Original Article

Correlation of Dermoscopic and Histopathologic Patterns in Leprosy – A Pilot Study

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Abstract

Background: Leprosy is a chronic granulomatous disease caused by Mycobacterium leprae. It is diagnosed based on clinical features and confirmed on the histological findings and peripheral slit-skin smear staining. Dermoscopy is a handy, easily accessible tool to diagnose this granulomatous disease and classify patients based on the immunological and clinical response. **Methods:** A single spot observational analysis was conducted in a tertiary hospital in North India. Patients attending the leprosy clinic and admitted patients for institutional therapy on the day of the study were enrolled in the cohort. The clinical and histological findings were correlated with the characteristic dermoscopy findings. A total of 50 patients were included in the study. All patents included in the study were on multidrug therapy and anti-lepra reaction drugs for a duration of less than 6 months. **Results:** The dermoscopy findings correlated with the clinical and histological findings. Tuberculoid poles of leprosy classically showed loss of hair and skin pigment along with absence of white dots as sweat glands in dermoscopy. Lack of blood vessel changes ruled out any lepra reaction. Lepromatous pole of leprosy on the other hand showed characteristic xerosis and white scaling on dermoscopy in the background of hypotrichosis and hypopigmentation. Leprosy reactions were characterized by blood vessel changes and arborizing blood vessels were characteristic in erythema nodosum leprosum, and a diffuse erythema was a clue toward diagnosing type I lepra reaction. Interestingly, clofazimine-induced pigmentation was picked up characteristically on dermoscopy as a "honey comb pattern". **Conclusion:** Dermoscopy is certainly a handy tool in aiding the diagnosis of leprosy, lepra reactions, and course of therapy. Characteristic patterns during the course of leprosy would certainly facilitate a quick and definitive diagnosis of patients suffering from leprosy. Also, patient drug compliance particularly to clofazimine can also be picked up objectively on dermoscopy.

Keywords: *Dermoscopy, histopathology, leprosy*

Introduction

Leprosy is a chronic granulomatous disease caused by Mycobacterium leprae. It is diagnosed based on the cardinal features of hypoaesthetic light-colored skin patches, thickened peripheral nerves, and presence of acid fast lepra bacilli in slit-skin smear samples. It is classified into a spectrum of clinical presentations as per the Ridley–Jopling classification based on the clinical, histological, and immunological response of the patient. Lepra reactions are acute inflammatory response during the chronic latent course of the disease. Type I lepra reaction is a type IV hypersensitivity response manifesting as neuritis and inflammation of the preexisting skin patches. Type II lepra reaction on the other hand is a type III hypersensitivity response which manifests as tender erythematous evanescent nodules along with systemic signs and symptoms. Antileprosy drugs particularly clofazimine also has dermatological manifestations and causes a diffuse hyperpigmentation of the skin.[1]

Dermoscopy of late has been a significant noninvasive tool to aid in the diagnosis of granulomatous diseases.[2] This technique provides additional information to the dermatologist at a submacroscopic level that may help differentiate between two or more cutaneous conditions that are hardly distinguishable with the naked eye. This study was performed with the aim to highlight the various dermoscopic findings in patients with leprosy. This is the first study of its kind considering the fact that dermoscopy can aid in differentiating and in diagnosing the various skin findings of

How to cite this article: Chopra A, Mitra D, Agarwal R, Saraswat N, Talukdar K, Solanki A. Correlation of dermoscopic and histopathologic patterns in leprosy – A pilot study. Indian Dermatol Online J 2019;10:663-8.

Received: August, 2018. **Accepted:** May, 2019.

