

Clinical and Epidemiological Characteristics of Patients Presenting with Cutaneous Leishmaniasis to the General Practice Departments (Outbreak; Tozeur, Tunisia, 2016) Managing Cutaneous Leishmaniasis Outbreak in General Medicine (Tozeur, Tunisia, 2016)

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Abstract

Background: We aimed at describing, by an active investigation, an outbreak of Cutaneous Leishmaniasis (CL) occurred in Dghoumes, an area near a natural reserve (NR), with high animal density and low economic level, in south Tunisia.

Methods: we performed a prospective study, from September 2015 to August 2016. All cases with confirmed diagnoses of CL were included (n=173).

Results: Median age was 15 years (IQR: 5-34). Outbreak covered six months. We notified a density of 34 cases per 100 Km² during outbreak. The Annual attack rate (AAR) of CL was 6.06 cases /1000 inh. Among children under 5 and, "Dghoumes" inhabitants AARs reached respectively 14.46 and 23.94 per 1000 inh. The risk of developing CL for inhabitant near NR was 21 folds higher than in other distant region. We have emphasizes a relation-ship between monthly attack rates and distance from NR to neighborhoods of cases (b=-7.63; p=0.000). In the first half of November the rise of CL cases was quite large (b=16.0; p=0.000) followed by a slow decrease (b=-2; p=0.000). Overall the 173 cases of CL had 231 lesions altogether. The face or the neck, were affected in 23.2% of cases. During follow up, complete recover was noted among 60% of patients.

Conclusions: CL, responsible for outbreak, attacked highly children, inhabitants in region with high animal density and low economic conditions.

Keywords: Cutaneous-leishmaniasis; Outbreak-investigation; Environmental-factors; Epidemiology

Introduction

Leishmaniasis continues to be a large cause of morbidity worldwide, mainly in the Middle East and South America [1,2]. Cutaneous leishmaniasis (CL) is the most common form of the disease [3]. The only prevention method is to avoid the parasite transmission by sand fly bites. Skin lesions tend to heal spontaneously at the expense of disfiguring and stigmatizing scars resulting in a considerable impact on life quality. CL can occurred on sporadic, endemic or endemo-epidemic form. An epidemiological update on CL based on data reported in 2014, classified Tunisia as high-burden country, with an incidence rate of 5.67/10 000 inhabitants in endemic areas. The Tunisian national efforts of CL control are essentially limited to a mandatory report [4,5]. Active surveillance system and effective interventions attesting epidemic preparedness and response are rare. Degache is an endemo-epidemic region in which active surveillance can curb the epidemic progression. We aimed at describing, by an active investigation, an outbreak of CL occurred in Degache (Tozeur, Tunisia) from September 2015 to August 2016 and at analyzing epidemic determinants.

Methods

Study design and settings

We performed a prospective study from September 01, 2015 to August 31, 2016 in the area of Degache part of Tozeur Governorate (Tunisia). Degache cover 998 square kilometers, it's located in the

eastern part of Tozeur in the south west of Tunisia and it include 28543 inhabitants (inh). It is a desert arid area with a total annual rainfall of 92.4 mm; greater in June and November. It includes the localities of Degache, Sabaa Byar, Mahassen, Bouhlal and Dghoumes. Degache is close to some ten kilometers to a Natural Reserve (NR) covering an area of 80 km². Distance from NR to CL cases neighborhoods was calculated using Google map.

Studied population

All patients covered by Degache public health care centers, having a confirmed diagnosis of CL were included regardless to their age or gender. The CL was defined according to mandatory criterion. We used the distribution of the population of Degach according to the last population census performed in 2014 by the National Institute of Statistics [6].

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Diagnosis

CL diagnosis was based on clinical features (supported by epidemiological data) and laboratory testing. The direct parasitological diagnosis is considered the gold standard in because of its high specificity. This is typically undertaken by histopathological examination of fixed tissue or parasite *in vitro* culture from material from suspected lesions. Microscopical diagnosis of CL is performed by the direct identification of amastigotes in Giemsa-stained lesion smears of biopsies, scrapings, or impression smears [7].

