Post-Kala-Azar Dermal Leishmaniasis in a Patient Treated with Injectable Paromomycin for Visceral Leishmaniasis in 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 woman came to the outdoor patient department (OPD) of Rajendra Memorial Research Institute of Medical Sciences, Patna, India, in April 2009 with multiple maculopapular and nodular nonnumb patches spread all over the body but more marked on the face and arms. She had a history of visceral leishmaniasis (VL) in April 2007 and was treated with injectable paromomycin (Gland Pharma) at a dose of 15 mg/kg of body weight, deep-intramuscular injections, for 21 days in the indoor ward of our Institute. The patient was cured of VL and found negative for Leishmania donovani bodies in the splenic aspirate on the 22nd day. She did not have any clinical signs and symptoms of VL in the next 2 years, but she noticed macular lesions on the face about 3 months after 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 the rK-39 strip test. The skin snip examination was positive (2+) for L. donovani bodies. PCR from blood and skin snip was also positive.

After confirmation of PKDL, she was admitted to the indoor ward and given a first course of amphotericin B at a dose of 1 mg/kg of body weight daily for 30 infusions. After an interval of 15 days, a second course of amphotericin B at the same dose and duration was administered. At the end of the second course of treatment, the skin lesions had almost disappeared. Microscopic examination of skin snip, collected from the same site, was negative for L. donovani bodies. In follow-up for 2 years after the end of treatment, the patient was found to be clinically cured. No adverse event was observed during either the treatment or the 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 to 15% in India (6). In Sudan, the lesions usually develop during the treatment or within 6 months of VL treatment, whereas in Indian PKDL cases, they appear after 2 to 3 years (2). PKDL has also been reported to develop even 10 years after VL treatment.

PKDL plays an important role in the interepidemic 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 hypopigmented 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 L. donovani bodies in the skin snip or biopsy specimen. The macular lesions are the most difficult to diagnose. rK-39 strip test and PCR are positive in cases of PKDL. In about 20 to 30% of PKDL cases, newer techniques using nested PCR with skin smear have higher sensitivity (83%) (3, 6).

The treatment of PKDL is another very important aspect as there is still 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 to 120 injections with a gap in between), thereby leading to side effects, mainly cardiovascular (myocarditis) and arthritis. Amphotericin B is another important alternative, but again, the treatment is quite long, i.e., about 3 or 4 courses, with nephrotoxicity and hypokalemia as the main side effects (4). In the case presented here, two courses of 30 injections of amphotericin B were administered, each at a dose of 1 mg/kg of body weight intravenously in 5% dextrose, with an interval of 15 days between the courses. We did not observe any side effects in this case. A repeated course of Ambisome (liposomal amphotericin B) at a 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). A 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 a better cure rate in the 12-week arm (unpublished data). Its major side effects include diarrhea, vomiting, and increases in alanine transaminase (ALT), aspartate transaminase (AST), blood urea nitrogen (BUN), and serum cre-
atinine. The main drawback of this drug is that, being an antineo-
plastic agent, it cannot be given to pregnant and lactating women.

In conclusion, it is to be stressed that the kala-azar elimination
program will not be effective until PKDL, the known source of
Leishmania infection, no longer remains in the population. The
kala-azar elimination program 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 sodium antimony gluconate (SAG). However, a few cases of
PKDL have also been reported after treatment with amphotericin
B. Similarly, we have reported a case in which PKDL developed
after successful VL treatment with miltefosine and even Ambi-
some (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 therapies,
such as Ambisome-miltefosine, Ambisome-paromomycin,
and miltefosine-paromomycin, need to be followed for a min-
imum period of 3 to 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 mono-
therapy and that such treatment can be effective in the VL
elimination program in the Indian subcontinent.

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REFERENCES

2. Dutta M, Ghosh TK. 1983. Review of current status of leishmaniasis epi-
demiology, p 97–102. Proceedings of the Indo-UK Workshop on Leish-
maniasis. Indian Council of Medical Research, New Delhi, India.
detection of Leishmania donovani in clinical samples from patients with
kala-azar and post-kala-azar dermal leishmaniasis. J. Clin. Microbiol. 39:
849–854.
4. Singh S, Sundar S. 1995. Treatment of post-kala-azar dermal leishmania-
5. Singh SP, et al. 2011. Options for active case detection of visceral leish-
maniasis in endemic districts of India, Nepal and Bangladesh, comparing in
endemic districts of India, Nepal and Bangladesh, comparing yield, feasi-