Leprosy in Childhood

34

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34.1 Epidemiology, Sources, and Way of Infection

Although leprosy was universally "eliminated as a public health problem" (defined as a registered prevalence of less than 1 case per 10000 population) in 2000, new cases of leprosy continue to be seen in people from endemic areas, including children (less than 14 years of age) (see Chap. 36 for more information).

Annual statistics on leprosy for 2018 report that among the total of 208,619 new leprosy cases, 16,013 involved children, corresponding to 7.6% of all new cases [1]. The number, although modestly decreasing over the past 5 years, is still significant and used as a strong indicator of continuing transmission of the disease and a useful marker of undiagnosed cases in the community.

Incidence of childhood leprosy in endemic areas is mainly due to overcrowded housing favoring increased aerial exposure to *M. leprae* and poor hygienic conditions favoring skin diseases, mostly itching (ectoparasitosis, pyoderma, mycoses) that facilitates transdermal penetration of *M. leprae*.

A strong factor in childhood leprosy is the presence at home, among family members or close neighbors, of an adult suffering from the disease. Fifty percent of leprosy cases in children occur in household contacts. Among familial contacts, there is a fourfold risk of developing leprosy if the index case is suffering from multibacillary (MB) leprosy as compared to paucibacillary (PB) leprosy.

Among children with leprosy, the age group with the higher incidence is between 5 and 14 years of age (with only 5–6% less than 5 years of age) [2]. This is explained by the disease's long incubation period of approximately 3–5 years.

Although leprosy should not be expected in infant, because of its long incubation period, cases of leprosy in children less than 1 year of age, although very uncommon, were reported [3]. In this regard it should be considered that *M. leprae* can

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enter the body, other than respiratory tract and skin, through other routes, such as the transplacental and/or by breast milk in women affected with untreated multibacillary leprosy. For instance, the transplacental pathway is demonstrated by the finding of viable *M. leprae* in the placenta of untreated multibacillary women and in the umbilical cord of their newborns [4].

Even if it is universally accepted that an intimate and prolonged contact with an untreated multibacillary patient is necessary to contract leprosy and that the disease has a long incubation period, occurrence of leprosy in infants of a few months of life suggests additional hypotheses on the pathogenesis. The short incubation period of only a few weeks in the case of infants could be explained by the fact that the immune system not fully developed in infant would allow the *M. leprae*, penetrated transplacentally, to rapidly develop the disease. Moreover, laboratory observations show that the generation time of *M. leprae* can be much faster than commonly reported in literature (26 h instead of 12–13 days).

Nevertheless, from an epidemiological point of view, the passage of bacilli by transplacental route, although possible, is less important than direct contact as demonstrated by the fact that when babies are removed from their lepromatous mother until the age of 6 months, childhood leprosy significantly decreases [5].

Sex ratio in child leprosy is uncertain and differs among studies. Thus, there is no evidence that allows us to establish any significant difference in prevalence between the sexes.

The genetics of leprosy has been investigated in children affected with leprosy by conducting studies on monozygotic and dizygotic twins. The findings confirm the existence of a genetic mechanism controlling susceptibility to both leprosy infection and clinical manifestation (for a thorough exposure on this topic, see Chap. 3).

34.2 Natural History After Contact With *M. leprae*

Upon penetration of *M. leprae* in the human body, varying outcomes may occur:

(1) No overt evidence of infection appears, and the child never develops leprosy.
(2) Early lesions of leprosy may appear. They may remain stationary for variable time and disappear entirely in a few months as a result of self-healing due to an effective immunological response leaving no trace or in a minimal form. In these cases the temporary clinical manifestations are more frequently hypopigmented macules difficult to be detected.
(3) The lesion/s may progress, and the child (or in adulthood) develops advanced leprosy.

34.3 Clinical Presentation of Advanced Leprosy

34.3.1 Clinical History

In case of advanced leprosy, skin and nerves may be variably affected in children, and all clinical forms may develop.

