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Original Research Paper

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CAN DERMOSCOPY DIFFERENTIATE BETWEEN TUBERCULAR AND NON-TUBERCULAR GRANULOMATOUS DISEASES: A CASE-CONTROL STUDY

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ABSTRACT **Background:** Lupus vulgaris (LV) and tuberculosis verrucosa cutis (TBVC) are commonly presenting forms of cutaneous tuberculosis with clinical appearance mimicking other chronic granulomatous diseases. There is limited data on whether the dermoscopic features of LV and TBVC described in literature can help in differentiating it from them. Hence, this study was conducted to enumerate the dermoscopic features of LV and TBVC and compare with those of other non-tubercular granulomatous diseases. **Methods:** The study was a prospective case-control study. Dermoscopic features of LV and TBVC were compared with those of non-tubercular granulomatous diseases such as leprosy, granuloma annulare, sarcoidosis. Dermoscopic features were recorded as per international dermoscopic society parameters and those modified for skin of colour. **Results:** Both cases and controls showed similar findings of presence of scales, vessels and structureless areas. White structureless areas, linear branching vessels, dotted vessels, white and brown scales, follicular plugs, follicular red dots, yellow dots and globules were more common in cases than controls. Erythema and yellow structureless areas were more common in controls than in cases but all these differences were not statistically significant. Presence of yellow scales in cases was the only finding which was statistically significant. **Conclusions:** Dermoscopic findings of LV and TBVC are not helpful in differentiating it from other granulomatous diseases. In pigmented skin, white structureless areas are more common than yellow structureless areas in LV and TBVC.

KEYWORDS : dermoscopy, tuberculosis, granulomatous diseases, lupus vulgaris.

INTRODUCTION

Lupus vulgaris (LV) and tuberculosis verrucosa cutis (TBVC) are commonly presenting forms of cutaneous tuberculosis with clinical appearance mimicking other chronic granulomatous diseases like leprosy, sarcoidosis, cutaneous leishmaniasis, granuloma annulare and deep fungal infections. Other forms of cutaneous tuberculosis like scrofuloderma and tuberculids have different and distinct clinical morphology. Diagnosis of LV and TBVC is made by clinico-histopathological correlation, demonstration of the organism which is often difficult and response to trial of anti-tubercular therapy which can take weeks to show results.

Dermoscopy is a non-invasive, quick tool for assessment of cutaneous neoplasms like melanoma, basal cell carcinoma and pigmented nevi but its use has expanded to many more dermatological conditions. There is limited data on whether the dermoscopic features of LV and TBVC are specific and if it can help in differentiating it from other granulomatous diseases. Hence, this study was conducted to enumerate the dermoscopic features of LV and TBVC and compare with those of other non-tubercular granulomatous diseases.

MATERIALS AND METHODS

The study was a prospective case-control study conducted at a tertiary care centre over 12 months. Cases were defined as patients diagnosed clinically and on histopathology as LV or TBVC and responded to standard anti-tubercular therapy (ATT) in 5 weeks. Treated or on treatment cases of LV, TBVC, tuberculids, other types of cutaneous tuberculosis with different morphology, pregnant and lactating women, those with HIV were excluded. Controls were defined as patients diagnosed clinically and on histopathology as any other non-tubercular granulomatous disease such as leprosy, granuloma annulare, cutaneous leishmaniasis, sarcoidosis, necrobiosis lipoidica. Consecutive cases and controls presenting to the authors and giving informed consent were included. Detailed clinical evaluation, skin biopsy for histopathology, culture for *M.tuberculosis*, non-tubercular mycobacteria, fungal culture, mantoux test, chest radiograph and ultrasound abdomen hemogram, liver and kidney function tests, blood sugar (fasting), urine routine and microscopy were done in all. Culture and PCR for leishmania was done only in clinically suspected cases or where LD bodies were seen on histopathology. Clinically suspected cases of LV and TBVC were started on antitubercular treatment and re-evaluated at 5 weeks. If there was no improvement at 5 weeks, then the patient was re-evaluated for drug resistant TB or other diagnosis and removed from cases. Dermoscopy was done using a handheld dermoscope Dermlite™ DL4 (3Gen Inc., San Juan Capistrano, CA, USA) with 10× magnification attached to a Smartphone (iPhone 10, Apple Inc., Cupertino, CA, USA). Dermoscopic features of all plaques were recorded as per international dermoscopic society parameters and those modified for skin of colour.[1] The presentation of the categorical variables was done as number and percentage (%). The quantitative data were presented as means ± SD. The comparison of qualitative variables were analysed using the Chi-Square test or Fisher's exact test. Data entry was done in Microsoft EXCEL spreadsheet and the final analysis was done with Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 25.0. For statistical significance, p value<0.05 was considered statistically significant. Institutional ethics committee clearance was taken.

