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RESEARCH ARTICLE

CLINICOPATHOLOGIC SPECTRUM OF HISTOID LEPROSY

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ABSTRACT

Background: Histoid leprosy (HL) is an uncommon variant of lepromatous leprosy with distinct clinical and histopathological features.
Methods: In 10 years (2005-2014), 385 cases of leprosy were diagnosed on histopathology and out of these, 13 cases (3.37%) were of histoid leprosy.
Results: The male/female ratio was 2.25:1. 10 cases (76.9%) were in 30-60 year old age group. The commonest skin lesions encountered were nodules over normal looking skin in 10 (76.9%) cases. The most common sites involved were upper and lower limbs in 8 (61.5%) cases. The various clinical differential diagnoses given were leprosy, dermatofibroma, neurofibroma, sarcoidosis, xanthoma, erythema nodosum leprosum and molluscum contagiosum. The main histopathological features were epidermal atrophy and a well-circumscribed dermal area packed with spindle-shaped histiocytes. All the cases were highly positive for acid-fast bacilli.
Conclusion: Histoid leprosy usually presents as nodules over a normal looking skin and can have different clinical diagnoses. For confirmation, histopathological correlation is must.

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INTRODUCTION

Histoid leprosy (HL) is an uncommon variant of lepromatous leprosy, characterized by cutaneous/subcutaneous nodules and plaques present over apparently normal skin. The term Histoid leprosy was coined by Wade in 1963, as a histological concept of bacillary-rich leproma composed of spindle-shaped cells, along with the absence of globus formation. It exhibits a fibromatoid tendency in the chronic form.Histopathologic findings include epidermal atrophy as a result of dermal expansion by the underlying leproma and an acellular band (Grenz zone) located immediately below the epidermis. The leproma consists of fusiform histiocytes arranged in a whorled, crisscross or storiform pattern containing acid-fast bacilli (AFB) (Vora *et al.,* 2014). HL was described in patients who were on inadequate and irregular dapsone therapy. However, occasional cases of de-novo HL can occur (Sehgal *et al.,* 2005).Clinical findings are well-defined, skin-colored or erythematous, shiny papules, plaques, cutaneous and subcutaneous nodules arising from apparently normal skin. In contrast, lesions of classical lepromatous leprosy arise from infiltrated skin. HL responds to multibacillary therapy with dapsone, clofazimine, and rifampicin. Adding a newer drug, ofloxacin, minocycline, or clarithromycin, may rapidly reduce the bacillary load and destroy mutant strains (Nair *et al.,* 2006). This can mimic many other dermatoses and can be missed clinically (Nair and Kumar, 2013). Rare variants of leprosy pose a diagnostic challenge even to astute clinicians and histoid leprosy is one such form of disease with unique clinical and histopathological features (Kaur *et al.,* 2009). Therefore this study was conducted to elucidate the cardinal clinical features, differential clinical diagnoses, and diagnostic salient histopathological features.

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MATERIALS AND METHODS

The present retrospective study was conducted in Department of Pathology, Government Medical college, Chandigarh with compiling of the data from archival records over a period of 10 years from 2005 to 2014. The cases which were clinically and histopathologically diagnosed as HL were included.The clinical features including age and sex distribution, type of skin lesions and the neurological features were noted. The skin biopsies were routinely processed and stained with hematoxylin and eosin and lepra stains. The histopathologic features including epidermal atrophy, grenz zone, collection of cells in dermis and spindle shaped cells were noted. The lepra stained slides were examined under oil immersion for bacillary index (BI).

