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Case Series

Histoid Leprosy: Case Series from Non-Endemic Region in Post-Elimination Era

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Histoid leprosy (HL) is a rare variant of lepromatous leprosy (LL) with unique histopathological findings and a characteristic bacterial morphology. HL occurs in highly bacilliferous patients such as LL or borderline LL and indicates the reservoir of infection. We report the clinical, histopathological and bacteriological features of three patients with de novo HL. The patients presented with asymptomatic skin papules on the face and trunk over a couple of years. Their past medical and family history was non-contributory. There were multiple, discreet, shiny, dome-shaped, skin-coloured to erythematous papules and nodules are seen on the face, trunk and extremities. Slit skin smeared showed the bacteriological index of 5+. Skin biopsy was done, and histopathology revealed a sub-epidermal grenz zone under atrophic epidermis and a collection of histiocytes in a whorled pattern in the dermis. A few macrophages are seen in the dermis. One of our cases presented with type 2 lepra reaction after completion of anti-leprosy treatment. Occurrence of de novo cases of HL from a non-endemic area may pose problems of missing/delay in the diagnosis and threat in the process of eradication of leprosy. It raises the question of the efficacy of conventional duration of multidrug therapy in some of such patients, thus necessitating studies to closely monitor or follow-up these cases for relapse or transmission of disease among close contacts and measures to control them.

Keywords : Histoid Leprosy, Elimination, Non-endemic Area

Introduction

Histoid leprosy (HL) is characterized by cutaneous and/or subcutaneous nodules and plaques on apparently normal skin with unique histopathological findings and a characteristic bacterial morphology (Seghal et al 1985). India has achieved the goal of leprosy elimination (prevalence of less than 1/10,000) as a public health problem at the national level by December 2005, as set by the National Health Policy. Although prevalence has come down at the national and state level, new cases are being continuously detected in several parts of India. The occurrence of HL, a rare form of multibacillary leprosy in a non-endemic area, highlights the problems (of missing/delay in the diagnosis) in eradicating leprosy as HL is highly-bacilliferous form and reservoir of drug-resistant bacilli. Herein, we report three cases of histoid leprosy presented to the Dermatology Out Patient Department (OPD) during 2017 and 2018.

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Informed consent has been taken from all the patients to publish the clinical information and images anonymously.

Case Reports

Case 1

A 26-year-male patient presented to Dermatology OPD with asymptomatic skin lesions on the face for 2 years. He had a history of epistaxis, three episodes in the last six months, and foul-smelling nasal discharge. The patient had consulted a nearby non-dermatologist for these complaints, took treatment, and there was no improvement of the condition. Cutaneous examination revealed madrosis and saddle nose deformity. Multiple, grouped, shiny, erythematous papules and plaques over normal skin were seen on the face, neck, trunk and upper extremities (Fig. 1). Bilateral ulnar and radial cutaneous nerves were slightly thickened and non-tender. There was hypoesthesia of both hands and feet. There was no motor deficit. Slit skin smear (SSS) from earlobes and eyebrows showed numerous long, slender lepra bacilli, lying singly or clumped. Bacteriological index on Ridley scale (Ridley 1964) was 6+. Histopathology revealed the whorled appearance of histiocytes in the dermis below the atrophic epidermis. A few foamy macrophages were also seen. Fite-Faraco staining (Chacko & Desikan 2008) showed abundant, elongated bacilli with tapering end among a few macrophages (Fig. 2). He responded well to one-year MB-MDT.

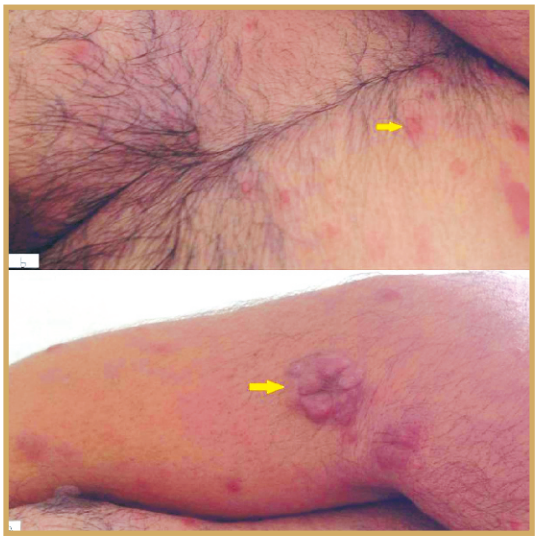

Fig 1 : a) solitary, shiny, smooth erthematous plaque with a few discreet nodules seen on the elbow. b) multiple, dome-shaped, erythematous discreet papules and nodules seen on abdomen.

