2

A 7-Year-Old Girl from Peru With a Chronic Skin Ulcer

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Clinical Presentation

History

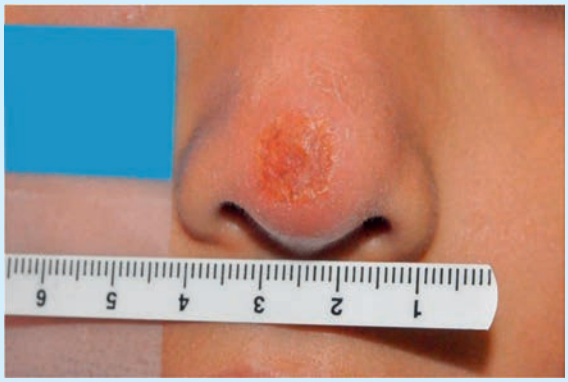
A 7-year-old girl who lives in the Peruvian capital, Lima, is brought to a local clinic because of a chronic skin lesion on her nose. The lesion appeared 4 months ago as a small nodule and slowly turned into an ulcer. It is a bit itchy but not painful. There is no history of trauma. The girl is otherwise healthy. Six months ago, she travelled to a valley on the western slopes of the Andes.

Clinical Findings

The lesion is a localized ulcer on the nose (Fig. 2.1). The borders of the ulcer are indurated and there is a plaque-like infiltration of the surrounding skin. The whole lesion is about 2 cm in diameter. There are no palpable lymph nodes. She is afebrile and the rest of the physical examination is normal.

Questions

1. What are your differential diagnoses?
2. How would you approach this patient?



• **Fig. 2.1** Lesion at first consultation.

Discussion

A 7-year-old Peruvian girl presents with a painless ulcerative skin lesion on her nose, which has been present for the past 4 months. There are no systemic symptoms.

Answer to Question 1

What Are Your Differential Diagnoses?

Infectious diseases that can cause similar lesions in the face are cutaneous leishmaniasis, sporotrichosis, cutaneous tuberculosis and infection by *Balamuthia mandrillaris,* a free-living amoeba.

Although common bacterial infections of the skin that are partially treated or masked as a consequence of traditional remedies (e.g. chemical burns) are another possibility; this is less likely in our case given the chronic nature of the lesion. Cutaneous anthrax and tularaemia could be considered in the differential diagnosis of lesions located on the extremities, but the latter is endemic in the Northern hemisphere only, and the long duration without any further symptoms does not fit with either infection. In addtion, cutaneous anthrax tends to present with considerable localized oedema not seen in this case.

Cutaneous leishmaniasis is a common, vector-borne, parasitic disease that affects people living in or travelling to endemic areas. It typically begins as a small papule on air-exposed parts of the skin, progresses to a nodule or plaque and then turns into an ulcer with raised borders. The ulcer is painless unless there is bacterial superinfection. Patients may have several lesions.

Sporotrichosis is caused by *Sporothrix schenckii,* a dimorphic fungus that is found in soil and on plants. It enters the skin through direct inoculation (e.g. thorny plants or animal scratch). The disease usually starts with a papule that turns into a tender ulcer. Lesions can spread along draining lymphatic vessels. Sporotrichosis occurs throughout the world as a sporadic disease of farmers and gardeners. This disease is hyperendemic in parts of the Peruvian Andes, where it often affects children and typically produces facial lesions.

However, our patient did not travel to such a hyperendemic place.

Cutaneous tuberculosis is an uncommon manifestation of tuberculosis. It occurs by direct inoculation of mycobacteria into the skin of non-sensitized individuals (e.g. children) or as a result of reactivation in persons with previous immunity against mycobacteria. As our patient lives in a poor neighbourhood with a high incidence of tuberculosis, we cannot rule out this diagnosis. Not only *Mycobacterium tuberculosis,* but also environmental mycobacteria, *Mycobacterium marinum* and *Mycobacterium leprae* can cause ulcerating skin lesions.

B. mandrillaris is a free-living amoeba that may cause a highly fatal disease. It usually starts as a painless plaque, often after local trauma. *Balamuthia* lesions are characterized by reddish or purplish infiltrations; ulceration is uncommon. The most frequent location of the initial lesion is the central face, over the nose. In a few months, it can progress to the brain causing granulomatous amoebic encephalitis. If this occurs, the survival time is usually less than 8 weeks.

The most likely diagnosis in our case is cutaneous leishmaniasis, because of the frequency of leishmaniasis in the valley our patient had travelled to and the characteristic presentation (localized painless ulcer with raised edges).

Answer to Question 2

How Would You Approach This Patient?

Gently clean the lesion with water, remove the scab and take a closer look at the process underneath. A definitive diagnosis of cutaneous leishmaniasis requires the demonstration of the parasite through microscopic examination, culture or molecular techniques.

The simplest approach is to scrape with a lancet under the edges of the lesion, and use the obtained material for a smear examination with Giemsa staining, looking for *Leishmania* amastigotes. The sensitivity of this technique is about 70%, decreasing as the duration of the lesion increases. The specificity is 100%.

Culture can be done on samples obtained by fine-needle aspiration or biopsy taken from the edge of a lesion. In reference centres, polymerase chain reaction (PCR) is used to confirm the presence of *Leishmania* and to identify the species.

The Montenegro or leishmanin skin test detects delayed immune response against *Leishmania* antigens and is sometimes used as a diagnostic aid. It can be negative in early stages of the disease and cannot distinguish current from past infection.

