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Original Research Article

Correlation of Clinico-Histopathological and Dermoscopic Diagnosis of Leprosy Patients

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Abstract:

Background: Mycobacterium leprae causes a chronic, infectious illness known as leprosy. Histological observations as well as peripheral slit-skin smear staining confirm the clinical diagnosis. This granulomatous disease can be diagnosed and patients can be classified based on their immunological along with clinical response using dermoscopy. This study was conducted to determine the connection among clinico-histopathological and dermoscopic diagnoses of leprosy patients, as well as to assess the significance of dermoscopy in the diagnosis of leprosy.

Method: Seventy leprosy patients participated in the investigation. A comprehensive history, complete general physical as well as local examination, skin biopsy, and dermatoscopy were performed. There was a correlation between its findings with clinical and histopathological observations.

Results: The incidence is highest among those aged 21 to 40 (51.4%), with a male preponderance of 60%. The average duration of illness for the plurality of patients (45.7%) was less than six months. The most prevalent complaint was patches of hypopigmented epidermis. Clinically, there were more multibacillary cases (51.4%). Histopathologically, the higher numbers of patients were Lepromatous (37.1%) and Tuberculoid type (25.7%). Maximum Clinico-histopathological correlation was seen between Multibacillary Leprosy and LL type (75.76%) and between Pauci-bacillary Leprosy and TT type (54.05%). Maximum, Dermatoscopic-histopathological correlation was found between Lepromatous Pole and LL type (72.22%) and between Tuberculoid Pole and TT type (52.94%). Also, highly significant correlation was seen between clinical and Dermatoscopic diagnosis.

Conclusion: Dermoscopy is unquestionably a useful diagnostic instrument for leprosy and lepra reactions. Although dermoscopy alone may not be able to diagnose atypical leprosy lesions, dermoscopy as a diagnostic tool has enormous potential for the early detection of leprosy.

Keywords: Leprosy; Mycobacterium leprae; Dermoscopy; Histopathological; Multibacillary; Lepromatous; Tuberculoid.

Introduction

Leprosy, also referred to as Hansen's disease, is believed to be one of the earliest human diseases. In spite of our nation's January 2006 declaration of leprosy eradication, the disease is still endemic in numerous states. India is responsible for 1,33,717 (58.7%) of the estimated 2.27.849 new cases detected globally in 2009 [1]. According to the Ridley–Jopling classification, depending upon the clinical, histological, along with immunological response of the patient, it is classified into a spectrum of clinical manifestations [2]. Leprosy can be diagnosed by a variety of methods, including an extensive clinical evaluation of lesions on the skin and the peripheral nerves, evidence of the Acid-Fast Bacilli (AFB) within slit skin smears by Ziehl-Nielsen staining, Histopathological subsection, evidence of bacilli by modified Fite-Faraco procedure, and FNAC of nerves [3]. Even though the clinical diagnosis is predicated on characteristic hypopigmented areas with sensory loss, there are wide variations in the clinical and histopathological analysis of such hypopigmented skin lesions. Type I lepra reaction is a type IV hypersensitivity response characterised by neuritis

and inflammation of the preexisting cutaneous regions. Type II lepra reaction, on the other hand, is a type III hypersensitivity response that manifests as delicate erythematous evanescent nodules in addition to systemic symptoms. Anti-leprosy medication, specifically clofazimine, has dermatological side effects and induces widespread hyperpigmentation of the skin [4].

Dermoscopy has recently become an important noninvasive diagnostic tool for granulomatous diseases. This technique provides the dermatologist with additional information at a submacroscopic level that may aid in distinguishing between multiple cutaneous ailments that are difficult to distinguish with the unaided eye. In addition to thorough clinical information and a bacilloscopic examination, therefore, skin biopsies play an integral part in the diagnosis of leprosy. In addition, histopathological examination allows us to determine the immunological condition of the patient, allowing us to predict the response to treatment [5]. The purpose of this investigation was to highlight the numerous dermoscopic findings in leprosy patients. Clinical and histological outcomes were eventually correlated with the findings. There are correlations between the clinical, histopathological, and dermoscopic diagnoses of leprosy patients, and the purpose of this study is to evaluate the significance of dermoscopy in the diagnosis of leprosy.

