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A Case Report

Histoid Leprosy

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ABSTRACT

Histoid Leprosy is a variant of lepromatous leprosy with characteristic clinical and histopathological features. Usually it is occured in lepromatous patients who relaps after dapsone monotherapy, in those with dapsone resistance , sometimes even after multidrug treatment, or at times, de novo with characteristic clinical and histopathological features. A 36 years old male, originated from Papua, visited to the skin outpatient clinic with translucent shiny nodules on the left elbow and thumb for the last 18 months. The nodules were multiple, painless and firm. There were nasal congestion, tickening of ear lobes and loss of eye brows. Patient did not have any history of previous antileprotic treatment. Routine blood examination was normal. Bacteriological examination of slit skin smear revealed acid-fast bacilli of Bacterial Index 4+ and Morfologic Index 10%. Histopathology of skin suggested lepromatous leprosy of histoid type with characteristic interlacing bundles of spindle shaped cells. Anti-PGL1 antibody (ELISA) revealed high titer of IgM (>5.300 u/ml) and also IgG anti PGL-1 (>5.300 u/ml). Polymerase chain reaction examination test to detect M.leprae was positive and direct sequencing of M.leprae isolate shows no mutation, which means no resistancy to MDT treatment. Treatment with MDT-WHO regiment give clinical improvements and the histoid lesions disappered after 3 months treatment.The histoid form of leprosy in this case developed without any prior treatment of anti leprotic drugs (de novo). Some theoretical aspects of the patho-mechanism of histoid leprosy are discussed.

Key words: *Histoid Leprosy, lepromatous leprosy, de novo*

BACKGROUND

Histoid leprosy is an uncommon variant of lepromatous leprosy with characteristic clinical, histopathological and bacteriological findings.[1,2,9] Clinically it is characterized by multiple discrete shiny, smooth, painless, succulent, globular, protuberant, firm, skin colored to yellow brown nodules and papules on normal appearing skin.[5,12] Slit skin smear from histoid lesions shows abundant acid fast bacilli appear long when compared to ordinary lepra bacilli.[15] The mean baseline Bacteriological Index was 4–6 (range 3–6). The mean Morfological Index was 4% (range 0–10%).[9] Histopathologically the epidermis shows Grenz zone and the dermis shows sheets of round to spindle-shaped histiocytes.[6,16] Wade described this pattern in 1960 and 1963 in patients from the Phillipines. Almost 50 years after its description by Wade, it remains an interesting enigmatic form of leprosy mostly reported from India. Histoid leprosy occurs in lepromatous patients who relapse after dapsone monotherapy, in those with dapsone resistance, sometimes even after multidrug treatment, or at times, *de novo*.[7,8,9]

The pathogenesis of this rare and unusual variant of leprosy still remains unresolved. The interplay of genetic factors, immune response and treatment received in a given patient seems to influence the manifestations of histoid leprosy.[9]

Treatment of histoid leprosy includes not only antimycobacterial chemotherapy, but also patient education about the disease, treatment of reactions, monitoring for and care of nerve damage, care of any disability, social support, physical and occupational therapy, and rehabilitation.[8] Although, there is no clear recommendation regarding the treatment regimens for histoid leprosy, it has been treated on the lines of multibacillary leprosy[9] and its managed by initially giving ROM therapy with Rifampicin 600 mg, Ofloxacin 400 mg, Minocycline 200 mg once, which is followed by multidrug regiment therapy.[7,12]

CASE REPORT

A 36 years man, army soldier, originated from Papua, visited to the skin clinic with transluscent shiny nodules on the left elbow and thumb for the last 18 months. These nodules were multiple, firm, and painless. This complaint was accompanied with nasal congestion. After 12 months, he noticed tickening of the ear lobes and loss of his eye brows. There was no history of any other painful eruptions or constitutional symptoms. No complaint of epistaxis or eyes involvement, as well as enlargement on his genital or pain on joints. There were no history of decrease of sweating on his body, nor dryness of the skin. No complaint about ulcer on his feet and any deformity of hands and feet. Family history of the same disease was denied. He never got any medication or taking any antileprosy drugs. Two years ago, he was operated for a single of nodule on his face at army hospital but no further information about the diagnosis.