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Access this article online

Website: www.idoj.in

DOI: 10.4103/idoj.IDOJ_297_18

Quick Response Code:

leprosy. The findings were subsequently correlated with the clinical and histological findings. The most important criteria to be considered when using dermoscopy in leprosy are as follows: (1) scaling patterns and atrophy, (2) the arrangement/morphology of vascular structures, (3) colors, (4) follicular, sweat gland and appendageal abnormalities, and (5) specific features (clues). Finally, dermoscopic findings must be interpreted within the overall clinical context of the patient (duration of illness, personal/family history, number, location, morphology and distribution of the lesions, histopathology, etc.) because only the combination between such data can really enhance the diagnostic accuracy in the field of diagnosing leprosy.

Methods

This was a pilot study and 10 patients were enrolled in the borderline tuberculoid (BT) pole of leprosy considering that this was the most common presentation of leprosy. A total of 10 patients were enrolled with lepromatous pole of leprosy and 10 patients each were enrolled with types I and II reactions of leprosy, respectively. Patients who had clofazimine-induced pigmentation were also included, just to complete the list of common dermoscopic findings in patients with leprosy. The study was conducted at a tertiary care hospital in India. Patient consent was obtained for clinical photographs, dermoscopy recording, and histopathological examination. All patients with signs of different poles of leprosy and lepra reaction were included in the study. All the patients were on multidrug therapy during the course of the study and the study did not alter the therapeutic intervention for the patients. A handheld Heine Delta® 20 T dermatoscope along with Nikon 3400 DSLR 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). A single spot observational analysis was conducted in a tertiary hospital in North India. Patients attending the leprosy clinic and admitted patients for institutional therapy on the day of the study were enrolled in the cohort. The clinical and histological findings were correlated with the characteristic dermoscopy findings. A total of 50 patients were included in the study. All patients included in the study were on multidrug therapy and antilepra reaction drugs for a duration of less than 6 months. The histopathological findings were reported by a pathologist and dermoscopic findings were reported by a dermatologist as a blinded procedure and the results were correlated.

Results

A total of 50 patients were enrolled in the study as a single point observational study. The average age of the patients was 28.4 years (21–64 years) and 32 (64%) patients were males and 18 (36%) were female. The mean duration of the diagnosed disease duration was 4 months (1–16 months). All skin lesions were biopsied using hematoxylin and eosin (H and E) stains. Dermoscopic patterns were observed by a blinded observer and then clinical correlation was drawn based on the clinical diagnosis and histopathological and dermoscopic findings.

BT leprosy had white areas on dermoscopy as the most consistent pattern in all the patients along with partial loss of hair follicles. Yellow globules were noted in 8 of 10 patients with BT leprosy. Absence of white dots in the form of absent sweat glands was the characteristic feature with the absence of blood vessel changes [Figures 1-3]. The white areas on dermoscopy indicate eccrine gland openings and the yellow globules are suggestive of sebaceous units in the absence of hair follicles. Histopathology of BT leprosy showed epidermal atrophy, loss of skin appendages, and well-defined dermal granulomas with absence of acid-fast bacilli on special stains. Both dermoscopy and histopathology correlated with the absence of skin appendages. Also, the absence of blood vessel changes on dermoscopy and simultaneous absence of increased vascularity on histopathology ruled out a lepra reaction. Thus, dermoscopy showed white areas along with sparse hair follicles and yellow globules which were correlated as loss of skin appendages on histopathology in BT leprosy.

Lepromatous leprosy [Figure 4] showed patchy xerosis and scaling over his right leg. Histopathology of lepromatous leprosy lesion [Figure 5] showed (H and E stain at 40× magnification) a thinned out epidermis and Grenz zone, followed by sheets of macrophages. The associated infiltrate is usually sparse and mainly lymphocytic. Figure 6 shows dermoscopic findings in lepromatous leprosy in the form of partial loss of hair follicles, dry xerotic skin, and white characteristic scaling. Dermoscopic findings of

