Differential Diagnosis of Leprosy: Skin

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Interaction between *Mycobacterium leprae* (*M. leprae*) and the host's immune system results in a wide range of lesions on the skin, giving rise to either mono- or polymorphous clinical aspects.

In active leprosy, these clinical aspects are characterized by [1]:

- Macules, which appear red in light-skinned patients and coppery in dark-skinned patients or are hypopigmented
- Papules, in groups or along the edges of hyperergic lesions
- Nodules, either scattered or in groups
- Plaques, caused by coalescence of papules or nodules or by infiltration of macules

In the hyperergic forms (TT, BT), skin lesions have asymmetric distribution, as well as early involvement of peripheral nerve autonomic branch leading to anhidrosis. This gives to lesions a dry, rough, and opaque appearance. Xerosis of lesions may cause pityriasiform desquamation.

Leprosy reactions are characterized by acute appearance of nodules and plaques, or by increase in erythema, infiltration, and edema in preexisting lesions.

On reactional lesions, vesicles, bullae, and ulcers may also appear.

Scaling occurs in healing lesions of type 1 leprosy reaction. Around subsiding erythema nodosum lesions, there could be collarette scaling.

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Residual lesions consist of hyperchromic macules, scars (resulting from ulcerative lesions), and atrophy occurring upon dissolution of the dermic infiltrate secondary to *M. leprae* elimination.

Trophic skin lesions following damage to peripheral nerves include ulcers, sclerosis, and scars.

This broad range of manifestations prompts us to take into consideration numerous skin diseases to be distinguished from leprosy in differential diagnosis.

13.1 Macule

A macule is a circumscribed, flat lesion with different surrounding skin color, which in leprosy may be due to:

- Erythema: the macule appears red in light-skinned patients, whereas in dark-skinned patients, the erythema gives the lesion a coppery color.
- Hypopigmentation: more easily detected in dark-skinned patients. The diminished pigmentation in leprosy is homogeneous and never complete; hypopigmentation is more pronounced in paucibacillary forms.
- Hyperpigmentation: the hyperchromic macule is to be regarded as a residual lesion. In the course of treatment with clofazimine, slate-gray hyperpigmentation appears in light-skinned individuals in affected areas exposed to sunlight. Macules in leprosy are:
- Permanent.
- Roundish or oval in shape.
- Nonpruriginous.
- Without vesicles.
- Chronic in evolution.
- Resistant to topical therapies.

13.1.1 Erythematous Macule

The erythematous macule is the only basic lesion which may be present in every clinical form of leprosy.

The single macule of indeterminate leprosy (I) is the most difficult lesion to diagnose; sensitivity and sweating are normal or slightly decreased. Only histopathology may help in diagnosis.

Large macules with asymmetric arrangement, in the paucibacillary hyperergic forms (TT, BT), where the surface appears rough and dry, show evidence of early reduction in sensitivity, sweating, and hair growth. These lesions can develop a ring-shaped appearance.

Patients presenting a large number of lesions with asymmetric arrangement also present *M. leprae* on skin smear.

Large macules with symmetric arrangement, with bizarre shapes and annular arrangement, are typically present in the central part of the spectrum (BB). Here, skin smear will be positive.

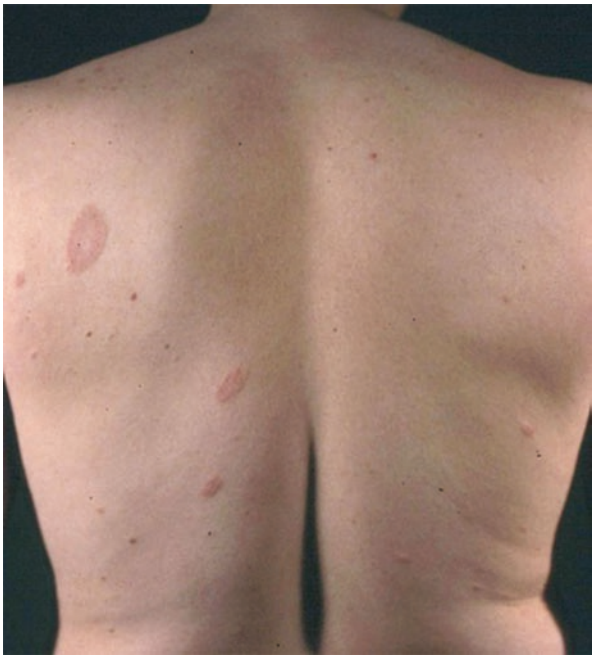

Fig. 13.1 Gibert's pityriasis rosea. Annular herald patch and few small secondary macules

Numerous small macules without anesthesia with symmetric arrangement are typical of multibacillary forms (BL, LLs). The diagnosis is confirmed by the presence of AFB.