Indeterminate leprosy (I) is an early and transitory stage of leprosy characterized by one of a few hypopigmented macules with indefinite margins lasting from 2 to 5 years (Fig. 34.1). Greater attention must be dedicated to detect them by using proper light when visiting and accurately examining all the skin surface. Most of the lesions are bacteriologically negative and disappear in a few months leaving no trace or in a minimal form. When spontaneous healing does not occur, this form evolves into one of the subtypes in the spectrum of the disease (Fig. 34.2).

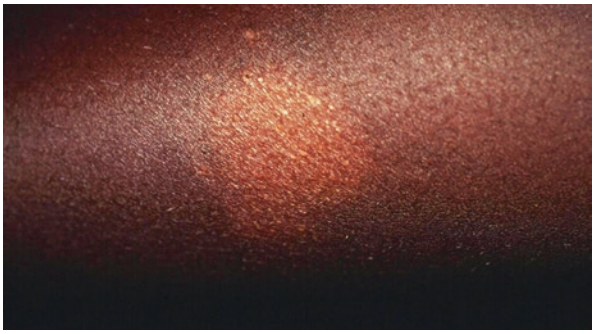

Fig. 34.1 I leprosy. Coppery macule, normal sensitivity, smooth surface and ill-defined edge

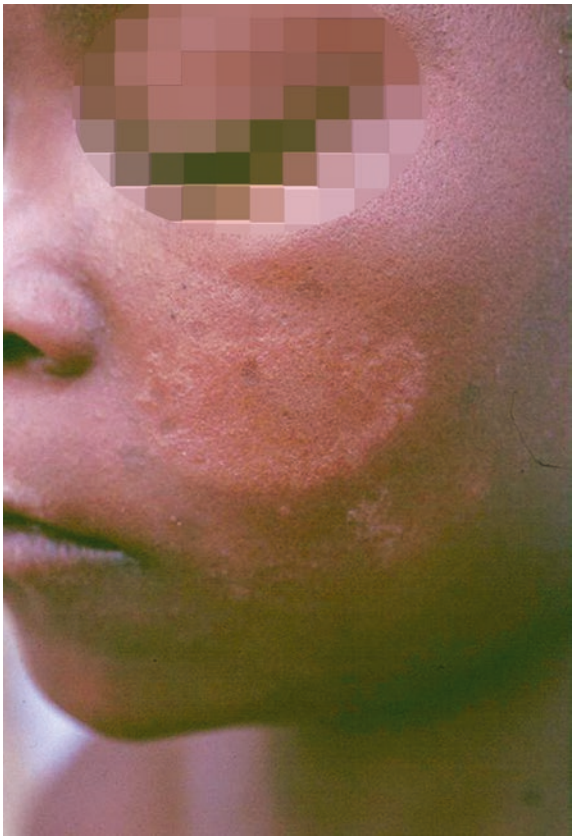

Fig. 34.2 I leprosy evolving into a hyperergic form

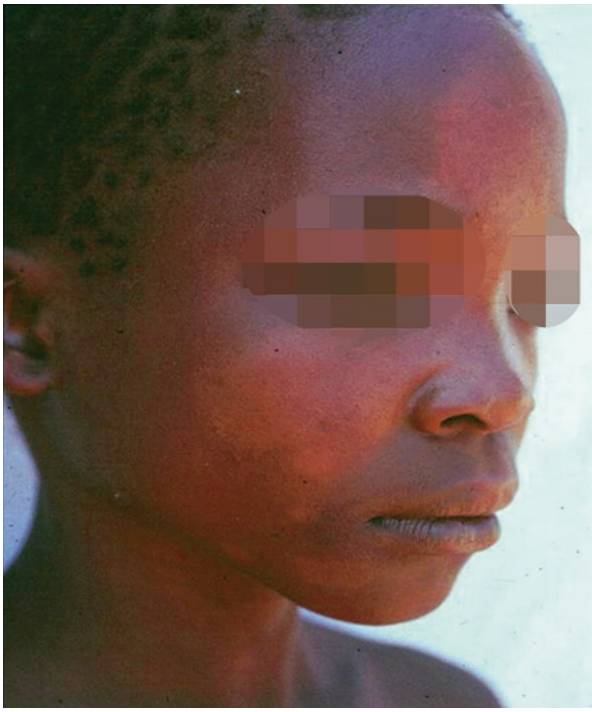

Fig. 34.3 BT leprosy. Large hypopigmented macule with well-defined margins and satellite lesions