Materials and Methods

This cross-sectional study was carried out at the outpatient unit of the Department of Dermatology in a tertiary hospital in Maharashtra from October 2019 to September 2020 with approval from the Institutional Ethical Committee and written informed consent from each participant. A total of 70 leprosy patients from every age group and both sexes who had not received anti-leprosy medications prior to visiting the OPD were selected at random and enrolled in the study. Excluded from this research were patients who had previously received MDT, those unwilling to provide informed consent, and expectant women. In accordance with the standard protocol, a detailed patient history and a comprehensive general as well as local examination were conducted on each patient. Investigations and a Slit-skin smear were performed on every patient. Consenting patients underwent skin biopsies for histopathological analysis in every case. All clinically diagnosed cases of leprosy yielded skin biopsies that were stained with Haematoxylin and Eosin as well as Modified Fite's staining techniques. Examining sections stained with Modified Fite's stain for Acid-Fast Bacilli. Based on the Ridley and Jopling Scale [2], histopathological findings were classified as Polar Tuberculoid (TT), Borderline Tuberculoid (BT), Mid-Borderline (BB), Borderline Lepromatous (BL), and Polar Lepromatous (LL).

A handheld ILLUCO dermatoscope IDS - 1100 along with Nikon 3400DSLR camera was used for recording dermoscopic images. Both polarized and nonpolarized modes were used for recording the dermoscopic findings and ultrasound gel was used as the interface. In particular, polarized light non-contact dermoscopy was usually preferred over conventional non-polarized light contact dermoscopy as the latter may reduce the vessels (due to pressure) and/or scaling (when using a liquid interface) visibility, even though some clues are better seen with nonpolarized light devices (i.e., more superficial findings, such as scaling and absence of hair follicle–like structures).

Statistical Analysis

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi square test, Fisher Exact tests were used as test of significance for qualitative data continuous data was represented as mean and standard deviation. Paired t test was used as test of significance to identify the mean difference between two quantitative variables for comparison.

Results

The research included 70 leprosy patients of both genders and of all ages. The higher incidence in the age group of 21-40 years (51.4%) with male predominance (60%). Mean age of the patients was 38.94±15.23 years, ranged from 10 to 75 years.

Most of the patients were belonging to Hindu community (94.3%), graduates (30%), unskilled workers (28.6%) and more than 2/3rd of the patients (77.1%) were married as shown in table 1.

Table 1: Socio-Demographic profile of the patients

Socio-Demographic data		Frequency	Percentage
Age Group (Years)	≤20	07	10.0
	21 to 40	36	51.4
	41 to 60	18	25.7
	>61	09	12.9
Sex	Male	42	60.0
	Female	28	40.0
Religion	Hindu	66	94.3

	Muslim	03	4.3
	Christian	01	1.4
Education	Primary	12	17.1
	Secondary	16	22.9
	Highschool	14	20.0
	Graduate	21	30.0
	Postgraduate	07	10.0
Occupation	Housewife	16	22.9
	Student	15	21.4
	Unskilled	20	28.6
	Semi-skilled	08	11.5
	Skilled	05	7.2
	Professional	06	8.6
Marital Status	Married	54	77.1
	Unmarried	16	22.9

Only 7 (10%) patients had history of contact with case of leprosy. 48.57% had only patches and 51.43% patients had patches with visible impairment. 45.7% had duration of symptoms since ≤ 6 months and 23 (32.9%) had duration of symptoms from 6 months to 1 year. Mean duration of symptoms was 10.36 ±9.93 months. Out of total 70 patients, 13 (18.6%) had 1 patch, 20 (28.6%) had 2 to 4 patches and 37 (52.8%) patients had ≥ 5 patches. At the time of clinical examination, 4 (5.7%) were having Type – I reaction & 11 (15.7%) were having Type - II reactions. Almost half patients, 51.4% were diagnosed to have Multi-bacillary Leprosy and 48.6% patients were diagnosed to have Pauci-bacillary Leprosy, (Table 2).