Single or groups of a few macules of indeterminate or tuberculoid leprosy must be distinguished from the macules occurring in fixed drug eruption, early-stage morphea, Lyme disease, and cutaneous mycosis and from the herald patch of Gibert's pityriasis rosea (Fig. 13.1).

The clinical evolution enables the formulation of the diagnosis: hyperpigmentation with self-resolution (fixed drug eruption), sclerosis (morphea), and erythema migrans (Lyme disease). Tinea corporis presents peripheral fine scaling, microvesicles, and itching.

The numerous small macules with symmetrical arrangement of multibacillary leprosy must be distinguished from syphilitic roseola by positivity of lues serological tests. Gibert's pityriasis rosea has erythematous macules with peripheral scaling and heals by autoresolution. Tinea corporis disseminata should also be considered in differential diagnosis.

Ring-shaped and circinate lesions with asymmetric arrangement are typical in the hyperergic form of the leprosy spectrum, presenting anesthesia and having raised edges; they must be differentiated from numerous other diseases. Absence of desquamation and vesiculation, together with lack of itching, enables exclusion of many dermatologic diseases. In differential diagnosis, the following must be included: tinea corporis (Fig. 13.2), Gibert's pityriasis rosea, lichen ruber planus, erythema annulare centrifugum, erythema multiforme, and subacute lupus

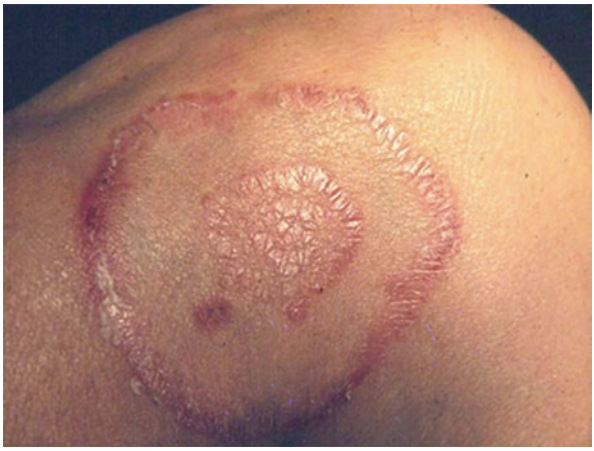

Fig. 13.2 Tinea corporis, large target lesion. Note vesicles on the external border, not present in leprosy. Target lesions can be observed in the BB form of leprosy, which presents skin lesions with symmetric arrangement and acid-fast bacilli

erythematosus. In the early stage of trypanosomiasis (*Trypanosoma gambiense*), erythematous annular patches occur on limbs and upper thorax.

13.1.2 Hypochromic Macule

Due to color loss which can be present in leprosy, macules are hypochromic, so in differential diagnosis, each skin disease with achromic macules has to be excluded: achromic nevus, nevus anemicus, and vitiligo. These diseases may coexist with leprosy in the same patient [2].

The hypopigmented variety of pityriasis versicolor, often localized on the upper trunk, shoulders, and arms, is more easily observed in Western countries during the warmer months of the year. In the active phase, hypochromic macules are characterized by pityriasiform scaling. When observed under Wood's light, macules show pale yellowish fluorescence. The shape and size of macules are variable as a result of coalescence of initial small lesions.

