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Leishmaniasis Recidivans in a Palestinian Bedouin Child

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In February 2005, a 12-year-old Palestinian Bedouin child with a small lesion on his upper cheek just below the right eye was referred to Leishmania Research Unit medical laboratory in Jericho for diagnosis of suspected cutaneous leishmaniasis. He lived in a rocky desert area by Wadi-Qelt, approximately 4 km from Jericho City center and attended the school in the adjacent Aqabat Jabr refugee camp, which borders Jericho City. He remained confined to this area for the few months before the lesion's appearance. The lesion was less than 1 cm in diameter, was bacterially clean, and had a small encrusted crater in its center. The lesion was 2 months old when first examined. There were no indications of previous cutaneous leishmaniasis, but other family members described having been exposed to cutaneous leishmaniasis. The family's residential area was rocky and cavernous with a continuously flowing stream that provided Jericho with drinking and irrigation water. There were irrigated banana plantations nearby. Extracellular amastigotes were seen in tissue smears stained with Giemsa stain (Figure 1). These parasites were identified as *Leishmania tropica* by DNA analysis. This was done by amplifying the internal transcribed spacer-1 of the ribosomal RNA genes, using a Gene Amp PCR-system 9700 (Applied Biosystems, Foster City, CA) followed by restriction fragment length polymorphism.[1,2] The DNAs of leishmanial species reference strains were included for comparison (Figure 2). The patient was treated with sodium stibogluconate injected intralesionally at 10 mg/kg/d every other day for 3 weeks, then twice a week for 2 months, and once a week thereafter for 3 months. The lesion seemed to re-epithelialize during the 3 months from February to early May. The patient was lost to follow-up until November 2005, when he returned with a small, red, smooth macule. This enlarged, and papules typical of Leishmaniasis recidivans appeared at its margins. Microscopic examination and DNA analysis were repeated and again showed the presence of *L tropica*. The patient was treated with intralesional sodium stibogluconate for another 5 months. The patient returned a third time in April 2006, 14 months after initial presentation, with a more severe and destructive nodular condition (Figure 3). Microscopic examination and DNA analysis were repeated, during which 2 tubes of rabbit blood-agar semisolid medium were inoculated with tissue aspirate to isolate the parasite. This time, no amastigotes were seen in the stained smears, and the internal transcribed spacer-1-PCR results were negative, but culture medium in 1 tube grew promastigotes. The lesion remained active throughout further treatment. The Bedouin family said they would apply a traditional therapy.

Leishmaniasis recidivans (LR) caused only by *Leishmania tropica* is a rare form of cutaneous leishmaniasis (CL). It appears as a chronic nonhealing or relapsing lesion that becomes visible on or at the edge of a scar produced by a primary cutaneous ulcer and as metastases to other parts of the skin. It may persist for more than 20 years[3] or may relapse after 43 years.[4]

This is the first reported case of a suspected CL recidivans in the Jericho district, which has been a classical focus for *Leishmania major* and only recently has harbored *L tropica*.[1] In West Asia, CL recidivans has been reported in Iran[5] and Iraq[6] and has been observed in up to 6% of the population in Sanliurfa in southern Turkey.[7]

Several types of drugs are commonly used for the treatment of CL, including pentavalent antimonials and paramomycin, a topical ointment. Antimonials are still considered a first-line drug.[8] Sodium stibogluconate may be administered intravenously or intramuscularly, with a recommended dosage of 20 mg/kg/d for 15 to 20 days, while meglumine antimonate should be given only intramuscularly. There have been no studies on the efficacy of sodium stibogluconate in the Jericho area of Palestine, although it has been used in Jericho for the past 2 decades.

The dosage and treatment schedule used in this patient, although different from the standard treatment protocol, has previously demonstrated good results in treating CL in Jericho. One group reported that monotherapy similar to that described herein was effective in treating CL.[9] In the past 5 years, however, *L tropica* has been recorded in the Jericho area in high percentages relative to *L major*, leading to an increase in resistant cases. The *L tropica* parasite is known to be less responsive to the standard treatment than *L major*.[1,10,11]

Polymerase chain reaction (PCR)-based species determination is crucial to review the natural history and response to medication of the various *Leishmania* species causing CL, especially in areas with more than 1 endemic *Leishmania* species, as in Jericho. As this case showed, culturing the parasite in cases of LR is important. At the third presentation, both PCR and microscopic examination failed to confirm the parasite's presence. This probably resulted from an uneven distribution of the parasite in the

sample; the LR papules generally contain few parasites. Therefore, it is important to employ several different diagnostic procedures and to sample from several sites to compensate for the high failure rate of detection techniques, as is also the case with New World leishmaniasis due to *Leishmania braziliensis*.[12]

The reasons for relapse after treatment of the boy's lesion remain unknown. The patient may have failed to fully comply with the therapy schedule or the lesion may have been caused by a resistant strain. Failure to take regularly scheduled treatment may cause the emergence of drug resistance, as has occurred in Bihar, India.[1] In addition, other factors associated with treatment failure cannot be excluded, including body weight and native immune status, both of which have been associated with treatment failure.[13]

A second-line medication, amphotericin B (deoxycholate), was suggested to the patient. This medication, which is highly nephrotoxic, has not been shown to be entirely effective in clearing the infection either.[14] Owing to the economic hardships following the Palestinian general election in January 2006, neither the Ministry of Health nor the family could afford to try amphotericin B, which, as a second-line drug, is not available cost-free from pharmaceutical companies, as are many first-line essential medications. Hence, the Bedouin family considered using traditional therapy using a mixture of gunpowder and garlic, but this was never done, for fear of disfiguring the child's face.