Table 1. Clinical features of Histoid Leprosy (n=13)

Case no	Age/sex	Duration	Lesion type and location	Loss of sensation	Symmetric Nerve thickening	Clinical diagnoses suggested
1	80/M	1 year	N ,L	+	-	ENL, LL
2	34/M	6 months	N, T	-	-	HL
3	19/F	6 months	N, U	+	+	HL
4	48/F	8 months	N, L	-	-	EN
5	40/F	15 days	P, L	-	-	Sarcoidosis, Dermatofibroma
6	31/M	6 months	N, Ear lobule	+	+	Leprosy
7	58/F	8 months	N, U & L	+	+	HL
8	32/M	8 months	N, T	-	-	HL, Dermatofibroma, Cutaneous Neurofibroma
9	30/M	8 months	P, U	+	+	HL
10	11/M	1 year 6 months	N, Face & ear lobule	-	-	HL, Sarcoidosis,Xanthoma
11	39/M	1 year	P, T	-	-	HL
12	30/M	1 year	N, U & L	-	-	ENL
13	30/M	3 months	N, L	-	-	HL

ENL,Erythema nodosum leprosum; H L, Histoid leprosy; LL, Lepromatous leprosy; L, lower limb; N, nodule; P, papule; T, trunk; U, upper limb.

Table 2. Histopathological features and Bacillary indexes

Case no	Epidermal atrophy	Grenz zone	Pseudo capsule	Wellcircumscribed area of cells in the dermis	Spindleshaped HistioCytes	ScantyLymphocytic infiltrate	BI(+)
1	+	+	+	+	+	-	5.34
2	+	+	+	+	+	-	6
3	+	-	+	+	+	-	5.5
4	+	+	-	+	+	-	5
5	+	-	+	+	+	-	5
6	+	-	-	+	+	-	6
7	+	+	-	+	+	-	6
8	+	-	-	+	+	-	5.3
9	+	-	-	+	+	-	6
10	+	-	-	+	+	-	5
11	+	-	-	+	+	-	5
12	+	-	+	+	+	+	6
13	+	-	-	+	+	-	6

Table 3. Clinicopathologic differential diagnosis of histoid leprosy

Diagnosis	Histoid leprosy	Dermatofibroma	Cutaneous neurofibroma	Erythema nodosum leprosum	Xanthoma	Cutaneous sarcoidosis	Molluscum contagiosum
Clinical details	Well-demarcated cutaneous and subcutaneous nodules, often multiple	Poorly circumscribed; c/s- white, homogeneous, pigmentation ++	Circumscribed, non - encapsulated tumour of dermis, solitary/multiple	Red, hot, tender nodules. Associated with systemic manifestations	Solitary/ multiple tumor like lesions	Erythema nodosum or brown red jelly like papules or plaques with central clearing, systemic disease+	Small, waxy , umbilicated papules
Microscopy	Epidermal atrophy Spindle cell proliferation of macrophages, resemble storiform tumour	Epidermal changes; dermis: spindle cells in a storiform pattern, foam histiocytes, giant cells, pale cytoplasm, Blood vessels, sclerosis	Loosely spaced spindle cells and wavy collagenous strands, elongated wavy nuclei	Polymorphs infiltrate macrophage granulomas, vasculitis +	Foamy histiocytes engulfing lipid droplets, multinucleated giant cells,fibrosis	Epithelioid cell granulomas (naked granulomas), fibrinoid necrosis, asteroid bodies±	Epidermis acanthotic,and show numerous molluscum bodies(intracytoplasmic inclusions)
Ancillary studies (AFB, Special stains and IHC)	BI=6	CD68	S-100	Granular broken AFBs	Fat stains	Reticulin stain	Electron microscopy

AFB,Acid fast bacilli; BI, Bacillary index;IHC,Immunohistochemistry

RESULTS

Out of a total of 385 cases of leprosy, 13 (3.37%) were diagnosed as histoid leprosy. There were 9 males and 4 females and the male to female ratio was 2.2:1. Maximum no of cases (76.9%) were in the age group 30-60 years. The oldest patient was 80 years and the youngest was 11 years old. None of the patients had a family history of leprosy. Eight (61.53%) patients were known cases of leprosy and gave a history of irregular treatment while five (38.46%) cases did not give a past history of leprosy.