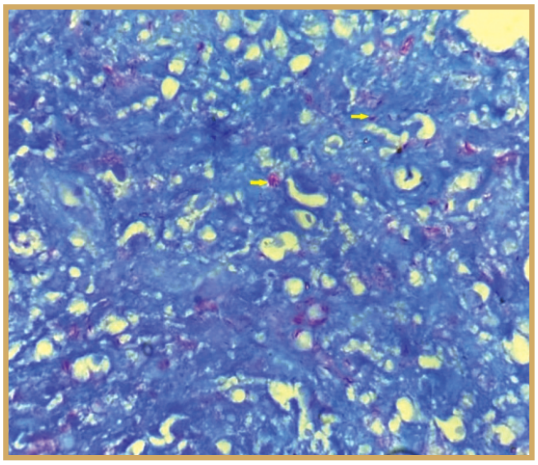

Fig. 2 : Numerous elongated acid fast lepra bacilli with tapering ends seen in histoid habitus. (Fite-Faraco stain, 100x)

Case 2

A 22-year-married female presented to our Dermatology OPD with asymptomatic skin lesions for 4 months. She had not consulted any doctor earlier as skin lesions were asymptomatic. She had a history of tingling and numbness of her hands and feet. There was no history any other chronic illness. There was no history of Hansen's disease in the family members. On examination, she had multiple, skin-coloured, discreet to grouped papules and nodules on the face (Fig. 3),

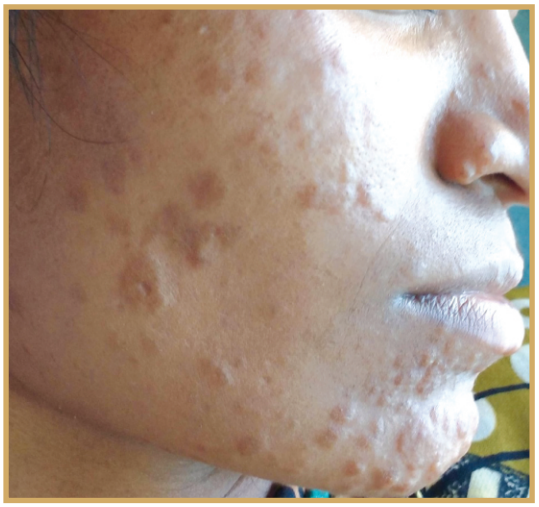

Fig 3 : Multiple skin-colored grouped papules seen on cheek and chin.

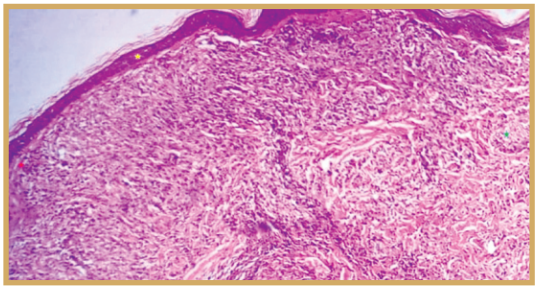

Fig 4 : Yellow star shows atrophic epidermis, red star shows sub-epidermal grenz zone with green star showing storiform-appearance of histiocytes in dermis. (H & E, 400x).

bilateral arms, forearms, thigh and abdomen. Peripheral nerve examination revealed thickened, non-tender, left popliteal and ulnar nerves. Slit skin smear from bilateral earlobes showed bacteriological index of 4+. A skin biopsy was done from the forearm papule. Histopathology showed atrophic epidermis, sub-epidermal grenz zone and storiform-appearance of histiocytes in the dermis (Fig. 4). The patient responded well to one-year MB-MDT with complete resolution of

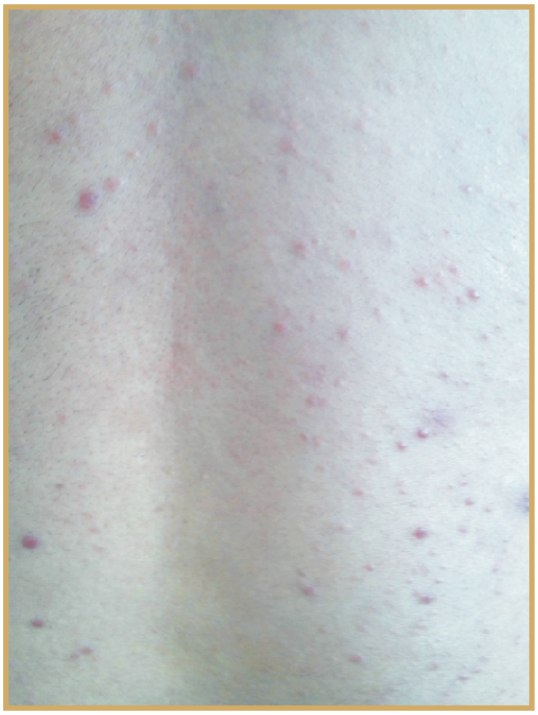

Fig 5 : Multiple, discreet, erythematous, dome-shaped papules seen on normal skin of back.

cutaneous lesions and presented with ENL lesions 6 months after completion of MDT. Relapse of HD was ruled out on the basis of history and clinical examination. The patient responded well to the tapering doses of corticosteroids.