Theoretically, LR caused by *L tropica* is treated with antimony administered either intramuscularly or intravenously for long periods with close supervision of the liver enzymes, glutamic-oxaloacetic transaminase, glutamic pyruvic transaminase, and amylase. The medical staff of the Jericho Health Department preferred administering sodium stibogluconate intralesionally in this patient because of the complexity of follow-up. In relapsing cases in which chronicity is maintained, combined treatment should be considered.[15] Surgical intervention is an option but is not generally recommended. Thermotherapy and cryotherapy should not be ruled out when the lesion is small and has not been very destructive.[16]

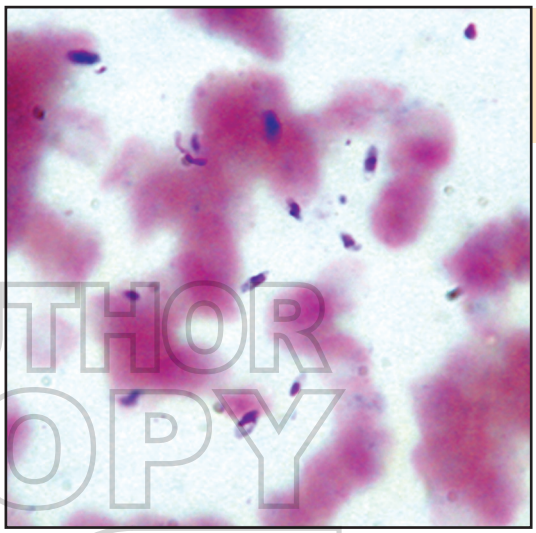

Figure 1. *Giemsa-stained smear showing extracellular amastigotes (original magnification ×1000).*

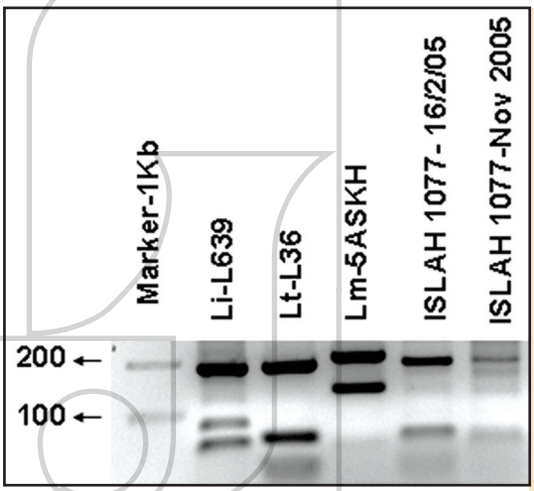

Figure 2. *Restriction fragment length polymorphism analysis of the amplified internal transcribed spacer-1-Gene Amp PCR products (Applied Biosystems, Foster City, CA) following digestion with* HaeIII*: left to right, the World Health Organization reference strains of* Leishmania infantum *(MHOM/TN/1980/IPT1),* Leishmania tropica *(MHOM/AZ/1974/SAF-K27), and* Leishmania major *(MHOM/TM/1973/5ASKH); leishmanial DNA from the patient's samples taken in February 2005; and leishmanial DNA following the relapse in November 2005.*

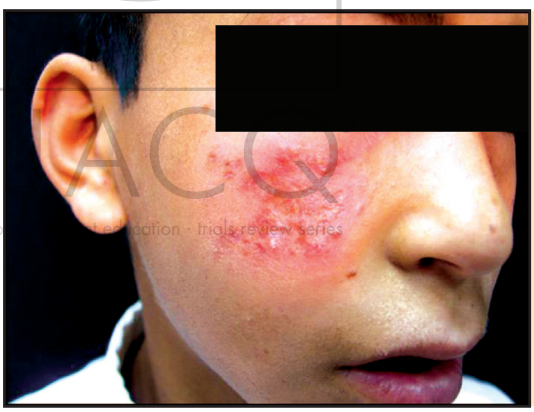

Figure 3. *The 12-year-old Palestinian boy with Leishmaniasis recidivans, showing small papules at the edge of the central lesion after several months of almost complete cure. After 5 months of antimony treatment following relapse, promastigotes were isolated, while the microscopic examination and internal transcribed spacer-1-Gene Amp PCR (Applied Biosystems, Foster City, CA) results were negative.*

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