Cutaneous Leishmaniasis: a 10-Year Experience in a Canadian Reference Centre for Tropical Diseases

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Abstract

Background: Cutaneous leishmaniasis (CL) is increasingly encountered in returned travellers and migrants to non-endemic countries such as Canada. Diagnosis is often delayed or missed because of the lack of awareness.

Methods: A retrospective descriptive study was performed including all the laboratory confirmed diagnoses of CL between January 2008 and October 2018 for which complete clinical data was available at the J.D. MacLean Centre for Tropical Diseases, Montreal.

Results: Forty-eight patients met criteria for inclusion (median age: 43.5 years (range: 1 - 75); male: 28 [58%]). Median time from onset to diagnosis was 89 days (IQR: 76). At initial presentation, New World (NW) CL (n=33) presented more often as ulcers (n=28 [85%]) compared to Old World (OW) CL (n=15) that mostly presented as plaques (n=9 [60%]); p=0.001. PCR had the highest sensitivity (98%) compared to smear, histopathology, and culture (64%-68%). The most common species identified for the NW CL was *Leishmania (V.) panamensis* in 23 patients (70%) and for the OW CL, *L. (L.) major* in 7 patients (47%). Liposomal amphotericin B (L-AmB) was the most used initial treatment in 20/38 (53%). Thirty-five patients completed their follow-up, 11 (69%) responded successfully to one course of L-AmB and adverse events were reported in 30% of patients. Complete cure was achieved within 1 year in 32 patients out of 35 (91%).

Interpretation: CL in non-endemic regions is often diagnosed late. Diagnosis should be confirmed by molecular testing. L-AmB is easily available but shows modest response and adverse events are common.

Introduction

Cutaneous and mucosal leishmaniasis (CL and ML respectively) are protozoan infection transmitted by the bite of female sandflies. This neglected tropical disease affects 600 000 to 1 million new individual annually. [1] Close to 20 *Leishmania* spp. are involved in human CL/ML and belong to 2 main subgenera, *Leishmania* and *Viannia.* Cutaneous leishmaniasis cases mainly occur in the Americas (New World (NW)) as well as in the Mediterranean basin, the Middle East, and Central Asia (Old World (OW)).

The clinical presentation of cutaneous leishmaniasis depends on various factors including the acquired species, strains, and virulence factors as well as host characteristics, such as age, gender, and immune status. [2,3] The lack of awareness of CL in the returned travellers and migrants amongst primary care physicians in non-endemic countries as well as the varied clinical manifestations may result in delayed diagnosis. [4]

Polymerase chain reaction (PCR) has the best sensitivity (97-100%) for the diagnosis of CL/ML compared to direct visualization of parasite (33-57%) or culture (67%). [5] Speciation is an important step in CL diagnosis and an invaluable tool to inform therapeutic approaches and prognosis and should be performed when available. [2,6]

Treatment of CL can be challenging, as there is no universally applicable approach. Management should be individualized based on several factors such as: *Leishmania* species, host immune status, location, size and number of lesions and presence of mucosal involvement. [6]

Treatment is believed to reduce scarring, and prevent disease progression, dissemination, subsequent ML, and relapse. [5-7]

The J.D. MacLean Centre for Tropical Diseases, one of the largest tropical medicine centres in North America, provides medical care to travellers, migrants, and refugees. It is also part of the GeoSentinel Surveillance Network (www.geosentinel.org). Recent study looking at CL/ML in travellers and migrants over the past 20 years by the GeoSentinel surveillance network has demonstrated a slow increase of cases per 10 000 travellers encountered in the past decade. [8] Very few studies have reported the clinical experience of North American tropical medicine clinics in diagnosis and outcomes of CL. [9,10]

We report the clinical, microbiological characteristics and the treatment related outcomes of all CL cases encountered over a 10-year period in our centre. By sharing our experience, we aim to raise awareness of CL among clinicians who may encounter these cases, including general practitioners, dermatologists, and infectious diseases specialists.