Case 3

A 54-year-male patient presented to our Dermatology OPD with complaints of tingling and numbness of hands and legs for one year. There was no history of epistaxis. Patient had no history of diabetes mellitus or hypertension. There was no past history of treatment taken for Hansen disease. On cutaneous examination, he had multiple, discreet, eythematous, dome-shaped papules over normal-looking skin of the back (Fig. 5), abdomen and face. All peripheral nerves were just palpable and non-tender. There was no evi-

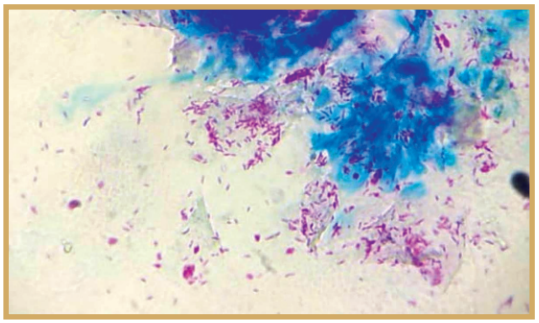

Fig 6 : Multiple, long, slender acid fast bacilli with tapering ends seen in slit skin smear. (ZN stain, 100x)

dence of motor-deficit, but sensory loss was noted on hands and feet. SSS from earlobes, eyebrows showed numerous, elongated lepra bacilli (Fig. 6). Bacteriological index was 5+. Histopathological findings confirmed the diagnosis of histoid leprosy. The epidermis was atrophic; dermis showed sub-epidermal grenz zone and whorled appearance of spindle-shaped histiocytes and a few foam macrophages in the dermis. Fite-faraco stain revealed plenty of singly-lying elongated bacilli among the macrophages. On the basis of clinical and laboratory findings, HL was diagnosed, and multibacillary-multidrug therapy was started. Patient responded to the conventional dose of MB-MDT and there was no evidence of any reaction during follow up period.

Discussion

HL is a rare variant of lepromatous leprosy (LL) first described by Wade in 1960 as a histological concept of bacillary-rich leproma composed of spindle-shaped cells, along with the absence of globus formation (Wade 1960). HL mainly occurs in the settings of dapsone monotherapy patients (as a relapse indicating earlier response), inadequate or irregular treatment (exhibiting mutant organisms) or seen as de novo cases. The etiopathogenesis is not known but may occur as a result of modified hypersensitivity reaction of the cellular type that results in an inhibition of the lesional expansion, but not in the destruction of the bacilli within the histoid lesion (Kontochristopoulos et al 1995). Immunohistochemical analysis had shown reduced numbers of all dendritic populations in the epidermis and a gradual reduction in HLA-DR expression on keratinocytes in histoid lesions. In spite of the presence of abundant macrophages, resembling morphologically activated ones, they lack the functional ability to kill the bacilli and produce cytokines like IL-2 and INF-γ. This proves the absence of well-organized granuloma and a high number of bacilli in histoid lesions (Kontochristopoulos et al 1995).

Clinical features may vary from small papules to subcutaneous nodules to cutaneous plaques appearing on normal-looking skin. These nodules are usually dome-shaped or succulent, globular, and protuberant, shiny, skin-colored or erythematous, fixed, soft to firm in consistency. Commonly involved sites are the face, extremities, back, buttocks and over bony prominences. All three of our patients had multiple erythematous to shiny, dome-shaped discreet papules over the normal-looking skin of the trunk and extremities. In severely affected patients, nodules have also been seen on the hard palate, buccal mucosa and glans penis (Ramanujam & Ramu 1969). Occasionally, the lesions may be pedunculated and umbilicated, resembling molluscum contagiosum. Pedunculated, umbilicated and mucosal nodules were not seen in our patients. Lepra reactions are rare in HL, although in a few studies, ENL was reported (Kaur et al 2009, Seghal & Srivastava 1987, Kalla et al 2000). One of our patients developed ENL reaction after six months of completion of multidrug therapy. Singh et al have reported a single case of HL with type 1 reaction (Singh et al 2015). A brief review of

