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Original Article

The Burden of Histoid Leprosy in Post Elimination Era

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Histoid leprosy is a rare variant of lepromatous leprosy, may occur de novo or may occur in cases earlier treated with dapsone monotherapy. Demographic, clinico-histopathological and treatment details of biopsy proven cases of histoid leprosy, collected retrospectively from the leprosy clinic of tertiary care hospital of SMS Medical College, Jaipur. During the study period of 5 years (2011-2016), 28 (2.98 %), patients had histoid leprosy among total 937 patients of leprosy. Most were in 21 – 40 years of age group with M: F ratio 2.5: 1. Histoid lesions developed with primary diagnosis of lepromatous leprosy in (71.4%) and de novo in (28.6%). Predominant site of involvement was upper extremity (85.7%) and most common presentation was subcutaneous nodules, Nerve thickening seen in (85.7%), and ulnar nerve being most common. Neuritis and disabilities were present in 6 and 16 patients respectively. Type 2 reaction seen in17.9% (5/28) patients. Biopsy and slit skin smear of all cases were done. Most (25/28) cases responded well to standard one-year multibacillary drug therapy (MDT), it had to be extended in three cases up to 2 years. Histoid leprosy may occur de novo or may be due to inadequate therapy, resistant strains, earlier dapsone monotherapy. Although India as whole has achieved leprosy elimination in January 2006, however new cases continue to be reported. Occurrence of histoid leprosy specially with changed morphology of the lesions and poor histopathological correlation needs to be investigated as these cases may be important source of infection even in low endemic situations.

Key words : Histoid Leprosy, Multidrug Therapy, Drug Resistance

Introduction

Leprosy has varied and occasionally unusual presentations, which can pose diagnostic dilemma and treatment challenges to clinicians worldwide. Histoid leprosy is a rare variant of lepromatous leprosy characterized by distinct morphological and histopathological appearance. Despite being a rare entity, the higher load of lepra bacilli in these cases makes it a concern as a reservoir for leprosy. This variant was initially described by Wade in 1963 (Wade 1963). It was first observed in multi bacillary patients, on irregular and/or inadequate dapsone monotherapy, but later de novo cases were also encountered (Sehgal & Srivastava 1987). Although India as whole has achieved leprosy elimination in December 2005 (Sengupta 2018), two states of Bihar and Chhattisgarh are yet to attain elimination (Desikan 2012).

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Histoid leprosy cases though rare have been reported from India (Sehgal & Srivastava 1988, Kalla et al 2000, Kaur et al 2009). Our centre receives high load of leprosy patients from adjoining parts of Northwestern India. A systematic retrospective analysis of our leprosy case records was carried out to study various epidemiological, clinical and histopathological characteristics of the patients with histoid leprosy seen over a period of 5 years.

Materials and Methods

The records of leprosy cases, who attended our leprosy clinic during April 2011 to March 2016, were retrospectively analyzed. A total of 937 case records were analyzed and biopsy proven histoid leprosy cases were included in the study. Case of leprosy was defined as a person showing one or more of the following features: hypopigmented or erythematous skin lesions with definite loss of sensation, involvement of the peripheral nerves, as demonstrated by definite thickening with loss of sensation and skin smear positive for acid-fast bacilli. As the study is retrospective so we used clinical classification system of leprosy suggested by WHO expert committee (WHO 2012).

Demographic, clinical, treatment and histopathological details of these patients from their records were collected. Clinical examination included number and type of lesions, sites involved, new/defaulter case, nerve involvement, reactions and disability. WHO's classification of leprosy (1988) was used to classify the patients. The other categories of leprosy were classified according to Indian classification system of leprosy like pure neuritic leprosy (IAL 1982). Type 1 reaction was defined as increased erythema and edema in pre-existing lesions with or without the appearance of new lesions or neuritis. Type 2 lepra reactions were defined as the appearance of tender evanescent erythematous nodules associated with fever, with or without neuritis or systemic manifestations. World Health Organization (WHO) disability grading was used to grade disability in patients.

