CASE REPORT

Histoid leprosy with Type 1 reaction

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Summary A sixty-one years old man presented with multiple nodules and plaques of different sizes, distributed on the face, trunk, buttocks and lower extremities. He had a history of prior treatment with dapsone monotherapy for Lepromatous leprosy (LL) thirty years ago. The patient was diagnosed with Histoid Borderline-Lepromatous Leprosy after clinical examination and the results of slit skin smears and histopathology that revealed histiocytic granuloma with spindle-shaped, non vacuolated histiocytes. Abundant acid-fast bacilli (AFB) were visible on Fite’s stain. Twelve weeks later, he developed a large erythematous plaque on axillary region and histopathology showed epitheliod and giant cells on background of the histiocytic granuloma. The diagnosis of type 1 leprosy reaction was made and the patient was treated with prednisone at 1 MG/kg body weight/day. The lesions regressed within four weeks and prednisone was slowly tapered (10 mg every 30 days) over four months. The anti-leprosy treatment was stopped after 24 months. Histoid leprosy rarely involves leprosy reactions. More frequently type 2 reactions were reported, but type 1 reactions are also possible as reported here.

Introduction

Histoid leprosy (HL) is a rare variant of multibacillary leprosy described by Wade,1 clinically characterised by firm, reddish, or skin-coloured, shiny, dome-shaped or oval papules and nodules on normal appearing skin. The term histoid derives by the histological finding of the dermal infiltrate composed by a predominance of spindle shaped cells or polygonal cells that may resemble a fibrohistiocytic tumor (dermatofibroma).2

HL was originally described as a manifestation of drug resistance after irregular or inadequate treatment with dapsone monotherapy or multi-drug therapy, but histoid
nodules may appear also de novo representing the first manifestation of lepromatous leprosy (LL).³

Lepra reactions in HL are rare. In the English literature, there are only few reports of Type 2 reaction and a case report of de novo HL developing Type 1 reaction after 10 weeks of multibacillary multi-drug therapy.⁴

Figure 1. Initial clinical exam. Multiples, erythematous, plaques on chest and dome-shaped nodules on arms.

Figure 2. Histopathology of biopsy taken from nodule. A. Histiocytic granuloma formed by spindle-shaped histiocytes. B. Abundance of acid-fast bacilli (AFB).
Case Report

A 61 year old man presented in January 2014, with multiple nodules on his entire skin. He had been treated with dapsone monotherapy for LL from 1961 to 1992 in another Health Centre. On physical examination we observed multiple, firm, shiny, cutaneous and subcutaneous nodules and infiltrated plaques of different sizes, distributed on the face, trunk, buttocks and lower extremities (Figure 1).

Bilateral ulnar and left fibular nerves were thickened but not tender. He showed a shortening of hand and feet digits (bone reabsorption) and he showed a disability degree of 3·67. He also had neurotrophic ulcers of left plantar surface. His weight was 89 Kg and he was using captopril for arterial hypertension.

Figure 3. Large erythematous annular plaque over the axillary region at the Type 1 reversal reaction.
The serological tests for HIV, Hepatitis B and C were negative. The routine blood biochemical tests showed no alterations.

A 4 mm biopsy of a skin nodule on his trunk revealed an atrophic epidermis and a grenz zone below the epidermis with a nodular infiltrate located mostly in the mid dermis, but extending until the subcutis and composed mainly by a spindle-shaped histiocytes arranged in a storiform pattern. Vacuolated histiocytes and few lymphocytes were also present in the infiltrate. Abundant acid-fast bacilli (AFB) uniformly stained (solid) were observed at Fite’s stain and they were longer than normal bacilli (Figure 2).

Two slit skin smears from a small nodule on the trunk and from the right ear lobe revealed a bacillary index of 4·5.

Histoid borderline lepromatous (HBL) leprosy was diagnosed, and because the previous dapsone monotherapy, drug resistance was suspected, and the patient started an alternative multidrug treatment (MDT) regimen with ofloxacin 400 mg/day, minocycline 100 mg/day, and clofazimine 300 mg/month and 50 mg/day for 24 months.

**Figure 4.** Dermis shows nodules with epithelioid cells, giant cells and lymphocytes on a background of histiocytic granuloma suggestive of Type 1 leprosy reaction.
Twelve weeks later, in April 2014, the patient presented with large erythematous, edematous, annular, plaques symmetrically located on axillary regions and also swelling of the hands. He still had nodular lesions on his skin and peripheral nerves remained similar to the previous examination. The patient had no constitutional symptoms (Figure 3).

Slit skin smears of plaques and right ear lobe revealed bacillary index of 3.0.

A skin biopsy of the left axillary region lesion showed epidermal atrophy. In dermis an inflammatory infiltrate composed predominantly by clusters of epithelioid cells on a background of vacuolated histiocytes. We observed rare giant cells and some lymphocytes but did not identify neutrophil in cells infiltrate. The subcutaneous tissue revealed no alterations. AFB showed a fragmented morphology (Figure 4).
The diagnosis of leprosy reaction Type 1 was made and prednisone 40 mg/day was added. The lesions regressed within 4 weeks and prednisone was slowly tapered (10 mg every 30 days) over 4 months.

