Cutaneous leishmaniasis: an increasing threat for travellers
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ABSTRACT
Analysis of the literature on cutaneous leishmaniasis in low-prevalence countries suggests an increase in imported cases that is attributable to the growing phenomenon of international tourism, migration and military operations in highly endemic regions. Cases of imported cutaneous leishmaniasis are often missed initially, but diagnosis can be made non-invasively by PCR using skin scrapings of lesions as starting material. Cutaneous leishmaniasis is an emerging threat for travellers and should be considered in all patients presenting with slow-to-heal ulcers.

Keywords  Cutaneous leishmaniasis, imported disease, leishmaniasis, PCR, travellers


Leishmaniasis is a parasitic disease transmitted by sand flies. It is characterised by a spectrum of cutaneous, mucocutaneous and visceral clinical manifestations that depend largely on the species of parasite involved and the host immune response. According to recent estimates, 1.5 million new cases of cutaneous leishmaniasis (CL) occur each year. More than 90% of cases occur in five countries in the Old World (Afghanistan, Algeria, Iran, Iraq and Saudi Arabia) and two countries in the New World (Brazil and Peru) [1]. CL in the Old World is caused by Leishmania infantum, L. major, L. tropica and L. aethiopica, which are found in southern Europe, the Mediterranean basin, the Middle-East and Africa. CL in the New World is mainly caused by members of the L. braziliensis complex (L. braziliensis and L. peruviana), L. mexicana, L. amazonensis and the L. guyanensis complex (L. guyanensis and L. panamensis).

In a prospective study performed during 1991–93 in a tropical disease unit in Paris, CL was identified in 3% of 269 patients with travel-associated dermatoses, ranking this disease eighth among all the observed causes of skin disease [2], while Herwaldt et al. [3] reported 58 imported cases of New World CL between 1985 and 1990 among travellers from the USA. An apparent increase in imported CL is indicated by the fact that at least 108 such cases were described in the English language scientific literature between 1999 and 2003, most of which involved travellers and military personnel (Table 1) [3–12]. Furthermore, at the beginning of 2004, the USA Department of Defense reported 522 confirmed cases of CL in soldiers deployed in south-west/central Asia [13]. In keeping with this apparent increase, four imported cases of Old and New World CL were diagnosed in Milan, Italy during a 16-month observation period that started in 2001.

The first case was an Italian male aged 26 years who had travelled extensively in Costa Rica and who presented 2 weeks after his return to Italy with three cutaneous ulcerated lesions on both legs. A skin biopsy from the largest ulcer yielded a positive microscopic diagnosis of amastigotes of Leishmania spp. which were identified after in-vitro culture as L. panamensis. PCR-restriction fragment length polymorphism (RFLP) analysis of DNA extracted from skin scrapings of the lesion identified the parasite as belonging to the L. braziliensis complex [14]. The patient was treated successfully with a course of parenteral liposomal amphotericin B (total dose, 1800 mg) and intra-lesional meglumine antimoniate.

The second case was an Italian male aged 63 years who developed two nodular skin lesions 3 months after returning from a 3-week trip to Tunisia and Morocco. The diagnosis of CL was
Table 1. Summary of case reports and series (1999–2003) reporting Old and New World imported cutaneous leishmaniasis in travellers

<table>
<thead>
<tr>
<th>Ref.</th>
<th>No. of patients/type</th>
<th>No. of lesions (no. of patients)</th>
<th>Localisation</th>
<th>Countries visited (no. of patients)</th>
<th>Species involved (no. of patients)</th>
<th>Method of diagnosis (no. of patients)</th>
<th>Observation period</th>
</tr>
</thead>
<tbody>
<tr>
<td>[4]</td>
<td>13/military personnel</td>
<td>1 (10); 2 (3)</td>
<td>NR</td>
<td>Belize (13)</td>
<td>L. braziliensis complex (13)</td>
<td>Skin biopsy (13); cutaneous PCR (13); culture 60</td>
<td>1998–99</td>
</tr>
<tr>
<td>[5]</td>
<td>1/Italian traveller</td>
<td>3</td>
<td>Hand</td>
<td>Brazil</td>
<td>L. viannia braziliensis</td>
<td>Dermal scraping and culture NR</td>
<td>NR</td>
</tr>
<tr>
<td>[6]</td>
<td>3/US military personnel</td>
<td>1</td>
<td>Face; temporal scalp; hand</td>
<td>Panama (3)</td>
<td>L. braziliensis panamensis</td>
<td>Skin biopsy (3); culture (3) NR</td>
<td>1997</td>
</tr>
<tr>
<td>[7]</td>
<td>5/German travellers</td>
<td>1</td>
<td>Face/neck (2); arm/hand (2); leg (1)</td>
<td>Costa Rica (1); Guatemala (1); Saudi Arabia, Turkey (1); Niger (1)</td>
<td>L. braziliensis panamensis (2); L. tropica (1); L. major (1); L. donovani (1)</td>
<td>Skin biopsy (3); skin culture (1); PCR 6</td>
<td>NR</td>
</tr>
<tr>
<td>[8]</td>
<td>1/Canadian traveller</td>
<td>1</td>
<td>Leg</td>
<td>Belize</td>
<td>L. braziliensis</td>
<td>Skin biopsy negative; culture; PCR NR</td>
<td>2000–02</td>
</tr>
<tr>
<td>[9]</td>
<td>35/German travellers</td>
<td>Mean, 2; range 1–6</td>
<td>Face (26%); upper extremities (42%); lower extremities (32%)</td>
<td>Peru (3); Brazil (2); Ecuador (2); French Guiana (2); Bolivia (1); Guatemala (1); Afghanistan (2); Syria (2); Turkey (2); United Arab Emirates (1); Egypt (2); Kenya (1); Libya (1); Malta (4); Sarp (4); France (1); Italy (3)</td>
<td>L. tropica (3); L. braziliensis complex (10); L. mexicana (1); L. donovani complex (8)</td>
<td>Skin smears (13); skin biopsy (14) cultures (9); PCR (6)</td>
<td>NR</td>
</tr>
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<td>[10]</td>
<td>25/French travellers; African migrants</td>
<td>NR</td>
<td>NR</td>
<td>Algeria (9); Senegal (5); Mali (4); Mauritania (3); Turkey (2); Tunisia (1); Spain, Italy (1)</td>
<td>L. major (7); MON-25 (4); MON-74 (2); L. tropica (1); L. infantum MON-34 (1)</td>
<td>Dermal scraping (19); skin biopsy (4); culture (17); PCR 24</td>
<td>1998–2001</td>
</tr>
</tbody>
</table>