RESULTS

Demographic features

The demographic data of 20 cases and controls each is given in Table 1. In cases, 18 were diagnosed as LV and 2 as TBVC (Figure 1). Mantoux ranged from 11-34 mm (average: 21.69 ± 7.06 mm). Two patients had systemic symptoms, 5 had family history of tuberculosis, and 2 had past history of tuberculosis.

The controls included borderline tuberculoid (BT) in 6, borderline lepromatous (BL) in 2, lepromatous leprosy (LL) in 1, granuloma annulare in 8, and one each of sarcoidosis, chromoblastomycosis and cutaneous leishmaniasis. There was no significant difference between cases and controls with respect to age, sex, and duration of disease.

Dermoscopic features

Overall, the commonest findings in both cases and controls were structureless areas (white and yellow), linear vessels with branches and white scales. The dermoscopic features of cases and controls separately are shown in table 2. The commonest dermoscopic finding in cases were scales (90%), vessels (75%) followed by structureless areas (65%) (Figure 2). In contrast, the commonest dermoscopic findings in controls were structureless areas (65%), vessels (50%) and then scales (35%) (Figure 3). In cases, yellow, white and brown scales were observed while in controls, only white scales were seen. The difference in presence of yellow scales in cases and complete absence in controls was statistically significant. Diffuse distribution of scales was common in both.

Dotted, linear, linear vessels with branches were seen in both groups. The distribution of vessels was clustered, peripheral or uniform in both groups with no difference. In cases, white structureless areas (50%) were more common than yellow (15%), while yellow(35%) was more common than white in controls(30%).

DISCUSSION

The prevalence of cutaneous tuberculosis is between 1.5% and 3.5% of all tuberculosis cases and around 1.5% of all extrapulmonary tuberculosis cases.[2-4] It constitutes 0.1% – 3.5% of all dermatology out-patients.[2-4] The commonest forms of cutaneous tuberculosis are scrofuloderma and lupus vulgaris followed by tuberculosis verrucosa cutis.[5]

The diagnosis of LV and TBVC is challenging because of their paucibacillary nature. The most reliable method of confirming diagnosis is histopathology which has very variable sensitivity between 65.7-100%.[6,7] The sensitivity of other methods is inconsistent and low such as 10-13.8% for AFB smear [8,9], 0.0-53.12% for culture of skin biopsy in L-J medium [10,11] and 25-74% for PCR.[12,13] Molecular methods have not yielded consistent results.[5,9,13] Mantoux test and interferon gamma release assay test are also not confirmatory for the diagnosis of cutaneous tuberculosis.[1] A therapeutic trial of 5 weeks of antitubercular drugs is frequently used to confirm the diagnosis in difficult cases, but it takes a long time [14,15,16] highlighting the difficulties in managing LV and TBVC.

The dermoscopic features of different granulomatous diseases including LV and TBVC have been described but their role in confirmation of diagnosis of LV and TBVC has not been discussed.[17,18,22-25] Previous studies on Indian patients have reported orange-yellow structureless areas and linear vessels with or without branches, white and yellow scales to be consistent findings.[22-24] One study mentions yellow-white globules and pinkish red background seen in 100% cases.[23] Other notable features include patulous follicles, milia-like cysts, white streaks, black dots/globules, perilesional halo, red globules and bluish hue.[22-24.] Similar findings were observed in this study too, but there were few differences. It was observed that white structureless areas were more common than yellow structureless areas (66.7% vs 20%), linear vessels with branches was the commonest vascular finding (75%), and diffuse distribution of scales was a common finding. Interestingly, instead of orange-yellow areas, focal bright white structureless areas have been reported in 92.3% patients with lupus vulgaris in type V and VI skin phototype in a retrospective study on darker skin phototype, similar to our observation.[25] The diagnostic accuracy of few dermoscopic features is high such as yellowish white globules for granulomatous histopathology (94.7%), bluish hue for orthokeratosis (89.47%), pink-red background for dilated vessels (84.21), and white structureless areas for dermal fibrosis (84.21%).[23] Besides these, other dermoscopic findings do not have a good diagnostic accuracy on histopathology.[23] We explain the higher frequency of white structureless areas as compared to yellowish structureless areas probably because the lesions in our study had more atrophy and scarring. Also, some authors have suggested that pigmented skin might be more prone to sclerosis, however no such documentation was found.[25] We also suggest that just as apple-jelly nodules on diascopy are seen less commonly in pigmented skin than fairer skin, similarly yellow structureless areas might be less common too.