Phlebotomine sandflies characteristics

With one week from eggs to larva, than 3 to 5 weeks to nymph form and 1 to 2 weeks for accomplishing adult form, its median lifetime is for 30 days. They fly slowly, female phlebotomine sting is short and repeated, several times are necessary to swallow the blood that it needs. Only a phlebotomine bug carrying the protozoan inoculates the disease. Infected animals can be an asymptomatic carrier of the protozoan and is therefore a source of transmission. The insect is particularly active from March to September (as soon as the temperature reaches 19/20°C) with a particularly increased risk in August and September. From the first cold, the risks disappear.

Data collection and statistical analysis

Data was prospectively collected using a standardized form including demographic characteristics (age, sex and origin). We also assessed clinical examination data counting location, number and type of the lesion 20. Results were presented to Tozeur health public responsible on November 2016. The epidemic curve was drawn up by counting CL cases in consecutive epidemiological weeks of the outbreak. The Annual Attack Rate (AAR) was calculated as a cumulative annual incidence by dividing the number of CL cases on population at risk. Monthly attack rates (MAR) have been also calculated according to locality. We drafted contingency tables to assess potential increased risk (with CI 95%) of CL according to gender, age group and locality. Statistical significance was determined with chi-square test of Pearson. All performed tests were bilateral and the significance level was set to 5%. We also performed a linear regression to calculate trend of outbreak, and the relation between MAR and distance from natural reserve of Dghoumes to cases neighborhoods.

Results

Description of outbreak

During one year, 173 cases of CL were monitored. Sex ratio was 1.1 and median age was 15 years (IQR: 5-34) years. The CL Annual attack rate (AAR) was 60.61 cases / 10 000 inh, it was 65.33 in men and 56.11 in women. The highest AAR was recorded among children under 5 reaching 144.59/10000 inh and among "Dghoumes" inhabitants reaching 239.39/10 000 inh. Compared to persons aged 40 and more, relative risk (RR) of CL was 5.2(CI 95%:3.3-8.1) for children under 5 and 3.6 (CI 95%:2.4-5.4) for inhabitants aged from five to nineteen years. Compared to the locality of Mahassen, which had the lowest, AAR, Degache and Bouhlal localities had three folds higher risk of cases occurrence. This risk increased to 21 folds for Dghoumes locality (Table 1). On an endemic baseline state, the outbreak of CL has begun in November 2015 and covered a period of six months until April 2016. In November the rise of CL cases was quite large (b=16.0; p=0.000). From 19 November to 31 January a slow decrease was notified (b=-2.1; p=0.000) than number of cases accelerate declining (b=-2.5; p=0.000). Outbreak finished with an endemic phase (Figure 1). The mean of Monthly Attack Rate (MAR) was 505.1/10000 inh. In the locality of Dghoumes, MARs were the highest. It was 46.9 in November, 61.69

	Cases (n)	AAR/1 000 Inh	RR	CI _{95%}
All	173	6.06		
Gender				
Female	82	5.61	1	-
Male	91	6.53	1.16	0.8-1.5
Age (years)				
≥ 40	27	2.77	1	-
20-39	41	4.31	1.55	0.9-2.5
5-19	67	10.00	3.6*	2.4-5.4
0-4	38	14.45	5.2*	3.3-8.1
Locality				
Mahassen	5	1.13	1	-
SabaaByar	13	3.00	2.63	0.5 -1.5
Dgueche center	41	3.59	3.16*	2.0 -4.9
Bouhlal	17	3.88	3.42*	2.1-5.5
Dghoumes	97	23.93	21.00*	15.0-29.4

Table 1: Annual attack rates of cutaneous leishmaniasis occurring in study region (September 2015 - August 2016).

