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Case Series

Blaschko-linear manifestations in polygenic inflammatory disorders

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ABSTRACT

This study delves into the intricate realm of Blaschko-linear dermatoses, initially described by Alfred Blaschko in 1901. The Blaschko lines forms V-shapes on the upper back, S-shapes on the abdomen, inverted U-shapes from the breast area to the upper arm, and perpendicular lines on the extremities. Blaschko's lines are attributed to the widely accepted theory of embryonic mosaicism in epidermal cells.

In this study, the Blaschko-linear manifestations of polygenic inflammatory disorders (BLMMPD) in Indian population is analyzed. Despite various studies on individual linear dermatoses, few Indian studies have explored the correlation between different Blaschko-linear dermatoses and their dermoscopic and histopathological features.

The study, conducted from July 2023 to December 2023, includes 28 cases of Blaschko-linear dermatosis of diverse spectrum. Those with dermatosis along blood vessels, lymphatics, nerve trunk and following koebnerization were excluded. The demographic details, clinical manifestations and dermoscopic-histopathological characteristics were documented. In our case series, Lichen striatus and Linear Lichen planus (LP) were noted to be the most common among linear dermatosis, with a notable female predominance (Male: female ratio 0.75:1) and unilateral distribution (85.7%) on the extremities. Other conditions were linear psoriasis, verrucous epidermal nevus, epidermal nevus, hypomelanosis of Ito and Blaschko-linear acquired inflammatory skin eruption (BLAISE). The clinical-histopathological correlation manifested in 64.2% of cases, while dermoscopy exhibited an even higher correlation in 92.8% of cases. While the distribution pattern of linear dermatoses by itself serves as a valuable diagnostic clue, specific diagnosis can be achieved with more accuracy with the help of distinctive dermoscopic features and correlating them further with histopathological features.

1. Introduction

Lines of Blaschko was first described by a German dermatologist, Alfred Blaschko in 1901. These are V-shaped lines in the upper back, S shape on the abdomen, inverted U-shape from the breast to upper arm and perpendicular lines down in the front and back of extremities.[1,2] It doesn't correspond to any known vascular, nervous, lymphatic structure, but represent growth pattern of skin. The lines are not visible under normal circumstances but becomes apparent when certain conditions affect the pigmentation or texture of the skin. Happle proposed to classify them as "superimposed segmental manifestation" and "isolated segmental manifestation".[3] Blaschko-linear dermatosis are included in the later category, the former, represents segmental manifestation of a supposed non-segmental lesion (e.g. Psoriasis). These disorders are named Blaschko-Linear Manifestations of Multifactorial Polygenic Disorders (BLMMPD).[4] Several studies on individual linear dermatosis are available, yet very few

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Indian studies have correlated various linear dermatosis with their distinctive dermoscopic and histopathological characteristics. The aim is to study the various clinical presentations, dermoscopic-histopathological correlation of various Blaschko-linear dermatosis.

2. Case Series

Institutional ethical committee approval was obtained. In this observational study, all patients with clinical findings of Blaschko-linear dermatosis who presented to our out-patient department between July 2023 to December 2023 were screened. Those with dermatosis along blood vessels, lymphatics, nerve trunk and following koebnerization were excluded.

After obtaining informed consent patients were enrolled. Demographic details, detailed history including onset, symptoms, duration, distribution, progression of lesion, morphology, systemic findings were collected using predefined proforma. Clinical examination, photography of lesions and dermoscopy (using HEINE DELTA 30 Dermoscope) was done for all patients. Biopsy was performed in all patients except for cases of hypomelanosis of Ito, as the patients did not consent. The histopathological and Dermoscopic findings were correlated. Data collected were appropriately analyzed and tabulated.

3. Result

The study encompassed 28 cases, with distribution as follows: Lichen striatus and linear lichen planus were observed in 28.5% of patients each (8 cases), linear psoriasis in 14.2% (4 patients), verrucous epidermal nevus in 10.71% (3 cases), linear epidermal nevus and Hypomelanosis of Ito in 7.14% (2 cases each). Only one case (3.57%) was identified as Blaschko-linear acquired inflammatory skin eruption (BLAISE). Biopsy was conducted for all patients except cases of Hypomelanosis of Ito.

The mean age at presentation was 17.92 ± 7.1 years (range 1-50 years), majority of patients were of age group 1-20 years contributing to 64.2% (18 patients). Male: female ratio 0.75:1 was seen, showing female predominance. The duration of the lesion ranged from 2months to 3 years. 20 cases were asymptomatic (71.4%) and itching noted in 8 patients (28.5%). Intense itching was seen in cases of linear lichen planus and BLAISE. 64.2% of the patient reported proximal to distal evolution of lesion.