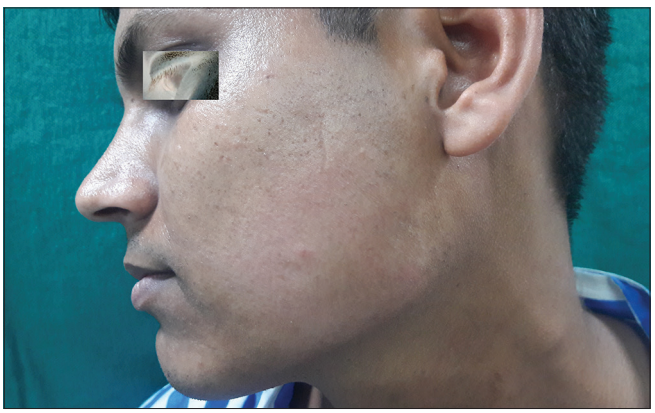

Figure 1: Borderline tuberculoid leprosy with a hypoaesthetic patch on the left side of face with a thickened greater auricular nerve

xerosis and shiny skin correlated with the histopathological feature of loss of skin appendages and epidermal atrophy. There are patchy areas of dry scaling and atrichia which is the striking feature of lepromatous leprosy.

Type 1 lepra reaction [Figure 7] shows a solitary large patch of leprosy on the trunk with signs in the form of erythema and induration. Type 1 lepra reaction lesion on histopathology (H and E stain at 40 × magnification) is shown in the form of loose and disorganized granuloma in the upper and mid-dermis, dermal edema, and variable cellular contents comprising epithelioid cells, lymphocytes, giant cells, and macrophages [Figure 8]. Figure 9 shows dermoscopic features of type I lepra reaction showing

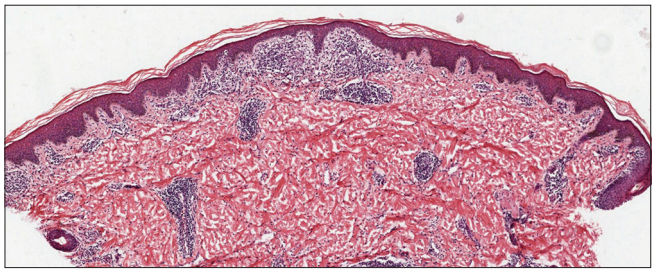

Figure 2: Borderline tuberculoid lesion showing granulomatous reaction in the upper dermis consisting of some Langhans giant cells, macrophages in tight clusters, and few accompanying lymphocytes. The infiltrate is also seen along nerves, vessels, and arrectores pilorum (H&E 40X)

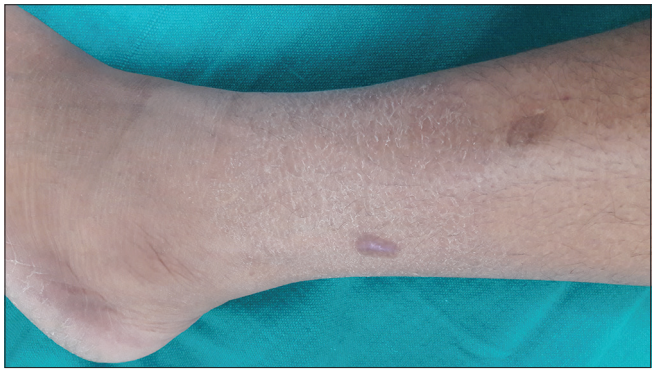

Figure 4: A Lepromatous leprosy showing xerosis and scaling along leg as part of glove and stocking distribution of lesions

Figure 6: Dermoscopic pattern in lepromatous leprosy showing partial loss of hair follicles, dry xerotic skin, and white characteristic scaling (Heine Delta® 20 T dermatoscope; 16×; polarizing)