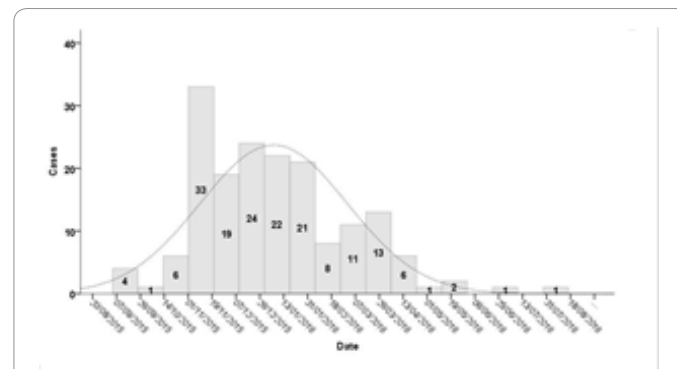


Figure 1: Endemo-epidemic curve for confirmed cutaneous leishmaniasis from September 2015 to August 2016 occurring in Degach, Tozeur (Tunisia). CL outbreak beginning in November 2015 covered a period of six months until April 2016. In November the rise of CL cases was quite large (b=16.0; p=0.000). A slow decrease was notified, from 19 November to 31 January (b=-2.1; p=0.000) then from February to 31 April (b=-2.5; p=0.000). Outbreak finished with an endemic phase (b=-0.6; p=0.000).

in December and 59.2 /10000 inh in January 2016 (Figure 2). We have emphases a relation-ship between MAR and distance from natural reserve of Dghoumes to neighborhoods of cases (b=-7.63; p=0.000). We have notified a density of 34 cases per 100 km² during outbreak.

Clinical features of the CL cases

Seven patients had a CL history. The median duration between CL symptoms and consultation was 30 days (IQR:11-45). Overall the 173 cases of CL had 231 lesions altogether, of them 51.2% had a single lesion (n=112), and seventeen cases presented with more than 5 lesions (range=1 to 13). Lesions occurred predominantly on the lower (49.6%) and on the upper (48%) limbs. The face or the neck, were affected in 23.2% of cases (Figure 3). The median lesion size was one cm. Clinical features were mainly scab (64%) or papule (16%). Although 6% (n=10) of the cases presented mixed features (Table 2). We noticed no disseminated leishmaniasis case, and cases with multiple lesions seemed to result from multiple inoculation sites.

Medical care

Glucantime have been prescribed in intra-lesion during 21 days

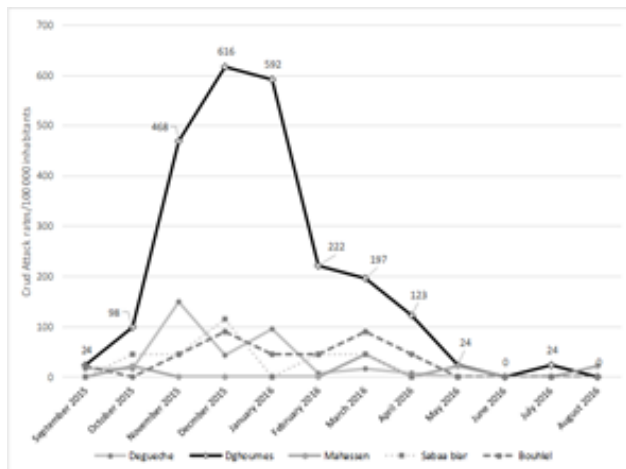


Figure 2: Monthly attack rates of cutaneous leishmaniasis/1000 inh according to the location (Tozeur; Tunisia); Sep 2015 - Aug 2016. The mean of monthly attack rate in the locality of Dghoumes, was 4.69 in November, 6.16 in December and 5.92 /1000 inh in January 2016.



Figure 3: Clinical features of cutaneous leishmaniasis cases. a) ulcerative and crusted form of CL on the leg; b) lupoid form of CL on the forearm; c) ulcerative form of CL on the leg; d) eczematiform of CL on the leg; e) lupoid form of CL on the forearm complicated by an erysipelatoid reaction following the glucantim intraliesional infiltration; f) sporotrichoid Form of CL on the forearm; g) impetigoid form of LC on the nose.

for 63.2% of patients while 20.8% received treatment in intra-muscular thru 15 days. Cryotherapy and Plaquenil have been prescribed respectively for 10.4% and 1.6% of patients, Nine patients have refused treatment. Twenty-eight and 18 patients have been treated respectively with antibiotics and antifungal for associated infections. During follow up, complete recover was noted among 60% of cases while 12.8% have not response to treatment.