Commonest site involved was lower limb (57.1%), followed by trunk (50%), upper limb (35.7%), neck (21.4%). Unilateral distribution was seen in 85.7% (24 patients), bilateral lesions in remaining 14.2% (4 Patients). Among the cases, 42.8% (12 patients) exhibited involvement of multiple Blaschko's lines, while non-segmental lesions were present in 21.4% of cases (6 patients). The most prevalent distribution observed was the narrow band pattern (71.4%), followed by the broad band and phylloid patterns. Majority of the patients (71.4%) had not received any topical or systemic treatment previously. No genital lesions and no involvement of palms and soles were identified in our study. A comprehensive presentation of patient characteristics is detailed in Table 1.

3.1. Lichen striatus

Eight patients, aged between 8 and 17 years, were diagnosed with Lichen striatus, exhibiting a male-to-female ratio of 1:3. Characterized by hypopigmented macules in a linear distribution, with a width ranging from 0.5cm to 1.5cm, these lesions were observed along the neck, extremities, and trunk. 2 patients had skin coloured papules. The duration of the lesions ranged from 8 months to 4 years. One patient reported itching and burning sensation. Multiple lines of involvement noted in 2 patients.

Dermoscopy showed whitish scar like areas, minimal scaling in 6 cases and surrounding area of pigment network in 4 case.[5] Histopathology showed parakeratosis, slight acanthosis, basal cell degeneration, melanophages and focal lichenoid interface dermatitis in the papillary dermis consisting of lymphocytes, histiocytes and plasma cells. Perivascular and peri-adnexal inflammatory infiltrate noted in 6 cases.[6]

3.2. Linear lichen planus (LP)

8 patients were diagnosed as linear LP in the age group between 10-50 years, with male-to-female ratio of 1:3. Violaceous flat toped papules and plaques were noted in a linear pattern of width 0.5 – 1.5cm. Duration of lesions was from 2- 12months. 6 cases presented with itching. Upper limb and lower limb were involved in 4 cases each, with lesions spilling over to trunk in 2 case. 4 cases had multiple Blaschko's lines involvement, 4 had non-segmental lesions, and 3 exhibited mucosal involvement. Dermoscopy showed blue-grey dots and globules (6/8 cases), red dots-globules (4/8 cases) and wickham's striae in all cases. Histopathology showed features of lichen planus including wedge shaped hypergranulosis, saw tooth appearance of rete ridges, basal cell degeneration, pigment incontinence and melanophages in the dermis. Colloid bodies were also noted in the epidermis.[7]

3.3. Linear psoriasis

4 male patients of linear psoriasis were included in this study, with age between 12- 36 years. They presented with hyperpigmented scaly plaques of 2years to 3 years duration over posterior aspect of left thigh and outer aspect of forearm, wrist. No evidence of trauma in the preceding lesions seen. Associated pitting of nails and non-segmental plaque psoriasis were present in 2 cases. Dermoscopy showed features of thick silvery white scales, and on

removing the scales, erythematous background and regular red dots and globules were seen. Corresponding biopsy findings include parakeratosis, Munro's microabscess, spongiform pustules of kogoj, regular acanthosis, supra-papillary thinning, dilated and prominent blood vessels in dermis and dermal papilla. Inflammatory infiltrate consisting of neutrophils and mononuclear cells on dermis and around blood vessels were noted.[8]

3.4. Verrucous epidermal nevus

3 cases belonging to age group 4 years to 12 years with scaly verrucous papules coalescing into linear plaque of width ranging from 1.5cm-2cm since birth were included in the study. Site involved includes behind the ear, arm and trunk. No symptoms of itching or signs of inflammation were noted. No neurological, ophthalmological and skeletal anomalies were noted in any of the cases. Dermoscopy showed brown exophytic structures in cerebriform pattern with ridges and furrows, brown dots and globules in all patients and follicular plugging (2/3 cases). Terminal hairs and fine white scales in few areas seen (2/3cases). Brown ring with hypopigmented areas in center were noted in all cases. Corresponding histopathology showed verrucous epidermal hyperkeratosis, papillomatosis and increased pigment in the basal layer.[9]

3.5. Linear epidermal nevus

2 male children of age 1, 3 years presented with brown-black pigmented macules, papules coalescing to form plaques of size ranging from 1.5- 2cm involving bilateral upper limb and lower limb in an interrupted pattern was seen. The lesions were asymptomatic and present since birth. Third degree consanguineous marriage in parents was observed in 1 case, but no family members had similar lesion. Multiple sites of involvement were noted in both cases, suggesting a systematized form. Neurological and ophthalmological evaluation were normal. Dermoscopy showed homogenous globular pigment pattern corresponding to histopathological finding of diffuse dense collection of pigment cell nests in epidermis.[10]