Physical examination of general state showed an alert male with the blood pressure was 120/90 mmHg, the pulse rates was 80 times per minute, the respiration rates was 20 times per minute and the body temperature was 36.5° C. From head and neck, there were no anemic, cyanotic, ictreus and respiratory distress. There were madarosis on his eye brows and tickening of his both ear lobes, but no lagophtalmus or nose deformity. There were tickening of N. Auricularis magnus dextra and sinistra. Heart and lungs were normal; liver and spleen were not palpable. On his upper extremities, there were no edema and warm on palpation. Bilateral medianus nerves were tickened but no glove anaesthetic pattern of the skin. There were nodules on his left elbow and thumb. On his lower extremities, there were tickening of N. Peroneus lateralis dextra and sinistra, without stocking pattern of anaesthesia of the skin. No deformities of extremities fingers.

Dermatological examination on the left elbow and thumb, the nodules were 2-4 cm in size, multiple, mobile with hard in consistency. Regular in contour with translucent shiny and sharply marginated. These lesions arising from apparently normal-looking skin. Crusting were positive (figure 1 a,b,c). On his ears, multiple, skin colored plaques varying in size from 0.2-0.5 cm on normal appearing skin (figure 2 a,b). There were madarosis on his bilateral eye brows (figure 2c).

Differential diagnosis of this patient were histoid leprosy, dermatofibroma, neurofibroma, histiocytoma and eritema nodosum leprosum.Laboratory examination revealed hemoglobin 12.0 g/dl, white blood cell count 11.500 K/uL. There was no abnormality from urinalysis

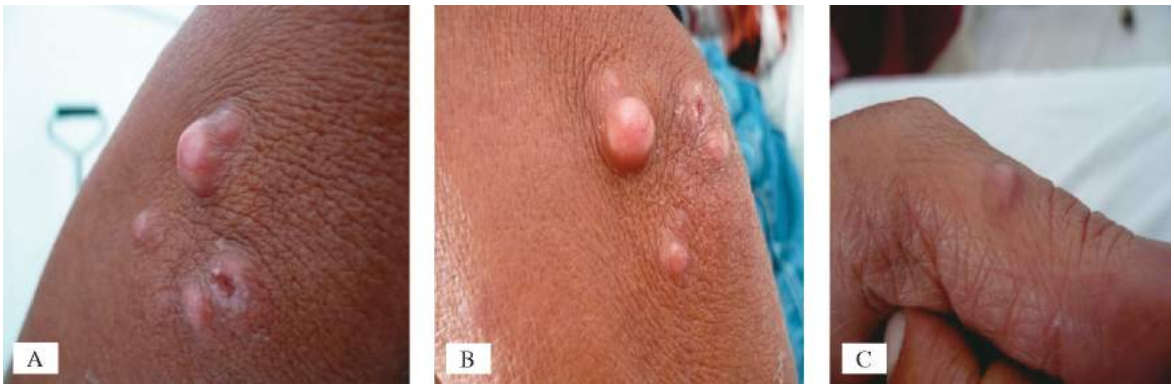

Figure 1. (A and B) The localization of lesions found in the patient. Translucent nodules located over an apparently normal skin on the left elbow. (C) Single nodule on the left thumb.

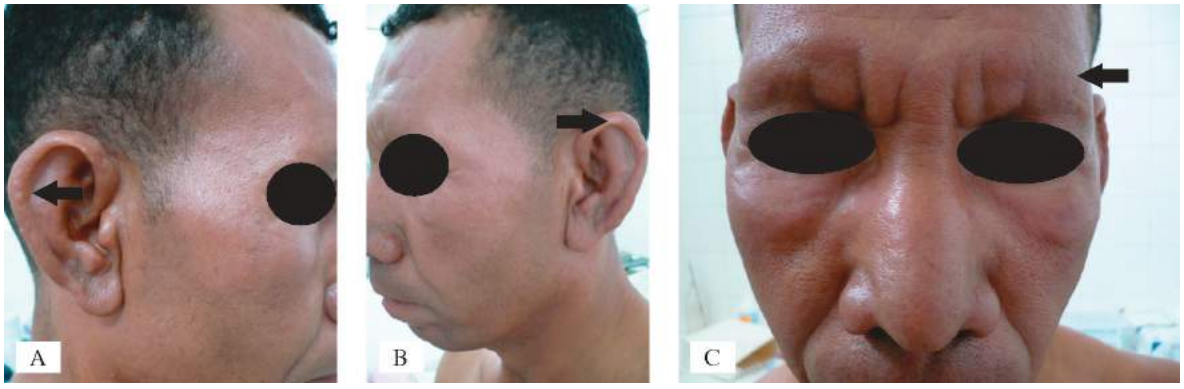

Figure 2. (A,B) Multiple, shiny skin nodules varying in size on the ear lobes. Note intervening normal looking skin. (C) Madarosis

and urine sedimentation. Bacterial examination from the ear lobe and shiny nodule smear for acid-fast bacilli showed a bacterial index (BI) of 4+ and a morfologic index (MI) of 10% (figure 3).