Characteristics	n	%
Location of CL lesions (n = 173)		
Legs	86	49.6
Arms	83	48.0
Face and neck	40	23.2
Trunk	7	4.0
Multiple locations	37	21.6
Number of lesions per case		
Single	89	51.2
2-4	61	35.2
>5	23	13.6
Size of lesion median in mm / M (IQR)	10	6-20
Type of the lesion		
Ulcerative and crusted	111	64
Lupoid	29	16
Ulcerative	19	11.2
Impetigoid	7	4
Psoriasiform	6	3.2
Sporotrichoid	1	0.8

Table 2: Clinical characteristics of the CL cases occurring in Dgach, Tozeur (Tunisia) from September 2015 to August 2016.

Discussion and Conclusion

In our study, we described an outbreak occurring in South West of Tunisia from September 2015 to August 2016. This work falls within an array of articles describing the LC epidemiological patterns in the community [8]. We estimated appropriate, to study epidemics in order to assess continuously eventual changes. For our results, during one year, 173 cases of CL were diagnosed in a region covering 998 square kilometers with an AAR of 60.61 cases/10000 inh. The highest AAR were recorded among children under four (RR: 5.2) and among "Dghoumes" inhabitants (RR: 21). CL, viral hepatitis and tuberculosis represented over 70% of notified compulsory diseases in Tunisia. Therefore, CL is the major public health problem for the country with three epidemic clinical forms. The most frequent one is caused by *Leishmania major* [9]. In 1982, an epidemic emerged in central Tunisia and expanded to the whole central and southern parts of the country, and since 2006, 15 from 24 governorates were considered as endemic. The epidemics were cyclic and annually, 2000 to 10000 cases were reported, Our data confirm the endemo-epidemic modality of occurrence of CL in this region. Tozeur is among the 10 main endemic governorates in Tunisia with 3,014 cases between 1998 and 2007 and a crud incidence rate of 30.86/10000 inh. Our study indicated that age group from one to 15 years had the highest rate, similar to studies performed by Kassiri et al. [10] and Akcali et al. [11]. Given that infection with *Leishmania* provides immunity against re-infection with the same parasite, most children will be immunized in endemic areas. It is important to pay more attention to undercount CL in this age group because of bacterial and fungal associated infections. The outbreak of CL has begun in November with a sudden rise ($b=16.0$; $p=0.000$). Followed by a slow decrease from February to May and finish with an endemic phase. Ajaoud M et al. [12] and Aoun K et al. [13], have notified a remarkable changes in the different months of year. In their study conducted on 2012 and 2013, the peak of emerging cases were observed in fall, mainly between September and November. In the present study (2015), the highest peak was in November. Our results were similar to those described by Toumi, This report was related to the activity of the sand flies (9) and the dominant of rural areas in this region [14] and may be related to the vegetation paucity. In urban regions, CL is endemic, with little seasonal variations. The locality of Dghoumes, covered the majority of the outbreak cases. We hypothesized that NR

of Dghoumes was the major cause of the outbreak. In fact the MAR decrease with moving away from natural reserve of Dghoumes ($b=-7.63$; $p=0.000$). Key factors include driving spatio-temporal dynamics of the disease are presently unknown. These might include dynamics of rodent populations, dispersal of vectors, climate changes, vegetation, soil type and establishment of dense human settlements in areas where a sylvatic transmission of leishmaniasis is high (rodent-vector-rodent cycle) [15,16].