3.6. Hypomelanosis of ITO

2 male Children of age 6months and 1.5 years presented with multiple hypopigmented macules and patches in whorls and streaks over trunk, gluteal region and both lower limbs along lines of Blaschko and were asymptomatic. Duration of lesion noted were 4 months and 1 year respectively. Few areas of blue-green pigmented macules suggestive of Mongolian spots were noted in back of 1^{st} child. Examination of CNS, eyes and skeletal system were normal in both patients. Dermoscopy showed presence of uniform faint pigment network, blotchy pigmentation and an irregular cloudy border. Biopsy was not done in both patients in view of parental concerns for invasive procedure.

3.7. Blaschko-linear acquired inflammatory skin eruption (BLAISE)

A 27-years old female, presented with sudden eruption of erythematous, itchy linear macules and papules along the lines of Blaschko of width 0.5cm involving left thigh for past 3 months. The lesion gradually progressed proximally and distally to involve abdomen and legs. Dermoscopy showed yellow structures in an erythematous background corresponding to the histopathologic features of spongiosis and diffuse band-like inflammatory infiltrate of lymphocytes, histiocytes with necrotic keratinocytes. Extension of inflammatory infiltrate along the eccrine sweat glands was noted. The diagnosis of BLAISE was established based on the presence of clinical features resembling blaschkitis, such as the onset in adulthood, erythematous and pruritic skin papules. Additionally, characteristics of lichen striatus, including distribution along the extremities and the presence of a lichenoid inflammatory infiltrate, were also observed in this patient.[11]

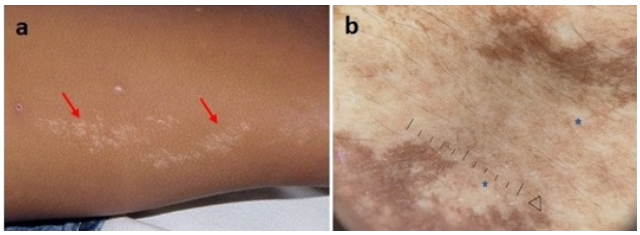

Figure 1: Lichen striatus clinical and dermoscopy images; a: Clinical image showing hypopigmented macules arranged in a linear distribution along the medial aspect of left leg (red arrow); b: Dermoscopy showing minimal scaling, whitish scar like areas (blue star)

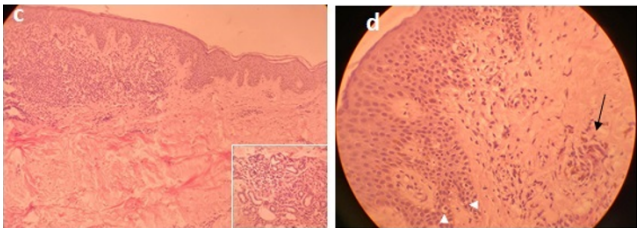

Figure 2: Lichen striatus histopathology images; **c:** HPE Low power view (4x), showing inflammatory infiltrate consisting of lymphocytes, histiocytes and plasma cells in DEJ perivascular region. Inset: High power view showing peri adnexal (peri-eccrine) inflammatory infiltrate; **d:** HPE High power view (40x), showing pigmented melanophages (black arrow) and vacuolation of basal layer (white arrow head).

Table 1: Patient characteristics

Characteristics	Findings	Number of patients	Percentage
Age	<10 years	10	35.7%
	11-20 years	8	28.5%
	21 30 years	6	21.4%
	31-40 years	2	7.14%
	41-50 years	2	7.14%
Sex	Male	12	42.8%
	Female	16	57.1%
Family history	Present	1	3.57%
Duration of lesions	< 6months	10	35.7%
	7-12	6	21.4%
	>1 year	12	42.8%
Symptoms	Asymptomatic	20	71.4%
	Itching	8	28.5%
Site	Neck	6	21.4%
	Trunk	14	50%
	Upper limb	10	35.7%
	Lower limb	16	57.1%

Table 2: Patients analysed based on their clinical,dermoscopic correlation with histopathology