Table 2: Clinical profile of the patients

Clinical profile		**Frequency**	**Percentage**
Contact History	Yes	7	10.0
	No	63	90.0
Presenting Symptoms	Patch	34	48.57
	Patch, Visible Impairment	36	51.43
Duration of Symptoms	≤ 6 Months	32	45.7
	6 Months to 1 Year	23	32.9
	> 1 Year	15	21.4
Number of Patches	1	13	18.6
	2 to 4	20	28.6
	≥ 5	37	52.8
Lepra Reactions	Type 1	04	5.7
	Type 2	11	15.7
Clinical Diagnosis	Multi bacillary	36	51.4
	Pauci-bacillary	34	48.6

After performing Dermoscopy, it was found that 36 (51.4%) patients had findings suggestive of Lepromatous Pole and 34 (48.6%) had findings suggestive of Tuberculoid Pole. After performing Histopathology, 26 (37.1%) patients found to have lepromatous leprosy (LL) followed by 18 (25.7%) had tuberculoid (TT) leprosy and 16 (22.9%) had borderline tuberculoid (BT) Leprosy, (Table 3).

Table 3: Dermoscopic and Histo-Pathological Profile

Dermoscopic Profile		**Frequency**	**Percentage**
Dermoscopic Diagnosis	Lepromatous Pole	36	51.4
	Tuberculoid Pole	34	48.6
Histopathological Diagnosis	LL	26	37.1
	BL	9	12.9
	BB	1	1.4
	BT	16	22.9
	TT	18	25.7

From the table 4, it was found that out of 33 case of Multi-bacillary Leprosy (Clinically), 75.76% cases were LL, 21.21% cases were BL and only 1 case was diagnosed as BB (Histologically). Out of 37 case of Pauci-bacillary Leprosy (Clinically), 54.05% cases were TT, and 45.95% cases were BT (Histologically). Maximum correlation was found between Multi-bacillary Leprosy and LL type (75.76%) and between Pauci-bacillary Leprosy and TT type (54.05%). Highly significant correlation

was seen between clinical diagnosis and histopathological diagnosis. (p value <0.05).

Table 4: Clinico-Histopathological correlation of Leprosy

Histopathological Diagnosis	Clinical Diagnosis				Total	
	Multi-bacillary		Pauci-bacillary			
TT	0	0%	20	54.05%	20	28.57%
BT	0	0%	17	45.95%	17	24.29%
BB	1	3.03%	0	0%	1	1.43%
BL	7	21.21%	0	0%	7	10.0%
LL	25	75.76%	0	0%	25	35.71%
Total	33	100%	37	100%	70	100%

From the table 5, it was found that out of 36 cases of Lepromatous Pole on dermatoscopy, 29(80.56%) cases were found to be multi-bacillary, based on clinical diagnosis and out of34 case of Tuberculoid Pole on dermatoscopy, 30 (88.24%) cases were found to be pauci-bacillary, based on clinical diagnosis. Highly significant correlation was seen between clinical diagnosis and Dermatoscopic diagnosis, (p value <0.05).