The commonest skin lesions encounteredwere nodules over normal looking skin in 10 (76.9%) cases (Figure 1). Papules were seen in rest three cases (23.07%). The most common sites involved were upper and lower limbs in 8 (61.5%) cases followed by trunk in 3 (23.07%) cases. Two patients (15.38%) presented with ear lobule infiltration and one of them had face lesions also. The salient clinical features are given in Table 1. The histopathologic features included epidermal atrophy with a subepidermal Grenz zone and a well-circumscribed dermal area of closely packed spindle-shaped histiocytes in a storiform

pattern. All the cases were highly positive for AFB (Figures 2-4). Bacillary index ranged from 5+ to 6+ (mean 5.54).

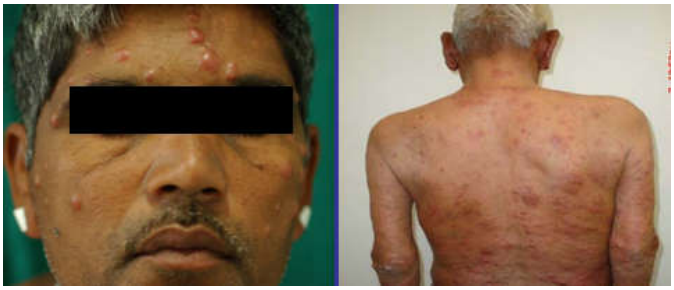

Figure 1. Multiple nodular lesions over face and back arising on normal skin

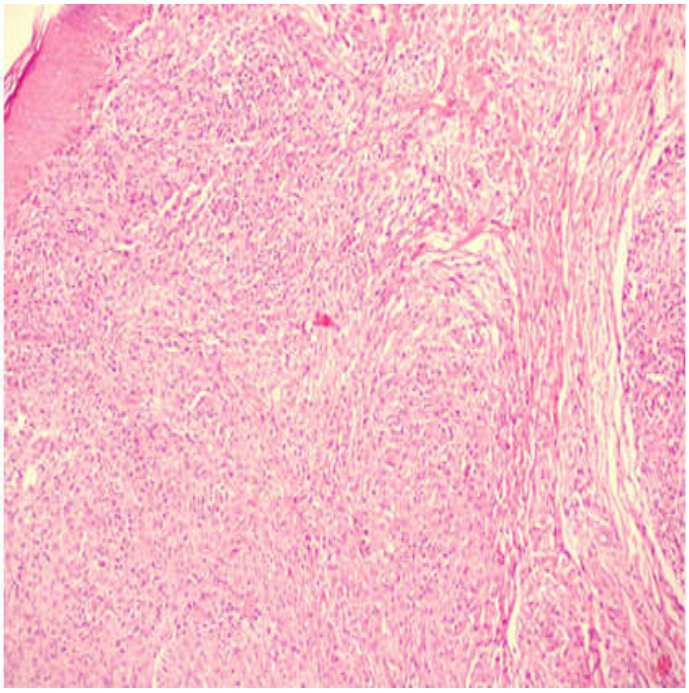

Figure 2. Photomicrograph showing epidermal atrophy and spindle shaped histiocytes in dermis arranged in storiform pattern. (H & E X 100)

