, December 2009, pp. 303–306

A new focus of visceral leishmaniasis in the Himalayas, India

Sujeet Raina[a], D.M. Mahesh[a], Rashmi Kaul[b], Kaushal S. Satinder[a], Dilip Gupta[a], Ashok Sharma[a] & Surinder Thakur[a]

[a]*Department of Medicine,* [b]*Department of Pathology, Indira Gandhi Medical College, Shimla, India*

Key words Himalayas – India – visceral leishmanisis

Visceral leishmaniasis (VL), commonly known as kala-azar in Indian subcontinent is a major public health problem and >90% of cases are from India, Bangladesh, southern Sudan, Nepal and north-east Brazil. VL affects more than 1,00,000 persons every year in India and occurs epidemically and endemically in well-defined areas in the eastern parts of the country, mainly Bihar, West Bengal, the eastern districts of Uttar Pradesh, Assam and the foothills of Sikkim[1]. Despite its widespread geographic distribution, leishmaniasis in humans is often focal within an endemic area, leading to 'hotspots' of disease transmission[2].

Visceral leishmaniasis is a disease of low altitude; it does not occur in altitudes over 2000 ft (600 m)[3]. However, cases have been reported from natives of sub- Himalayan region, India. The existence of a pocket of the disease and vector in the Kumaon (350–900 m above mean sea level) and Garhwal (1500–2500 m above mean sea level) region of the non-endemic north Indian hilly state of Uttarakhand has already been established recently[1,4]. Few sporadic cases have been reported from Himachal Pradesh in the past but details about altitude are not available[5,6]. In an another report from this state two cases of VL were diagnosed in natives living at an altitude of 2300 and 3000 m respectively[7]. However, the incidence of the disease is still increasing, and 18 cases of VL have since been recorded from January 2003 to December 2007. In this report, we present results of epidemiological, clinical investigative and therapeutic features of these cases identified in this new focus. The possible mode of its introduction in the region is postulated.

The study was conducted in the Department of Medicine, Indira Gandhi Medical College, Shimla (Himachal Pradesh), India. Eighteen cases were diagnosed over a five year period from January 2003 to December 2007. The patients of our study were diagnosed as VL by clinical findings and confirmed by demonstration of amastigotes (*Leishmania donovani* bodies) in bone marrow smears of 15 patients and in splenic smears of three cases. None of our patients reported to have been out of the state or district during the three years preceding onset of symptoms. All the patients lived in a rural area and were engaged in cattle rearing and agricultural and horticultural activities, four were state government employees and one was a student. All the patients except one lived in a sub-alpine valley along the Satluj river that leads to the mountain deserts of the tribal district of Kinnaur and adjacent area of Shimla and Kullu districts (Fig. 1).

Eight patients belonged to Kinnaur district, seven were from Rampur subdivision of Shimla district and two patients were from Nirmand subdivision of Kullu district. One patient belonged to Beas river valley area in Hamirpur district. The altitude of these areas ranges between 924 and 2960 m above the mean sea level. The terrain of the Kinnaur district is dry and sandy with loose rocks. The minimum temperature in the winter at the district headquarters is –7°C and maximum is 13°C. The minimum temperature in the summer at the district headquarters is 8°C and maximum is 25°C . The average temperature is 1.5°C and

Fig. 1: Study area showing geographic distribution of patients. Figures in parentheses depict number of patients from that location.

16.2°C in December and June, respectively. The annual average rainfall is 28.1 mm and the snowfall ranges from 64 to 1399 mm. In Kullu district, the maximum temperature is 38.8°C and minimum is 5.2°C in winter. The average rainfall in the Kullu Valley is 80 cm. Heavy frost occurs during December to February. Snowfall generally occurs during December and January. In Rampur area of Shimla district, the rainfall as well as temperature is slightly higher and the area does not get snowfall[8].