Table 5: Clinico-Dermatoscopic correlation of Leprosy

Dermatoscopic Diagnosis	Clinical Diagnosis		Total
	Multi-bacillary	Pauci-bacillary	
Lepromatous Pole	29 (80.56%)	7 (19.44%)	36 (100%)
Tuberculoid Pole	4 (11.76%)	30 (88.24%)	34 (100%)
Total	33 (47.14%)	37 (52.86%)	70 (100%)

Out of 36 cases of Lepromatous Pole on dermatoscopy, 72.22% were LL and 25% were BL and only 1 case was BB (based on histopathology). Out of 34 cases of Tuberculoid Pole on dermatoscopy, 52.94% were TT and 47.06% were found to be BT type of Leprosy, based on histopathology. Maximum correlation was found between Lepromatous Pole and LL type (72.22%) and between Tuberculoid Pole and TT type (52.94%), (Table 6).

Table 6: Dermatoscopic-Histopathological correlation of Leprosy

Dermatoscopic Diagnosis	Histopathological Diagnosis				
	TT	BT	BB	BL	LL
Lepromatous Pole	0 (0%)	0 (0%)	1(2.78%)	9 (25%)	26 (72.22%)
Tuberculoid Pole	18(52.94%)	16(47.06%)	0 (0%)	0 (0%)	0 (0%)
Total	18(25.71%)	16(22.86%)	1(1.43%)	9(12.86%)	26(37.14%)

Histopathology Findings

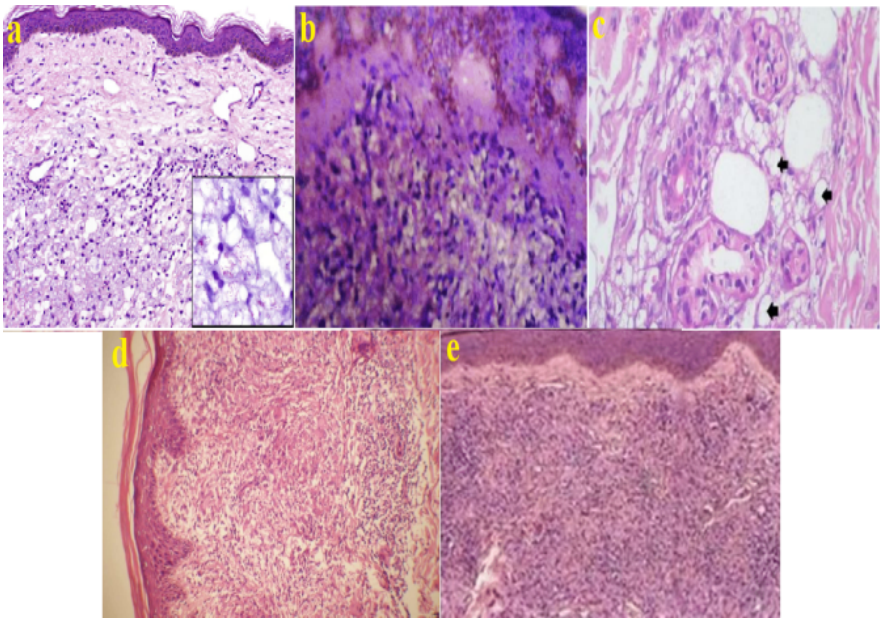

Figure 1: Histopathological findings of- a) Lepromatous Leprosy (LL); b) Borderline Lepromatous Leprosy (BL); c) Borderline Leprosy (BB); d) Borderline Tuberculoid Leprosy (BT); e) Tuberculoid Leprosy (TT)