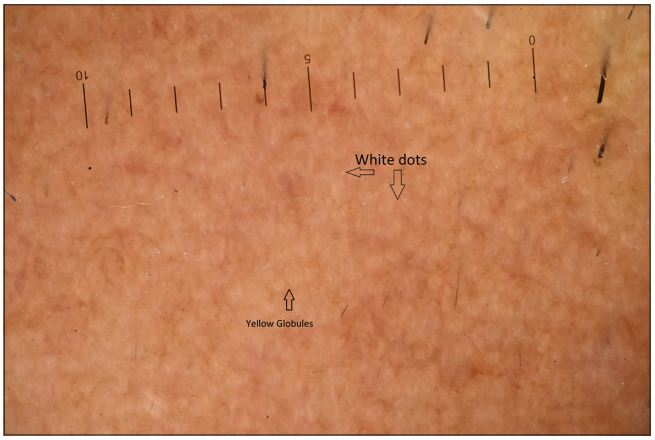

Figure 3: Dermoscopic pattern in borderline tuberculoid leprosy showing white areas with loss of hair follicles. In between yellow globules can be seen which was the hallmark apart from white areas demonstrating hypopigmentation. Absence of blood vessels rules out lepra reaction (Heine Delta® 20 T dermatoscope; 16×; polarizing)

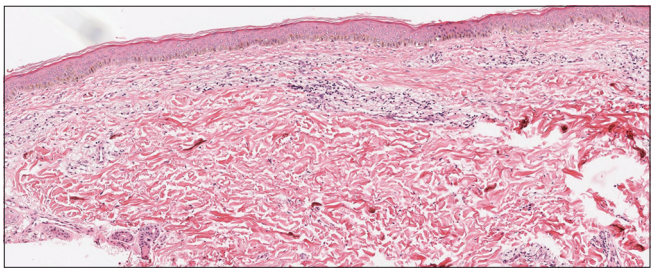

Figure 5: Lepromatous leprosy lesion showing a thinned out epidermis and Grenz zone, followed by sheets of macrophages. The associated infiltrate is usually sparse and mainly lymphocytic (H&E 40X)

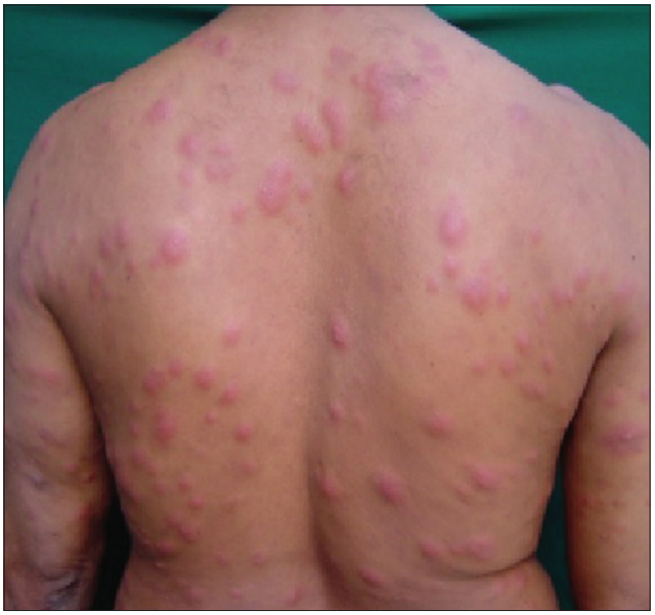

Figure 7: Multiple erythematous plaques on the back depicting type 1 lepra reaction

characteristic diffuse erythematous background and branching telangiectatic vessels 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.

The clinical, histological, and dermoscopic features of erthema nodosum leprosum or type II lepra reaction are shown in Figures 10-12. Figure 10 shows tender erythematous to hyperpigmented nodules along the forearm. The histopathology image shows dense neutrophilic infiltrate along the upper dermis along with perivascular lymphocytic infiltration, foamy histiocytes, and lobar panniculitis, and the dermoscopic images describe branching blood vessels in the background of hyperpigmentation and features of lepromatous leprosy. Dermoscopy and histopathology were consistent in demonstrating branching blood vessels in the background of hyperpigmentation.

