Post Kala-azar Dermal Leishmaniasis in a patient treated with Injectable Paromomycin for Visceral leishmaniasis-First case report from India.


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Post Kala-azar Dermal Leishmaniasis (PKDL) is a skin manifestation that usually develops after treatment of Visceral Leishmaniasis (VL), a major public health problem in India. The diagnosis and management of PKDL is complex. This is the first case report from India in which PKDL occurred after paromomycin treatment for VL in an Indian patient.

Case Report

A 40 year old lady came to the outdoor patient department (OPD) of Rajendra Memorial Research Institute of Medical Sciences, Patna, India in April 2009 with multiple macula-papular and nodular non-anesthetic patches spread all over the body, more marked on the face and arms. She had previous history of Visceral leishmaniasis (VL) in April 2007 and was treated with injectable Paromomycin (manufactured by Gland Pharma) in the dose of 15 mg/kg body weight, deep intramuscular for 21 days in the indoor ward of our Institute. The patient was cured for VL and found negative for Leishmania donovani (LD) bodies in the splenic aspirate on 22nd day. She did not have any clinical signs and symptoms of VL in the last 2 years, but she noticed macular lesions on the face after about 3 months of VL treatment. She did not bother to visit us because she was not aware of Post Kala-azar Dermal Leishmaniasis (PKDL) and did not have any other complaints. When the macular lesions started progressing into nodular form, spreading all over the body, she came to the OPD for medical advice. The patient was serologically positive with rK39 strip test. The skin snip examination was found positive (2+) for LD bodies. PCR from blood and skin snip was also found positive.

After confirmation of PKDL, she was admitted in the indoor ward and given first course of Amphotericin B in the dose of 1 mg/kg body weight daily for 30 infusions.
After an interval of 15 days, the second course of Amphotericin B in the same dose and duration was repeated. At the end of second course of treatment, the skin lesions had almost disappeared. Microscopic examination of skin snip, collected from the same site, was found negative for LD bodies. On follow-up for 2 years after end of treatment, the patient was found clinically cured. No adverse event was observed either during the treatment or follow up.

Discussion

Post Kala-azar Dermal Leishmaniasis (PKDL) is a dermatitis which tends to develop after treatment for visceral leishmaniasis (VL) in about 50% of VL cases in Sudan and 5–15% in India (6). In Sudan, the lesion usually develops during the treatment or within 6 months of VL treatment whereas in Indian PKDL cases it appears after 2–3 years (2). PKDL has also been reported to develop even after 10 years of VL treatment. PKDL plays an important role in the inter-epidemic period as a reservoir of leishmania infection and its manifestation involves different types of dermal lesions indicating different levels of disease aggravation. In India, PKDL appears either with hypo pigmented macules that may coalesce and spread over the body or in the form of erythematous eruptions that lead to the formation of papules, nodules, and plaques or combinations thereof with progression of the disease (6). A loss of acquired immunity may partially explain the periodicity of VL incidence peaks every 10 to 15 years.

The gold standard for diagnosis of PKDL is still demonstration of LD bodies in the skin snip or biopsy. The macular lesions are the most difficult to diagnose. rK-39
strip test and PCR is positive in cases of PKDL. In about 20-30% of PKDL cases, newer techniques using nested-PCR with skin smear have higher sensitivity (83%) (3, 6).

Treatment of PKDL is another very important aspect as still there is no specific treatment guideline. Sodium stibogluconate (SSG) has been tried and is still being used, but it has to be given for a very long duration (90-120 injections with a gap in between), thereby leading to side effects mainly cardio-vascular (Myocarditis) and arthritis. Amphotericin B is another important alternative but again the treatment is quite long i.e. about 3-4 courses with nephrotoxicity and hypokalaemia as the main side effects (4). In this presented case, two courses of 30 injections each in the dose of 1 mg/kg body weight intravenously in 5% Dextrose with an interval of 15 days between each course were administered. We did not observe any side effects in this case. Repeated course of Ambisome (liposomal Amphotericin B) in the dose of 2.5 mg/kg for 20 injections is another alternative with minimal side effects but considering its high cost it does not seem feasible (4). Dose-finding study of Miltefosine, an oral drug for VL, comparing 2.5 mg/kg for 8 weeks and 12 weeks for treatment of PKDL revealed better cure rate in 12 weeks arm (unpublished data). Its major side effects include diarrhea, vomiting, raised Alanine Transaminase (ALT), Aspartate Transaminase (AST), Blood urea nitrogen (BUN) and serum creatinine. The main drawback of this drug is that, being an anti-neoplastic agent, it can not be given to the pregnant and lactating women.

In conclusion, it is to be stressed that the Kala-azar elimination programme will not be effective till PKDL, the known source of Leishmania infection, will remain in the population. The ensuing Kala-azar elimination programme aims to eliminate Kala-azar from the Indian Subcontinent by 2015 and PKDL by 2018 (5). Hence, PKDL cases need
to be diagnosed and treated along with acute VL cases. PKDL previously was said to occur mainly after treatment with SAG. However, few cases of PKDL have also been reported after treatment with Amphotericin B. Similarly, we have reported a case which developed PKDL after successful VL treatment with miltefosine and even Ambisome (1). This is the first case report from India where PKDL developed after treatment for VL with paromomycin. The VL patients who have been treated with combination therapy like Ambisome-Miltefosine, Ambisome-Paromomycin and Miltefosine-Paromomycin need to be followed for a minimum period of 3-5 years for development of PKDL. If these patients do not develop PKDL, it may be hypothesized that combination therapy with two drugs is better than monotherapy and that can be of effective use in the VL Elimination Programme in the Indian subcontinent.

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References


