Case Report:

Sodium stibogluconate as first-line treatment for post kala-azar dermal leishmaniasis

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ABSTRACT

An 18 year-old-girl, a resident of Buxar District of Bihar State, India, presented with hypopigmented rash on face of six months duration. Superficial sensations were intact. There was history of being treated for prolonged fever two years ago, for about three weeks. Based on history, clinical and microscopic examination, she was diagnosed to have post kala-azar dermal leishmaniasis. Treatment with parenteral sodium stibogluconate was initiated, to which she responded satisfactorily. This case highlights the classical lesions of Indian type of PKDL and reiterates the fact that sodium stibogluconate should still be considered first line therapy as it is a cheap, yet efficacious drug.

Key words: *Post Kala-Azar Dermal Leishmaniasis, Visceral Leishmaniasis, Sodium Stibogluconate*

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INTRODUCTION

Post kala-azar dermal leishmaniasis (PKDL) is a distinct clinical entity that usually occurs after visceral leishmaniasis (VL) caused by parasite *Leishmania donovani.* PKDL is characterized by diverse dermal lesions ranging from hypopigmented patches to erythematous papules and nodules. VL has its home in the plains of the Ganges and Brahmaputra. It has been known to occur epidemically and endemically in the Eastern sector of the country viz. Assam, West Bengal, Bihar, eastern districts of Uttar-Pradesh, foot-hills of Sikkim and to a lesser extent in Tamil Nadu and Orissa. Presently, the endemic states are Bihar, Jharkhand, Uttar Pradesh and West Bengal. Currently about 52 districts of Bihar, 11 districts of West Bengal, 4 districts of Jharkhand and 6 districts of Uttar Pradesh are affected by kala-azar.[1] We report the classical presentation and successful use of sodium stibogluconate as a first line treatment in a patient presenting with PKDL.

CASE REPORT

An 18-year-old girl, a resident of Buxar Dist. of Bihar, India, presented with rash on the central part of her face of six months duration. Rash was insidious in onset and gradually progressive. It was not associated with erythema or pruritus. She denied history of any drug intake, prior to the onset of rash. There was no history of fever or any constitutional symptoms. On persistent questioning, she gave a history of being treated for fever two years back with hospitalization period being about three weeks. However, there were no documents available to substantiate these facts.

General condition of the patient was stable. There was no pallor, cyanosis, or lympadenopathy. Dermatological examination revealed hypopigmented, shiny, succulent,

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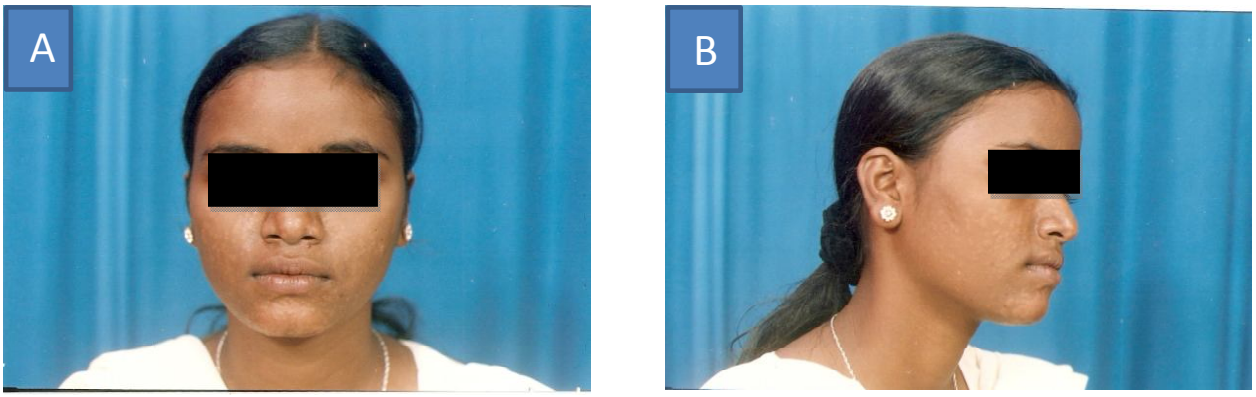