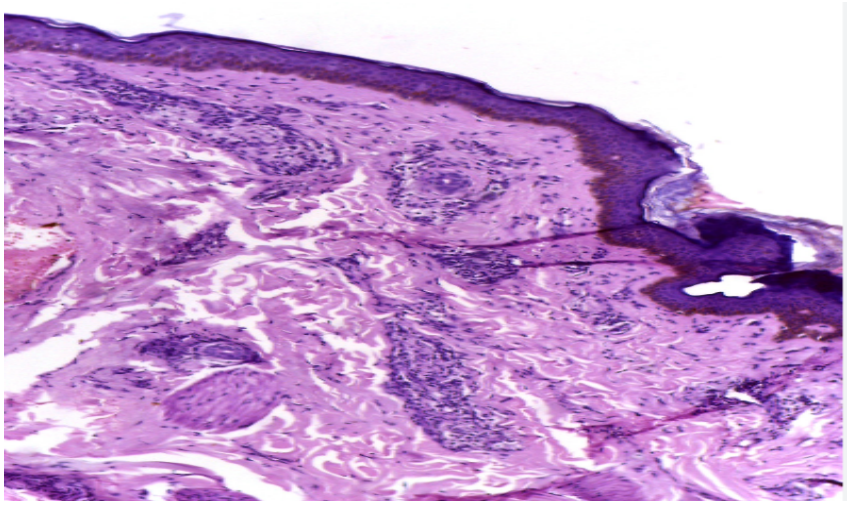

Figure 2: Histopathological findings of Type -2 Lepra Reaction

Dermoscopic Findings

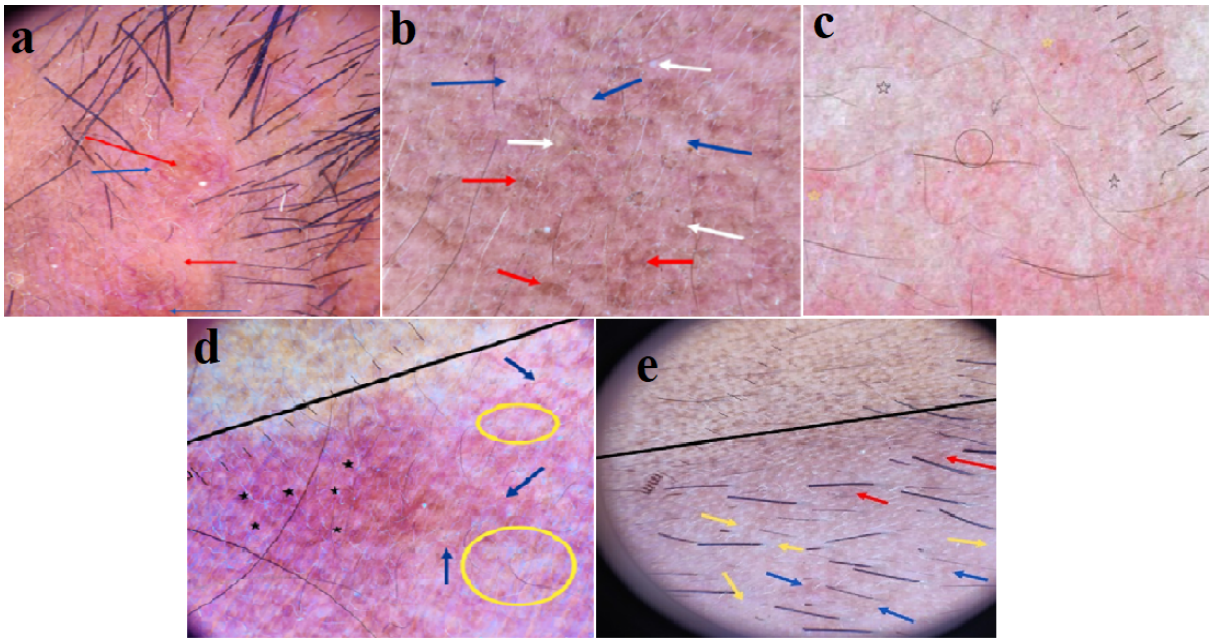

Figure 3: Dermoscopy of – a) Lepromatous Leprosy (LL); b) Borderline Lepromatous Leprosy (BL); c) Borderline Leprosy (BB); d) Borderline Tuberculoid Leprosy (BT) and e) Tuberculoid Leprosy (TT)