Of the 18 VL cases, 15 were males and three were females. The median age was 34 yr, with the oldest patient being a 65 yr old man and the youngest an 18 yr old girl. All the patients reported fever. The duration between the onset of fever till diagnosis varied from six weeks to one year with the median period being three months. Other clinical features reported were weight loss in all the patients, epistaxis in five and diarrhoea in three. Splenomegaly was found in all the cases and massive splenomegaly was noted in 14 cases. Hepatomegaly was detected in 11 patients. Lymphadenopathy was seen in eight cases. Significant axillary lymphadenopathy was noted in seven patients, cervical lymphadenopathy in three and retroperitoneal in two patients. Amastigotes (*Leishmanaia* bodies) were isolated on FNAC from lymphnodes in two patients. Three patients had pedaledema and ascites was present in two. None of the patients had jaundice or hyperpigmentation. Eight patients were also evaluated for their HIV status and all were found negative. All the patients were anaemic. Dimorphic anaemia was the commonest type of anaemia. Leucopenia was present in seven patients and thrombocytopenia in six patients. The differential leucocyte count revealed relative lymphocytosis in eight patients. ESR was raised in 14 patients. Five patients had hypoalbuminemia.

Serum transaminases were raised in six patients though bilirubin was normal in all the patients. Renal functions were deranged in two patients. All patients were administered sodium stibogluconate at a dose of 20 mg/kg/day for 4 wk. Clinical cure was achieved in 14 out of 18 cases. Four patients died during the treatment in the hospital. The parameters for a favourable therapeutic response were disappearance of symptoms and resolution of splenic size and lack of recurrence of symptoms during six months of follow-up.

The clinical picture in our cases is generally similar to that already established in Indian patients but certain clinical features need emphasis because of uncommon manifestations. Leishmanial lymphadenopathy, an interesting feature noticed in our cases has been stressed as an extremely rare feature in Indian kala-azar. Most of our cases were relatively fair skinned, and none of them had hyperpigmentation.

The present report of a visceral leishmaniasis focus in a previously non-endemic area raises few basic questions about the understanding of kala-azar epidemiology in this area. The fact that all our patients had contracted the disease indigenously is suggestive of a local vector and probably a zoonotic reservoir. Six species of *Phlebotomus* and 15 species of *Sergentomyia* have been found in the northern mountain ranges of the Himalayas (Himachal Pradesh is situated in these ranges), with their distribution limited to particular ecoclimatic zones[9]. Survey of sandflies in the Himalayan region has established the presence of *Phlebotomus argentipes, P. longiductus* and *P. major* (Diptera: Psychodidae) in this area[9,10]. A new focus of localised cutaneous leishmaniasis and vector has already been established along the Satluj river valley in the mountainous region of non-endemic north-west Himachal Pradesh very recently. The characterization of *Leishmania* strains by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) of the ribosomal gene region of 10 biopsy specimens revealed presence of both *L. tropica* and *L. donovani* in these patients of localised cutaneous leishmaniasis[8]. Similar characterization of the *Leishmania* species by PCR is required in patients of VL.

Identification of the sandflies collected from the peridomestic environment of the patients of localised cutaneous leishmaniasis, revealed the presence of *P. longiductus, P. major* and *P. kandelaki* in this belt[8]. Their role as a vector for transmission of VL, in this particular region needs to be delineated by demonstrating similar strains of *Leishmania* in both the vector and the human host. Also lymphadenopathy, a common feature in this focus raises the possibility of a new vector or a variant of the disease. More epidemiological work is required in this naïve area.

The recent emergence of VL in this area of Himachal Pradesh appears to be due to construction activities, horticulture development, and establishment of new residential colonies leading to destruction of forests and intrusion into the sylvatic cycle. With the presence of major River Sutlej and few other small rivulets the hydroelectric potential of this area has been exploited in last 20 years. This has resulted in construction of at least three major and few minor hydroelectric power projects. The labourers employed are mainly from the known endemic areas of Bihar, Jharkhand, Uttar Pradesh and Nepal. It is still not clear whether the parasite has come from sylvatic cycle or introduced by migrant population. The cattle kept close to the houses by people in rural areas are also known to attract both anthropophilic, as well as zoophilic vectors[11]. Moreover, adaptation of the vector, as well as the parasite, to strange, often bizarre habitats is well-known. Two studies have indicated potential changes in the geographical distribution of the vectors. Modelling studies in south-west Asia have indicated potential range expansion of *P. papatasi* with global warming[12]. In Italy, VL caused by *L. infantum* is prevalent in the milder parts, where it is transmitted by *P. perniciosus.* Low temperature appears to be one of the main factors preventing its spread into northern Europe[13]. Indian kala-azar is a complete anthroponosis. There is no known animal reservoir involved in its transmission. However, kala-azar in several other parts of the world is a zoonosis,

involving canine reservoirs, principally dogs, foxes and jackals[4]. Epidemiological work is required in this area to substantiate the presence or absence of any zoonotic reservoir.

