Current Practice

Childhood leprosy: Facts, myths and mysteries

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Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* which targets skin and peripheral nerves[1]. In disseminated disease other organs can also be affected[2]. The earliest records on "leprosy like" disease come from Egypt, dating as far back as 1400 BC. However, the word 'leper' means 'scaly' in Greek. Ancient Indian writings describe the disease as "Kushth". Initially, leprosy patients were strictly isolated and segregated into leprosaria. In Sri Lanka, people were confined to leprosy hospitals. Society was hostile to people with leprosy and they were not allowed to move freely. Several statutory acts and laws were enacted against them. This further marginalized the leprosy sufferers and gave rise to the myth that the disease is highly infectious and incurable.

The WHO classifies leprosy as a Neglected Tropical Disease (NTD)[3]. This is because the attention of the WHO has been focused on killer diseases like human immunodeficiency virus (HIV), tuberculosis (TB), malaria and emerging infections like Ebola. NTD programme is an initiative aimed at tackling seventeen neglected diseases affecting over one billion people worldwide. NTDs often coexist and are associated with poverty. A good example of this is the coexistence of leprosy and TB. People afflicted with leprosy suffer silently and experience stigmatization and discrimination. Leprosy has become an important disease worldwide in view of associated peripheral nerve damage, its ability to cause permanent disabilities and stigmatization.

Mycobacterium Leprae: The organism was first described by G.A. Hansen of Norway in 1873, the first bacillus to be identified as a cause of human disease[4]. However, it remains a mystery as to why the organism cannot be grown in artificial media. It is an acid and alcohol fast intracellular organism[1]. Compared to *Mycobacterium tuberculosis* it has a slow division rate[1].

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Mycobacterium leprae is considered to be primarily a human pathogen. However, there is a long history of studies, evidence and arguments indicating possible non-human sources of the agent[5]. In recent times the organism has drawn the attention of many researchers. Work is been done to find out how it is able to transform mature Schwann cells to immature stem cells. This mechanism assures the organism's survival. It is believed to provide novel therapies for many degenerative disorders of the nervous system.

Epidemiology: The question of possible extra human sources of *Mycobacterium leprae* is important for epidemiology and control. The mystery of clinical disease in the individual with no apparent history of exposure to other known cases and clinical clustering of cases in certain areas of affected countries are two strong pieces of evidence that support the theory of the possible existence of extra human sources. However, none of this is conclusive evidence. The long incubation period, the inability to recall contacts and the fact that stigma leads to hiding of cases are possible ways as to how this could happen. Theoretically, recognition of such sources would help in control and possible elimination and ultimate eradication of the disease.

Transmission: Family clustering of cases indicates transmission by way of droplets inhalation[6]. Droplets are generated by sneezing, cough and nasal discharges of patients with lepromatous leprosy. Inoculation is another rare form of transmission[7]. This can happen by needle stick injuries or by inoculation of bodily secretions into minor abrasions. The latter mechanism is well described in South American literature. Congenital transmission has not been reported thus far, possibly because of the long incubation period.

Pathogenesis: *Mycobacterium leprae* causes tissue damage by several mechanisms including direct invasion, immunological attack of infected tissues both by humoral and cell mediated immunity and by causing peripheral nerve damage[1]. The abundance of nerves in the skin acts as a niche for the organism.

The main defense against *Mycobacterium leprae*, like other obligatory intracellular parasites, is cell mediated immunity[8]. If this response is robust, clinical features do not develop. A slightly weaker response allows the organism to gain a foothold and leads to the development of one or two skin lesions. It is this immunological response that leads to the development of clinical manifestations. However, if the organism overcomes the immunological attack, dissemination results leading to the development of multiple skin lesions and involvement of other organs[8].

Classification: A disease is classified for many reasons. With regard to leprosy, classification is necessary for the treatment of disease subtypes, management of reactions and predicting outcomes. The first international classification was attempted in 1931 in Manila[9]. After several unsatisfactory attempts, a comprehensive classification was proposed by Ridley and Joplin in 1962[10]. This classification was based on immunology, histopathology and clinical features. With subtle modifications, this has withstood the test of time. However, as the majority of leprosy sufferers live in countries with poorly developed healthcare infrastructure, a simplified classification became a necessity. This compelled the WHO to divide the disease into two simple types namely, pauci-bacillary (PB) and multi-bacillary (MB) leprosy. This was done by counting the number of skin lesions. If the number is five or less then it is considered as PB leprosy and more than five as MB leprosy[11]. An important aspect of the disease, the nerve damage, was not considered in this classification. This was subsequently corrected. A patient with a positive slit skin smear for AFB is regarded as a MB case irrespective of the number of skin lesions. Similarly, presence of two or more affected peripheral nerves is considered as a case of MB leprosy. For countries like ours, with a well-established health care network, the WHO classification is used for treatment purposes only.