Methods

We conducted a retrospective descriptive study of patients with CL diagnosed or referred to the J.D. MacLean Centre for Tropical Diseases between January 2008 and October 2018. All patients with a confirmed diagnosis of CL by a positive smear, histopathology, culture and/or PCR were included in the study. Patients with no laboratory-confirmed diagnosis as well as patients with Post Kala-azar Dermal Leishmaniasis (PKDL) were excluded. Cases assessed only by teleconsultation for whom follow-up was not available were excluded. The data was collected from

the patients' electronic medical charts and included demographics, travel history, clinical presentation, diagnostic methods, and treatments. The purpose of travel was adapted from GeoSentinel Surveillance Network definitions. [8] The primary outcome evaluating the clinical response to treatment in this study was defined as the complete reepithelialisation at 1 year after the initiation of treatment. [11]

Data Analysis

Descriptive statistics were used to summarize patients' demographic, epidemiologic, clinical and treatment data. Missing data were excluded from the analysis. Categorical variables were expressed as frequencies and percentages and were compared between OW and NW CL using Chi-square (X2) and Fisher's exact test, where appropriate. Continuous variables were expressed as mean and standard deviation or as median and interquartile range (IQR) for non-normally distributed variables. Continuous variables were compared between the OW and NW CL groups using the Student's T-test or the Mann-Whitney Test for non-normally distributed variables. Differences between groups were considered significant if P-value < 0.05. Sensitivity of the different methods of detection was evaluated using a composite reference standard defined as a lesion clinically and epidemiologically consistent with leishmaniasis and at least one positive laboratory test. Statistical analyses were performed using STATA version 14.2.

The study was approved by the McGill University Health Centre research ethics review board.

Results

A total of 48 patients were included in our study. Table 1 describes the demographic and clinical characteristics of the returned travellers and migrants. Twenty-eight patients (58%) were

male, and the median age was 43.5 years (IQR=34; range=1-75). Five patients (10%) were below age of 18 (1-12). The patients' regions and countries of birth are presented in Supplemental Table 1. The median time from initiation of symptoms to diagnosis was 89 days (11-496) and patients consulted a median of 2 physicians before being seen in our reference centre (Table 1). The most common region of exposure for OW CL are Middle East (5/15, 33 %), North Africa (5/15, 33%) and Sub-Saharan Africa (3/15, 20%) (Table 1). For NW CL, the most common countries of exposure were Costa Rica (11/31; 35%), followed by Mexico (7/31; 23%). A comprehensive list of all countries of exposure can be found in Supplemental Table 2. The most common purposes of travel were tourism (n= 24, 50.0%) and visiting friends and relatives (VFR) (n= 7, 14.6%). Travellers who presented with NW CL were more likely to travel for tourism and those presenting with OW CL were more likely VFR travellers (p=0.028) (Table 1). Migration-related cases accounted for 10.4% (n=5) and amongst those cases, 3 patients were refugees. The median duration of travel was 42 days (IQR:69) and 12.5% of patients travelled for 2 weeks or less. Only 22.9% (11/48) of the patients had a diagnosis of CL established before coming to our centre. Overall, 19 patients (40%) consulted a dermatologist before being referred to our center. Two of those 19 patients (10.5%) had a diagnosis of CL established before being referred.

Clinical characteristics of the lesion stratified by geographical area of exposure (OW vs NW) are presented in table 2. Patients with OW CL presented more often with a plaque (n=9; 60%), whereas most of the patients diagnosed with NW CL presented with an ulcer (n=28; 85%), (p<0.001). A total of 9 patients (19%) presented with adenopathy, all of which were diagnosed with NW CL (p=0.025). No patient in this study had mucosal involvement. Figure 1 presents the distribution of the skin lesions. The face and neck (n=14, 29%) and the lower extremities (n=15,

31%) were the main area involved. PCR had the best sensitivity by far (98%) compared to the other diagnostic methods (64-68%). More details on the diagnostic methods used and their sensitivity are found in Table 3. Speciation was available for 43 of the 48 CL cases. The top 3 species were *Leishmania (V.) panamensis* (53.5%), *Leishmania (L.) mexicana* (16.3%) and *Leishmania (L.) major* (16.3%). The detailed distribution of species can be found in Supplemental Table 3.

Information regarding treatment plan was available for 47 patients (98%) (Table 4). Patients who did not receive treatment were either lost to follow-up or were clinically cured when referred to our centre. Overall, the most used first-line treatment was liposomal amphotericin B (n=20; 53%). Out of the 38 patients who received a first-line treatment, 13 received a second-line treatment. The most used treatments in second line were L-AmB (n=4; 31%) and oral fluconazole (n=3; 23%).

