Research Article / Araştırma Makalesi

Evaluation of Pediatric Cutaneous Leishmania Cases

Pediatrik Kutanöz Leishmania Olgularının Değerlendirilmesi

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Abstract: Cutaneous Leishmaniasis (CL) is a disease caused by leishmania-type protozoans, which is transmitted by the bite of infected female phlebotomine sandflies and is characterized by ulcerated nodular lesions. Twenty-one pediatric cutaneous leishmania cases followed by pediatric infectious diseases and dermatology were included in the study. The demographic and clinical characteristics of the patients, the local or systemic treatments, and side effects were analyzed retrospectively. 14 (66%) of the patients were female and 7 (34%) were male. The mean age of the cases was 6.4 years. Fifteen of the patients were refugees (seven of the patients were from Iraq, and eight of them were from Syria). Ten of the patients (47%) had lesions only on the face, 6 (28%) were both on the face and hand, 4 (20%) were on the lower extremities. Seven patients (34%) had a single lesion, fourteen had multiple lesions and seven had more than four lesions. Amastigote was observed in the microbiological examination of skin scraping samples of 13 patients. Intralesional therapy was given to 15 patients, systemic treatment was given to 6 patients, and 2 patients refused systemic treatment. Five patient was given meglumine antimoniate, one patient was given amphotericin B. In one patient, side effects such as facial swelling, rash, and edema developed after amphotericin b, and the treatment was changed to meglumine antimoniate. Leishmaniasis is a chronic disease caused by flagellate protozoa of the genus Leishmania. especially in endemic countries. CL has become a relatively common condition all over the world due to international travel, migration, and refugees. Cutaneous Leishmania should be considered when there are chronic, painless skin lesions outside of endemic areas.
Keywords: Cutaneous Leishmania, Child, Endemic Area, Refugees

Özet: Kutanöz Leishmaniasis (KL), enfekte dişi tatarcık sineğinin ısırması ile bulaşan ve ülsere nodüler lezyonlarla karakterize, leishmania tipi protozoanların neden olduğu bir hastalık olup, dünyanın bazı bölgelerinde endemik olarak görülmektedir. Çalışmaya çocuk enfeksiyon hastalıkları ve dermatoloji tarafından takip edilen 21 pediatrik kutanöz leishmania olgusu dahil edildi. Hastaların demografik ve klinik özellikleri, aldıkları lokal veya sistemik tedaviler ve yan etkileri retrospektif olarak incelendi. Olguların 14'ü (%66) kız, 7'si (%34) erkekti. Olguların ortalama yaşı 6.4 yıldı. Hastaların 15'i mülteciydi (hastalardan yedisi Iraklı, sekizi Suriye'liydi). Hastaların 10'unda (%47) sadece yüzde, 6'sında (%28) hem yüzde hem de elde, 4'ünde (%20) alt ekstremitede lezyon vardı. Yedi hastada (%34) tek lezyon, ondördünde çoklu lezyon ve yedi hastada dörtten fazla lezyon vardı. 13 hastanın direk mikroskopik incelemesinde amastigot gözlendi. 15 hastaya intralezyonel tedavi, 6 hastaya sistemik tedavi verildi, 2 hasta sistemik tedaviyi reddetti. Beş hastaya meglumin antimoniat, bir hastaya amfoterisin B verildi. Bir hastada amfoterisin b sonrası yüzde şişlik, kızarıklık ve ödem gibi yan etkiler gelişti ve tedavi meglumin antimoniat olarak değiştirildi. Kutanöz Leishmaniasis, leishmania cinsi protozoalarının neden olduğu kronik bir hastalıktır. Uluslararası seyahat, göç ve mülteciler nedeniyle sadece endemik bölgeler değil, tüm dünyada nispeten yaygın bir durum haline gelmiştir. Endemik bölgelerin dışında kronik, ağrısız cilt lezyonları olduğunda Kutanöz Leishmania düşünülmelidir
Anahtar Kelimeler: Kutanöz Leishmania, Çocuk, Endemi, Göç, Mülteci

