Cutaneous Leishmaniasis – A Case Series from Dresden

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Abstract

Leishmaniasis is world-wide one of the most common infectious disorders caused by protozoa. Due to the climate change, there is a risk of further spread of the disease to central and northern Europe. Another important issue is the high number of refugees from Syria since Syria is one of the hot spots of Old World leishmaniasis. We report on single-centre experience with leishmaniasis in the capital of Saxony, Dresden, during the years 2001 to 2017. We noted a substantial increase in the last five years. Once a very rare exotic disorder in Germany, cutaneous leishmaniasis has become a reality and physicians should be aware of it. A significant number of cases are from Syrian refugees; other cases had been acquired in the Mediterranean region!

Introduction

The climate change has the potential for distribution and epidemiology of skin diseases. In case of infectious dermatoses, climate may modulate the distribution of both, pathogens and vectors [1].

Leishmaniasis is a protozoal disease with cutaneous, mucocutaneous and visceral subtypes. World-wide, about two million people are affected. Pathogens are Trypanosoma-like Leishmania with the major subgenera Leishmania and Viannia. Around 20 species have been identified so far.

Cutaneous leishmaniasis is classified into Old World- and New World- disease. Also, there is mucocutaneous and visceral leishmaniasis, also known as Kala-Azar [2].

The classical distribution of leishmaniasis is Central and South Americas, China, Sri Lanka, the Indian subcontinent, North, East, West and Central Africa, Middle East, and the Mediterranean. Transmission occurs by blood-sucking female insects of the genus Phlebotomus (Old World) and Lutzomyia (New World). Pathogen reservoir includes rodents, canine, feline, and humans. The incubation period may vary between some weeks and several months. The protozoa are located intracellular and modify the host response reactions immunologically [3].

Entomological investigations suggest changes in the geographical distribution of Leishmania vectors. An increased risk for vectors has been calculated for the European Atlantic coast, Austria, Germany, and Switzerland [4]. In Germany, there are two possible mosquito vectors, i.e. Phlebotomus (P.) mascittii and P. perniciosus [5]. In Northern Italy, Ixodes ricinus had been identified as another possible vector since 7.5% of all tick bites had a positive polymerase chain reaction (PCR) for Leishmania (L.) infantum [6]. PCR plus sequencing and/ or multiple restriction enzyme
digestions (RFLP) is now considered as gold standard in diagnosis [7].

We report on cutaneous leishmaniasis cases, diagnosed and treated at our department during the years 2001 - July 2017.

Patients and Methods

This is a single-centre retrospective study using the patient files at the academic teaching hospital Dresden-Friedrichstadt from January 2001 to July 2017. All patients that could be identified by diagnosis of cutaneous leishmaniasis were included.

Results

We identified nine patients – 6 males and three females – with age between 1.5 years and 33 years. Five patients were refugees from Aleppo, Syria (Table 1).

Table 1: Cutaneous leishmaniasis 2001-17 (PR, partial remission; CR, complete remission)

| No. | Age (years) | Sex | Infection site | Clinical presentation | Diagnosis | Treatment and outcome |
|-----|-------------|-----|----------------|-----------------------|-----------|----------------------|
| 1⃣  | m           | 10  | head-neck      | plaque, nose          | Histology | Glucantime 3 x 200 mg/d |
| 2⃣  | f           | 3   | head-neck      | plaque, nose          | Histology | Glucantime 3 x 200 mg/d |
| 3⃣  | f           | 5   | hands          | plaque, nose          | Histology | Glucantime 3 x 200 mg/d |
| 4⃣  | f           | 6   | head-neck      | plaque, nose          | Histology | Glucantime 3 x 200 mg/d |
| 5⃣  | f           | 10  | head-neck      | plaque, nose          | Histology | Glucantime 3 x 200 mg/d |
| 6⃣  | f           | 9   | head-neck      | plaque, nose          | Histology | Glucantime 3 x 200 mg/d |
| 7⃣  | f           | 14  | head-neck      | plaque, nose          | Histology | Glucantime 3 x 200 mg/d |
| 8⃣  | f           | 2   | head-neck      | plaque, nose          | Histology | Glucantime 3 x 200 mg/d |
| 9⃣  | f           | 1.5 | head-neck      | plaque, nose          | Histology | Glucantime 3 x 200 mg/d |