Table 1 : Histoid leprosy - comparison with reported cases by others

Reference	Age	Sex	Duration	Site	Clinical presentation	Previous history of anti-leprosy treatment taken	Peripheral nerve involvement	Slit Skin Smear Bacterio-logical index (BI)	Histopathological examination	Lepra reactions
Present case 1	26 years	M	2 years	Face, neck, trunk and upper ext-remities	Madrosis, saddle-nose deformity, multiple, grouped shiny papules and plaques, similar findings as reported by other authors	Nil	Bilateral ulnar and radial cutaneous nerves, thickened, non-tender	6+	Spindle-shaped histiocytes with a few macrophages seen below the atrophi epidermis	Nil
Present case 2	22 years	F	4 months	Face, abdomen, upper extremities and thigh	Asymptomatic, multiple, papules & nodules	Nil	Left ulnar and common per-oneal nerve thickened and non-tender, asymmetrical nerve involve-ment seen in this case un-like cases reported by other authors	4+	atrophic epidermis, sub-epidermal grenz zone and stori-form-appearance of histiocytes in dermis	Type 2 reaction occurred after 6 months of completio n MDT

Present case 3	54 year	M	1 year	Face and trunk	Multiple, discreet erythematous dome-shaped papules over the normal skin	Nil	Symmetric thickening of nerves in both extremities, non-tender	5+	Whorled appearance of histiocytes under atrophic epidermis	Nil
Singh et al (2015)	42 year	F	-	Face, trunk, and extremities	Asymptomatic multiple papules, plaques, and nodules		B/L common peroneal and posterior tibial nerves thickened and non-tender	Ranged from 4+ to 6+ from various sites	spindle-shaped, non-vacuolated histiocytes in a whorled pattern with an abundance of AFB. Papillary dermal edema with plenty of lymphocytes scattered between the histiocytic granulomas	Type 1 reaction seen after 10 weeks of MB-MDT
Nair & Kumar (2013)	43 years	M	8 months	Trunk, both upper and lower limbs	Papules and nodules, Superciliary madrosis, earlobe infiltration seen	Nil	Symmetric nerve involvement	-	-	Type 2 reaction developed after 5 months of MDT
Tiwary et al (2017)	24 years	M	1 year	Face with lips, both extremities, back, buttocks, genitalia	Asymptomatic papules, nodules and plaques	Nil	ulnar, common peroneal, posterior tibial and great auricular nerves were bilaterally thickened, but non-tender.	6+	epidermal atrophy, grenz zone and numerous spindle-shaped non-vacuolated histiocytes arranged in interlacing whorls	Not seen

literature about reported cases is shown in Table 1. Histological features are striking with the presence of circumscribed nodular lesions with spindle-shaped histiocytes, sub-epidermal grenz zone and abundant lepra bacilli. The cells are arranged in an intertwining pattern, and some cases may resemble fibrohistiocytictumors. These classical features, such as epidermal atrophy, grenz zone and storiform the appearance of histiocytes were seen in our patients. Lepra bacilli in HL are numerous in number, thin and longer than the usual bacilli of leprosy and are aligned along the long axis of the cell without the distortion of the cell (histoid habitus). Occasionally there are a few foamy macrophages seen (Sehgal & Srivastava 1985). One of our male patients' histopathology had shown the presence of a few macrophages in the dermis.

Differential diagnosis include sarcoidosis, molluscum contagiosum and leukaemia cutis. The presence of hilar lymphadenopathy, lung and bone involvement helps in differentiating this condition. The absence of nerve thickening, sensory loss or absence of AFB in slit skin smear and histopathology helps in differentiating molluscum contagiosum from HL. Leukemic cutis may be easily differentiated by the presence of pruritus, absence of AFB in SSS and by blood examination. Histological differential diagnosis include fibro histiocystictumors, which can be easily ruled by the absence of elongated AFB in the cells.

In most of the Indian studies, HL has responded well to the conventional MB-MDT. Only a few authors have used adjunctive therapy of ofloxacin, pefloxacin or Mycobacteria w vaccine to decrease the bacillary load (Vora et al 1985, Talwar 1999). Histoid leprosy is also known to be caused by drug-resistant bacilli (Seghal & Srivastava 1985). Microbiological confirmation of drug-resistant strains with mouse footpad inoculation was not done in our study because the facility was unavailable. As our cases responded well to MB-MDT, drug resistance in our cases is unlikely. This is the limitation of this study.

Conclusion

Though HL usually occurs in highly bacilliferous patients such as LL or borderline LL, a few de novo HL cases have been reported. Diagnosis and differentiation of HL from lepromatous leprosy and other forms of leprosy as well as other conditions relevant in differential diagnosis are important as these cases require close follow up. Although ENL in HL is reported to be rare, it does occur in a few patients, as seen in one of our cases. Though there is a response to treatment with conventional MB MDT in some of such patients, long-term follow-up studies are required to monitor relapse. Hence, the occurrence of HL may pose a threat in eradicating leprosy. So, there is a need for a complete microbiological and molecular investigations for drug resistance in such cases and measures to control them.

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