Case Report

Lepromatous leprosy: a case simulating verrucous carcinoma

A 59-year-old immigrant from China presented with a rapidly-enlarging exophytic growth on his left heel for 4 months. He was also found to have peripheral neuropathy, Charcot's joint, diffuse erythematous papules and acquired ichthyosis. Classical histologic features of leprosy were noted, together with atypical verrucoid proliferation. The diagnosis of lepromatous leprosy was made after clinical-pathological correlation and confirmation by polymerase chain reaction.

Keywords: Digitate papules, lepromatous leprosy, leprosy, multibacillary leprosy, verrucous carcinoma

Introduction

The cutaneous manifestations of leprosy are vast. We report a case of lepromatous leprosy with classical clinical and histological features, but also co-existing with verrucoid growth, which is seldom encountered.

Case report

A 59-year-old man was referred to the Orthopaedic Tumour Clinic for a fungating growth on his left heel for four months. It was asymptomatic but growing rapidly. There was no history of trauma or contact with fish. He had a history of closed fracture on the same ankle that was treated conservatively in childhood, and carcinoma of rectum, now in remission, following surgery and chemo-radiation therapy 12 years ago.
Clinically, the mass was 4×5 cm, with verrucous surface and irregular border (Figure 1). There was no satellite lesion or regional lymphadenopathy. The provisional diagnosis by the orthopaedic team was squamous cell carcinoma. MRI excluded deep fascial invasion. Wide local excision followed by staged skin graft was performed.

The patient was referred to the dermatology team when the histology suggested otherwise. On further enquiry, he complained of insidious onset of dry skin, sensation loss of the extremities causing frequent scald injuries after handling hot water and progressive painless deformity of left ankle from which he reported difficulty finding appropriate shoes. Social history revealed that he was born and immigrated from a village in Guangdong 40 years ago, but he did not recall any history of similar condition among his close family members. On examination, he had slight saddle-nose deformity, Charcot's joint on the left ankle (Figure 2), acquired ichthyosis on the limbs, multiple non-descript ill-defined erythematous papules on the back (Figures 3 & 4) and enlarged ulnar nerves on palpation. Peripheral neuropathy was confirmed on nerve conduction study.

Histologically, there was verrucoid epidermal hyperplasia without invasion, atypia or increased mitotic activities (Figure 5). There were patchy mixed inflammatory lymphohistiocytic infiltrates and some plasma cells. Globi formation was noted with foamy histiocytes (Figures 6 & 7). Ziehl-Neelsen stain and Wade-Fite stains showed abundant acid-fast bacilli (Figure 8), while PAS, Grocott, Warthin-Starry and Gram stains were all negative. Polymerase chain reaction (PCR) analysis of paraffin tissue was positive for Mycobacterium leprae DNA but not M. tuberculosis. A second skin
biopsy on a papule on the back also showed identical histology (Figure 6).

The diagnosis of lepromatous leprosy was made and the patient was started on rifampicin, dapsone and minocycline in hospital. There was no observable reaction on treatment and the graft was taking well. Screening for HIV and diabetes was negative. On discharge, he was referred to the Leprosy Skin Clinic for continuation of multi-drug therapy and contact tracing.
Leprosy is a chronic granulomatous infection of the skin and peripheral nerves. It is transmitted by *Mycobacteria leprae* (*M. leprae*), an obligate intracellular Gram-positive bacillus with acid-fast property and affinity for macrophages and Schwann cells. It is a global disease affecting all races, highly endemic in Africa and South America, and prevalent in developing countries in South-East Asia and parts of China. With the introduction of WHO multi-drug therapy (MDT), the disease is now controlled with decreasing prevalence. In fact, Hong Kong is declared by WHO to be eliminated from leprosy\(^1\) with its incidence of 0.088/10000 population. In the 1950s and 60s, the majority of leprosy patients in Hong Kong (90%) were born in China,\(^2\) while in recent years, imported leprosy from South East Asian countries accounted for the majority.