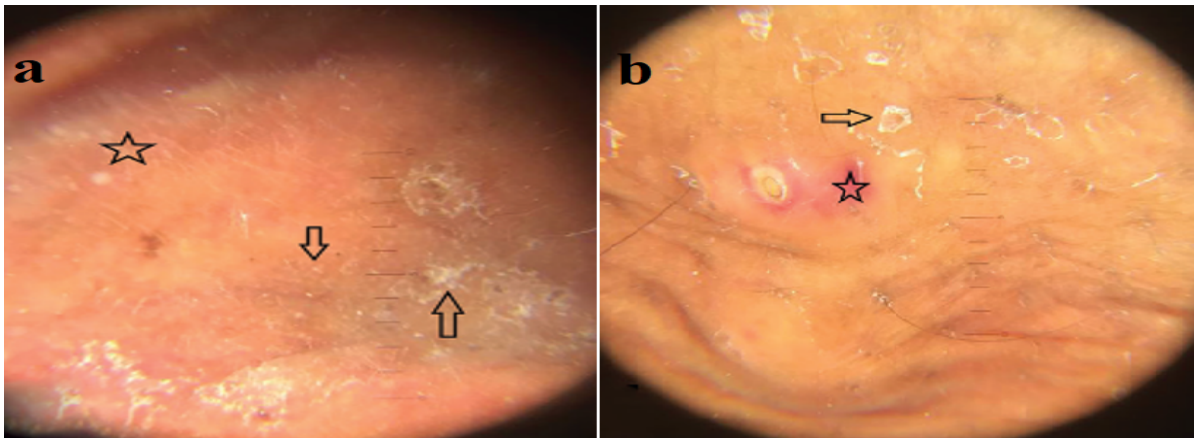

Figure 4: a) Dermoscopy of Type -1 Lepra Reaction; b) Dermoscopy of Type -2 Lepra Reaction

Discussion

In the present study, a total of 70 clinically diagnosed leprosy patients were examined and were subjected to clinical and histopathological examination as well as dermoscopic diagnosis, which included various aspects of the lesions, like number and site of lesions, type of disease. Almost half of the patients, 36 (51.4%) were from the age group of 21 to 40 years with mean age of patients was 38.94±15.23 years, ranged from 10 to 75 years. Consequently, the age distribution in the present analysis correlates well with other studies [7–9]. This age group is more susceptible to the disease due to their mobility along with increased contact opportunities. Males greatly outnumber females, 1.5:1 male to female ratio. Regarding sexuality, the results of the present investigation are comparable to those of the aforementioned studies [5-7]. The illness is more prevalent in men due to their outdoor occupations and greater susceptibility to infection. Maximum cases (28.6%) were unskilled workers followed by 16 (22.9%) were housewife and 15 (21.4%) were students. Similar observation was noted in the study by Ramanjanayalu et al [8], in that 41% of patients were unskilled workers.

Out of 70 patients, 34 (48.57%) had patches only and 36 (51.43%) patients had patches with visible impairment which is correlated well with study done by Mohan N et al [9] and Giridhar M et al [10]. In current study, 45.7% had duration of symptoms since ≤ 6 months and 23 (32.9%) had duration of symptoms from 6 months to 1 year. Mean duration of symptoms was 10.36 ±9.93 months, ranging from 1 month to 4 years. Thus, the majority of patients possessed the illness for less than one year. This is due to the earlier arrival of patients to the facility. Comparable findings were seen by Chopra A et al [5] and Ramanjanayalu et al [8].

At the time of clinical examination, out of total 70 patients, 15 (21.4%) cases showed Type-I and Type -II reactions. 4 (5.7%) were having Type – I reaction & 11 (15.7%) were having Type -II reactions. These findings are supported by Mohta A et al [7], Bhatia AS et al [11] and Shivamurthy V et al [12].