Previously, dermoscopic findings of other granulomatous diseases have been reported such as white areas, partial loss of hair follicles, yellow globules, yellowish-orange structureless areas surmounted with branching vessels in BT leprosy; loss of pigment network, focal areas of hyperpigmentation and white shiny streaks in BL; and partial loss of hair follicles, dry xerotic skin and white scaling, yellow globules and yellowish orange structureless areas in LL. [17,18] Interestingly, BT leprosy which clinically shows atrophy also showed white structureless areas as a consistent finding on dermoscopy.[17,26]

The specificity of dermoscopic findings to LV and TBVC has not been evaluated previously as controls were not taken. In our study, it was seen that on comparing with other granulomatous non-tubercular diseases, only yellow scales was statistically significant specific finding which helped to differentiate LV and TBVC from other non-tubercular granulomatous diseases. Yellow-orange or white structureless areas, yellow dots and globules, linear vessels with branching and scales, though are common findings in LV and TBVC, they do not help to differentiate it from other granulomatous diseases. Histopathology and response to ATT is still required for confirming the diagnosis.

The limited number of patients was a limitation of the study.

CONCLUSION

Dermoscopic findings of LV and TBVC are consistent with findings of granulomatous diseases, but none are helpful in differentiating it from other granulomatous diseases. Yellow scales are the only findings which were statistically significant. In pigmented skin, white structureless areas are more common than yellow structureless areas.

Figure legends:

Figure 1: Clinical variants of cutaneous tuberculosis seen in the study. Fig 1a: Lupus vulgaris. Figure 1b: Tuberculosis verrucosa cutis

Figure 2: Dermoscopic features of cutaneous tuberculosis. Fig 2a: Dermoscopy of lesion showing yellow structureless area (Dermlite 4, polarised mode, 10X). Fig 2b: Dermoscopy of lesion showing white structureless area (Dermlite 4, polarised mode, 10X). Fig 2c: Dermoscopy of lesion showing yellow globules (Dermlite 4, polarised mode, 10X). Fig 2d: Dermoscopy of lesion showing vessels with branches and white scales (Dermlite 4, polarised mode, 10X). Fig 2e: Dermoscopy of lesion showing yellow scales (Dermlite 4, polarised mode, 10X).

Figure 3: Clinical image and dermoscopy of BT hansen's. Fig 3a: Clinical image of BT hansen's showing a well-defined hypopigmented plaque on the arm. Fig 3b: Dermoscopy of BT hansen's showing yellow- white structureless areas (red arrow) with erythema (white arrow) (Dermlite 4, polarised mode, 10X) .

Tables

Table 1 : Demographic Profile of Cases and Controls

	Cases	Controls	p-value
Mean age (years)	29.85 ± 15.3	38.45 ± 23.21	P = 0.3426
Gender Male Female	8	9 11	P = 0.3483*

Duration of disease (months; Mean ± SD)	31.15 ± 35.17	17.25 ± 23.21	P = 0.1484*
Mode of onset Chronic Acute	 17 3	 16 4	P = 0.6812*
Site	Leg - 6 Arm- 4 Foot- 3 Hand-3 Buttock-2 Earlobe-1 Cheek-1	Face-6 Hand-5 Back-3 Arm-2 Foot- 2 Leg-2	P = 0.0804*