In total, 35 of the 48 patients (73%) included in the study had a complete follow-up 1 year after initiation of treatment. Of these, 32 (91%) were cured. Amongst patients who completed their follow-up, 11 patients (69%) responded successfully to one course of treatment with L-AmB. When L-Amb was used either as the first or second-line treatment, the cure at one year was 75%. Adverse events were evaluated for 20 patients (80%) of the 24 who received L-AmB either as the first or second-line treatment. A total of 6 patient (30%) experienced adverse effects. Three (50%) of these patients had acute kidney injury. The other adverse effects reported were shortness of breath during infusion, increased pancreatic enzymes and fatigue. In patients with OW CL, 12

(80%) had a complete follow-up after 1 year and 10 (83%) were cured whereas in patients with NW CL 23 (70%) had a follow-up after 1 year and 22 (96%) were cured.

Discussion

Our clinic has seen an increased number of annual cases of CL throughout the years, from 9 cases (2008 to 2009) to 16 cases (2017 to 2018). This recent increase has also been reported by the GeoSentinel Surveillance Network over the last decade as well as in a recent retrospective observational study in Sweden. [8,12] Patients diagnosed with NW CL were more likely to travel for tourism. The most represented countries were Costa Rica followed by Mexico which are very popular tourist destinations for our population. In Central America, Costa Rica reports the highest burden of CL with estimated annual incidence of 3500 to 5700 cases. [13] As previously reported, NW CL is increasingly seen in tourist travellers and may represent a change in popular travel destinations with travel in Latin America being increasingly common. [8,14] Traveller's' behaviour, such as ecotourism, may also result in increased risk. On the other hand, OW CL was seen mostly in VFRs who travelled to North Africa, West Africa and Middle East. This reflects the regions of origin of our migrant population. A similar difference in purpose of travel between OW and NW CL has been described recently. [8] Amongst all cases, 10% were related to migration and 3 patients were refugee from Iran, Syria, and Haiti. Two of the refugees were children, both age 12 at diagnosis and both presenting with chronic lesions of 6 to 12 months duration before diagnosis was made. This highlights the vulnerability of this group to acquire leishmaniasis, as well as their difficulties in accessing care.[15] The median duration of travel was 42 days (IQR: 69 days) but in 12.5% of cases, the travel duration was 2 weeks or less, which illustrate that CL is not only an

infection of long-term travellers.[8] This also reinforces the need for better pretravel counselling about protective measures to minimize vector exposure. [6]

The median time between symptoms and diagnosis was 89 days (range 11-496) and patients consulted a median of 2 physicians (range: 0-5) before being referred to our centre. This illustrates the diagnostic challenges and the lack of awareness of CL in non-endemic settings. Delayed diagnosis has also been observed in other case series. [16-18] Interestingly, diagnostic delay is also observed in endemic settings such as Spain. [17] This finding could also partly be explained by referral bias, with more complex and atypical cases being referred to our centre.

Although the numbers are small, it appears that there is a difference in morphology at initial presentation between OW and NW CL. We observed that OW CL initially presented more often as plaques, whereas NW CL presented more commonly as ulcers ($p<0.01$). NW CL was also more frequently associated with adenopathy ($p=0.025$). *Leishmania (V.) panamensis* was the most common species diagnosed in our patients. This illustrates the propensity of species of the *Viannia* subgenus to cause a significant inflammatory response with lymphatic involvement. [14,16,19] *Leishmania (L.) major* was the most identified species among the OW CL with 57% of the lesions presented as plaques. Patients were diagnosed between 50 and 102 days after the initiation of symptoms. *Leishmania (L.) major* can spontaneously heal within approximately 2 to 6 months, therefore, the healing process may have started in those patients before diagnosis was made, with an impact on the morphology seen (plaque rather than initial ulcer) at initial presentation to our centre.[6]. No cases of mucosal leishmaniasis were seen in our centre during the study period. Several species of the *Viannia* subgenus have a strong association with mucocutaneous and

mucosal leishmaniasis, *Leishmania (V.) braziliensis* having the strongest association. Only 3 patients were diagnosed with *L. (V.) braziliensis* with *L. (V.) panamensis* being the most common *Viannia* species in our study. The recently published GeoSentinel Surveillance Network analysis on CL has also demonstrated that all travel related cases of MCL were due to *L. (V.) braziliensis* despite *L. (V.) panamensis* being the most reported *Viannia* subgenus species. [8]