Figure 1: Frontal **(A)** lateral **(B)** clinical photographs of the patient showing succulent indurated plaques over the malar region, angle of the Mandible and chin

indurated plaques distributed over the malar region, angle of mandible and chin (Figures 1A and 2B). There was no associated erythema. The lesions were non-tender and non-ulcerative. Superficial sensations were intact. There was no peripheral nerve trunk thickening. Mucous membranes were unremarkable. Clinically, there was no hepato-splenomegaly. No cardiac abnormality was detected. Examination of chest and nervous system did not reveal any abnormality. A microscopical examination of Geimsa-stained smear prepared from biopsy material demonstrated the amastigote forms of leishmania parasites (Figure 2).

We made a clinical diagnosis favouring PKDL based on history of taking treatment for prolonged fever two years ago, patient's place of origin, site of rash, time - period of onset of rash and morphology of the rash. Other possibilities like leprosy, sarcoidosis, scleroderma and progressive macular hypomelanosis were excluded on diagnostic testing. The diagnosis was confirmed by presence of amastigote forms of leismania parasites in biopsy material from the lesions.

Patient was treated with parenteral sodium stibogluconate 850 mg i.m. per day for 30 days. The patient started showing satisfactory response from the third week of initiating SAG (Figure 3). The patient was followed up for one year. Lesions had resolved and there was no relapse.

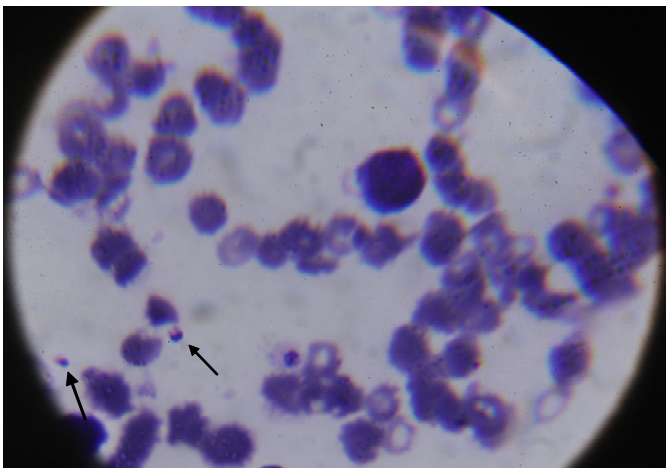

Figure 2: Photomicrograph of imprint smear from skin biopsy exhibiting the presence of Leishmanina Donovan bodies (arrows) (Giemsa, X 100)

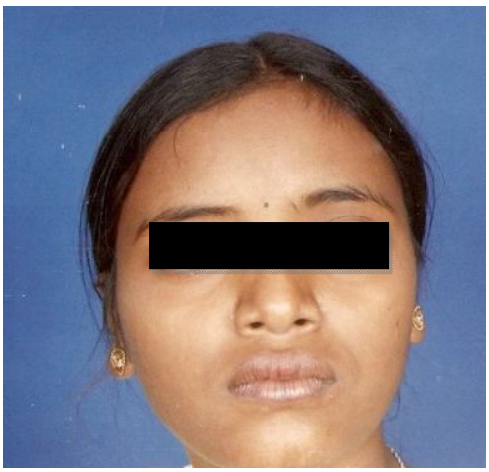

Figure 3: Clinical photograph after satisfactory resolution of post-kala-azar dermal leishmaniasis lesions

DISCUSSION

PKDL was first clinically described from Bengal in 1922.[2] PKDL is a dermatosis that usually occurs after visceral leishmaniasis caused by *Leishmania donovani* and characterized by diverse dermal lesions from hypopigmented pinpoint marks, erythematous papules, to nodules. The dermal lesions appear in individuals who are otherwise asymptomatic (in whom the visceral infection disappears), usually months to years after occurrence and effective treatment for classic kala-azar.[3]

PKDL is mainly found in India (5-10%), Sudan (50%), and Nepal after incomplete or partial treatment of VL cases with sodium stibogluconate. In India, 20% of cases of PKDL have no history of VL and its treatment, but on investigation, *Leishmania donovani* (LD) bodies can be shown in skin snips or biopsy. This type of skin lesion of PKDL may develop in asymptomatic cases of VL who had infection in the past where no kala-azar manifestations are seen.