The infection caused by *M. leprae* carries a long incubation period, from months to 20 years, averaging three to five years. The majority of exposed individuals do not develop disease. Host genetic and environmental factors influence individual susceptibility to infection and disease progression. In lepromatous leprosy, a predominant-Th2 response suppresses macrophage activity and cell mediated immunity while a heightened Th1 response is found in tuberculoid leprosy. Several leprosy susceptibility loci on chromosome 6 and 10 are found; and the presence of HLA allele DQ1 gears towards lepromatous expression. In a genome-wide association study in Han Chinese, novel association with NOD2, TNFSF15, RIPK2 are found, indicating heterogeneity of genetic susceptibility between ethnic groups.\(^3\) Transmission results from early childhood close contact with a source with high infectivity (lepromatous leprosy), and spreading by droplets of nasal or oral secretions. The household risk of acquiring disease in an endemic area is 10%. There are a few reports of infections acquired through open wound and fomites, and, recently, armadillos as a zoonotic transmission.\(^4\) Moreover, another species, *Mycobacterium lepromatosis*, has been found to cause diffuse form of lepromatous leprosy in Mexico and the Caribbean.\(^5\)

Our patient had classical clinical and histologic features of lepromatous leprosy, which represented the more severe spectrum of disease with multi-bacillary involvement and poor host immunity. What was atypical would be the late age of onset, very long incubation and verrucoid presentation. Most literature reported special forms of leprosy as histoid, dermatofibroma-like papules, digitate or shagreen-like patches. Verrucoid presentations are rare in leprosy and were found in few anecdotal reports of lepromatous leprosy with coexistent chromoblastomycosis,\(^6\) or in HIV-positive individuals.\(^7\) A more logical association would be squamous cell carcinoma arising from chronic unhealed leg ulcers, and even with that, verrucous carcinoma arising from such lesion was rarely reported.\(^8\) The underlying reason that our immunocompetent patient developed verrucoid growth was obscure. Without other supporting cutaneous suggestions of leprosy, the differential diagnosis would have been malignant tumours (squamous cell carcinoma, verrucous carcinoma,
cutaneous metastasis, amelanotic melanoma), or infection (giant condyloma, deep fungal infection, atypical mycobacterial infection or tuberculosis verrucosa cutis). A biopsy for histology and culture would be helpful to establish the diagnosis.

The diagnosis of leprosy is suggested by (1) the presence of skin lesions with definite sensory loss (except borderline lepromatous or lepromatous leprosy), (2) thickened peripheral nerves, or (3) the presence of acid-fast bacilli on skin smears or tissue biopsy.\(^9\) The sensitivity and positive predictive values based on the above diagnostic features are more than 95% in endemic countries.\(^10\) M. leprae cannot be cultured in artificial media. Newer techniques like serology for M. leprae antibody, phenolic glycolipid-1 (PGL-1), or PCR for M. leprae DNA detection are useful in multibacillary disease with high bacterial load. The sensitivity for serology ranges from 40% (paucibacillary) to 90% (multibacillary) and it can be used to monitor the effectiveness of treatment as its level declines with MDT. The sensitivity of PCR using M. leprae specific repetitive sequence in multibacillary disease is 80% and can be performed on skin or nasal biopsy specimen and extracts of slit skin smear.\(^11\) These tests are used more as identification tools rather than detection tools for leprosy, as the sensitivity for paucibacillary disease is low overall.

Standard multi-drug therapy with monthly supervised rifampicin 600 mg and clofazimine 300 mg, and daily self-administered dapsone 100 mg and clofazimine 100 mg was prescribed to our patient. He tolerated treatment well with counseling, psychological support and regular follow-up. Podiatry assessment and footwear adjustment was made. The relapse rate after two years of WHO-MDT is quoted to be 0.77% globally\(^1\) to 3% locally.\(^12\) In our locality, a more conservative approach is adopted with prolonged MDT until all skin lesions are inactive, followed by dapsone monotherapy for 10 years after the slit skin smear is negative.

In conclusion, although leprosy is a fading disease, clinicians should remain vigilant in the screening and diagnosis of leprosy in Hong Kong. Early specialist referral is recommended in view of its protean manifestations and infectious implications.

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**References**

1. World health organization leprosy fact sheet.