On clinical diagnosis, almost half patients, 36 (51.4%) were diagnosed to have Multi-bacillary Leprosy and 34 (48.6%) patients were diagnosed to have Pauci-bacillary Leprosy in contrast to case distribution seen in study by Shivamurthy V et al, majority of the patients were of PB type154 (77%) and the rest were of MB type 46 (23%) [12].

After performing Dermoscopy, it was found that 36 (51.4%) patients had findings suggestive of Lepromatous Pole and 34 (48.6%) had findings suggestive of Tuberculoid Pole. We have covered the entire spectrum of leprosy from tuberculoid pole to the lepromatous pole so that it becomes easy to differentiate it from other diseases having similar dermatoscopic finding. In a study by Chopra A et al, Tuberculoid poles of leprosy classically showed loss of hair and skin pigment and Lepromatous pole of leprosy on the other hand showed characteristic xerosis and white scaling [5].

After performing Histopathology, 26 (37.1%) patients found to have lepromatous leprosy (LL) followed by 18 (25.7%) had tuberculoid (TT) leprosy and 16 (22.9%) had borderline tuberculoid (BT) Leprosy. Only 9 (12.9%) patients found to have borderline lepromatous (BL), and 1 patient diagnosed to have mid-borderline (BB). Comparable findings were seen in a study by Shivaswamy KN et al [6], Mohta A et al [7] and Bhatia AS et al [11].

In the present study, maximum correlation was found between Multi-bacillary Leprosy and LL type (75.76%) and between Pauci-bacillary Leprosy and TT type (54.05%). Highly significant correlation was seen between clinical diagnosis and histopathological diagnosis. (p value <0.05) similar correlation was seen in study by Shivaswamy KN et al [6]. This is on par with the results of the study conducted by Moorthy BN et al [13], Sharma A et al [14] and Kalla G et al [15] in their study also showed a higher concordance with pole LL similar to our study. However, a high correlation was also noted with the other's pole TT, which was not seen in our study. Correlation is supposed to be better at poles LL and TT probably related to clinical and histological stability of the disease.

It was also observed in current study that the concordance was better in TT and LL rather than with BT or BL. This observation was also noted by Moorthy BN et al [13] and Sharma et al [14] in their studies. In mi borderline (BB) leprosy the correlation was low (3%). Even though it is on par with other studies like Moorthy BN et al [13] and Kar et al [16] such a low concordance could not be explained since we had only 1 case of BB.

Discordance between clinical and histopathological diagnosis can be explained on the basis that generally the diagnosis is made on clinical grounds alone, awaiting histopathological confirmation. It is possible that there is an individual observer bias also. Variation in different studies may be related to different criteria used to select the cases: choosing the biopsy site, age of the lesion, morphology of the lesion, immunological and treatment status of the patient, retrospective versus prospective studies.

The maximum correlation between Dermatoscopic and histopathology was found between Lepromatous Pole and LL type (72.22%) and between Tuberculoid Pole and TT type (52.94%). Dermoscopic findings correlated with histological

findings in most of the cases, adds it certainly as a handy tool in aiding the diagnosis of leprosy, lepra reactions, and course of therapy to facilitate a quick and definitive diagnosis of patients suffering from leprosy. Similar conclusions were seen in the study by Chopra A et al [5] and Ankad BS et al [17].

Lepromatous Leprosy (LL): Histopathology shows skin, epidermis is thin and atrophic. Upper dermis shows many granulomas composed of foamy macrophages. Juxta-epithelial layer shows granuloma free clear 5% ZN Stain strongly positive for lepra bacilli. Dermoscopy shows yellowish orange and structureless areas with yellow globules with signs of xerosis and shiny skin correlated with the histopathological feature of loss of skin appendages and epidermal atrophy. These findings are correlated with the previous studies [5, 7, 11].