Clinical features: Majority of children develop a single lesion. This could be either indeterminate tuberculoid or borderline tuberculoid (BT) leprosy. Indeterminate leprosy is the commonest type of leprosy seen in children who present early[12]. The lesion is often a hypo-pigmented ill-defined patch on the face[12]. This is often mistaken by parents and primary physicians as pityriasis alba or pityriasis versicolor. Indeterminate leprosy often heals without leaving a mark (Figures 1a and 1b).

Figure 1a: ***Early indeterminate patch***

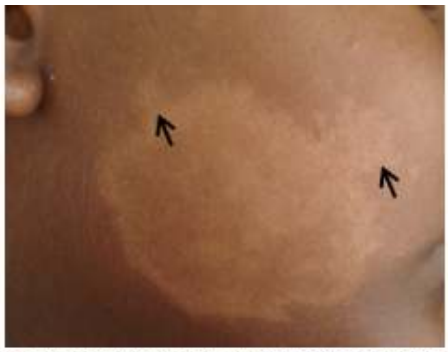

Figure 1b: ***Indeterminate leprosy downgrading to BT leprosy. Note pseudopodia (arrows).***

A patch of tuberculoid leprosy (Figure 2) is often well defined, round or oval in shape, with a raised edge. The colour of the lesion is determined by the complexion of the child, duration of the lesion or presence of a reaction. However, the hallmark feature is the impairment of sensation within the lesion. Demonstration of sensory impairment is subjective, and difficult to perform in young children. Finding a thickened nerve in the vicinity of the lesion or a thickened nerve trunk nearby or elsewhere is more reliable and an easy to elicit sign of the disease.

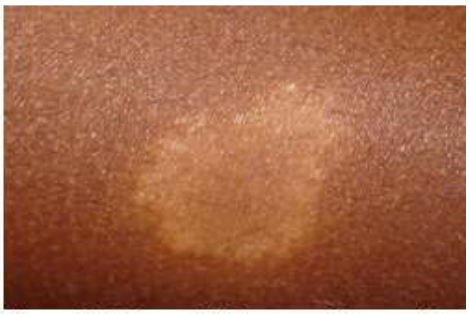

Figure 2: ***Tuberculoid leprosy. Note smaller size and well demarcated border.***

Lesions of BT leprosy are often larger, show pseudopodia or satellite lesions and have a tapering

outer edge. Most of the lesions show an annular configuration (Figure 3).

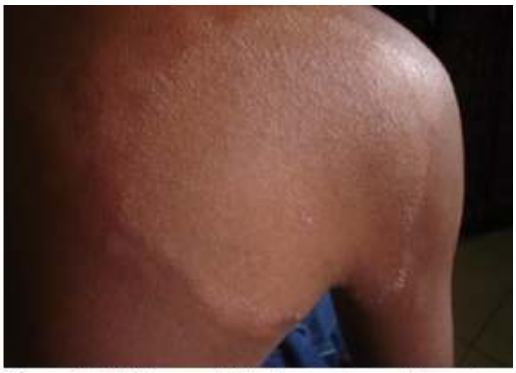

Figure 3: *BT leprosy. Note large size, erythematous border & satellite lesions.*

Not uncommonly, a large dry patch of erythema is seen. This is the maculo-anaesthetic type (Figure 4).

Figure 4: *BT leprosy. Note distribution of lesion along median nerve & flat thenar eminence.*

In dark children the lesions are coppery coloured (Figure 5) whereas in fair children the lesions are pink (Figure 6).

Figure 5: *BT leprosy: Note coppery colour*

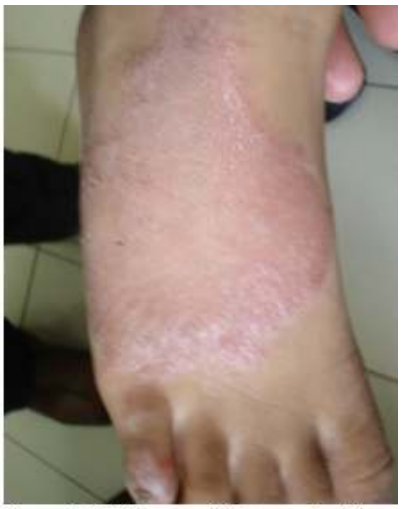

Figure 6: *BT leprosy, Note psoriasiform pink colour in a fair child.*

Both these lesions are associated with sensory impairment due to longer duration and associated type 1 reaction. If the reaction is severe, the lesions are elevated as erythematous plaques (Figure 7). Even the satellite lesions can be inflamed. Sensory changes similar to tuberculoid leprosy may occur.