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Received 01.07.2023 ***Accepted*** 18.09.2023 ***Online published*** 20.09.2023

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1. Introduction

Leishmaniasis is an infectious disease caused by the obligate intracellular parasites of Leishmania protozoan microorganisms, transmitted by the bite of the vector which is a female sandfly (phlebotom)(1). According to the data of the World Health Organization (WHO), approximately 12 million people in 98 countries all over the world have been infected with leishmaniasis, and it is reported that 350 million people live with that risk (2). Approximately 50 million people in our country are at risk for this infection. Previously, a very important part of them were reported from 9 endemic provinces, namely Şanlıurfa, Diyarbakır, Mardin, Osmaniye, Adana, Hatay, Kahramanmaraş and İçel (3). However, recently, there has been an increase in cases of leishmania in non-endemic regions due to the migration of refugees from endemic regions to our country and the world due to reasons such as wars, famine, and low socioeconomic status. Our country hosts more than 4 million refugees, especially those who escaped from the civil war in Syria (4). There are three forms of Leishmaniasis which are cutaneous, mucocutaneous, or visceral (VL), depending on the leishmania species and the reservoir host's immune response (5). CL starts as an erythematous papule in the area where the fly bites and takes the form of a painless, ulcerated nodule and plaque that has a necrotic center over time (6).

Diagnosis is made by tests such as microscopic examination, culture, and PCR from clinically suspicious cases. Showing the presence of leishmania amastigotes in the light microscope is the most common diagnostic method (7). There are intralesional and systemic treatment options due to the type of Leishmania parasite, the endemic region, and the location, number, and size of the lesion. The most commonly used and oldest therapeutic agents are pentavalent antimon compounds (8). The aim of this study is to investigate the cases of pediatric cutaneous leishmaniasis seen in a non-endemic city in the central <anatolia region in the west of our country. with the increasing number of refugees in our country after war and migration. For this reason, the clinical and epidemiological characteristics and treatment regimens of the cases followed up due to CL in our hospital were evaluated retrospectively.

2. Materials and Methods

Pediatric patients under the age of 18, who were followed up with the diagnosis of CL between March 2017 and November 2021 by the Department of Pediatric Infectious Diseases and Dermatology were included in our study. The study was started after the approval of the Eskişehir Osmangazi University Ethics Committee (date:15.02.2022, number:27). The data of twenty-one pediatric patients included in the study were accessed retrospectively from the hospital automation system. Parameters such as age, gender, nationality, immigration status, country, family history, physical examination findings; location, number, and time of lesions, type of diagnosis, local or systemic treatment type, treatment duration, pharmacological agents used, side effect profile of these drugs and prognosis were examined.

Statistical analysis

Descriptive statistics are given with mean and standard deviation for numerical variables, and numbers and percentages for categorical variables. Relationships between categorical variables were tested with the chi-square test. SPSS 22.0 Windows version package program was used in the analysis. $p<0.05$ was considered as significant.

3. Results

Thirty-nine pediatric CL cases followed in our hospital were included in the study. Eighteen of 39 cases were excluded from the study because their data could not be reached. Of the remaining 21 cases, 14 (66%) were girls and 7 (34%) were boys. The mean age of the cases was 6.4 years. Fifteen (71%) of the cases were immigrants (7 Iraqi, 8 Syrian immigrants). There was only one lesion in 9 (42%) cases, multiple lesions in 12 (57%) cases, and more than four lesions in 7 (34%) cases. While 12 (57%) patients had lesions only on the face, 6 (28%) patients had lesions