Paucibacillary forms (tuberculoid leprosy or TT and borderline tuberculoid leprosy or BT) are the commonest clinical type recorded. This is due to the fact that infection contracted in childhood and evolving into multibacillary leprosy would become apparent after puberty due to the long period of incubation. Furthermore cell-mediate response in children is more likely hyperergic as a consequence of the penetration of *M. leprae* through the skin (as described in Sect. 34.1).

The most frequent skin lesion of childhood paucibacillary leprosy is the hypopigmented macule with definite margins (Fig. 34.3). Other skin lesions are those of hyperergic leprosy: papules and plaques. Plaques may appear annular because of central healing. In most cases (90%), the lesion is single and located on the upper and lower limbs, followed by the trunk and face. Lesions are usually few in number, distributed monolaterally or bilateral (in the BT type) but asymmetrically.

When multibacillary leprosy develops (mid-borderline leprosy or BB, borderline lepromatous leprosy or BL, lepromatous leprosy or LL), it initially appears as multiple, small, nearly symmetrically distributed hypopigmented to coppery macules with indistinct borders. They may appear erythematous or reddish-brown and later on may develop into nodules (Fig. 34.4). With the time, the lesions diffuse symmetrically involving the entire skin.

Anesthesia of the skin lesions, as well in the areas of the affected nerves, occurs in TT and BT leprosy. It is easier to be diagnosed confidently in older children (12–14 years of age) especially if the lesion/s are on the limbs and trunk (more difficult on the face). By contrast, eliciting sensory loss to fine touch in young children

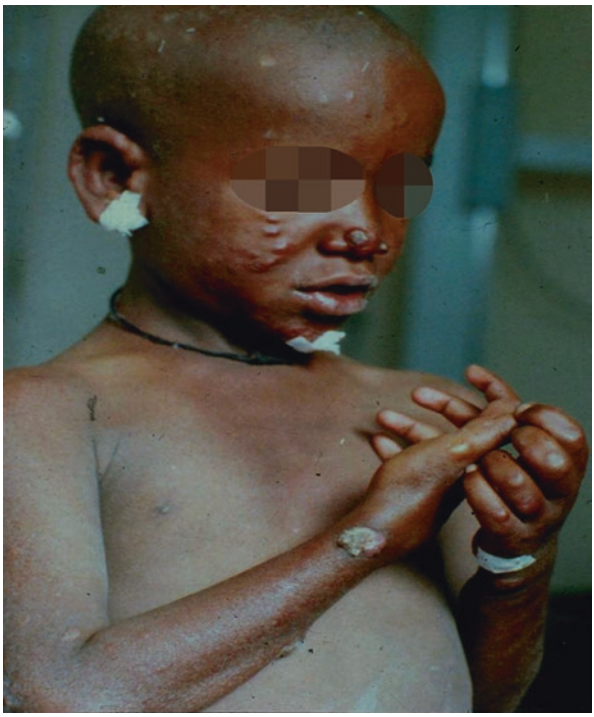

Fig. 34.4 BL leprosy (Courtesy of C. Travaglino)

is often inaccurate or even impossible. A loss of sensitivity can be evidenced in children of 3–4 years old or more, if they trust the examiner and understand what he wants. In these cases it is necessary to spend a few minutes with the little patient before the medical examination in order to gain his trust and friendship, for instance, by tickling and asking him where he was touched and then by repeating the game with his eyes closed. If you want to assess the tenderness of nerve trunks, it is better to slowly palpate and look at his eyes even before waiting for his reaction to the pain. The most affected peripheral nerve is the ulnar nerve, followed by the external sciatic-popliteal and large auricular.