Slit skin smear (SSS) and skin biopsy of these cases were studied. Bacteriological index (BI) was calculated in all the patients. Correlation of clinical diagnosis and histopathological findings was carried out. Multidrug therapy (MDT) was given to all patients according to WHO guidelines. Reactions and deformities were treated accordingly.

Results

During the study period of 5 years, a total of 937 leprosy patients attended our leprosy clinic of Department of Dermatology of SMS Medical College Hospital Jaipur. Of these, 28 (2.98%) patients had biopsy-proven histoid leprosy.

The mean age of patients was 34.5 years, ranged from 12 to 75 years. Maximum number (13/28; 46.4%) of patients belonged to the age group of 21 – 40 years followed by 41-60 years. Study included 937 patients with Male: Female ratio being 2.5: 1. The duration of disease at the time of presentation ranged from 1 month to 7 years. Majority (9/28; 32.1%) of the patients presented between 7 to 12 months. Eighteen patients belonged to poor or rural socio-economic background (Table 1).

Twenty-eight cases were histopathologically confirmed as histoid leprosy. Lepra bacilli in histoid cases were found to be well preserved, uniformly stained, long rod with tapering ends in SSS. Several striking features are seen in histoid histopathology, the most prominent being the circumscribed nature of the lesion, the predominance of spindle-shaped and /or polygonal cells, and an unusually large number of acid-fast bacilli. Other findings were epidermal atrophy, peri-appendageal mononuclear inflam-

Table 1 : Demographic profile of histoid cases studied (n=28)

Age in years			
Age groups	**Male (n=20)**	**Female (n=8)**	**Total**
Up to 20	3	2	5
21 – 40	9	4	13
41 – 60	7	2	9
Above 60	1	-	1
Duration			
Less than 1 month	2	-	2
1 – 6 months	4	2	6
7 – 12 months	7	2	9
1-2 year	4	3	7
More than 2 years	3	1	4
Socioeconomic background			
Rural	15	3	18
Urban	5	5	10

matory infiltrate, absence of appendages, clear grenz zone were noted. In 20 patients (71.4%) histoid lesions developed with primary diagnosis of lepromatous leprosy (LL) in 14 patients, borderline lepromatous (BL) leprosy in 3 patients, borderline (BB) leprosy in 2 patients and borderline tuberculoid in 1 patient. De novo development of histoid lesions were seen in 8 cases (28.6%). All the cases of histoid leprosy were new cases. Nodules/ subcutaneous nodules (Figs. 1 and 2) were the commonest lesion seen in 24 patients (85.7%), followed by infiltrated plaques in 6 patients and papule in 2 patients. Most patients had more than one type of lesion. Number of lesions varied from 1 to 100, majority (18/28, 64.3%) of them have 26 to 50 lesions, followed by 1 to 25 (6/28, 21.4%) and 51 to 100 (4/28, 14.3%). Most common site of involvement was upper extremity (24/28, 85.7%), followed by lower extremity (21/28, 75%), trunk (20/28, 71.4%) and face (18/28, 64.3%) (Table 2).

Nerve thickening was seen in 24/28 of histoid patients (85.7%), most commonly ulnar nerve followed by lateral popliteal nerve. Neuritis was observed in 6 patients. Grade 1 disability in hands and feet was seen in 7 and 8 patients respectively, while one patient had grade-2 disability in hand. Five patients (17.9%) had type 2 reaction during the course of disease.

SSS showed abundant bacilli occurring mostly in clusters. Bacilli were uniformly stained, slender with tapering ends and longer than the usual lepra bacilli. BI ranged from 3+ to 6+ with mean being 5.1. In addition to above findings histopathology showed atrophic epidermis due to dermal expansion by the underlying leproma (histoid nodule) and an acellular grenz zone immediately below the epidermis (Fig. 3). The leproma consisted of spindle shaped histiocytes arranged in different patterns. AFB+ bacilli (Fig. 4) were arranged in groups or parallel bundles along the long axis of the histiocytes. The expanding histoid leproma formed a pseudocapsule due to compression of surrounding tissue.