on the face and extremities, and 3 (14%) patients had lesions on the lower extremities. Eleven (52%) lesions were ulcerated nodular, 9 (42) were papular, and 1 (5%) were plaque (Figure-1). The mean onset time of the lesions was 3.5 months. Amastigote was detected in the microbiological examination of 13 (61%) cases (Figure-2). Intralesional treatment was applied to 15 of the cases (71%), systemic treatment was given to 6 of them (28%), and 2 cases refused systemic treatment. The mean duration of treatment in 15 cases given intralesional therapy was 3 sessions. Meglumine antimoniate treatment was given to 5 (83%) and Amphotericin-B treatment to 1 (17%) of the 6 patients who received systemic treatment. Of the 6 patients who were given systemic treatment, two received 20 days of treatment, and four received 10 days of treatment (Table 1). Only one patient developed side effects such as swelling of the face and lips and diffuse rash after systemic treatment. For that patient amphotericin-b treatment was discontinued and meglumine antimoniate treatment was started. The mean age of the Turkish patients was higher than the Syrian and Iraqi patients (p:0.03). While intralesional treatment was applied mostly to Turkish and Iraqi nationals, the systemic treatment rate was higher in Syrian patients (p:0.02). The number of patients with more than 4 lesions in Syrian nationals was higher than in Turkish and Iraqi patients (p:0.02) (Table 2).

Figure 1. Images of Cutaneous Leishmania Cases

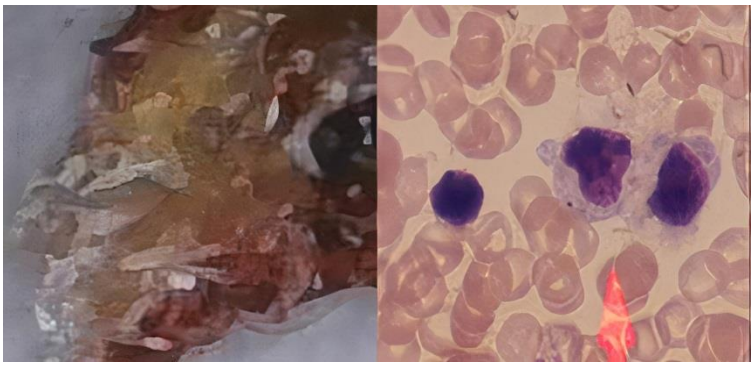

Figure 2. Nail Sign and Amastigote in microscopic examination

Table 1. Clinical distribution of all cases of cutaneous leishmania

Case Number	*Age month*	*Gender*	*Lesion Location*	*Lesion Number*	*Lesion Type*	*Lesion Time month*	*Local Treatment*	*Local Treatment Time*	*Systemic Therapy*	*Systemic Therapy Time*	*Microscopic Diagnosis*	*Nationality*	*Side Effect*
1	48	Female	Face	1	Papule	3	Yes	2	No		Amostigote	Syria	
2	132	Female	Face	1	Papule	12	Yes	2	No		Amostigote	Turkey	
3	156	Female	Face	1	Papule	6	Yes	2	No		Amostigote	Iraq	
4	24	Male	Face	1	Plaque	1	Yes	2	No		Amostigote	Iraq	
5	12	Male	Face	1	Papule	1	Yes	4	No		Amostigote	Iraq	
6	96	Female	Face	1	Papule	3	Yes	2	No		Amostigote	Turkey	
7	144	Male	Face	1	Ulcerated nodule	6	Yes	5	No		Amostigote	Syria	
8	96	Female	Face/Hand	3	Ulcerated nodule	1,5	Yes	2	No		-	Turkey	
9	84	Female	Face	3	Papule	1,5	Yes	1	Yes	20	-	Turkey	
10	168	Male	Leg	2	Papule	3	Yes	5	No		-	Turkey	
11	60	Female	Face/Hand	2	Papule	3	Yes	2	No		-	Iraq	
12	12	Female	Face	1	Ulcerated nodule	2	Yes	2	No		-	Iraq	
13	216	Male	Face	1	Ulcerated nodule	2	Yes	2	No		-	Turkey	
14	180	Male	Leg	2	Ulcerated nodule	2	Yes	2	No		-	Iraq	
15	18	Female	Face	7	Ulcerated nodule	2	No		Yes	20	Amostigote	Iraq	
16	60	Female	Face/Eyelid Body	6	Ulcerated nodule	6	No		Refuse		Amostigote	Syria	Edema/ Rash
17	48	Female	Face/Leg	5	Ulcerated nodule	2	No		Refuse		Amostigote	Syria	
18	24	Male	Face/Ear/ Neck	5	Ulcerated nodule	2	Yes	1	Yes	10	Amostigote	Syria	
19	48	Female	Face Body	5	Ulcerated nodule	3	No		Yes	10	Amostigote	Syria	
20	60	Female	Face	6	Ulcerated nodule	3	No		Yes	10	Amostigote	Syria	
21	24	Female	Leg	5	Papule	3	No		Yes	10	-	Syria	