The diagnostic method with the highest sensitivity was PCR (98%), confirming the findings of others. [3] The other methods (smear, culture, and histopathology) had sensitivity ranging from 64 to 68%. These numbers are consistent with what has been described in the literature. [5] The importance of speciation has been increasingly recognized as it facilitates the choice of optimal treatment and has an important prognostic value. Species can sometimes be inferred from region of exposure, but travellers may have multiple possible exposures and geographic distributions of some species is evolving. Systemic treatment is usually recommended for *Viannia* subgenus infection because it appears to reduce the risk for subsequent mucosal involvement. [2,6] Molecular speciation has not been well standardized, but various methodologies are available in most high-resource settings. [2]

Liposomal amphotericin B was used to treat 20 patients (53%), which represents the most used first-line treatment in our study. Amongst patients who completed the follow-up, 69% were cured at one-year. The cure was 75% when patient received L-AmB either as first or second-line treatment. L-AmB may be better tolerated and is more readily available than pentavalent antimony in Canada which explains why it is the most used agent in our centre. There are no controlled clinical trials of L-AmB treatment for CL and available data comes mainly from observational

studies. The response rate is variable, in the range of 72-88% in some studies of OW and NW species, and more recent studies have described response rates as low as 46% when looking at cure at 90 days and 63% when delayed healing and second course of L-AmB were included. [20-26] Thirty percent of patients who received L-AmB experienced adverse events with acute kidney injury being the most common (50%). Adverse events rates of L-AmB in the treatment of CL has been reported to be as high as 46-53%. [23,25]

A strength of our study is the inclusion of detailed clinical and outcome data. Our centre includes the national reference laboratory for parasitology, which allow easy access to speciation, and results were available for most of our cases. Documentation of treatment response at standardized time points was difficult to obtain retrospectively. Also, 27% of the patients were lost to follow-up within a year. Some of these were returned to their consulting institution for further treatment and follow-up, other may have been cured which could have underestimated our cure rate.

In conclusion, increased travel and migration had led to increased number of cases of CL over recent years. The use of L-AmB is common in North America because it is familiar and easily available, but we add to the literature showing that response rates are modest and adverse events are common. More studies are needed to better understand the role of L-AmB for CL compared to other agents. Physicians' awareness is essential to identify patients with chronic skin lesions who are at risk for CL.

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Competing Financial Interests

The authors declare no competing financial interests.

Contribution

All authors serve as guarantors of the work, and all critically appraised the manuscript for content. A.L.—construction and querying of study database; data collection and interpretation, literature search, drafting the manuscript; revision and critical appraisal of the manuscript. F.L.—construction and querying of study database; data collection, literature search, drafting the manuscript, analysis and interpretation, revision and critical appraisal of the manuscript. K.B. .—data collection and interpretation; revision and critical appraisal of the manuscript. M.N.—laboratory data collection, revision and critical appraisal of the manuscript. CPY—data interpretation, revision and critical appraisal of the manuscript. M.S.—data interpretation, revision and critical appraisal of the manuscript. M.D.L.—contribution to drafting, literature search, data

interpretation, revision and critical appraisal of the manuscript. S.B. — study conception and design; construction and querying of study database; data collection, analysis and interpretation; literature search, drafting the manuscript, supervision, revision and critical appraisal of the manuscript.

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FIGURE 1 CAPTION

Locations of the main lesion for each patient (n=48).

No significant differences were identified between OW and NW CL (p=0.24).

OW CL: Old World Cutaneous Leishmaniasis; NW CL: New World Cutaneous Leishmaniasis