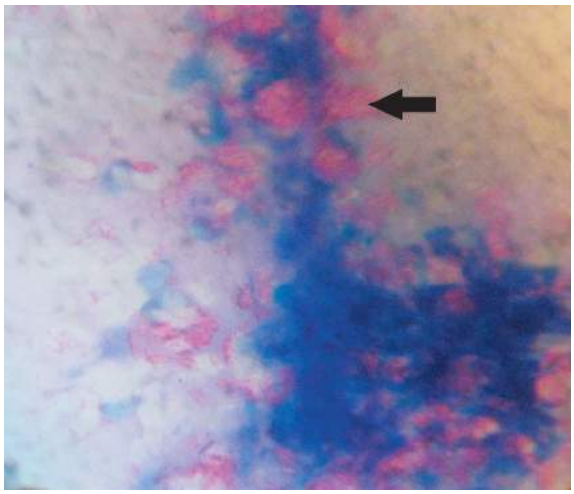

Figure 3. Slit skin smear from ear lobe and nodule showed bacilli in globi,numerous and appear long with tappering ends (Ziehl Neelsen staining). (Magnification 1000×)

Biopsy specimen of the nodules showed a well-circumscribed area of the dermis packed with many acid-fast organisms and foamy macrophages, consistent with histoid leprosy. Fite-Faraco stain demonstrated cells packed with lepra bacilli with a characteristic interlacing bundles of spindle-shaped histiocytes (figure 4 a,b,c).

Elisa examination of anti PGL-1 examination revealed IgM > 5300 u/ml and IgG > 5300 u/ml with cut off for IgM: 605 u/ml and IgG: 630 u/ml. PCR examination from nasal and skin swabs were positive and no mutation.Polymerase Chain Reaction to detect *M.leprae* using the LpF-R/Lp 1–2 nested primers were positive from skin smear, nasal swab and blood specimens. The results of drug resistance study using direct sequencing method for *rpoB, folP* and *gyrA* areas of *M.leprae* revealed no mutation, which means that the bacilli still sensitive to Rifampycin, Dapsone and Quinolone treatment.

The patient was treated with Rifampicin 600 mg and Ofloxacin 400 mg daily for ten days therapy initially, then followed by WHO-MDT therapy for Multibacillary Leprosy. Improvement of clinical symtomps have been achieved after 3 months therapy and nodule lesions were disappeared. The treatment is continuing and the patient is still under monitoring.

DISCUSSION

Histoid leprosy is uncommon variant of lepromatous leprosy.[7] The term 'histoid leprosy' was first coined by Wade in 1960 as a histological concept of bacillary rich leproma composed of spindle-shaped cells along with an absence of globus formation. Since then few case series have been published, mostly from India [9] It constitutes 1.2–3.6 % of all leprosy cases, however, studies regarding this form of disease are rare.[9,11] This variant of leprosy is considered as a well-recognized expression of multibacillary leprosy characterized by typical clinical, histopathological, immunological and bacteriological findings.[3] Based on the history, physical examination, and supported by laboratory result as well as histopathology, bacteriology and serology examination we diagnosed this patient as Histoid Leprosy.

The histoid lesions commonly appear as smooth, shinny, hemispherical, dome-shaped, nontender soft to firm nodules which may be superficial, subcutaneus or fixed deeply under the skin and plaques or pads appearing on otherwise normal-looking skin.[4,6,8] In this case, nodules/subcutaneus translucent shinny nodules were the morphological pattern and a significant proportion of this patient, arising from apparently normal skin. There are three type lesions of histoid leprosy; subcutaneus nodule, cutaneus nodule, and cutaneus plaque.[4] In this case, the patient showed all of the typically condition features of histoid leprosy, like cutaneus nodules on his elbow, subcutaneus nodules on his left thumb and he also had skin colored plaques over the ear lobes. The nodules of histoid lesions which occur over the extensor surface of the extremities, back, buttock and face. They may be localized to bony prominences, especially around the elbows and knees.[6] In this case, bony prominences around the elbow and thumb were the sites of involvement. Leprosy bacilli in slit skin smear of a patient