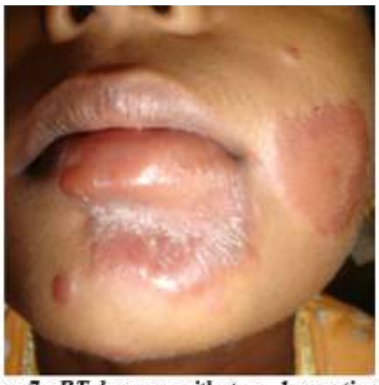

Figure 7: *BT leprosy with type 1 reaction: Note features of inflammation & scaling indicative of type 1 reaction. Two satellite lesions are also visible*

An unusual form of PB leprosy in children is the Souza-Campos nodule of leprosy (nodular leprosy of childhood)[13]. This results from close contact with an infected parent or grandparent. Morphological patterns include papulonodules, wheel like lesions and lichenoid lesions. They occur on the face, chest and limbs. (Figure 8)

Figure 8: *Note non-nodular lepromatous leprosy on the grandmother's face.*

MB forms of leprosy are rare in children. An occasional child with borderline tuberculoid leprosy may down grade towards the lepromatous spectrum. Such a case may demonstrate the development of skin coloured papules and nodules which are full of organisms (Figure 9).

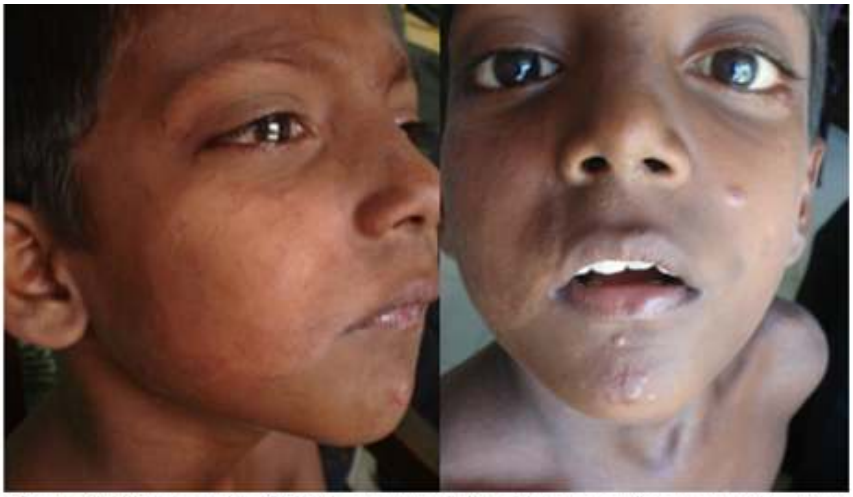

Figure 9: *Note patch of BT leprosy and development of new papules away from main lesion.*

Peripheral nerve damage: Peripheral nerves are targeted by *Mycobacterium leprae* due to their lower temperature and abundance of Schwann cells[14]. When a nerve trunk is involved it often leads to a mixed sensory motor neuropathy. In addition to the functional impairment, such nerves are often irregularly thickened. Commonly affected nerves are the ulnar nerve at the elbow (Figure 10), common peroneal around the neck of fibula, and the superficial radial cutaneous nerve at the wrist. In comparison to adults, thickening of greater auricular nerve is uncommon in children possibly because of lesser degree of trauma. The affected nerves are all superficial and subjected to repeated trauma.

Figure 10: *Ulnar claw hand. Note hypo-pigmented patch over wrist*

Dactylitis: Though mentioned as a manifestation of leprosy since ancient times, no details can be found in any textbook of leprosy. Dactylitis denotes inflammation of a digit[15]. In leprous dactylitis several mechanisms are involved. It is seen in tuberculoid to lepromatous spectrum of the disease. (Figure 11)

Figure 11: *Note dactylitis of the right thumb due to lesional involvement*

Reactions: Lepra reactions are acute inflammatory episodes often precipitated by chemotherapy. However a small number of patients have features of reactions at the time of presentation. Generally two types of reactions are encountered, type 1 reaction and type 2 reaction[16]. The latter is also known as Erythema Nodosum Leprosum[16] (Figure 12), a form of acute systemic vasculitis resulting from wide spread deposition of immune complexes. Patients are acutely ill with fever, arthritis, red eyes and painful skin nodules. They require high dose oral steroids for a longer period of time. In type 1 reactions the existing lesions show acute inflammation (Figure 13). If a nerve trunk is involved paralysis occurs. This again is treated with oral steroids. Fortunately both types of reactions are rare in children.