Pityriasis alba is rather common in children, as cutaneous manifestation of atopy (Fig. 13.3). Clinically, it appears with roundish, oval patches with faded margins. It is erythematous in the early stages. Later the erythema subsides, leaving a hypopigmented lesion with dry surface and occasionally fine scaling. The face is the most heavily affected area, but lesions may also appear on the upper part of the thorax, arms, buttocks, and thighs (Fig. 13.4). The macule (either single or multiple) shows diameter of less than 2 cm when located on the face and larger when occurring on the trunk. The eruption persists for months, with the appearance of new lesions and self-resolution of older ones. In Western countries, the lesions become more evident in summer because of the pigmentation of surrounding skin.

Oval or roundish hypopigmented macules may constitute a residue of inflammatory lesions (postinflammatory hypopigmentation) of either bacterial (impetigo), fungal (tinea corporis), or viral infections (herpes zoster), or allergic contact dermatitis.

Early post-kala-azar dermatitis may consist in hypopigmented macules occurring simultaneously with bilateral distribution in several areas of the body (thorax, back, arms, and neck).

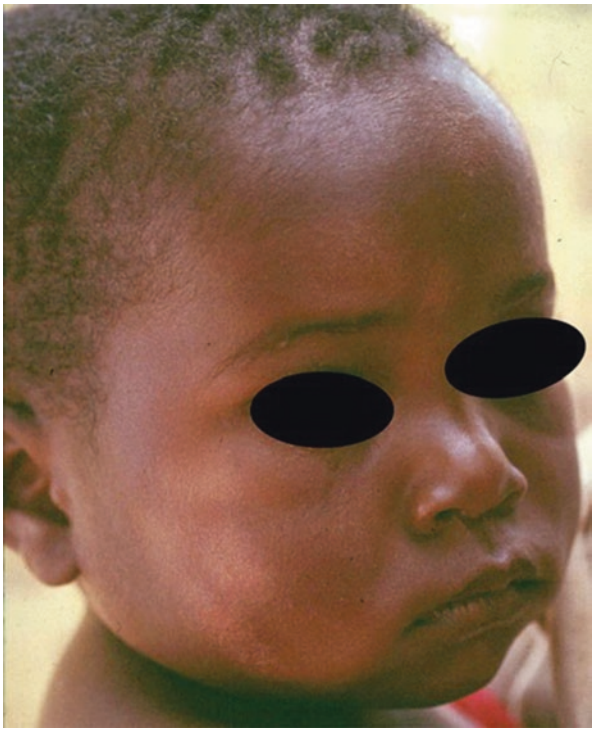

Fig. 13.3 Pityriasis alba

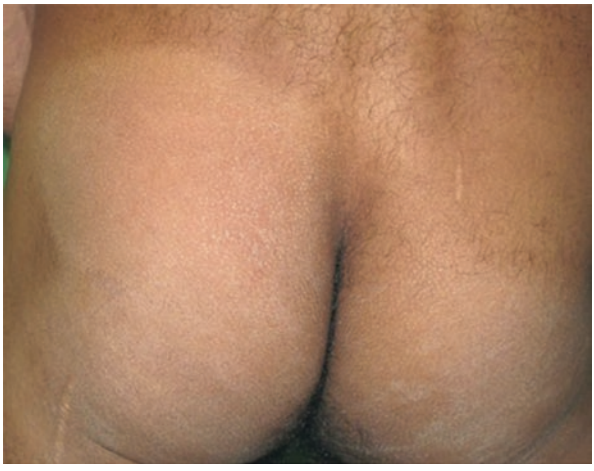

Fig. 13.4 Pityriasis alba. Sensitivity in hypochromic lesions is present

13.1.3 Hyperchromic Macule

This can be a residual sign of cutaneous involvement in leprosy. Case history, along with the possible presence of active leprosy lesions at the same time, can clarify the diagnosis.

Some cases of tuberculoid leprosy have been reported as "primary hyperchromic" macules by authors on account of the successful therapeutic response [3].

Differential diagnosis may include residual lesions of postinflammatory hyperpigmentation, Kaposi's sarcoma, morphea, erythema dyscromicum perstans, and fixed drug eruption. One may take into consideration tinea nigra, clinically characterized by brownish macules localized on palms and soles, and the hyperchromic form of pityriasis versicolor. In epidermomycosis, detection of fungus with KOH enables clear diagnosis.

13.2 Papule

A papule is a circumscribed, superficial, solid, elevated lesion. In hyperergic forms (TT, BT), they assume asymmetric distribution.