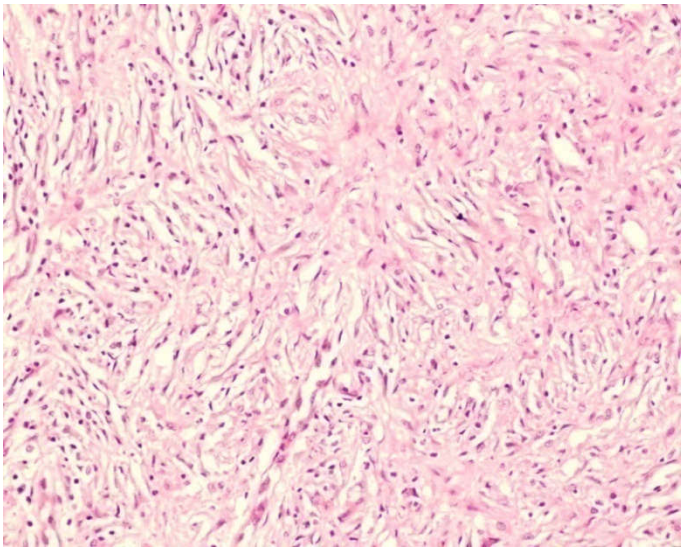

Figure 3. Photomicrograph showing the storiform pattern of interlacing bundles of spindle-shaped cells reminiscent of fibrous histiocytoma. (H & E X 200)

Spindle shaped macrophages were packed with AFB which were longer than ordinary lepra bacilli. The histopathological features and bacillary indexes are given in Table 2.

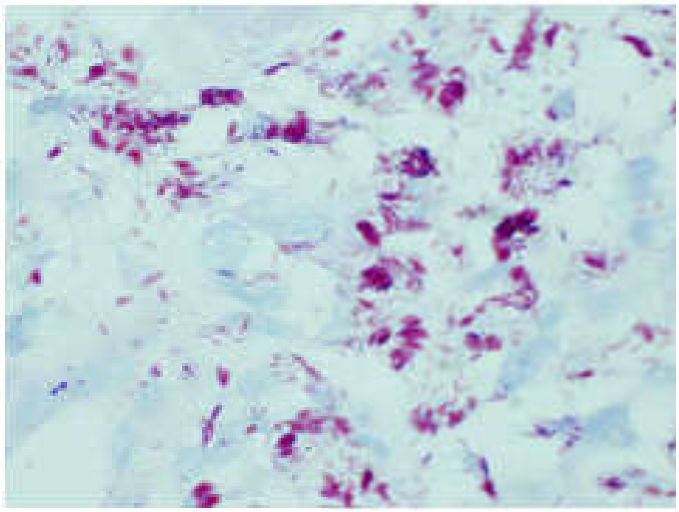

Figure 4. Photomicrograph showing heavy bacillary index (AFB stain X 1000)

DISCUSSION

HL constitutes 1.2 – 3.6% of all leprosy cases, however studies regarding this form of disease are rare (Rinasari *et al.,* 2010). In India, its incidence among patients with leprosy is estimated to be 2.79–3.60% (Gupta, 2015).The total number of cases in this study was 13,incidence being 3.37%indicating the rarity of HL.A previous similar study by Nair and Kumar 2013 had incidence of 2.05%.The study by Kaur *et al.,* 2009had an incidence of 1.8%, Mendiratta *et al.,* (2011) 1.14%, and by Kalla *et al.,* (2000) 2.8%, all indicating again the rarity of HL. There is a male preponderance inprevious studies (Manoharan *et al.,* 2008). The male:female ratio is 2.2: 1 in thisstudy, however it is lesser than the studies done by Kaur *et al.,* 2006 (5.7 : 1) and Sehgal and Srivastava (1988) (8.2 : 1). 30-60 year old age group accounted for maximum no of cases (76.9%), the mean age being 35 years, in contrast to studies by Sehgal and Srivastava (1988), and Kalla *et al*. (2000) where the 20–40-year-old age group was most commonly affected. HL is an uncommon variant of lepromatous leprosy that usually follows treatment failure. Occasionally it occurs de novo without any history of previous inadequate or irregular treatment (Bhat *et al.,* 2015).