Cases of PKDL are of considerable epidemiologic importance, because these act as reservoirs of parasites. Transmission of parasite from PKDL cases to other individuals by infected phlebotomine sandflies may have been the cause of massive epidemic of kala-azar in Bihar in the 1970s.[4] It is also found in Africa (2%) but rare in China. No cases have been reported from Mediterranean areas and Central and South America.[5] Poverty, overcrowding, malnutrition, polygamy, illiteracy, and poor domestic conditions facilitate the growth of this disease, which is a major public health problem in India.[6]

PKDL probably has an important role in interepidemic periods of VL, acting as a reservoir for parasites. There is increasing evidence that the pathogenesis is largely immunologically mediated; high concentrations of interleukin 10 in the peripheral blood of VL patients predict the development of PKDL[2]. During VL, interferon-gamma (IFN-γ) is not produced by peripheral blood mononuclear cells. After treatment of VL, peripheral blood mononuclear cells start producing interferon ã, which coincides with the appearance of PKDL lesions due to IFN-ã producing cells causing skin inflammation as a reaction to persisting parasites in the skin. PKDL is essentially a clinical diagnosis, because the dermato-pathological sampling of patients is impractical, and there is lack of definitive laboratory sampling. Demonstration of LD bodies in the slit smear or by culture of the skin tissue is considered to be the *gold standard* for diagnosis of PKDL.[7] Molecular methods like real-time polymerase chain reaction (PCR) are expensive, cumbersome, and require trained personnel and costly equipment.[8]

Treatment is always needed in Indian variety of PKDL and the condition is known for its refractoriness to various modalities of treatment. Antimonial compounds like sodium stibogluconate is the drug of choice for the treatment of VL[9]. Usually, it is administered 20 mg/kg/day for 30 days parenterally upto 120 days. Sodium stibogluconate which used to be a very potent drug for treatment of VL. However, resistance to this drug has emerged and the cure rate in the endemic districts of Bihar is presently as low as 30%-40% with this drug.[10] Moreover, its prolonged administration, as required in PKDL, can limit its use, particularly because of its cardiotoxicity. However, the drug is cheap and is readily available. Our patient, though hailing from Bihar where resistance to this drug is widely present, responded satisfactorily to treatment with sodium stibogluconate.

Pentamidine isethionate is imported for use in PKDL. Its limiting factors are expense and

unacceptable toxicity of causing irreversible diabetes mellitus. Amphotericin-B, both imported and indigenously available, has been used for a considerable length of time with a high efficacy rate. Repeated courses of amphotericin B have been found to be superior to sodium stibogluconate[11] for treatment of PKDL, with a smaller duration in the dose of 1mg/kg body weight i.v. infusion daily or alternate day for 15-20 infusions. Dose can be increased in patients with incomplete response with 30 injections. Liposomal Amphotericin-B in the dose of 2.5 mg/kg body weight is another alternative but is expensive.[12] The only oral drug, which is effective, is miltefosine in the dose of 2.5 mg / kg / day for 28 days with 95% efficacy rates[13]. Inj. paromomycin 15 mg/kg body weight can be used for about 3 weeks. Development of oral sitamaquine may augur well for future combination therapies.

In conclusion, we feel that other than the districts of North Bihar where resistance to pentavalent compounds is found in 30%-40%, in other endemic regions, in a resource poor country like India, compounds like sodium stibogluconate will still remain the first-line therapy of PKDL. Oral miltefosine is available in Bihar National Leishmaniasis control programme but its prolonged half-life raises concern for emergence of resistance. So, it should be judiciously used, to remain a potent option for resistant cases.

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