Clinical Features

The median duration of the CL symptoms was 30 days (IQR:11-45). Patients may not recall the initial sand fly bite that leads to CL which explained essentially by the painless character of the lesions, and so, a lack of reported bites should not be used to exclude the diagnosis. Incubation periods can vary from a few days to many months, and skin lesions may initially be ignored or misdiagnosed. In our study the extent of lesions seemed to result from multiple inoculation sites. In fact, the half of cases presented more than one lesion and a lesion size greater than 1 cm. In literature, CL usually presents as a small papule that enlarges and ulcerates at its center to produce a volcano-shaped wet lesion. Alternatively, the lesion may not ulcerate but remain as a smooth nodule or the surface may become hyperkeratotic, which are both described as dry lesions. The thickened edge is characteristic of CL and usually correlates with the lesion activity [17,18]. In this study, lesions of CL were mainly located on the lower limbs (49.6%) followed by upper limbs (48%), face and neck (23.2%) and trunk location (4%). These results corroborate with those obtained by Abda et al. [4] and Hjira et al. in Morocco [19]. These locations are exposed parts of the body exhibited at bites of sand flies [20]. Our results are explained by the clothing habits of the population in Degache which are characterized by low coverage of the upper and lower limbs. Furthermore, we found that the single lesions were observed in 51.2% of patients, and 23.6% of patients showed multiple lesions, These results are comparable to those noted by Abda et al. with an average lesion number of 1.9 ± 1.8 per patient [21] and by Kassiri H et al. who described that 48.8% of the cases had only one ulcer on their bodies, Killick-Kendrick R illustrated that sand flies complete their feeding in one biting. CL lesions may become large (>5 cm) but are rarely larger than 10 cm in diameter, and any ulceration rarely penetrates into subcutaneous tissues, except for cartilage in the pinna of the ear. In this study, we found that the median size of CL lesions was 1 cm with range between 1 mm to 5 cm. It is comparable to the study of Khazaei et al. with a size of 1 cm in 53.18% of cases. According to clinical forms of CL, in our study, the ulcero crustous forms was the most represented (64%). Our finding was comparable with rates noted by Fenniches et al., Fathy FM et al. in Libya and Hjiri N et al. in Morocco. The predominance of the ulcero crustous form in our serial, also noted in other studies in North Africa, was explained by the frequency of CL to *Leishmania Major*, which is characterized by multiple lesions, localization at the regions discovered especially at the limbs associated with the short duration of evolution of disease. Many clinical presentations are possible during CL, verrucous, vegetative impetigoid, pseudotumoral, lupoid, psoriasiform, ulcerative, erythematous, nodular forms, sporotrichoides etc. [22]. This clinical polymorphism depends not only on the genetic characteristics of the parasite, but also on the immunological status of the host. Complications of CL include secondary infection and disfiguring scars. Secondary infections should be treated to avoid prolongation of the healing time, Disfiguring scars may improve in appearance over 6 to 12 months and should not be considered for surgical revision any earlier than this because of the risk of local recurrence. The natural history of CL is that all forms will eventually resolve spontaneously apart chronic

manifestations. The time taken for spontaneous resolution, however, can vary considerably and spontaneous cure is obtained in less than 8 months.

Prevention

Regarding the results of this study, it is assumed that the CL in Degach is an endemic rural type of Leishmaniasis. Therefore, the appropriate preventing measures should be considered to reduce the occurrence of outbreak. There is currently no chemoprophylaxis or immune-prophylaxis (vaccination) available to protect against CL. In the EMR (Eastern Mediterranean region), prevention strategies are based mainly on vector and reservoir control measures, this latter component being very important. In Tunisia, actions to induce environmental changes, such as destroying rodent burrows and planting trees around human habitations, have significantly contributed to the fall in the incidence of the disease among human populations. We have notified insignificant environmental interventions in Degach especially nearest NR of Dghoumes.

Conflict of Interest

The authors have nothing to disclose concerning this manuscript.

Funding Body

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Ethical Considerations

The study was conducted under the aegis of the regional public health authorities. Clinical investigation has been conducted according to the principles expressed in the Declaration of Helsinki. An oral informed consent, have been obtained from the participants, All samples (dermal smears) and data were collected and treated with respect to confidentiality and anonymity obligations. Photographs were taken and used for scientific purposes and among consenting patients, No incentives were proposed to the participants to the study.

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