Erythematous/coppery papules are frequently associated with other basic lesions, favoring polymorphous clinical aspects.

Red or coppery papules are grouped together along the edges of the ring-shaped lesions, forming clinical aspects to be distinguished from Leiker's granuloma multiforme (Fig. 13.5) [4], localized or widespread granuloma annulare (Fig. 13.6), lichen ruber planus, late secondary syphilis, post-kala-azar dermatitis, and secondary late yaws (Fig. 13.7).

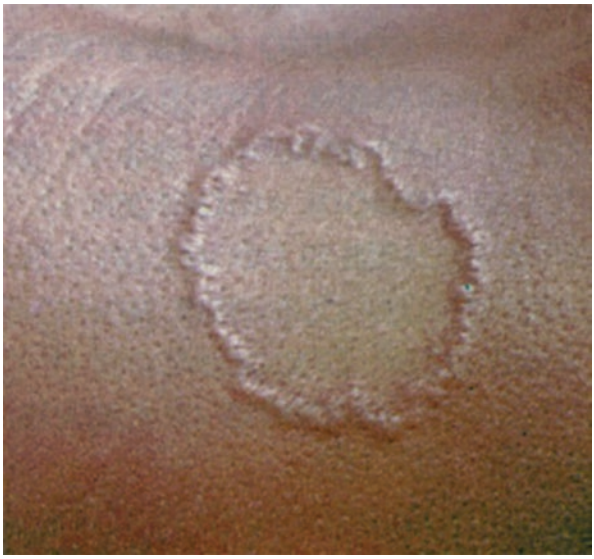

Fig. 13.5 Leiker's granuloma multiforme. This lesion was easily confused with TT leprosy before being identified by Leiker. Clinically, there is no impairment of sensitivity

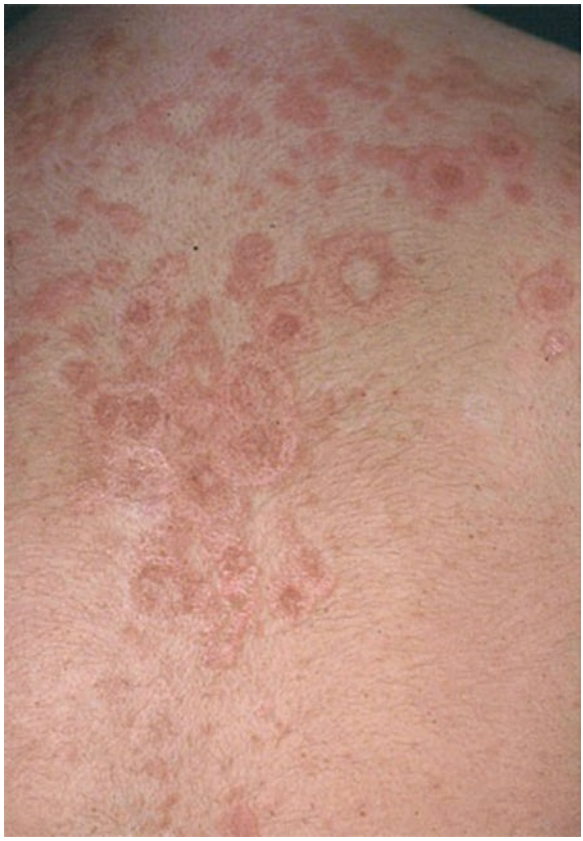

Fig. 13.6 Widespread granuloma annulare. Annular aspect, symmetric distribution; the differential diagnosis is BB leprosy, but—of course—in lesions of granuloma annulare, there are no AFB

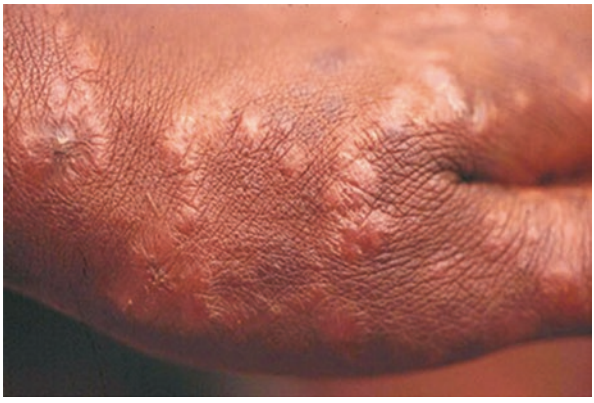

Fig. 13.7 Secondary late yaws. Asymmetric bilateral lesions; the differential diagnosis is with BT leprosy. Clinically, there is no impairment of sensitivity

13.3 Nodule

A nodule is a circumscribed, solid lesion that in leprosy is typical of multibacillary forms. The nodule is due to an inflammatory infiltrate in the whole dermis except the papillary layer.