The incidence of de novo histoid patients is now increasing (Kaur *et al.,* 2009). It is evidenced by de novo cases in this study (38.46%) compared with another major study by Kaur *et al.,* 2009 where de novo cases of HL accounted for only 12.5%. The detection of large number of de novo cases could be due to high index of suspicion for leprosy maintained in our centre.As suggested by Palit and Inamadar, the histoid form could serve as a reservoir of leprosy and as a source of new cases. This could pose a serious threat to national leprosy elimination program (Palit and Inamadar, 2007). Literature states that the lesions are usually located on the posterior and lateral aspects of the arms, buttocks, thighs, dorsum of the hands, lower part of the back, and over the bony prominences, especially over the elbows and knees (Annigeri *et al.,* 2007). In more severely affected cases, mucosal and genital lesions have also been recorded. The palms and soles are usually not affected in histoid leprosy (Sehgal *et al.,* 1985). Histoid lesions

have also been reported along the course of the peripheral nerve trunks and cutaneous nerves (Manoharan *et al.,* 2008). The ulnar nerve is the most common nerve involved (Kalla *et al.,* 2010). Ear lobe infiltration seen in 15.38% of the cases in this study and 58.82% by Nair and Kumar is a unique feature as other studies mention ear lobe infiltration as a rare feature of HL (Sehgal and Srivastava, 1987 & 1988). The characteristic histopathological features of HL are epidermal atrophy, subepidermal grenz zone, collection of spindle shaped histiocytes in dermis forming pseudocapsule and positive staining for AFB (Wade, 1963; Sehgal and Srivastava, 1987; Ridley, 1980). It is not unusual to locate a few foci of chronic inflammatory cells in the sections (Sehgal *et al.,* 2009).There are three histological variants of histoid Hansen's, namely, pure fusocellular, fusocellular with epithelioid component, and fusocellular with vacuolated cells.The third pattern is mostcommonly observed (Patnaik *et al.,* 2008). A peculiar phenomenon the tuberculoid contamination may be seen in cases of subcutaneous histoid lepromas. This is because of the occurrence of well-defined foci of epithelioid cells, located within the lesion substance or in the encircling fibrous tissue encapsulation. No satisfactory explanation of their occurrence is postulated, but it is likely that tuberculoid contamination may well represent the tuberculoid component of the earlier borderline leprosy (Sehgal *et al.,* 2009).

HL has high bacillary index, mean BI of 5.54. The bacilli of the histoid lesions constitute one of the most distinctive and intriguing features. The acid-fast bacilli are longer than the usual lepra bacilli (Sehgal and Srivastava, 1987 & 1988; Ridley, 1980).They are consideredas mutant bacilli resulting from the development of drug resistance against dapsone monotherapy. Spindle-shaped histiocytes are arranged in groups or parallel bundles aligned along the long axis of the cell, a ''histoid habitus'' (Sehgal *et al.,* 2009). The AFB is not found in globi formation, as they do not secrete any glial substance (Vora *et al.,* 2014).When HL occurs in the appropriate clinical setting, that is, in a patient of lepromatous leprosy on antileprosy therapy, the diagnosis is rarely a problem. Problems in diagnosis may occur when the preceding LL leprosy is missed or is not evident (Boyd and Robbins, 2005; Wood *et al.,* 1985; Chakrabarti *et al.,* 1997). HL clinical mimics include xanthomas, neurofibroma, dermatofibroma, reticulohistiocytosis, or cutaneous metastasis. These can be differentiated from histoid leprosy on the basis of its characteristic histopathology, the absence of lepra bacilli on slit skin smear and nerve thickening (Monga *et al.,* 2008). Barring histiocytoma, which may be a differential on histopathologic examination, all the other conditions may be mistaken for HL on clinical examination, thus rendering histopathological examination crucial to the correct diagnosis (Sehgal *et al.,* 2009). Various differentials of HL and their differentiating features are given in Table 3.

Conclusion

- Histoid leprosy usually presents as nodules over a normal looking skin and can have different clinical diagnoses. For confirmation, histopathological correlation is must.
- Despite its rarity, histoid leprosy poses a challenge to the leprosy eradication program because of its multibacillary character.
- A high index of suspicion is thus essential for surveillance of new and relapse cases, rather than to wait for voluntary reporting.

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