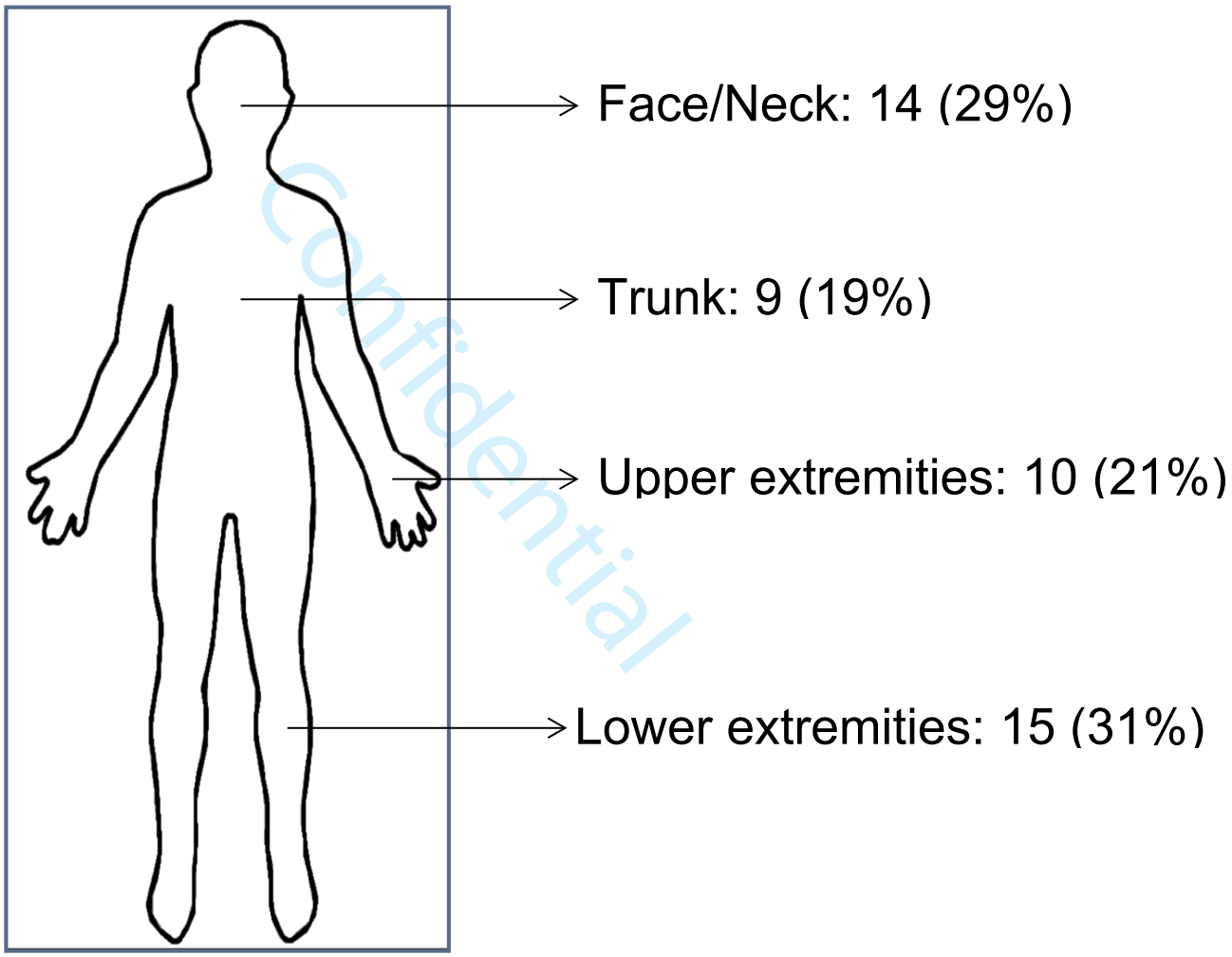

Table 1. Demographic and clinical characteristics of 48 returned travellers and migrants presenting to our tropical diseases centre with CL and comparison between OW and NW CL

	Total (n=48)	OW CL (n=15)	NW CL (n=33)	p-value
Gender, n (%)				
Male	28 (58.3)	7 (46.7)	21 (63.6)	0.269
Female	20 (41.7)	8 (53.3)	12 (36.4)	
Age				
Median (IQR)	43.5 (34)	53 (31)	36 (30)	0.247
Immune status, n (%)				
Immunocompetent	46 (95.8)	14 (93.3)	32 (97.0)	0.559
Immunocompromised	2 (4.2)	1 (6.7)[a]	1 (3.0)[b]	
Region of exposure, n (%)				
North/Central America	24 (50.0)	-	24 (72.7)	-
South America	9 (18.7)	-	9 (27.3)	
North Africa	5 (10.4)	5 (33.3)	-	
Sub-Saharan Africa	3 (6.3)	3 (20.0)	-	
Middle East	5 (10.4)	5 (33.3)	-	
South/Central Asia	1 (2.1)	1(6.7)	-	
East Asia	1 (2.1)	1(6.7)	-	
Purpose of travel, n (%)				
Tourism	24 (50.0)	5 (33.3)	19 (57.6)	0.028
Visiting friends and relatives	7 (14.6)	6 (40.0)	1 (3.0)	
Work/business	5 (10.4)	2 (13.33)	3 (9.09)	
Education/Research	2 (4.2)	0	2 (6.06)	
Volunteer/Aid worker	5 (10.4)	1 (6.7)	4 (12.1)	
Migration	5 (10.4)	1 (6.7)	4 (12.1)	
Duration of travel for non-migrant travellers (days)				
Median (IQR)	42 (69)	60 (74)	36 (48)	0.475
Time from the initiation of symptoms to diagnosis (days)				
Median (IQR)	89 (76)	98.5 (78.5)	84 (77)	0.180