Nodules characterize the anergic forms (BL, LLs) and have symmetric distribution (except in some anecdotal cases), and many AFB are present. These nodules have slow onset and can be red/coppery or of normal skin color. Edges are vague, are firm in consistency, and when they protrude are defined as tuberous lesions.

The differential diagnosis may include Recklinghausen disease (Fig. 13.8), sarcoidosis (Fig. 13.9), Oriental sore (cutaneous leishmaniasis), anergic cutaneous leishmaniasis, post-kala-azar dermatitis [5], onchocerciasis (Figs. 13.10 and 13.11), mycetoma, keloids, Kaposi's sarcoma, and skin lymphoma [6].

Wade's "histoid" leprosy is characterized by the presence of scattered nodules which are hard in consistency and distinctly delimited from the surrounding skin.

These lesions must be differentiated from several diseases, including dermatofibroma, anergic cutaneous leishmaniasis, molluscum contagiosum, and keloids.

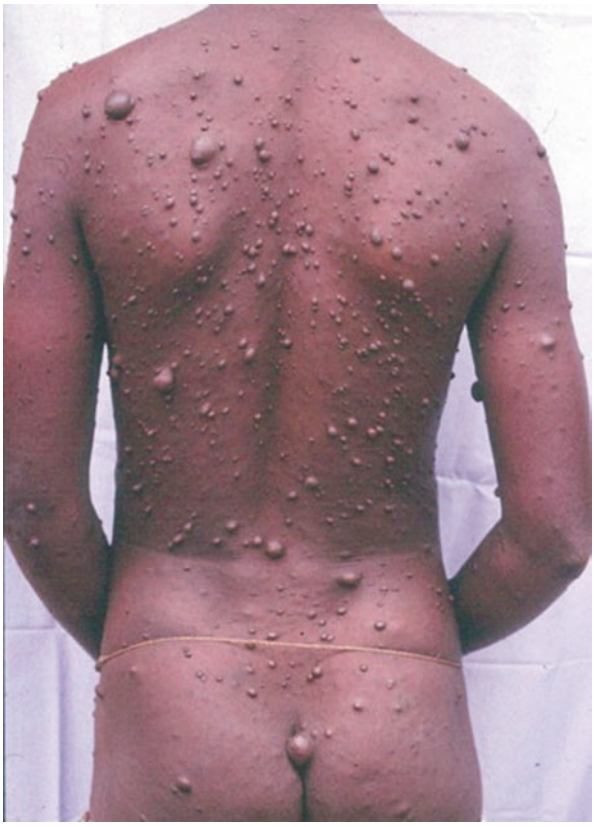

Fig. 13.8 Recklinghausen disease. Cutaneous neurofibromas: soft, sessile, dome-shaped, pedunculated

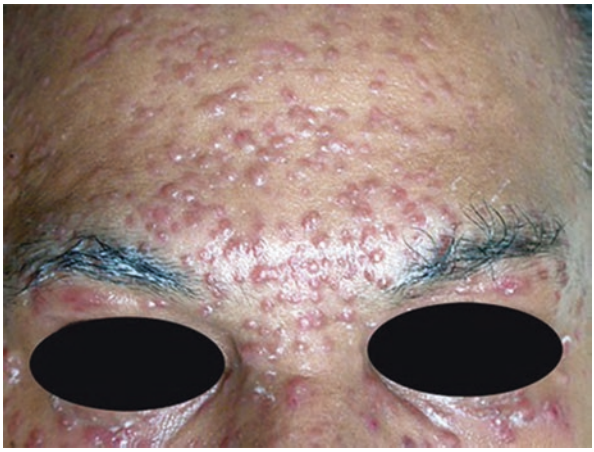

Fig. 13.9 Sarcoidosis. Symmetric distribution of nodules; there are no AFB in lesions