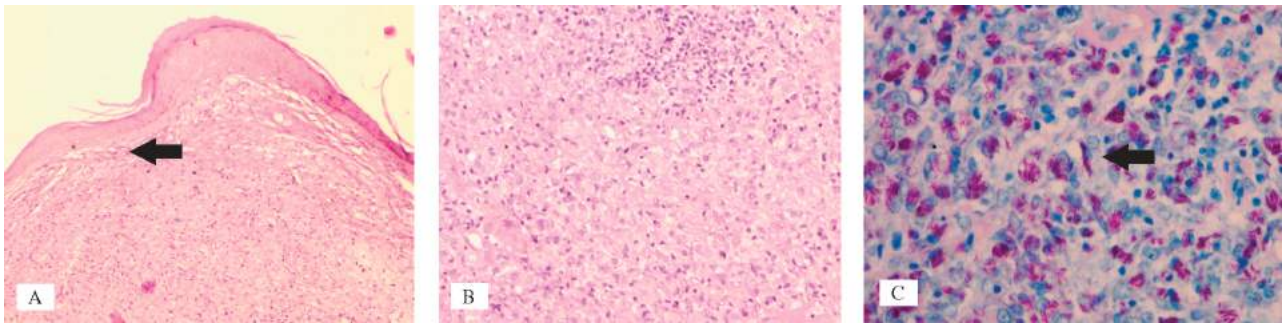

Figure 4. Skin biopsy showing (A) Epidermal atrophy with Grenz zone. (B) Domination of histiocytes (Magnification 1000x). (C) Spindle shaped histiocytes, foamy macrophages. Special Fite-Faracomethod

