JCM
Journals.ASM.org

Post-Kala-Azar Dermal Leishmaniasis in a Patient Treated with Injectable Paromomycin for Visceral Leishmaniasis in India

Krishna Pandey, V. N. R. Das, Dharmendra Singh, Sushmita Das, C. S. Lal, N. Verma, S. Bimal, R. K. Topno, N. A. Siddiqui, R. B. Verma, P. K. Sinha, and Pradeep Das

Rajendra Memorial Research Institute of Medical Sciences (Indian Council of Medical Research), Agamkuan, Patna, Bihar, India

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-

Received 1 October 2011 **Returned for modification** 31 October 2011
Accepted 14 January 2012
Published ahead of print 25 January 2012
Address correspondence to Krishna Pandey, drkrishnapandey@yahoo.com.

doi:10.1128/JCM.05966-11

atinine. The main drawback of this drug is that, being an antineoplastic 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 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 therapies, such as Ambisome-miltefosine, Ambisome-paromomycin, and miltefosine-paromomycin, need to be followed for a minimum 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 monotherapy and that such treatment can be effective in the VL elimination program in the Indian subcontinent.

ACKNOWLEDGMENTS

No funding or conflicts of interest are reported by any of the authors.

We thank Sri Naresh Kumar Sinha (technical assistant) for the help rendered by him in the preparation of the manuscript.

REFERENCES

1. **Das VNR, et al.** 2009. Development of post kala-azar dermal leishmaniasis (PKDL) in miltefosine-treated visceral leishmaniasis. Am. J. Trop. Med. Hyg. **80**:336–338.
2. **Dutta M, Ghosh TK.** 1983. Review of current status of leishmaniasis epidemiology, p 97–102. Proceedings of the Indo-UK Workshop on Leishmaniasis. Indian Council of Medical Research, New Delhi, India.
3. **Salotra P, et al.** 2001. Development of a species-specific PCR assay for 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 leishmaniasis. Int. J. Dermatol. **34**:668–669.
5. **Singh SP, et al.** 2011. Options for active case detection of visceral leishmaniasis in endemic districts of India, Nepal and Bangladesh, comparing in endemic districts of India, Nepal and Bangladesh, comparing yield, feasibility and costs. PLoS **5**:e960.
6. **Zijlstra EE, El-Hassan AM.** 2001. Leishmaniasis in Sudan: post kala-azar dermal leishmaniasis. Trans. R. Soc. Trop. Med. Hyg. **95**(Suppl 1):S59–S76.