Table 2 : Clinical profile of histoid patients (n=28)

Parameters	Male (n=20)	Female (n=8)	Total
Primary diagnosis			
TT	-	-	-
BT	-	1	1
BB	2	-	2
BL	1	2	3
LL	10	4	14
De novo Histoid leprosy	7	1	8
Type of lesion*			
Nodule	18	6	24
Plaque	3	3	6
Papule	2	-	2
Number of lesions			
1-25	4	2	6
26-50	13	5	18
51-100	3	1	4
Site of involvement*			
Face	15	3	18
Trunk	15	5	20
Upper limb	17	7	24
Lower limb	16	5	21
Nerve thickening	17	7	24
Neuritis	4	2	6
Grade 2 disability *			
Hand	6	2	8
Feet	6	1	7
Eye	-	-	-
Reaction			
Type 1	-	-	-
Type 2	5	-	5
History of treatment	-	-	-
Bacillary Index			
3+	2	1	3
4+	3	2	5
5+	4	1	5
6+	11	4	15

*Some patients had more than one entity

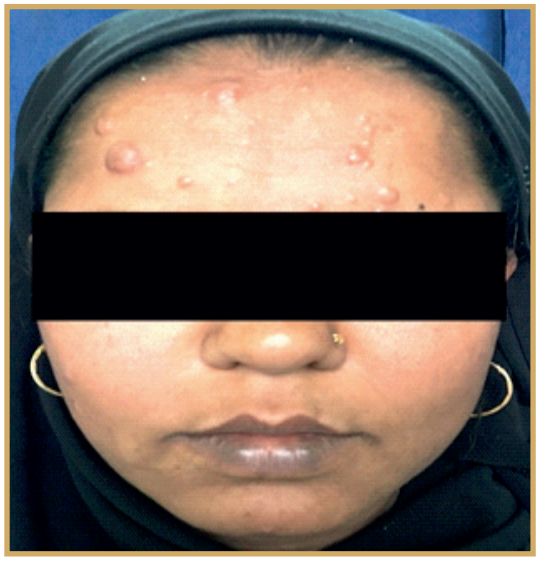

Fig. 1 : Multiple well defined discrete skin-colored subcutaneous nodules over forehead

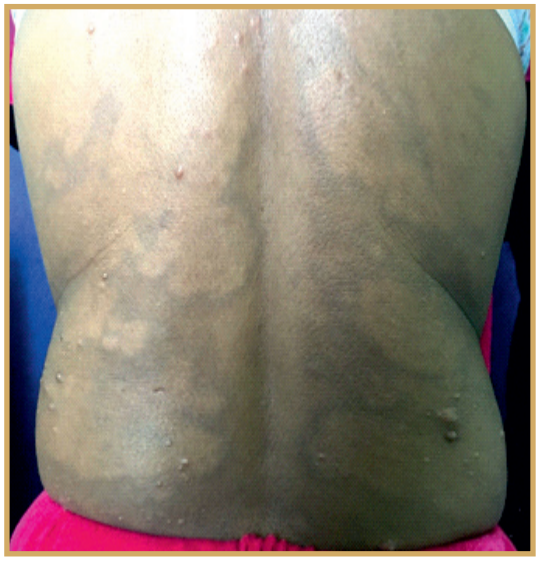

Fig. 2 : Multiple discrete well defined hypo pigmented patches and skin-colored nodules over trunk

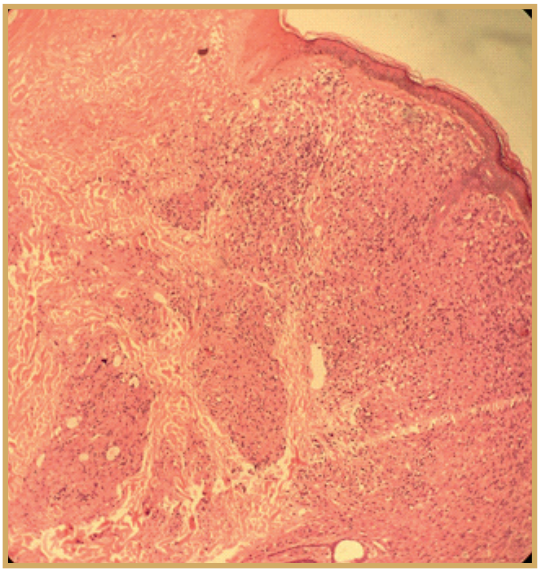

Fig. 3 : H&E-stained histopathological section on 10 X magnification shows epidermal atrophy, flattening of rete ridges, conspicuous grenz zone, and perivascular and perifollicular infiltrate of spindle shape histiocytes.