Although the clinical presentation was more or less classical, the first diagnosis was other than kala-azar in most of the cases. The correct initial diagnosis was made more often with greater awareness and experience of the occurrence of this disease in this area. Initial failure to suspect kala-azar in this area might cause a diagnostic delay. It is important to mention that 14 patients responded to sodium stibogluconate treatment and had a favourable therapeutic response without recurrence of symptoms during 6 months of follow-up.

References

1. Verma SK, Ahmed S, Shirazi N, Kusum A, Kaushik RM, Barthwal SP. Sodium stibogluconate-sensitive visceral leishmaniasis in the non-endemic hilly region of Uttarakhand, India. *Trans R Soc Trop Med Hyg* 2007; *101:* 730–2.
2. Desjeux P. The increase in risk factors for leishmaniasis worldwide. *Trans R Soc Trop Med Hyg* 2001; *95:* 239–43.
3. Park K. Leishmaniasis. In: Park K, editor. *Park's Textbook of Preventive and Social Medicine*. VI edn. Jabalpur, India: Banarsidas Bhanot 2007; p. 256–8.
4. Singh S, Biswas A, Wig N, Aggarwal P, Sood R, Wali JP. A new focus of visceral leishmaniasis in sub-Himalayan (Kumaon) region of northern India. *J Commun Dis* 1999; *31:* 73–7.
5. Naik SR, Rao PN, Datta DV, Mehta SK, Mahajan RC, Mehta S, *et al*. Kala-azar in north-western India: a study of 24 patients. *Trans R Soc Trop Med Hyg* 1979; *73:* 61–5.
6. Dutta U, Rajwanshi A, Rayat CS, Sakhuja V, Sehgal S. Kala-azar in Himachal Pradesh: a new pocket. *J Assoc Physic India* 1984; *32:* 1072–3.
7. Mahajan SK, Machhan P, Kanga A, Thakur S, Sharma A, Prasher BS, *et al*. Kala-azar at high altitude. *J Commun Dis* 2004; *36:* 117–20.
8. Sharma NL, Mahajan VK, Kanga A, Sood A, Katoch VM, Mauricio I, *et al*. Localized cutaneous leishmaniasis due to *Leishmania donovani* and *Leishmania tropica*: preliminary findings of the study of 161 new cases from a new endemic focus in Himachal Pradesh, India. *Am J Trop Med Hyg* 2005; *72:* 819–24.
9. Kaul SM, Jain DC. Distribution of phlebotomine sandflies (Diptera: Psychodidae) according to the physiographic divisions of India. *J Commun Dis* 1995; *27:* 155–63.
10. Kulkarni SM, Bhat HR, Modi GB. Survey of phlebotomid sandflies from the Himalayan region, India (Diptera: Phlebotomidae). *Indian J Med Res* 1978; *67:* 583–8.
11. *Control of leishmaniasis*. Geneva: World Health Organization. *WHO Tech Rep Ser* 1990; *793:* 66–94.
12. Cross ER, Hyams KC. The potential effect of global warming on the geographical and seasonal distribution of *Phlebotomus papatasi* in Southwest Asia. *Environ Health Perspect* 1996; *104:* 724–7.
13. Kuhn KG. Global warming and leishmaniasis in Italy. *Bull Trop Med Int Health* 1999; *7:*1–2.

Corresponding author: Dr Sujeet Raina, Fire Officers Building, Stokes Place, Shimla–171 002, India.
E-mail: sujeetrashmishera@yahoo.co.in

Received: 17 November 2008 *Accepted in revised form:* 11 October 2009