NR, not reported.
established by microscopy of one of the lesions. PCR-RFLP analysis of skin scrapings from the ulcer borders identified *L. major* as the causative agent, with subsequent confirmation after in-vitro isolation by isoenzyme electrophoretic characterisation. Meglumine antimoniate treatment was administered intra-lesionally, resulting in complete healing of a lesion localised to the chest, but complete resolution of a second lesion on the leg required an additional 6-week course of oral itraconazole.

The third case was an Italian male aged 28 years who presented with an ulcerated nose lesion that appeared a few days after returning from a 4-week stay in Mexico, where he had engaged in extensive outdoor activities. Microscopic examination of a skin biopsy revealed amastigotes of *Leishmania* spp., and PCR-RFLP analysis of a skin scraping identified the *L. braziliensis* complex. The patient was treated with a short course of intravenous pentamidine isethionate, resulting in complete healing of the lesion.

The fourth case involved a soldier from Afghanistan, aged 23 years, who was deployed in Italy for 2 months and who developed three cutaneous lesions. Histopathological examination of an ulcerated foot lesion revealed *Leishmania* tissue amastigotes, identified by PCR-RFLP as belonging to the *L. aethiopica-L. tropica* group. The patient was treated with a short course of intra-venous pentamidine, resulting in rapid clinical improvement of all lesions.

*CL* may present as single or multiple lesions that generally occur on parts of the body exposed to sand fly bites. The appearance of the lesions is quite variable, depending on the species of parasite involved and on the genetic and immunological background of the host. In all four cases described above, the diagnosis of *CL* was missed initially by the general physician, and the patients had been treated inappropriately with systemic antibiotics before being referred. Similarly, in the large retrospective USA study [3], the 58 patients interviewed had consulted a mean of 2.1 physicians (range, 1–7 physicians) before the diagnosis of *CL* was considered, and a median of 112 days (range, 13–1022 days) elapsed from the time the lesions were first noticed and treatment with sodium stibogluconate. Since many physicians in western countries have limited experience of diagnosing *CL* in returning travellers, diagnostic delays and inappropriate management are to be expected.

In addition to a low awareness of *CL* among general physicians, the problem arises of how to achieve a definitive diagnosis. Although histopathological examination is useful in excluding other diagnoses, its sensitivity in diagnosing *CL* may only be 14–18% [15–17]. PCR appears to be the best method for confirming a diagnosis of *CL*, with a sensitivity of 98–100% and a specificity of 100% at the genus level [3,6,10,11]. Faber *et al.* [18] compared PCR with traditional diagnostic techniques (i.e., skin test, culture and histopathology) and found that PCR exhibited no significant difference in sensitivity when compared with the combined results of the three traditional tests, and had the highest sensitivity when used as a single diagnostic procedure [18]. In the cases reported from 1999 to 2003 (Table 1), PCR was positive in 67 of the 68 instances in which it was performed, while in the four cases described above, it was possible to readily amplify specific *Leishmania* sequences from skin scrapings of the lesions, thus avoiding skin biopsies that may be undesirable when involving certain areas of the body such as the face. There was complete concordance between the results obtained by PCR-RFLP and isoenzyme typing methods.

The final issue regarding imported *CL* is the choice of therapeutic agent. Factors that may influence this decision include: (i) the absence of evidence-based data regarding travellers; (ii) the possible high toxicity associated with parenteral treatment for a benign self-healing disease (with the exception of New World *CL* where there is a risk of mucosal dissemination); (iii) the compliance of the patient; and (iv) the lack of availability of appropriate drugs, especially pentavalent antimonial agents, in certain countries [19].

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