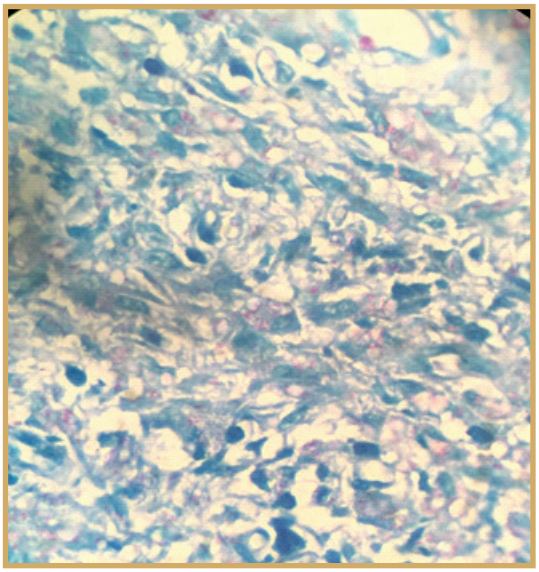

Fig. 4 : Fite-Faraco stain of tissue section on 100 X magnification shows numerous red colored acid-fast bacilli.

Most cases responded well to multibacillary drug therapy (MDT) of 1 year. Three patients had to be given an extended therapy for 2 years due to inadequate response.

Discussion

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 (so conspicuous in ordinary leproma) (Bhat et al 2015). Clinically it is characterized by multiple discrete shiny, smooth, painless, firm, skin colored to yellow brown, cutaneous, and, or subcutaneous nodules, papules, and plaques, on apparently normal skin, primarily affecting the back, buttocks, face and extremities. This type usually occurs in patients due to irregular or inadequate therapy, resistant strains (primary resistance to dapsone) or dapsone monotherapy (Wade 1963, Sehgal & Srivastava 1987). The disease has also been reported to arise de novo without any prior history of any anti leprosy treatment (Bhat et al 2015, Dimri et al 2012, Pandey et al 2015).

Histopathology is unique showing epidermal atrophy due to dermal expansion by underlying leproma and acellular band (Grenz/Unna band) below the epidermis. Dermis consists of fusiform histiocytes in a whorled, criss-cross or storiform pattern. The histoid nodules expand rapidly forming pseudocapsules of compressed collagen at the periphery, often associated with central liquefaction necrosis (Manoharan et al 2008). The histiocytes have numerous acid-fast bacilli arranged in parallel bundles along their long axis with or without globus formation (Sehgal et al 1987). These bacilli are usually well-preserved, solid uniformly staining long rods with tapering ends, distinctly longer than ordinary lepra bacilli. So far, the correlation is concern as many of the studies have shown discordant results. Sehgal et al reported good correlation of histopathological findings in 44% cases (Sehgal et al 1985b). However, in our study the histopathological findings were matched in only 8 (28.5%) cases with their primary clinical diagnosis of histoid leprosy. Majority of the cases (71.5%) had discordant histopathological findings. It may be due to spectral instability of these cases.