Number of physicians consulted before visit in our reference centre[c]				
Median (range)	2 (0-5)	2 (1-5)	2 (0-3)	0.311
Number of course of systemic or topical antibiotics before visit in our reference centre[d]				
Median (range)	1 (0-4)	1 (0-3)	1 (0-4)	0.381

[a]Patient had Systemic Lupus Erythematosus (SLE) on 5 mg of prednisone and hydroxychloroquine 400 mg daily

[b]Patient living with Human Immunodeficiency Virus (HIV) with CD4 count of 512 cells/ul

[c]Data missing for 2 patients

[d]Data missing for one patient

Table 2. Clinical characteristics of the lesions and comparison between OW and NW CL groups.

	Total	OW CL	NW CL	p-value
Number of lesions, n (%)				
Median (range; IQR)	2.54 (1 – 11;2)	3 (1 – 11; 2)	1 (1 – 11; 1)	0.077
Single	23 (48)	5 (33)	18 (55)	0.173
Multiple	25 (52)	10 (67)	15 (45)	
Size*, n (%)				
Average Longest diameter (cm)	3,5 (± 2,3)	3,4 (± 2,5)	3,6 (± 2,2)	0.163
>5 cm	35 (75)	12 (80)	23 (72)	0.754
<5 cm	12 (25)	3 (20)	9 (28)	
Morphology, n (%)				
Ulcer	33 (69)	5 (33)	28 (85)	0.001
Plaque	12 (25)	9 (60)	3 (9)	
Nodule	3 (6)	1 (7)	2 (6)	
Lymphangitis, n (%)				
Yes	7 (15)	1 (7)	6 (18)	0.295
No	41 (85)	14 (93)	27 (82)	
Adenopathy, n (%)				
Yes	9 (19)	0 (0)	9 (27)	0.025
No	39 (81)	15 (100)	24 (73)	
Bacterial coinfection, n (%)				
Yes	11 (23)	3 (20)	8 (24)	0.746
No	37 (77)	12 (80)	25 (76)	

OW CL: Old World Cutaneous Leishmaniasis; NW CL: New World Cutaneous Leishmaniasis

* n=47 for this variable.

Table 3. Sensitivity of the diagnostic methods used.

	Count	Positive result	Sensitivity*
Smear	37	25	68%
Histopathology	28	18	64%
Culture	37	24	65%
PCR	43	42	98%

*Sensitivity was evaluated using a composite reference standard including lesion clinically and epidemiologically consistent with cutaneous leishmaniasis and at least one positive test.

Table 4. First and second line treatments used to treat cutaneous leishmaniasis.

	First-line treatment			Second-line treatment		
	Total (n=47)	OW (n=15)	NW (n=32)	Total (n=16)	OW (n=8)	NW (n=8)
Local (n, %)	2 (4)	2 (13)	0 (0)	4 (25)	3 (37.5)	1 (12.5)
Systemic (n, %)	36 (77)	12 (80)	24 (75)	9 (56)	3 (37.5)	6 (75)
No treatment (n, %)	9 (19)	1 (7)	8 (25)	3 (19)	2 (25)	1 (12.5)
Specific treatment, n (%)	Total (n=38)	OW (n=14)	NW (n=24)	Total (n=13)	OW (n=6)	NW (n=7)
Liposomal amphotericin B	20 (53)	4 (29)	16 (67)	4 (31)	1 (17)	3 (43)
Oral fluconazole	10 (26)	5 (36)	5 (21)	3 (23)	1 (17)	2 (29)
IV pentavalent antimonial	4 (11)	3 (21)	1 (4)	2 (15)	1 (17)	1 (14)
Topical paromomycin	1 (2.5)	1 (7)	0 (0)	2 (15)	1 (17)	1 (14)
Pentamidine	1 (2.5)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
Topical paromomycin with fluconazole	1 (2.5)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
IL pentavalent antimonial	1 (2.5)	1 (7)	0 (0)	1 (8)	1 (17)	0 (0)
Cryotherapy	0 (0)	0 (0)	0 (0)	1 (8)	1 (17)	0 (0)

OW CL: Old World Cutaneous Leishmaniasis; NW CL: New World Cutaneous Leishmaniasis

IV=intravenous, IL=intralesionnal.