*chi-squared Test

Table 2: Comparison of Dermoscopic Features of Cases vs Controls

Dermoscopic features	Frequency in cases (n=20)	Frequency in controls (n=20)	Total N=40	p-value
Presence of vessels	15 (75%)	10 (50%)	25 (62.5%)	
Type of vessels				
Dotted	6 (30%)	2 (10%)	8 (20%)	0.388*
Linear	2 (10%)	4 (20%)	6 (15%)	0.192*
Glomerular vessels	1 (5%)	0 (0%)	1 (2.5%)	1*
Linear with branches	6 (30%)	4 (20%)	10 (25%)	1*
Distribution of vessels				
Clustered	3 (15%)	1 (5%)	4 (10%)	0.077
Peripheral	8 (40%)	2 (10%)	10 (25%)	
Uniform	3 (15%)	7 (35%)	10 (25%)	
Presence of scales	18 (90%)	7 (35%)	25 (62.5%)	
Colour of scales				
White	14 (70%)	7 (35%)	21(52.5%)	0.294*
Yellow	11 (55%)	0 (0%)	11 (27.5%)	0.008*
Brown	6 (30%)	0 (0%)	6 (15%)	0.137*
Distribution of scales				
Central	2 (10%)	1 (5%)	3 (7.5%)	0.288*
Diffuse	12 (60%)	5 (15%)	17 (42.5%)	
Patchy	4 (20%)	0 (0%)	4 (10%)	
Peripheral	0 (0%)	1 (5%)	1 (2.5%)	
Follicular findings	5 (25%)	1(5%)	6 (15%)	
Follicular plugs	3 (15%)	0 (0%)	3 (7.5%)	0.167*
Follicular red dots	2 (10%)	0 (0%)	2 (5%)	
Perifollicular scar	0 (0%)	1 (100%)	1 (2.5%)	
Other structures	15 (75%)	18 (90%)		
Erythema	4 (20%)	11 (55%)	15 (37.5%)	0.08*
Yellow structureless areas	3 (15%)	7 (35%)	10 (25%)	0.283*
White structureless areas	10 (50%)	6 (30%)	16 (4%)	0.056‡
Specific clues				
Yellow dots and globules	7 (35%)	3(15%)	10 (25%)	0.283 *

* Fisher's Exact Test

Keywords: dermoscopy, tuberculosis, granulomatous diseases, lupus vulgaris.