In India, prevalence of histoid leprosy is estimated between 1.8% to 3.2% (Kalla et al 2000, Kaur et al 2009, Sehgal & Srivastava 1988). While the prevalence in our study was found to be 2.98%. Maximum number of patients belonged to 21-40 years age group as observed in other reports (Kalla et al 2000, Sehgal & Srivastava 1988). Male preponderance was seen in our series, M:F ratio being 2.9:1. This is comparable to the study of Kalla et al (2000) they reported a M:F ratio of 2:1 and lower to the ratio reported by Sehgal & Srivastava (1988) (8.2:1) and Kaur et al (2009) (5.7:1). Clinically, histoid lesions are characterized by painless, firm, discrete, smooth, and globular, skin colored to yellowish brown cutaneous and subcutaneous nodules and plaques appearing on otherwise normal-looking skin, ranging in size from 1.5 to 3.5 cm and are usually 3-50 in number. In our patients, most common morphological pattern was nodules/ subcutaneous nodules and majority of them had 25-50 lesions. The lesions are usually located on the face, back, buttocks and extremities and over bony prominences, especially around the elbows and knees. In our study, upper extremities were the commonest site followed by buttocks and thighs. In accordance to other studies, ulnar nerve was the commonest nerve affected nerve in our patients (Kalla et al 2000, Kaur et al 2009, Sehgal & Srivastava 1988).

Reactions are considered uncommon in histoid leprosy. There are very few reported

cases of ENL developing in patients with histoid leprosy (Kaur et al 1993, Kumar et al 1997, Sehgal et al 1985a, Vasavi & Reddy 2012). In our study, 5 patients (17.9%) developed type 2 reaction, which is higher than the observations of Sehgal and Srivastav (1988) (1/23, 4.3%) and Kalla et al (2000) (2/25, 8%). Whereas, in the study by Kaur et al (2009), 40% (16/40) case experienced ENL. The author hypothesized that ENL reactions are not common in established histoid disease, although they can be a commonly observed phenomenon in each patient during transition to manifest histoid, similarly higher incidence of ENL in our patients might have been because of transitional state in majority of them.

De novo histoid leprosy is considered in patients, who directly present with asymptomatic papulo-nodular eruptions without other sign and symptoms of leprosy and can't be classified according to prevalent classification system of WHO and Ridley Jopling and had no past history of leprosy. It is difficult in diagnosis as it may mimic lepromatous leprosy, neurofibroma and dermatofibroma. None of the patients in our study had history of taking any anti-leprosy treatment, which is comparable to observations of Kaur et al (2009) (3/40, 7.5%). De novo development of histoid lesions without any evidence of other lesions of the disease, were seen in 8 cases (28.6%). It is considered that histoid leprosy occurs in patients with LL who relapse after receiving inadequate treatment or dapsone monotherapy. However, in our study none of the histoid leprosy case had been treated in past for leprosy. It may be due to increase health awareness and easily available health care facilities helps patients in early recognition and treatment. On other hand it may be a distinct entity in the leprosy spectrum or may be because of distinct variant of lepra bacilli or may have developed due to downgrading of BL/LL lesions. All the patients were treated with 1 year course of MDT MB except 3 cases; they were given 2 years extended MDT MB.

Conclusion

In conclusion, histoid leprosy may occur de novo without any evidence of lesions of other presentations of the disease, or history of pervious inadequate or irregular treatment or dapsone monotherapy. As per the criteria laid, the leprosy has been eliminated in India; the prevalence of histoid leprosy remains alarming. The new cases are still coming with varied morphological presentation, without any prior inadequate treatment. Hence, these patients form a potential reservoir of infection due to their high bacillary load. As these cases continue to occur in the 'post elimination era', prompt diagnosis and treatment has become essential to decrease the chances of transmission to general population. We advocate that histopathological examination should be done in all the cases for prompt and accurate diagnosis, many of times these cases may be misdiagnosed as their lesions may mimic other disorders. The morphologically the lepra bacilli in histoid leprosy is slightly different than usual cases hence genomic study of this bacilli should be done.

Limitations

As it is a retrospective study some data regarding history of contact with diagnosed case of leprosy was not available. Further, drug resistance/ sensitivity testing for *Mycobacterium leprae* is not available in our institution to obtain any data about presence of drug resistance in such cases. The facilities for genomic/genetic analysis of lepra bacilli were not available at our center so it could not be done. Lastly, the percentages / proportions may not reflect true picture at population level.

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