If leishmaniasis is ruled out, the following tests can be useful for the diagnosis of alternative causes of our patient's lesion: smear microscopy and culture in Sabouraud's medium (for sporotrichosis), a purified protein derivative (PPD) skin test (for tuberculosis) and, if necessary, a histopathological examination of a biopsy specimen.

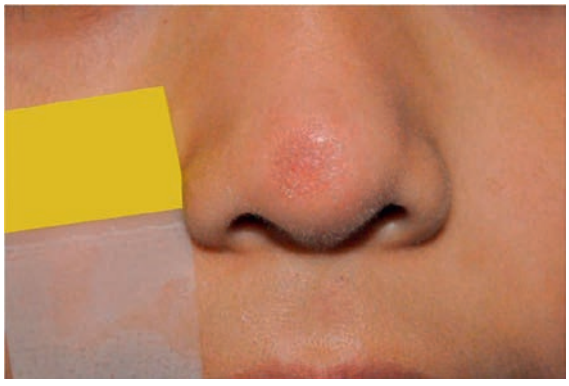
The Case Continued…

The scab was removed revealing an ulcer with cobblestone-patterned bottom and raised edges, typical of cutaneous leishmaniasis. The microscopic examination of a sample obtained by scraping was negative. The leishmanin skin test was positive. PCR was also positive; and the infecting species was identified as *Leishmania (Viannia) peruviana.*

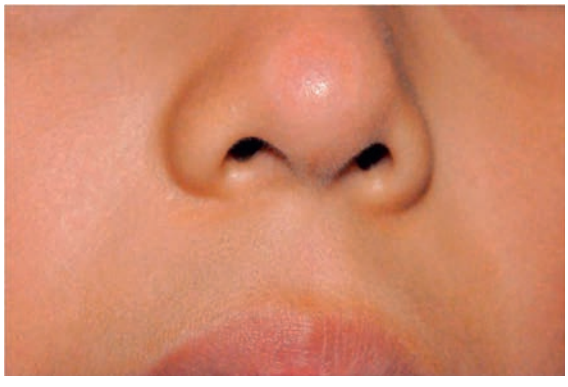
With a definitive diagnosis of cutaneous leishmaniasis, treatment was started with intravenous sodium stibogluconate (SSG, 20 mg/kg/day for 20 days) which is the first-line treatment of choice for cutaneous leishmaniasis caused by *L. (V.) braziliensis* or *L. (V.) peruviana* in Peru. In addition, the girl received topical imiquimod therapy, which was administered every other day for 20 days. Imiquimod, is an immune-modulating drug, which may be used as part of the therapy for facial lesions and relapses. The response after 20 days of treatment was good (see Fig. 2.2).

Treatment failure occurs in almost one quarter of patients after a first course of SSG monotherapy in Peruvian series, usually within 3 months. Follow-up is therefore recommended. Factors linked to treatment failure include young age and short stay in endemic area (as in this case) as well as recent onset of disease ($\leq$5 weeks), multiple lesions, and *L. (V.) braziliensis* infection (not present in this case). At the third month of follow-up, our patient did not have any signs of relapse (Fig. 2.3).

The treatment of cutaneous leishmaniasis is challenging because SSG has a high failure rate and several side effects, including myalgia, arthralgia, loss of appetite, nausea, fever, increased levels of liver and pancreatic enzymes, reactivation of varicella zoster virus and cardiotoxicity, which can lead to



• **Fig. 2.2** Follow-up image after 20 days of treatment.



• **Fig. 2.3** Follow-up image of the scar 3 months after the end of treatment.

prolongation of QT-segment, severe arrhythmias and death. Information about the safety of this drug in children is limited. It is also unclear from the literature if there are safe and effective alternatives to SSG in children with *L. (V.) peruviana* infection. This is particularly relevant because, in endemic areas, cutaneous leishmaniasis often affects children.

SUMMARY BOX

Cutaneous Leishmaniasis

Cutaneous leishmaniasis (CL) is caused by protozoa of the genus *Leishmania.* Some 20 *Leishmania* species are associated with human disease. CL can be anthroponotic or zoonotic (reservoir: small mammals). The parasite is transmitted by sand flies of the genus *Lutzomyia* (New World) and *Phlebotomus* (Old World). Of the estimated 1.5 million annual cases, 90% occur in Afghanistan, Pakistan, Iran, Syria, Saudi Arabia, Algeria, Brazil, Colombia and Peru.

The incubation period between sand fly bite and appearance of skin lesions ranges from weeks to months. Clinical manifestations depend on characteristics of the parasite and the host immune response. Localized cutaneous leishmaniasis is the most common form. Some species of the *Leishmania Viannia*-complex can produce mucosal lesions resulting in disfiguring disease.

The lesions can heal spontaneously; this is more common in Old World (>50%) than in New World leishmaniasis (<20%). The aim of treatment is to accelerate healing, reduce scarring and decrease the risk of metastasis and recurrence. Topical therapy is recommended for Old World CL and for New World CL caused by species not belonging to the *Leishmania Viannia*-complex. This topical approach consists of intralesional pentavalent antimony, paromomycin cream and/or cryo- or thermotherapy. Systemic therapy is indicated for CL caused by species of the *Leishmania (Viannia)*-complex, which may lead to disfiguring mucocutaneous leishmaniasis. In addition, systemic treatment should be given when lesions are extensive or when topical treatment fails. Pentavalent antimonials are the first-line systemic treatment of choice for all New World forms except *L. guyanensis,* for which pentamidine is recommended. Miltefosine and azoles are alternatives.

Amphotericin B deoxycholate and liposomal amphotericin B are second-line drugs.

Further Reading

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