All the cases of leprosy after 3 months of therapy comprising capsule clofazimine who had developed diffuse hyperpigmentation along face and upper trunk were also included in the study [Figure 13]. The histopathology of clofazimine-induced hyperpigmentation [Figure 14] (H and E stain at 40 × magnification) highlights a band of deposition of dark pigment along epidermis along with increased melanin deposition in the epidermis.

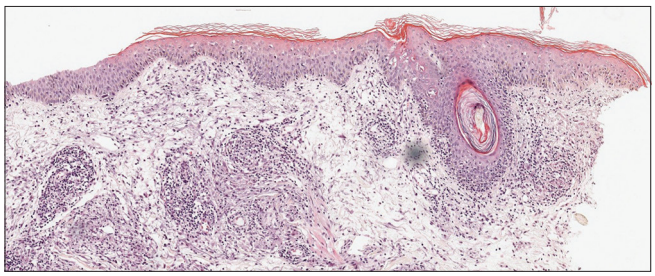

Figure 8: Type 1 lepra reaction lesion (H and E stain at 40 × magnification) showing a loose and disorganized granuloma in the upper and mid-dermis, dermal edema, and variable cellular contents comprising epithelioid cells, lymphocytes, giant cells, and macrophages (H&E 40X)

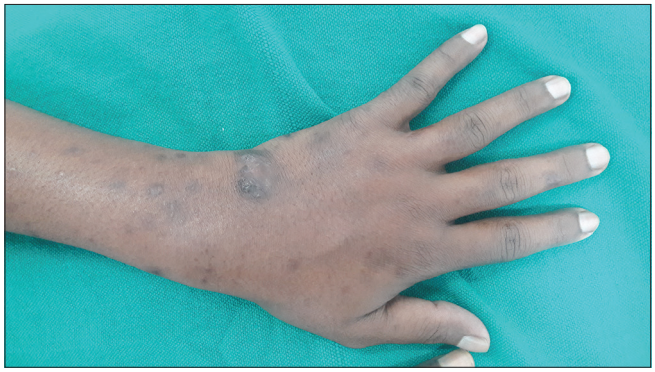

Figure 10: Erythema nodosum leprosum showing erythematous to hyperpigmented indurated nodules along left forearm and wrist

The dermoscopic features of clofazimine-induced hyperpigmentation showed characteristic honeycomb pattern with yellow to white globules interspersed along a black background as shown in Figure 15. There was a strong correlation in the histopathological finding of pigment deposition and the dermoscopic finding of yellow and white globules. Findings were also correlated from normal skin of the same patients which did not have dermoscopic features of pigment change and the skin biopsy also did not show any pigment deposition. Ideally, untreated patients with leprosy should have been recruited since MDT initiation (Multi drug therapy for Leprosy including Dapsone, Clofazimine and Rifampicin) can alter the morphology of the lesions (resolution of granuloma, reactions, and clofazamine-induced pigmentation). This study, however, wanted to examine patients without denying them any treatment, which would have been unethical. Also, leprosy being a chronic illness, 3–6 months of therapy is unlikely to cause any gross structural and histological changes in most patients.

Discussion

Dermoscopy helps in the diagnosis of infectious and inflammatory conditions by demonstrating a characteristic