Table 2. Clinical and epidemiological features of cutaneous leishmania cases

	Total n:21 (%)	Turkish Patients n:6 (%)	Syrian Patients n:8 (%)	Iraqi Patients n:7 (%)	p
Age (year)	6.4 (1-18)	11 (7-18)	4.7 (2-12)	5.5 (1-15)	**0.03**
Gender					0.7
Female	14 (66)	4 (67)	6 (75)	4 (57)	
Male	7 (33)	2 (33)	2 (25)	3 (43)	
Lesion Location					0.6
Face	12 (57)	4 (67)	3 (38)	5 (72)	
Leg	3 (14)	1 (17)	1 (12)	1 (14)	
Multiple	6 (28)	1 (17)	4 (50)	1 (14)	
Lesion Number					0.4
Single	9 (43)	3 (50)	2 (25)	4 (57)	
Multiple	12 (57)	3 (50)	6 (75)	3 (42)	
>4 lesions	7 (33)	0 (50)	6 (75)	1 (14)	
Lesion Type					0.3
Papule	9 (43)	4 (67)	2 (25)	3 (43)	
Plaque	1 (5)	0 (0)	0 (100)	1 (14)	
Ulcere-nodule	11 (53)	2 (33)	6 (75)	3 (43)	
Lesion Time (month)	3.6	3.8	3.5	2.5	0.1
Local Treatment	15 (71)	6 (100)	3 (38)	6 (86)	**0.02**
Systemic Treatment	6 (28)	1 (17)	4 (50)	1 (14)	**0.05**
Microscopic Diagnosis (Amostigote)	13 (62)	2 (33)	7 (88)	4 (57)	0.09

4. Discussion

CL is a parasitic disease that is endemic in nearly 80 countries around the world, including the Southeast regions of our country. While almost all of the approximately 1.5 million new cases per year were reported from these endemic regions in the past, cases have been reported from all countries in recent years due to wars, famine, and migration (9). Our country hosts more than 4 million refugees, especially from endemic regions such as Syria and Iraq. Kaman et al. reported 16 pediatric CL cases from Ankara province, which is not one of the endemic regions of our country (10). In our study, we found 21 pediatric CL cases in Eskişehir, which were not endemic leishmaniasis. This, in parallel with the recent literature, supports that the frequency of CL cases has increased in non-endemic regions after wars and migrations (11,12).

In our study, pediatric CL was more common in girls than boys. In the study of Cömert et al. and Kireçci et al., CL was more common in girls, while in the study of Kaman et al., it was more common in boys (10,13-14). The fact that CL cases are more common in girls in immigrants can be explained by the fact that more women work in open areas such as fields and gardens. In our study, CL lesions were most commonly found on the face, followed by the feet and hands. Similarly, Kaya et al. and Kaman et al. reported that CL lesions were most common in the face and neck region (10-11). We attributed this to the fact that sandflies infect more open areas such as the face and neck.