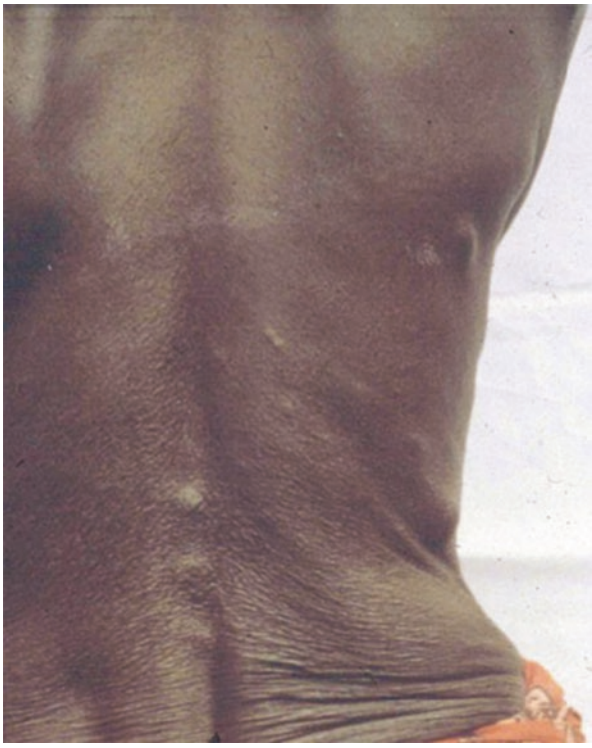

Fig. 13.10 Onchocerciasis. Subcutaneous nodules located on bone prominences; severe pruritus is present; from Nunzi E, Leiker DL (1990) Manuale di Leprologia. AIFO-Italia, Bologna

The nodules of acute erythema nodosum leprosum (ENL), which are localized in the dermis and hypodermis, must be differentiated from nodular vasculitis, having different etiology. The diagnosis could be difficult when ENL represents acute onset of leprosy. Medical history and AFB presence in "cooler" areas of the body (earlobes, extensor aspect of elbows and knees, and upper side of fingers) will help in diagnosis.

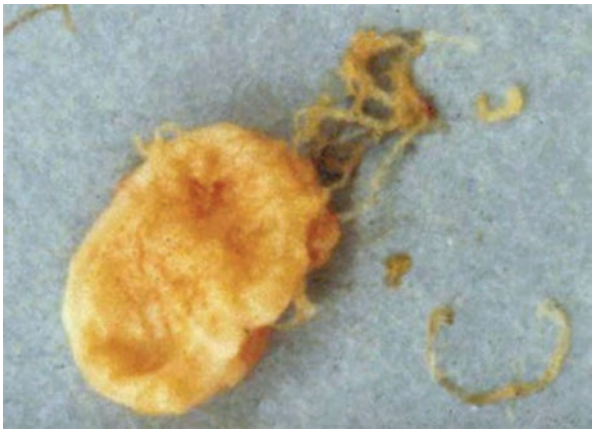

Fig. 13.11 Onchocerciasis. Section of nodule containing adult filariae

13.4 Plaque

A plaque is an elevated, roundish area caused by either spread and coalescence of papules and nodules or central granulomatous infiltration of a macule.

In the hyperergic part of the spectrum, plaques can assume annular appearance with central healing.

Differential diagnosis may include cutaneous leishmaniasis, lupus vulgaris, atypical mycobacterioses, late secondary syphilis, sarcoidosis [7, 8], and mycosis fungoides (Fig. 13.12).

In these lesions, it can be difficult to determine the loss of sensitivity, while presence of AFB and histopathological examination permit diagnosis.

13.5 Diffuse Infiltration

Diffuse cutaneous infiltration is a characteristic of polar lepromatous leprosy (LLp) and must be differentiated from skin lymphoma, actinic reticulosis, and diffuse cutaneous leishmaniasis.

In diffuse infiltration of the skin due to leprosy, slit-skin smear is positive.