with histoid leprosy are numerous.[9] Slit skin smear from histoid lesions shows abundant acid-fast bacilli occuring in clusters, singly or tightly. The histiocytes and macrophages are packed with lepra bacilli characteristically longer than ordinary lepra bacilli and with tappering ends.[4,6,9] Bacteriological index may be 3+ to 6+ and morphological index may be 0 to 10% or very high.[9] Slit skin smear from our patient were taken by standard methods from the skin and nodule, its revealed abundant organisms occuring in globi, appearing long with tappering ends as compared with lepra bacilli in patients with other types of leprosy. The bacteriological index and morphological index from our patient revealed 4+ and 10%. The microscopic pathology of histoid leprosy evolves with time and is altered by therapy. It is imperative to take biopsy of the entire lesion early in its evolution and before the administration of multidrug therapy.[6] In this case, we did an excisional biopsy to taken the entire lesion. Histopathology finding is unique in histoid leprosy.[6] Histopathological features in Haematoxylin - Eosin and Ziehl-Neelsen stained skin biopsy specimens were studied to confirm the diagnosis of histoid leprosy, as suggested by Sehgal and Srivastava and Wade.[9] Classical histopathology findings include epidermal atrophy as a result of dermal expansion by the underlying leproma and an acellular band (Unna band) located immediately below the epidermis. This dermal expansion of histiocytes pushes aside the dermal collagen resulting in the formation of pseudo capsule. The leproma consists of fusiform histiocytes arranged in a whorled, criss-cross or storiform pattern. These histiocytes resemble fibroblast and it is suggested than these fibroblast-like macrophages may have arisen from tissue histiocytes rather than from blood monocytes. Usually there is epidermal atrophy with a subepidermal Grenz zone and a well-circumscribed dermal area of closely packed spindle-shaped histiocytes foaming interlacing bands and whorls surrounded by a pseudocapsule. Foamy macrophages may be found. However, epidermal atrophy is the rule of thumb in histoid leprosy.[6] Histopathological findings in this case included a free subepidermal zone (Grenz) and intertwining of strands of spindle-shaped histiocytes, and also epidermal atrophy as a striking features of histoid leprosy. Rapid molecular-type assays have been developed for detection of *M. leprae* directly from patient specimens using available genetic data. These assyas have been based primarily on the amplification of *M. leprae*-specific sequences using polymerace chain reaction (PCR) and identification of the *M. leprae* DNA fragment. This technique has been applied not only to skin biopsy samples but also to several different types of specimens.[4,15] We performed this examination to identify of acid-fast organisms and to detect any mutation. PCR examination of our patient taken from nasal and skin swab showed positive result and no mutation. PCR is indicated to identification of acid-fast organisms when bacilli are numerous but tissue site, clinical history, or their circumstances are questionable. PCR has thus generated new approaches to the detection and identification of *M. leprae* and, coupled with mutation detection analyses, has the ability to provide rapid drug susceptibility results from specimens taken directly from the patient. PCR can provide an excellent adjunct to clinical and histopathological diagnosis of leprosy.[5,8] Histoid leprosy has been reported generally to manifest in patients after long-term dapsone monotherapy, irregular or inadequate therapy, developing as relaps after successful treatment or even appearing *de novo* without a prior history of any antileprosy treatment[6] like in this case. *De novo*, means, without any previous lesions or treatment, thus without the possibility of being relapsing cases.[10,13] The pathogenesis of histoid leprosy still remains unresolved.[4] The interplay of genetic factors, immune response and treatment received in a given patient seems to influence the manifestations of histoid leprosy. Despite the presence of adequate numbers of macrophages, it has been claimed that they lack the functional property to kill bacilli that exist in high numbers in histoid lesions. It is possible that under the influence of *M. leprae* antigens they lose their bacteriolytic property or produce 'suppressor' cytokines, such as interleukin-10, that adversely inhibit T cell-mediated responses to *M. leprae*.[4,9] When histoid leprosy occurs in the appropriate clinical setting, that is, in patient of lepromatous leprosy on antileprosy therapy, the diagnosis is rarely a problem. Problems in diagnosis may occur when patients, particularly travelers, are present in nonendemic areas where the level of suspicion and familiarity with leprosy is low or when the preceeding LL leprosy is missed or is not evident. Lepromatous nodules, erythema nodosum leprosum, von Reklinghausen disease and histiocytoma are the conditions that need to be evaluated for the differential diagnosis of histoid leprosy. However, there are certain distinguishing features to be looked upon in cutaneous histoids. Unlike the resilient von Reklinghausen nodules, they are firm to palpation and also lack umbilication so typical of molluscum contagiosum.[6,14] Erythema nodosum lesions are red, hot, tender nodules; are associated with systemic manifestations; and tend to disappear and reappear.[6] Dermatofibroma is a common benign fibrous skin lesion, is also called a fibrous histiocytoma. It is due to a non-cancerous growth of dermal dendritic histicyte cells. In some cases it arises at the site of a minor injury, especially an insect bite or thorn prick. Dermatofibroma most often occur on the legs and arms. Once developed, they usually persist for years. They appears as firm-feeling nodules, often yellow-brown in colour, sometimes pink or quite dark. Lepromatous leprosy nodules arise from infiltrated skin. In contrast, lesions of histoid leprosy arise from apparently normal skin. Classical lepromatous leprosy presents with generalized symmetric lesions, while histoid lesions presents with localized asymetric lesions.[11]There is no clear recommendation regarding the treatment regimens for histoid leprosy. As some workers have considered it to be a variant of LL disease, it has been treated on the lines of multibacillary leprosy. Between 1982 and 1994, multibacillary patients were treated with 2 years MDT multibacillary regimen

(MBR) or until bacillary negativity, whichever was later. Between 1994 and 1998 and subsequently from 1999 onwards, multibacillary patients were treated with 2 years or 1 year fixed duration MDT MBR.[9] With the advent of the new era of more effective treatment (MDT) modalities available for multibacillary leprosy, the same regimens can be applied to the patients with histoid disease. Histoid leprosy being a highly bacillary form of leprosy and concern regarding the efficacy of fixed dose (12 months, after 1998). Researchers have used ofloxacin in combination with standard MDT MBR or pefloxacin alone in treatment. In this case, we have also used ofloxacin that may rapidly reduce the bacillary load. As we have known that ofloxcacin have a strong bactericidal effect like other drugs; minocycline, clarithromycin, and levofloxin.[8,11] It is the general belief that histoid disease requires longer for bacteriological clearance than does LL.[11] According to report of two cases in India, histoid leprosy was managed by initially giving ROM therapy with rifampicin 600 mg, ofloxacin 400 mg, minocycline 200 mg once, which is followed by MDT therapy.1[2] The disease responded satisfactorily. US National Hansen Disease Program (NHDP) treatment recommends minocycline 100 mg daily, which can be used as a substitution for dapsone in individuals who do not tolerate this drug. It can also be used instead of clofazimine, although evidence of the efficacy of its anti-inflammatory activity against Type 2 reactions is not as substantial as the evidence for clofazimine. Clarithromycin, 500 mg daily, is also effective against *M. leprae* and can be used as substitution for any of the other drugs in a multiple drug regimen.[8]

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