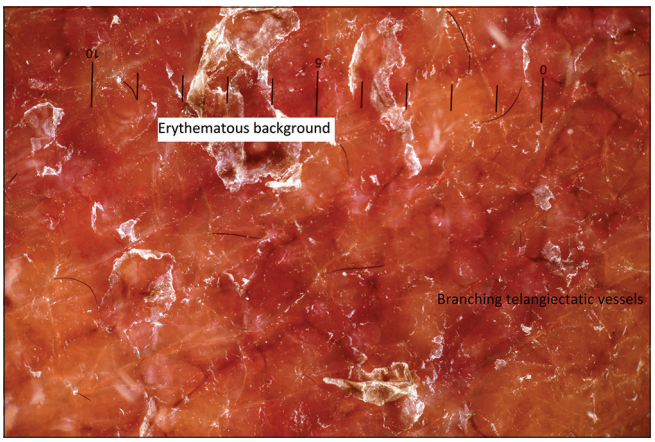

Figure 9: Dermoscopic features of type I lepra reaction showing characteristic diffuse erythematous background and branching telangiectatic vessels along with sparse hair follicles and scaling (Heine Delta®20 T dermatoscope; 16×; polarizing)

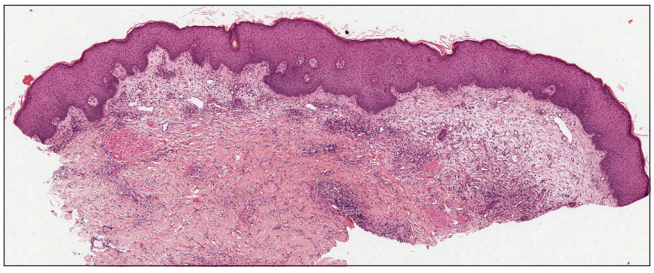

Figure 11: Type II lepra reaction lesion or erythema nodosum leprosum showing a dense infiltrate which extends into the subcutis, particularly around vasculature. In addition to epithelioid histiocytes with a large pink-bubbly cytoplasm, there is a dense neutrophilic infiltrate (H&E 40X)

Figure 12: Dermoscopic features of erythema nodosum leprosum showing ill-defined branching blood vessels in the background of characteristic hyperpigmentation and features of underlying lepromatous pole of leprosy (Heine Delta®20 T dermatoscope; 16×; polarizing)

pattern. The characteristic pattern of all granulomatous skin disorders on dermoscopy is presence of structureless orange to yellowish areas, which may be distributed in a diffuse or focal pattern. Leprosy is a granulomatous infectious disease with inflammatory reactions during its chronic course. In this study, Ridley–Jopling classification was used to classify leprosy histopathologically and clinically in all cases. Inflammatory diseases manifesting as granulomas and cutaneous infections exhibit useful patterns that can be diagnosed using dermoscopy. Sarcoidosis, lupus vulgaris, cutaneous tuberculosis, necrobiosis lipoidica, and granuloma annulare have been evaluated for dermoscopic patterns.[3] The characteristic findings on dermoscopy in any granulomatous dermatoses are related to the mass effect due to the presence of the compact and dense granulomatous infiltrate in the dermis and are better appreciated by applying slight pressure on the skin, due to the reduction in the skin erythema. Very few studies have evaluated the dermoscopic features in patients with leprosy. Dermoscopic patterns in 12 patients with BT leprosy have been shown to be useful in adding the diagnosis, based on the characteristic findings.[4] This study was conducted to assess the role of dermoscopy in aiding the clinical and histopathological findings in different common clinical presentations of leprosy. The absence of skin appendages is characteristic feature which aids in differentiating from other granulomatous conditions. Also, the characteristic yellowish to orange globules were not present uniformly in all the cases, and decreased white dots (absence of sweat duct openings) and branching blood vessels were additional differentiating features from other granulomatous diseases.

Of late, dermoscopy has been shown to be a useful tool in assisting the non-invasive diagnosis of several dermatological disorders.[5] Dermoscopy includes evaluating hair and scalp dermatoses in the form of trichoscopy,[6] nail or nailfold abnormalities as onychoscopy,[7] cutaneous