Figure 12: *Type 2 reaction. Note the inflammation &ear lobe involvement*

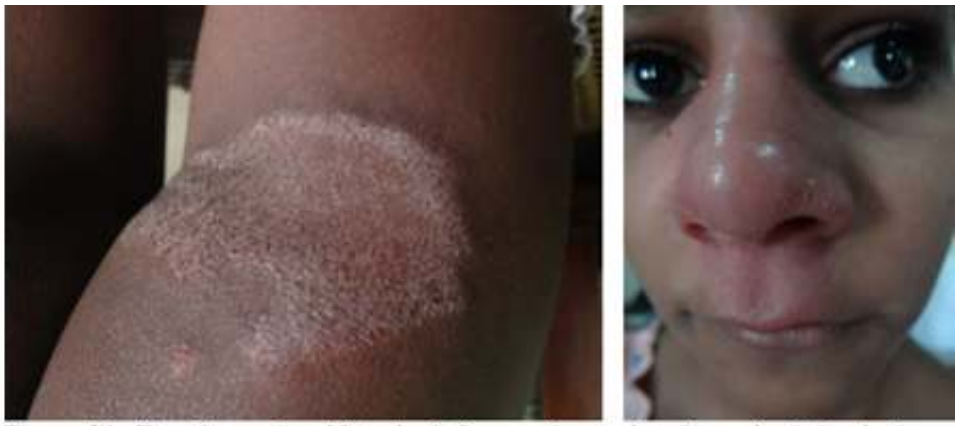

Figure 13: *Type 1 reaction. Note the inflammation and scaling of existing lesions*

Diagnosis: Diagnosis is clinical. In the past, emphasis was focused on finding cardinal signs of leprosy such as lesional anaesthesia, thickening of nerves and suggestive deformities which however are not present in all cases. Further, there are many protean manifestations of leprosy. Therefore, certain aspects in the history become important. These include duration of lesion, symptoms referable to peripheral nerve damage e.g. hyperaesthesia, living in an endemic area and presence of a known contact in the family. Skin lesions in such a scenario should be considered leprous in origin until proved otherwise.

Once a diagnosis of leprosy is entertained, the next step is to ascertain whether it is PB or MB, to assess the degree of nerve damage and to assess the suitability for chemotherapy. The number of skin lesions along with the number of thickened nerves determines whether the patient has PB or MB leprosy for treatment purposes. Less than six skin lesions are considered as PB whereas six or more lesions are considered as MB[11]. In recognition of importance of nerve damage, presence of two or more thickened nerves, irrespective of the number of skin lesions is considered as MB. At the time of diagnosis, if the organism can be demonstrated by a slit skin smear,

diagnosis of MB is entertained irrespective of the number of skin lesions. In doubtful cases and in cases where there is poor parental acceptance of the diagnosis skin biopsy can be performed.

Treatment: Multi drug therapy introduced by the World Health Organisation (WHO) in 1982 revolutionized the management of leprosy patients[17]. As a result, leprosy became a curable disease. Leprosy registers were abolished and leprosaria were closed. The duration of the treatment was reduced to six months for PB cases and twelve months for MB cases. Though not the ideal for all cases of leprosy MDT paves the way for integration of leprous services into the normal health services of the respective countries.

Rifampicin is the most potent anti-leprosy drug in MDT. It is given on a monthly basis, based on the slow division rate of M. leprae. The added benefit is the low cost. Dapsone for PB leprosy is given on a daily basis in order to prevent rifampicin resistance. Though a weak drug in the setting of good cell mediated immunity it is often adequate. Dapsone is combined with Clofazimine in MB leprosy to prevent rifampicin resistance. Though a cheap drug, clofazamine induced pigmentation is often troublesome (Figure 14). In view of the poor cell mediated immune response in MB cases, the three drugs are given over a period of one year.

Figure 14: ***Clofazimine induced pigmentation***

Prevention: It is believed that one day MDT will eliminate and help to eradicate the disease. This is by breaking the transmission in society. For this to happen, firstly leprosy patients in society should be detected. Secondly the living standard of the people needs to be improved. It is no secret that in Europe leprosy was eliminated before the advent of MDT. As the incubation period of leprosy is long, ultimate eradication of the disease will take several decades. A number of programmes have been introduced to detect new cases worldwide. WHO at present recommends contact tracing for all new cases. In a study done at the Lady Ridgeway Hospital, Colombo in 2007, 33% of index cases had a positive family contact[18]. Chemoprophylaxis is been contemplated in some countries. Emergence of rifampicin resistance is a concern not only to *Mycobacterium leprae* but also to *Mycobacterium tuberculosis*.

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