Twelve months later, in January 2015, the PCR of drug resistance for folP1, rpoB and gyrA genes associated with dapsone, rifampicin and ofloxacin resistance was available and the result was negative. Nevertheless, the anti-leprosy alternative treatment regimen was maintained.

The treatment regimen was continued for 24 months with excellent compliance and the patient was discharged in December 2015. Sustained clinical improvement was seen during the last year of treatment. Four months after discharge, the patient showed rare softened hyperpigmented nodules and diffuse clofazimine-associated hyperpigmentation (Figure 5).

In March 2016, a new biopsy from a residual nodule lesion of the right axillary region revealed an atrophic epidermis with an infiltrate composed by foamy histiocytic granuloma with giant vacuoles occupying the entire extent of the dermis. All bacilli were fragmented (Figure 6).

Discussion

HL was first described in 1963 by Wade on his collection of specimens of LL cases with a unique histopathology and characteristic bacterial morphology. The histological findings included epidermal atrophy and an acellular band (Unna band) located immediately below the epidermis. The granulomas resembled a tumor, composed by spindle-shaped histiocytes, in nodular arrangements in a whorled, storiform pattern that look like a dermatofibroma. AFB are very abundant and the bacilli had elongated morphology.5

HL was most likely to be found in old cases of LL which initially responded to treatment, but had later relapsed developing drug’s resistance.1 Since then there have been many reports and currently HL is a well-recognised variant of LL, which may occur before or during the treatment.3 In fact, in the last years the reports of HL de novo occurring also in patients naïve (without treatment) are increasing.6 In these cases, HL exhibits clinically multiple
symmetric firm dome-shaped or oval papules with a smooth bright surface and cutaneous, or subcutaneous nodules and plaques over apparently normal skin.

The slit skin smear from HL lesions shows abundant acid-fast bacilli singles or in clusters. The bacillary index may be 5+ to 6+ and these bacilli appear longer and show tapering ends when compared to common Lepra bacilli. Fite’s stain from fine-needle aspiration cytology is also positive in HL.

There is no evidence of global prevalence of HL. In India the incidence is estimated to be 2.79–3.60% among patients with leprosy. HL responds well to standard WHO multibacillary multidrug therapy. In cases of drug resistance alternative regimens should be used.

Leprosy reactions in HL have been only rarely reported in the English literature and regard mainly Type 2 reactions that have been described with different incidence.

Sehgal and Srivastava and Kalla et al. described a Type 2 reaction only in one out 23 and two out of 25 patients with HL, respectively. Contrarily Mendiratta et al. and Nair et Kumar reported a higher incidence with three out of 11 patients and four of 17 patients, respectively. Also Kaur et al. found a high incidence of Type 2 reactions in HL of 40% in a retrospective study of 40 cases from India. Patvekar et al. describe a man with histoid leprosy and Type 2 reaction with neural abscess.

We were able to find only a single case of Type 1 reaction in HL reported recently by Singh et al. They described a 42 year old woman with HL that after 10 weeks starting multibacillary multi-drug therapy developed pruritic, painful, erythematous and edematous papules, partly ulcerated plaques and nodules over the face, trunk and extremities, and a few ulcerated papules over the forearm. There was no nerve tenderness or sensory motor deficit consistent with Type 1 reaction. Biopsies taken from a plaque on the patient’s back and a nodule on her hand, revealed atrophic epidermis, preserved grenz zone, and papillary dermal edema with a plenty of lymphocytes scattered between the histiocytic granulomas. Quantities of elongated AFB were visible on Fite’s stain. She was started on prednisolone at 0.75 mg/kg body weight/day and resulted in symptomatic relief and healing of ulcerated papules within 4 weeks.

In our case at the time of diagnosis, the patient was classified as a histoid borderline lepromatous leprosy because of the clinical appearance, the histological features and the long-term dapsone monotherapy in the past.

Twelve weeks after starting therapy the patient developed a Type 1 leprosy reaction (reversal reaction) characterised by the rapid onset of large annular erythematous and edematous plaques on both axillary regions and his hands were swollen. The patient had no constitutional symptoms. The histopathology of biopsy material taken from a plaque on the right axillary region revealed atrophic epidermis, preserved grenz zone, dermal edema and clusters of mature epithelioid cells, rare giant cells and some lymphocytes between the histiocytic granulomas. The presence of dermal edema, epithelioid cells, giant cells and lymphocytes on a background of macrophage granuloma were suggestive of Type 1 leprosy reaction as previously described.

Revising the first description of Wade, we found that he described a peculiar phenomenon observed in some of his specimens of HL called ‘tuberculoid contamination’. In these cases he reported ‘tuberculoid foci’ seen in nodules with epithelioid cells in centre, almost free from bacilli, in contrast with the normal abundance of AFB in the surrounding tissue. He
called these features ‘tuberculoid contamination of histoid lesion’. The interesting issue is whether these cases represented Type 1 reactions not diagnosed at that time.

In conclusion, patients with HL develop more frequently Type 2 reactions, but also Type 1 reaction, even if they appear to be rare, they are possible as reported here and probably also originally by Wade.1

References