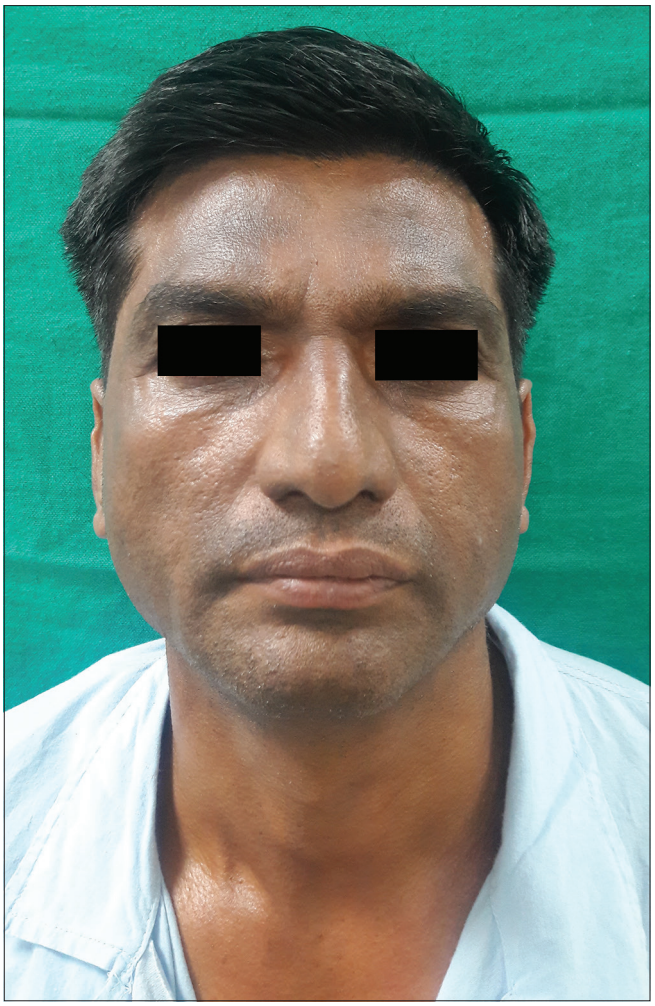

Figure 13: A case of leprosy after 6 months of therapy comprising capsule clofazimine: has developed diffuse hyperpigmentation along face and upper trunk

infections and infestations as entomodermoscopy,[8] and inflammatory dermatoses as inflammoscopy.[9]

Leprosy as a clinical spectrum includes hair and sweat gland abnormalities, pigment alterations as hypopigmentation as initial manifestation, erythematous during type I lepra reaction, dusky violaceous hue during erythema nodosum leprosum, and diffuse hyperpigmentation due to clofazimine. Leprosy also shows overlapping features of a granulomatous dermatoses and inflammatory changes during lepra reactions.

Dermoscopy could be a handy tool to delineate the area for skin biopsy as there is a histological correlation with histopathological findings. Also, dermoscopy could aid in deciding the pole of leprosy which is mainly a clinical diagnosis and histopathology substantiates the findings. Better correlation between histopathology and dermoscopy could add an additional tool in assessing patients with leprosy. Interestingly, clofazimine-induced pigmentation was picked up characteristically on dermoscopy as a "honey comb pattern" and this would help in confirming

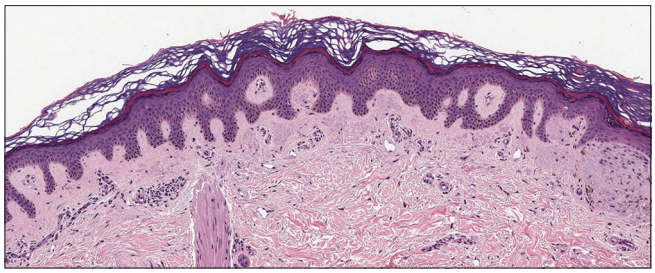

Figure 14: Histopathology of clofazimine-induced hyperpigmentation (H&E 40X) showing a band of deposition of dark pigment along epidermis with increased melanin deposition in the epidermis

patient compliance, duration of therapy, and response to multidrug therapy. Differential diagnosis of depigmented lesions like nevus depigmentosus and vitiligo could be differentiated as both the conditions will have normal skin texture and normal skin appendages without any xerosis or scaling. Leukotrichia may be appreciated in vitiligo.