In MB spectrum sensory loss is symmetrical and diffuse; the absence of pain precedes loss of touch sensitivity.

34.3.2 Reactions

Leprosy reactions are relatively rare in children under 15 years of age with varying frequencies in different studies [6]. In all of them, the Type 1 reaction is most commonly reported given that the most frequent clinical form is BT (Fig. 34.5). Older children, and those with borderline forms, are at higher risk for reactions (Fig. 34.6) [7]. Severe reactions are accompanied by fever, malaise, anorexia, swelling of the face and extremities, and neuritis. Rarely, the only manifestation of a reaction is an isolated neuritis.

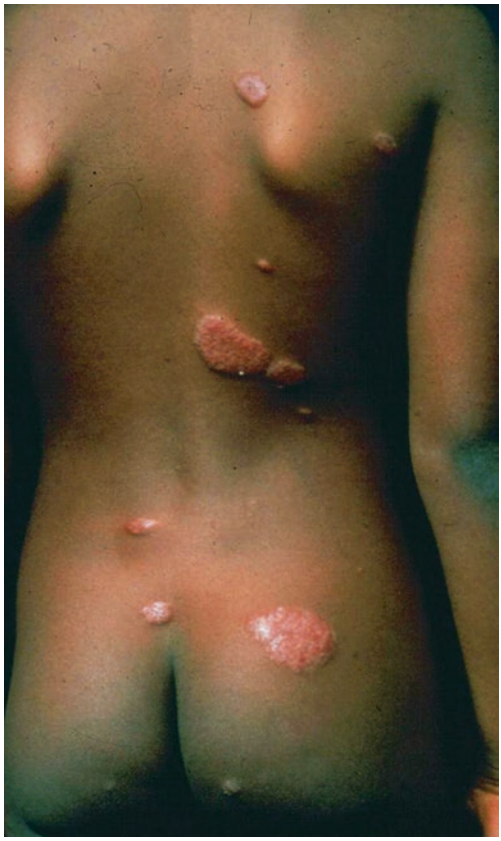

Fig. 34.5 Type 1 leprosy reaction in BT patient (before treatment). The same patient, under treatment, is presented in Fig. 26.3

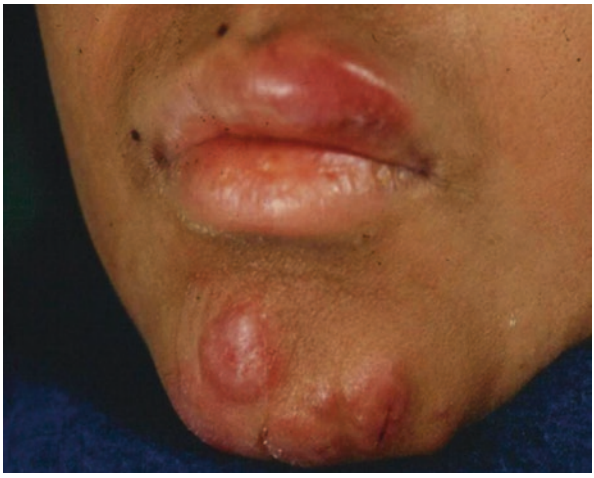

Fig. 34.6 Type 2 leprosy reaction (erythema nodosum leprosum). (From Massone C, Nunzi E (2009) Note di Leprologia. AIFO-Italia, Bologna)

34.4 Diagnosis

For a thorough explanation of the clinical diagnosis of leprosy, see Chap. 26.

Furthermore, when diagnosing leprosy in children, we should take into account some peculiarities.