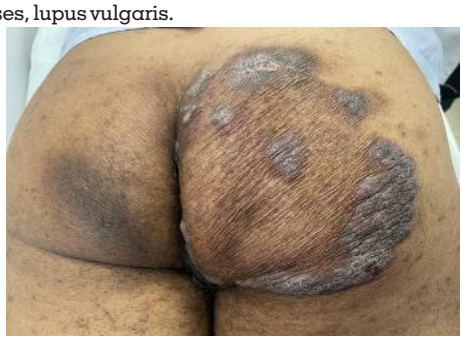

Fig 1 a

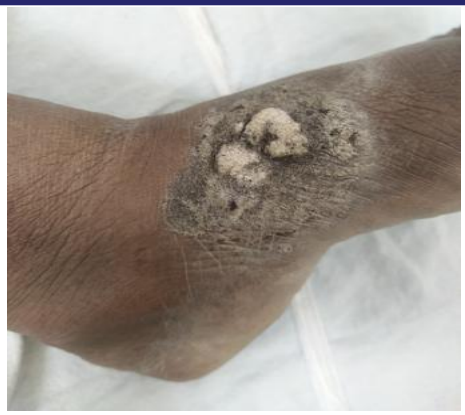

Fig 1b

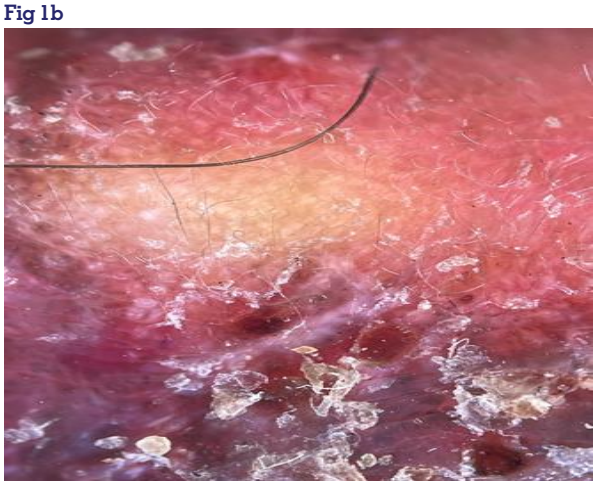

Fig 2a

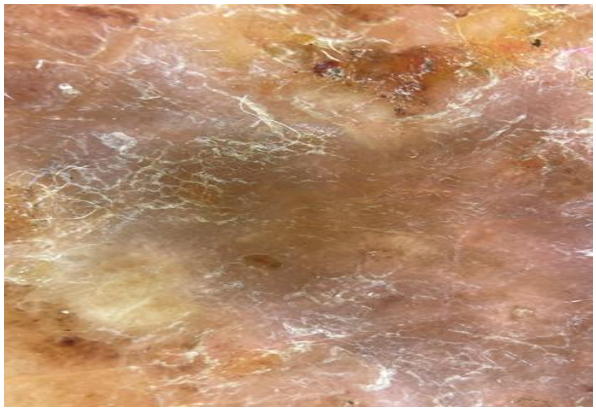

Fig 2b

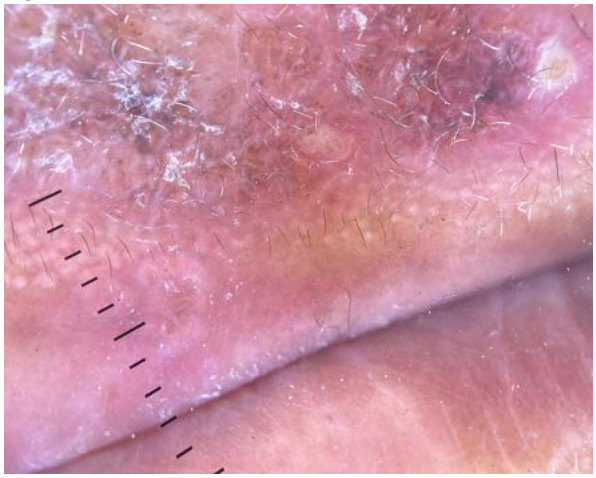

Fig 2c

Fig 2d

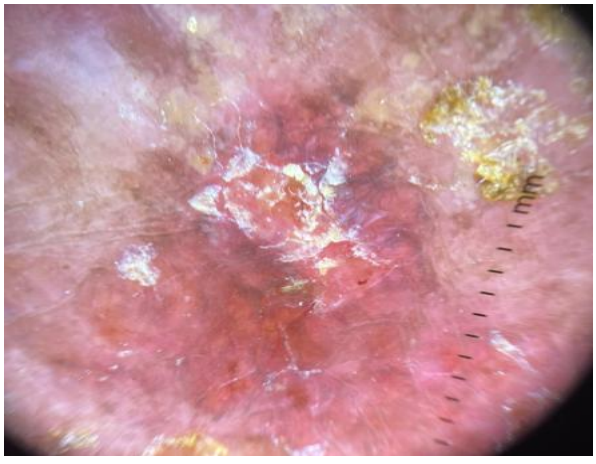

Fig 2 e

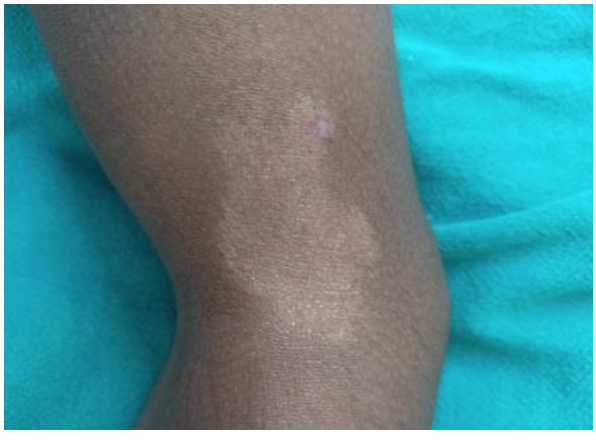

Fig 3 a

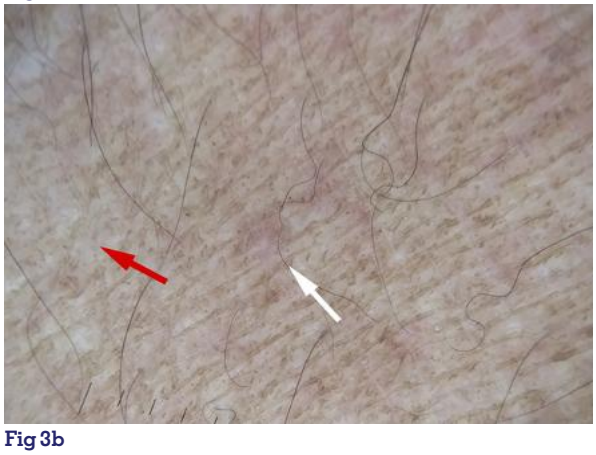

Fig 3b

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