13.6 Regional Manifestations

13.6.1 Eyebrows

In polar lepromatous leprosy (LLp), eyebrow involvement is characterized by diffuse infiltration with madarosis, and these features must be differentiated from other infiltrating pathologies: skin lymphoma and follicular mucinosis.

In hypothyroidism and secondary syphilis, thinning out of the external part of eyebrows can be noted, while generalized hair loss can be seen in alopecia areata totalis.

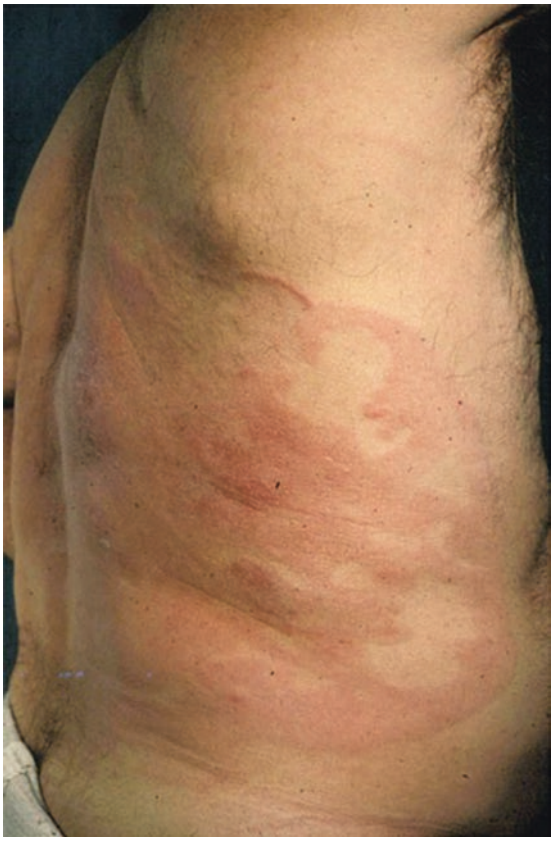

Fig. 13.12 Mycosis fungoides

13.6.2 Ear

The ear may be affected by isolated nodules or diffuse infiltration in lepromatous form. Differential diagnosis must be made with skin lymphoma and diffuse cutaneous leishmaniasis.

Infiltration of the earlobe may also be observed in lupus vulgaris and in lupus erythematosus.

13.6.3 Nose

In advanced stages of LLp, massive bacterial infiltration of the upper respiratory mucosa and of the nose can lead to collapse of the nasal pyramid. Differential diagnosis must be made in relation to mucocutaneous leishmaniasis and relapsing polychondritis (Fig. 13.13). Tertiary yaws may be characterized by an ulcerous and mutilating rhinopharyngitis (gangosa), but in this disease, serological tests for lues are positive

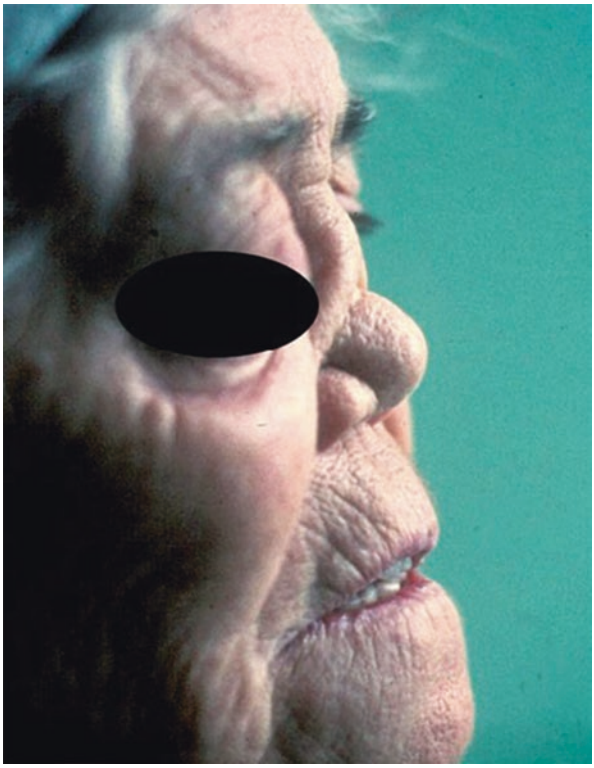

Fig. 13.13 Relapsing polychondritis may cause destruction of the nasal cartilage, resulting in a pseudo-saddle nose; from Crovato F in Leiker DL, Nunzi E (1986) Leprosy in the light skin. An illustrated Manual. AIFO-Italia, Bologna

13.6.4 Hands

Hands may be the site of specific localization of *M. leprae*. The skin of the back of the hands may be affected by diffuse infiltration in LL, resulting in atrophy after effective treatment.