In a large proportion of early cases of childhood leprosy, search for acid-fast bacilli (AFB) is negative because most of them are indeterminate, TT, or BT. However, in the presence of multiple erythematous macules with indefinite borders due to multibacillary leprosy, skin smears are positive with rates increasing with age [8].

Histopathology examination, other than being an essential cardinal step for leprosy diagnosis, particularly in non-endemic areas, is also a useful tool for accurate proper classification of leprosy and detection of any shift in the patient's position in the spectrum [9]. Due to the incompletely developed immune system of children, non-specific histological features may be encountered, particularly in indeterminate leprosy or in early phase of tuberculoid leprosy.

None of the serological markers identified in leprosy can be used as confirmatory tests for diagnosing leprosy in children. However, titration of anti-PGL-1 has been suggested to identify, among school children and household contacts, those at high risk of developing multibacillary leprosy [10].

34.4.1 Differential Diagnosis

The clinical suspicion of leprosy is facilitated in children with a familial case, more reasonably if multibacillary.

Diagnosis of leprosy in children should be based on the cardinal signs of leprosy (clinic, bacteriology, histopathology) (see Chap. 26).

Other skin diseases resulting in similar hypopigmented lesions such as pityriasis alba (Fig. 34.7), early vitiligo, birthmarks, and pityriasis versicolor should be considered in differential diagnosis of leprosy.

With regard to nerve involvement, inherited peripheral nerve disorders, e.g., hereditary sensory and sensory-motor neuropathies of various types, neurofibromatosis, neuropathies associated with developmental defects, and acquired neurological conditions, including traumatic neuropathies, should also be taken into consideration in differential diagnosis.

34.5 Treatment

The introduction of multidrug therapy (MDT) has been largely successful. Standard blister packs for children aged 10–14 years are available for both paucibacillary leprosy (dapsone 50 mg given daily; rifampicin 450 mg given once a month under supervision) and multibacillary leprosy (dapsone 50 mg given daily; rifampicin 450 mg given once a month under supervision; clofazimine 50 mg given every other

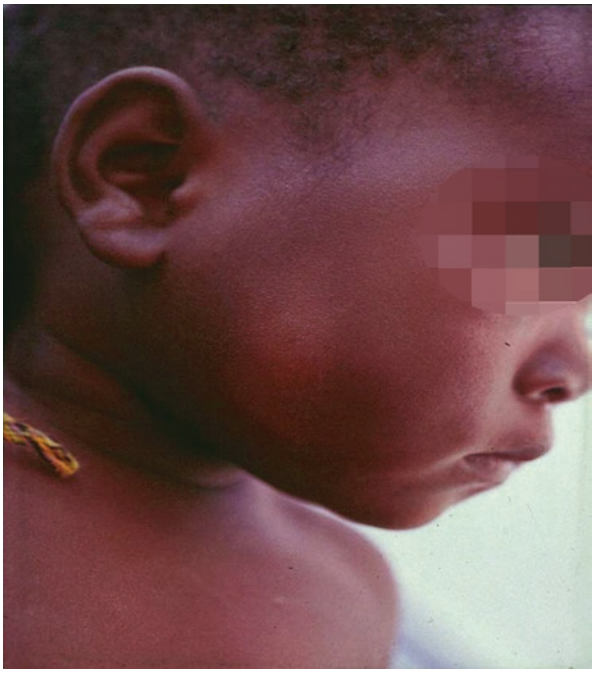

Fig. 34.7 Pityriasis alba. Coppery-colored macule with ill-defined margin

day and 150 mg given once a month under supervision). The paucibacillary regimen is administered for 6 months and the multibacillary for 12 months.

For children less than 10 years, the dose must be adjusted to body weight: (A) rifampicin, 10 mg/kg body weight monthly; (B) clofazimine, 1 mg/kg body weight daily and 6 mg/kg body weight monthly; and (C) dapsone, 2 mg/kg body weight daily.

In case of hypersensitivity to dapsone, clofazimine and rifampicin can be used in combination as an alternative to conventional MDT.