Borderline Lepromatous Leprosy (BL): Histopathology shows skin with granuloma in dermis. These granulomas are composed of foamy macrophages and lymphocytes. Granulomas are separated from epidermis by a clear zone. 5% ZN stain shows scattered lepra bacilli. Dermoscopic features included white, shiny streaks with relative sparing of appendages. No branching vessel was present. Our dermatoscopic patterns of White shiny streaks with relative sparing of appendages in BL leprosy showing correlations with Histopathological findings Perifollicular hyperkeratosis and have been shown to be useful in diagnosis, based on the characteristic findings. Similar findings are reported in Mohta A et al [7] and Bhatia AS et al [11].

Borderline Leprosy (BB): Histopathology shows skin with adnexa and a few scattered granulomas. These granulomas are formed by admixture of foamy macrophages, lymphocytes and epithelial cells. These granulomas have peri- neural distribution. 5% ZN stain shows few lepra bacilli. Dermoscopic features included focal white areas, distorted pigment network, ill-defined focal red areas with decreased white dots of eccrine and follicular openings. No similar comparative studies were found in this context.

Borderline Tuberculoid Leprosy (BT): Histopathology shows skin with thin atrophic epidermis without skin appendages. Dermis shows multiple granulomas in areas reaching up to epidermis. These granulomas are composed of epithelial cells, lymphocytes, and ill formed Langerhans giant cells. Lepra-bacilli couldn't be demonstrated. Dermoscopy, yellowish orange, structureless areas surmounted by branching vessels with patchy loss of the pigment network and diminished hair follicles were observed which were correlated as loss of skin appendages on histopathology in BT leprosy. Similar findings are reported in Chopra A et al [5] and Bhatia AS et al [11].

Tuberculoid Leprosy (TT): Histopathology shows skin with multiple granulomas in dermis. The granulomas are reaching up to epidermis. They are composed of epithelial cells, Langerhans giant cells and lymphocytes. Nerve twigs are destructed. Lepra bacilli are not seen. On dermoscopic evaluation of the lesional edge, orangish yellow and white structureless areas were seen with peripheral erythema surmounted by telangiectatic vessels and moderate loss of hair follicles but relative sparing of vellus hair. Histopathological finding of multiple dermal granulomas was correlated with dermoscopic findings of white structureless areas. Similar findings are reported in Mohta A et al [7] and Bhatia AS et al [11].

Type -1 lepra Reaction: Histopathology shows a loose and disorganised granuloma in the upper and mid-dermis, dermal edema and variable cellular contents, namely, epithelioid cells, lymphocytes, giant cells, and macrophages. Dermatoscopy shows yellowish-orange areas with characteristic diffuse erythematous background with increased vascularity along with sparse hair follicles and scaling. The histopathological vascular changes due to lepra reaction could be correlated to a greater extent on dermoscopy in the backdrop of leprosy changes. Similar correlations were also seen in a study by Chopra A et al [5].

Type -2 lepra Reaction: Histopathology shows presence of neutrophils in the granuloma was a uniform feature seen in all lesions. Some sections showed leukocytoclasia and papillary dermal edema. Dermatoscopy shows dilated blood vessels, increased erythema and whitecharacteristic scalingover the lesion.Dermoscopy and histopathology were consistent indemonstrating branching blood vessels in the backgroundof hyperpigmentation. Such findings on histopathology were also seen in a study by Chopra A et al [5].

Limitations of study

Due to the limited sample size, a larger number of leprosy patients in various stages and time frames must be evaluated. To support and strengthen the results we have obtained, additional research on a larger population is required, as are studies that identify incidents of leprosy and lepra reactions in a timely manner and to distinguish diagnostic dilemma cases.

Conclusions

In conclusion, it can be stated that dermoscopy is a useful diagnostic instrument for leprosy and lepra reactions. Unique trends during the progression of leprosy would surely facilitate the rapid and accurate diagnosis of leprosy patients. Although

dermoscopy alone may not be able to diagnose atypical leprosy lesions, dermoscopy as a diagnostic tool has enormous potential for the early detection of leprosy.

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