All cases were identified since 2013; there was not a single case before. The lesions developed up to 6 months before a diagnosis was confirmed. Major differential diagnoses were pyoderma and infected insect bites. The diagnosis was confirmed by histologic proof of intracellular amastigotes in eosin-hematoxylin or Giemsa stains. Four cases occurred in a single family. Here, we decided to confirm clinical diagnosis in the oldest child only. In another infant, infected with Sicily, polymerase chain reaction (PCR) was performed at the Benhard-Nocht-Institute for Tropical Medicine, Hamburg. PCR was positive for Leishmania spp., sequencing excluded L. braziliensis and L. major complex but confirmed L. donovani complex. Eventually, L. infantum infection could be delayed. Other infections were acquired during holidays in Northern Italy and Crete, Greece.

We used pentavalent antimonials (Glucantime) (n = 5), meglumine stibnite (n = 1), azole derivates (n = 2) or paromomycin ointment (n = 1) to treat our patients. Eight patients achieved a complete remission (CR), one achieved a partial remission (PR). In the latter two cases, treatment is continued. Treatment was well tolerated. To reduce the injection-associated pain, topical lidocaine/prilocaine ointment (EMLA® cream) was applied. We observed single delayed oedema after the second injection of glucantime on the cheek. With systemic corticosteroids, oedema disappeared within three days.

Cutaneous leishmaniasis healed leaving scars (n = 7) and/or post-inflammatory hyperpigmentation (n = 4).

Discussion

We identified nine cases of cutaneous leishmaniasis (Old World) in the last 16 years. All but one patient were infants, children and adolescents [8][9][10]. Five patients were from Aleppo, Syria, coming to Saxony as refugees. The most common sites affected, were head-and-neck region and hands not covered by clothes. In Aleppo and the surrounding northern area of Syria, L. major is the major pathogen [11]. L. infantum is the dominant species in Sicily [12].

In Germany 130 cases of leishmaniasis were registered from September 2000 and May 2007 with
96 cutaneous and mucocutaneous disorders. Tourists represented the greatest group [13]. In Europe EuroTravNet identified three hot spots for Leishmania infections in Europe, i.e. Spain, Malta, and Italy [14]. The largest outbreak of European leishmaniasis occurred in 2009 in Fuenlabrada, Spain, with 90 adult patients with either localised Leishmania lymphadenopathy or visceral leishmaniasis (81%) [15].

In recent years, refugees and asylum seekers from the Middle East and North Africa have become more important in that manner. The official number of refugees registered in Saxony was 69,900 in 2015. In May 2017, around 25,000 refugees and asylum seekers officially lived in Saxony [16]. Outbreaks of cutaneous leishmaniasis have been reported from refugee camps in Lebanon and Turkey [17][18][19], but neither from Switzerland nor Germany [20][21][22].

Another important source of infections are pets serving as a pathogen reservoir. Canine and feline infections from animals taken by tourists to endemic regions of the Mediterranean, and dogs and cats imported from there represent a risk factor for leishmaniasis spread in Central Europe [23].

Treatment is dependent on clinical symptoms. Miltefosine, pentavalent antimonials, paromomycin and azole derivates are treatment options. Recently, case reports about successful photodynamic therapy have appeared, but systematic trials are missing [7][9]. In general, the safety of drug therapy is good. The adverse effects associated with miltefosine were vomiting, nausea, ketosis, headache, diarrhea, and an increase in aminotransferases and creatinine. The most frequently reported clinical adverse effects of pentavalent antimonials and pentamidine were musculoskeletal pain, gastrointestinal problems, and headache. Electrocadiographic QTc interval prolongation and increase in liver and pancreatic enzymes were also seen [24]. We observed a facial edema after second injection with glucantime, that responded rapidly to systemic corticosteroids. The third injection was tolerated well.

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