Although development of resistance to first-line drugs is a main threat to the efficacy of MDT program, the alternative drugs recommended in adults (ofloxacin, moxifloxacin, minocycline) are contraindicated for prolonged use in children under 10 years of age. Thus, no alternative regimens are specifically designed for children.

Because lesions in children may undergo self-healing, in case of doubtful cases, it has been suggested to wait and keep the child under observation (untreated) for a period to see whether the skin lesion is improving or sensory loss is appreciated. However, in endemic areas, whenever prolonged clinical observation is not practicable or in the presence of family members affected with leprosy, even in doubtful cases, treatment is wisely recommended.

In the presence of a single lesion of paucibacillary leprosy, a unique administration of three drugs in combination has been used in children: rifampicin (300 mg), ofloxacin (200 mg), and minocycline (50 mg) (ROM therapy).

Relapses are mainly due to inadequate treatment. Several factors, such as child's refusal to swallowing tablets, side effects, drug hypersensitivity, lack of information, and education among the parents, may contribute to a lower compliance to

treatment. For these reasons, activities of information and education among patients and their parents may be implemented and are reported to improve treatment compliance.

Leprosy reactions are the main cause of neural damage and deformities. Thus, they should be identified and urgently as well as adequately treated to prevent disabilities.

Children with reactions (both type 1 and 2) require the prompt use of steroids (prednisolone 1 mg/kg/day) for prevention of nerve damage and deformity. Clofazimine can also be used for management of both type 1 and 2 reactions, generally recommended at 1.5–2 mg/kg three times daily for 1 month and then reduced by one dose per day each month. The maximum dose of 300 mg daily can be administered. Other drugs which can be used for reactions are hydroxychloroquine, methotrexate, azathioprine, cyclosporine, and nonsteroidal anti-inflammatory drugs like paracetamol, etc. Thalidomide is not recommended for children below 12 years old, due to the lack of safety information, but it might be used—if legally available—in adolescent boys.

34.6 Disability

Disabilities and deformities due to permanent damage to peripheral nerves are the most common cause of social stigma in leprosy. They affect psychologically and functionally both the children and their family members. A significant percentage of children affected with leprosy have their initial presentation with deformities suggesting delay in diagnosis [11]. Hence, an important factor to prevent disability in leprosy patient, other than adequate treatment of neural impairment, is early detection. Rehabilitative measures such as physiotherapy and corrective surgery should also be offered to selected patients.

34.7 Preventive Measures

The practice of removing the newborn from the multibacillary mother has fallen into disuse after the introduction of the MDT.

Nowadays preventive measures for leprosy include early diagnosis and management of active cases as well as their contacts. Household contacts should be evaluated annually for evidence of disease for at least 5 years and should be educated to seek immediate attention if suspicious cutaneous or neurologic changes develop. Because leprosy in children is essentially a disease of school age children, community education about leprosy along with school surveys should also be implemented for early detection and to prevent disabilities.

34.8 Vaccine and Chemoprophylaxis in High-Risk Contacts

See Chap. 28.

34.9 Effect of Childhood Leprosy on Community

Despite global efforts, discrimination and stigma associated with the disease are still present. Children affected with leprosy risk to be deprived of education or subjected to bullying and rejection due to stigma associated with the disease.

The child's psyche must be safeguarded at all costs. There is the common opinion that the sick child should not be informed of the diagnosis. He may be informed at a later age, if affected by a multibacillary form requiring a longer follow-up.

34.10 Conclusions

The high prevalence recorded for childhood leprosy is a strong indicator of recent transmission of the disease and a sign of failure of control programs targeted to the elimination of leprosy. The skill for diagnosing and managing leprosy is diminishing leading to missed and misdiagnosis of leprosy in infants and young children and occurrence of deformities and disabilities. For all the above, effective planning to bring down the incidence of leprosy and its complications in children should become a top priority in programs aiming to achieve the goal of elimination of leprosy.

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