Supplemental Table 1. Region and countries of birth of all travellers and migrants and those presenting with Old world and New world CL.

Region/country	Total, n (%)	OW CL, n (%)	NW CL, n (%)
North America	37 (77.1)	9 (60.0)	28 (84.8)
Canada	35 (72.9)	9 (60.0)	26 (78.8)
United States	1 (2.1)	0 (0.0)	1 (3.0)
Mexico	1 (2.1)	0 (0.0)	1 (3.0)
Central America/Caribbean	2 (4.2)	0 (0.0)	2 (6.1)
Belize	1 (2.1)	0 (0.0)	1 (3.0)
Haiti	1 (2.1)	0 (0.0)	1 (3.0)
South America	2 (4.2)	0 (0.0)	2 (6.1)
Colombia	1 (2.1)	0 (0.0)	1 (3.0)
Peru	1 (2.1)	0 (0.0)	1 (3.0)
Europe	1 (2.1)	0 (0.0)	1 (3.0)
France	1 (2.1)	0 (0.0)	1 (3.0)
Middle East/South Central India	5 (10.4)	5 (33.3)	0 (0.0)
Syria	2 (4.2)	2 (13.3)	0 (0.0)
Iran	1 (2.1)	1 (6.7)	0 (0.0)
Afghanistan	2 (4.2)	2 (13.3)	0 (0.0)
North Africa	1 (2.1)	1 (6.7)	0 (0.0)
Algeria	1 (2.1)	1 (6.7)	0 (0.0)

OW CL: Old World Cutaneous Leishmaniasis; NW CL: New World Cutaneous Leishmaniasis

Supplemental Table 2. Countries of exposure to CL

Country	Total (n, %) n=48	OW CL (n, %) n=15	NW (n, %) n=31*
Afghanistan	1 (2%)	1 (7%)	0 (0%)
Algeria	1 (2%)	1 (7%)	0 (0%)
Belize	2 (4%)	0 (0%)	2 (6%)
Bolivia	2 (4%)	0 (0%)	2 (6%)
Brazil	1 (2%)	0 (0%)	1 (3%)
Burkina Faso	3 (7%)	3 (20%)	0 (0%)
China	1 (2%)	1 (7%)	0 (0%)
Colombia	2 (4%)	0 (0%)	2 (6%)
Costa Rica	11 (24%)	0 (0%)	11 (35%)
Ecuador	1 (2%)	0 (0%)	1 (3%)
French Guinea	1 (2%)	0 (0%)	1 (3%)
Guatemala	1 (2%)	0 (0%)	1 (3%)
Iran	1 (2%)	1 (7%)	0 (0%)
Israël	1 (2%)	1 (7%)	0 (0%)
Mexico	7 (15%)	0 (0%)	7 (23%)
Morocco	2 (4%)	2 (13%)	0 (0%)
Pakistan	1 (2%)	1 (7%)	0 (0%)
Panama	1 (2%)	0 (0%)	1 (3%)
Peru	2 (4%)	0 (0%)	2 (6%)
Syria	2 (4%)	2 (13%)	0 (0%)
Tunisia	2 (4%)	2 (13%)	0 (0%)

OW CL: Old World Cutaneous Leishmaniasis; NW CL: New World Cutaneous Leishmaniasis

*There were 2 patients in the NW CL group where the country of exposure was not ascertainable.

Supplemental Table 3. *Leishmania* species and country of exposure

Leishmania spp.	Travellers and migrants (n=43)*	**Top countries**
New World n (%)	33	Costa Rica (11), Mexico (6), Bolivie (2), Colombie (2)
Leishmania (V.) panamensis	23	Costa Rica (11), Bolivie (2), Colombie (2)
Leishmania (V.) braziliensis	3	French Guinea (1), Belize (1), Peru (1)
Leishmania (L.) mexicana	7	Mexico (6), Belize (1)
Old World n (%)	10	Tunisia (2), Morocco (2)
Leishmania (L.) major	7	Tunisia (2), Morocco (2), Algeria (1)
Leishmania (L.) tropica	3	Pakistan (1), Israel (1), Syria (1)

*Speciation was available for 43 out of 48 travellers and migrants