In our study, 57% of the cases had multiple lesions. The number of cases with more than four lesions in Syrian nationals was higher than in Turkish and Iraqi patients (p:0.02). Contrary to our study, the number of cases with a single lesion was higher in studies conducted in India, Iran, and Pakistan (15,16). In the study of Aksoy et al. and Kaya et al. from our country, the number of lesions was higher in Syrian patients than in Turkish patients, as in our study (11,17). This may be due to the lack of facilities such as shelters and hygiene for Syrian refugees. In our study, ulcerated nodular lesions were present in 53% of the cases. The most common lesion type was reported as papule in the study of Layegh et al., plaque in the study of Bari et al., and ulcerated nodule in the study of Aksoy et al. (17-19). In our study, ulcerated nodules were more common in Syrian patients, whereas papular lesions were more common in Turkish patients. This may be due to the delay in admission to the hospital and the infected type of leishmania.

In the study of Aksoy et al., it was reported that intralesional treatment was more common, and in the study of Kaman et al., cases who were given systemic treatment were more frequent (10,17). In our study, 71% of the cases were given intralesional and 28% systemic treatment. The rate of intralesional treatment was higher in Turkish cases and the systemic treatment rate was higher in Syrian cases. This can be explained by the fact that in our study, the number of lesions in Syrian nationals was higher and they were not eligible for local treatment.

Although the basis of systemic therapy is pentavalent antimonial; It has been reported that amphotericin-b is an effective and alternative treatment modality in the presence of serious side effects, in cases that do not respond to treatment, and in the presence of multiple lesions (20-23). Similarly, in our study, meglumine antimonate was the most commonly used systemic therapy, and liposomal amphotericin B treatment was used in one patient. The main limitations of the study are the small number of cases and the inability to perform microbiological typing of the leishmania subspecies.

The most common and easily accessible method for the diagnosis of cutaneous leishmania is to detect amastigotes in direct microscopic examination from samples taken from suspicious lesions. Molecular methods such as PCR, which directly show the causative agent and can be identified, are other important diagnostic methods. In our study, amastigotes were seen in the microscopic examination of 61% of the cases,

but PCR or culture could not be performed in any of the cases. Similarly, Altınel et al. diagnosed 82.7% of cutaneous leishmaniasis cases by microscopic and pathological examination of smear samples taken from the lesion (24). In the most recent studies conducted in our country, Gürses et al. and Nalçacı et al. emphasized the importance of newly developed molecular methods in the diagnosis and typing of Leishmania (25,26). In our study, only microscopic examination was used in diagnosis and not molecular methods, which is one of the limitations of our study.

As a result, CL cases have become a public health problem for non-endemic regions as a result of migration from endemic regions to non-endemic regions due to war, famine, and economic reasons. CL should be kept in mind as a diagnosis, especially in long-lasting ulcerated nodular and papular lesions. It is important to detect the lesions early and to give intralesional and systemic treatment depending on the location and number of the lesions, especially in foreign patients. In addition, priority should be given to measures such as hygiene and cleaning measures, fighting against vectors, and increasing shelter options for the control of the disease.

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Ethics

Ethics Ethics Committee Approval: The study was approved by Eskişehir Osmangazi University Ethical Committee (Approval Date/ Number: 15.02.2022/27).
Author Contributions: Idea/concept: M.İ.N., Y.K., M.C.K., Ö.K., E.Ç.D. Design: M.İ.N., Y.K., M.C.K., Ö.K., E.Ç.D. Data Collection: M.İ.N., Y.K., M.C.K. Data Processing: M.İ.N., Y.K., M.C.K, H.K.E., K.B.Ç., N.D., T.U.,Analysis/Comment: M.İ.N., Y.K., M.C.K., Ö.K., E.Ç.D Literature research/review: M.İ.N., Y.K., M.C.K., Ö.K., E.Ç.D.Writing: M.İ.N., Y.K., M.C.K., Ö.K., E.Ç.D, All authors discussed the results and contributed to the final manuscript.
Conflict of Interest: No conflict of interest was declared by the authors.
Financial Disclosure: The authors declared that this study received no financial support.
Acknowledgment: The authors express their gratitude to the dental students who participated in the study by filling out the questionnaire.