Localization of *M. leprae* in the phalanx, occurring in LL, may lead to dactylitis and pathologic fractures of bones.

The most frequently observed consequences on the hands of leprosy patients are due to involvement of autonomic, sensitive, and motor branches of peripheral nerves. Dryness of the skin, anesthesia, and muscular paralysis favor the occurrence of traumatic cutaneous lesions that may lead to infections involving subcutaneous tissues and bones with ulcerations, fistulae, and scars.

Such polymorphous clinical aspect is included in differential diagnosis with syndromes affecting the peripheral nerves of the hands such as carpal tunnel syndrome, cervical rib syndrome, Dupuytren's disease, and progressive systemic sclerosis.

13.6.5 Lower Limbs

The lower limbs may also be the site of lesions of leprosy. Like the hands, most of the lesions on the lower limbs are due to involvement of peripheral nerves.

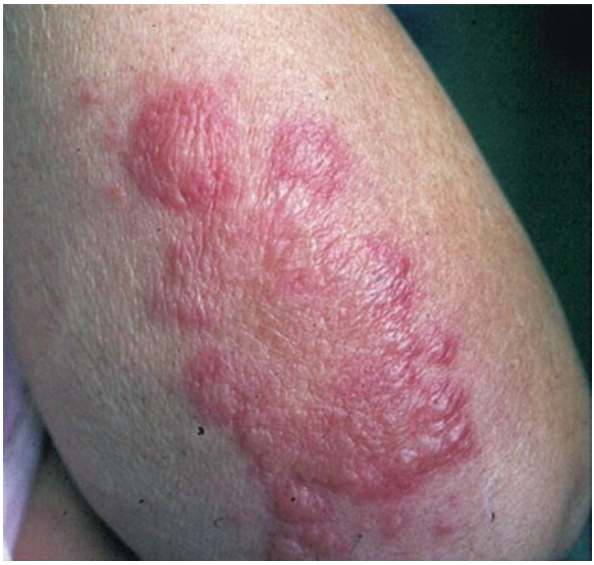

Fig. 13.14 Sweet's syndrome

In differential diagnosis, diseases which are characterized by trophic lesions, such as ulcers and bone reabsorption, must be considered.

Several diseases presenting ulcers and other disabilities on the lower limbs should be taken into account, including atypical nontubercular mycobacterioses, cutaneous tuberculosis, syphilis, cutaneous leishmaniasis, neoplasia, pyoderma gangrenosum, necrobiosis lipoidica, arterial hypertension, chronic venous insufficiency, sickle cell anemia, hereditary neuropathies, and diabetes mellitus.

13.7 Skin Manifestations in Leprosy Reactions

Type 1 leprosy reaction does not usually raise the question of differential diagnosis, since it often occurs in patients under treatment and is clinically characterized by modifications of preexisting lesions which involve an acute inflammatory phenomenon. In some cases, the patient may seek medical attention, for the first time, during type 1 leprosy reaction. This reaction must be differentiated from pathologies which begin acutely with inflammatory plaques, such as erysipelas and Sweet's syndrome (Fig. 13.14). In these cases, examination for AFB is negative. Diagnosis must be based on investigation of neuropathy and on histopathology.

Erythema nodosum leprosum (ENL), the main cutaneous expression of type 2 leprosy reaction, is characterized by acute eruptions of nodules. In BL, ENL may appear with plaques which are depressed in the center and becoming hyperpigmented. Differential diagnosis must be made with fixed drug eruption and nodular vasculitis, which have different etiology. Wheals caused by immunocomplexes can appear in type 2 leprosy reaction.

In acute onset of leprosy, anamnesis and AFB investigation will help in diagnosis.

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