White areas were noted in all lesions of leprosy not in reaction, which corresponds to a decreased number of melanocytes in the affected patches of leprosy. White areas were not described previously in granulomatous conditions, and this is understandably due to the presence of melanocytes, which can help us in differentiating it from other granulomatous infections. Lepra reactions have an erythematous hue and clofazimine induces a dark pigmented background.

Conclusion

Dermoscopic findings correlated with the clinical and histological findings in all the cases. This was a pilot study and further studies need to be conducted to diagnose cases of leprosy and lepra reactions well within time and to differentiate cases having a diagnostic dilemma. Dermoscopy is certainly a handy tool in aiding the diagnosis of leprosy, lepra reactions, and course of therapy. Characteristic patterns during the course of leprosy would certainly facilitate a quick and definitive diagnosis of patients suffering from leprosy.

Limitations

Considering this was a pilot study, more number of patients in different phases and timeline of leprosy need to be evaluated.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

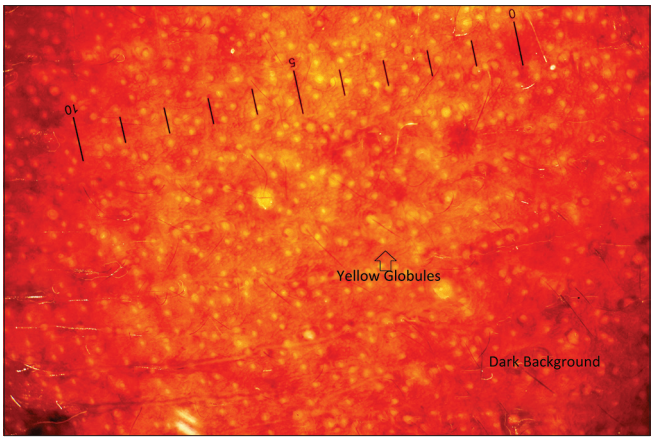

Figure 15: Dermoscopic features of clofazimine-induced hyperpigmentation showing characteristic honeycomb pattern with yellow to white globules interspersed along a dark to skin-colored background (Heine Delta®20 T dermatoscope; 16×; polarizing)

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Lockwood DNJ. Leprosy. In: Griffiths C, Baker J, Bleiker T, Chalmers R, Creamer D, editors. Rooks Textbook of Dermatology, vol. 1. 9th ed. Oxford: Wiley Blackwell; 2016. p. 28.1-10.
2. Lallas A, Giacomel J, Argenziano G, García-García B, González-Fernández D, Zalaudek I, *et al*. Dermoscopy in general dermatology: Practical tips for the clinician. Br J Dermatol 2014;170:514-26.
3. Micali G, Lacarrubba F. Possible applications of videodermatoscopy beyond pigmented lesions. Int J Dermatol 2003;42:430-3.
4. Ankad BS, Sakhare PS. Dermoscopy of borderline tuberculoid leprosy. Int J Dermatol 2018;57:74-6.
5. Errichetti E, Stinco G. Dermoscopy in general dermatology: A practical overview. Dermatol Ther 2016;6:471-507.
6. Miteva M, Tosti A. Hair and scalp dermatoscopy. J Am Acad Dermatol 2012;67:1040-8.
7. Lencastre A, Lamas A, Sá D, Tosti A. Onychoscopy. Clin Dermatol 2013;31:587-93.
8. Micali G, Lacarrubba F, Massimino D, Schwartz RA. Dermatoscopy: Alternative uses in daily clinical practice. J Am Acad Dermatol 2011;64:1135-46.
9. Errichetti E, Stinco G. The practical usefulness of dermoscopy in general dermatology. G Ital Dermatol Venereol 2015;150:533-46.