Diagnosis	Distribution % (cases)		Clinical-Histopathological correlation % (cases)	Dermoscopic Histopathological correlation % (cases)
	Multiple Blaschko's lines involvement	Non- segmental lesion		
Lichen Striatus (8)	25% (2)	-	50% (4/8)	87.5% (7/8)
Linear Lichen planus (8)	50% (4)	50% (4)	75% (6/8)	100% (8/8)
Linear psoriasis (4)	50% (2)	50% (2)	50% (2/4)	100% (4/4)
Verrucous epidermal nevus (3)	-	-	100% (3/3)	100% (3/3)
Linear epidermal nevus (2)	100% (2)	-	50% (1/2)	100% (2/2)
Hypomelanosis of Ito (2)	100% (2)	-	100% (2/2)	100% (2/2)
BLAISE (1)	-	-	0% (0/1)	0% (0/1)
All cases (28)	42.8% (12)	21.4% (6)	64.2% (18/28)	92.8% (26/28)

BLAISE – Blaschko-Linear AcquiredInflammatory Skin Eruption

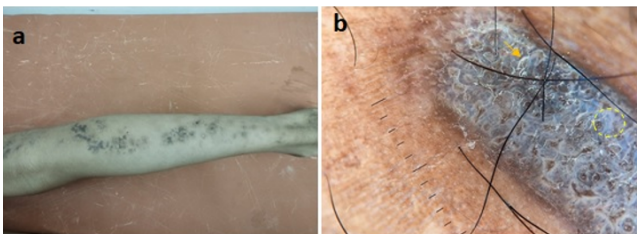

Figure 3: Linear lichenplanus clinical and dermoscopy images; **a:** Clinical image showing linear lichenoid papules and plaques along forearm; **b:** Dennoscopy showing Wickham's Striae (yellow arrow), Grey blue dots and globules (yellow dotted circle), Brownish- black dots & globules

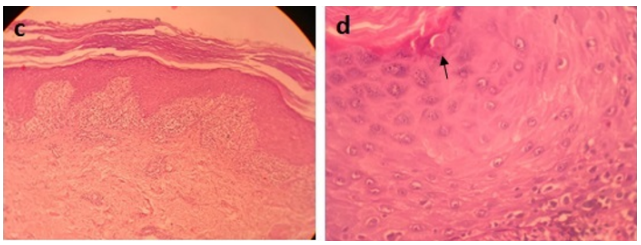

Figure 4: Linear lichen planus histopathological images; c: HPE Low power view (4x), showing hyperkeratosis, hypergranulosis, lichenoid infiltrate and saw-tooth rete pegs; **d:** HPE High power view (40x), showing wedge shaped hypergranulosis, colloid bodies (black arrow)

4. Discussion

Blaschko's lines are attributed to the widely accepted theory of embryonic mosaicism in epidermal cells migrating from the dorsal midline.[15] These lines represent boundaries between population of two distinct cell lines. Lyonization.[16]

Table 3: Summary of relationship of clinical, dermoscopic and histopathological features

Diagnosis	Clinical Findings	Dermoscopic findings	Corresponding Histopathological features
Lichen Striatus	Hypopigmented macules and patches in linear distribution	Minimal scaling Whitish scar like areas	Parakeratosis Reduced melanin pigment as a result of basal degeneration, Other findings: Focal inflammatory infiltrate consisting of lymphocytes, histiocytes and plasma cells, Dermal melanophages, peri-vascular and peri-adnexal inflammatory infiltrate
Linear Lichen planus	Lichenoid papules and plaques	Wickham's Striae Grey blue dots Red dots and globules Brownish- black dots & globules	Wedge shaped hypergranulosis Pigment incontinence- dermal melanin Dilated blood vessels in dermis Epidermal melanin Other findings: hyperkeratosis, lichenoid infiltrate, saw tooth appearance of rete pegs and colloid bodies
Linear psoriasis	Well demarcated, erythematous scaly plaque	White scales Regular red dots and globules Pinkish background	Hyperkeratosis with air trapped inside Dilated torturous capillaries in thinned out dermal papillae Inflammatory infiltrates Other findings: parakeratosis, regular elongated rete ridges, Munro's micro-abscess, spongiform pustules of kogoj.
Verrucous epidermal nevus	Verrucous pigmented plaques	White scales Comedo like opening Brown dots and globules Brown circle with hypopigmented center Cerebriform pattern Dotted vessels	Verrucous epidermal hyperkeratosis Dilated infundibula with keratinocyte plugging Papillomatosis Increased pigment in the basal layer Confluence of rete ridges Tips of dilated capillaries
Linear epidermal nevus	Pigmented macules and patches	Globular pattern Homogenous pattern	Pigment nests in dermis Diffuse dense collection of pigment nests (in basal layer) Other findings: hyperkeratosis, papillomatosis, broad flat rete ridges
Hypomelanosis of Ito	Hypopigmented macules and patches in whorls and streaks	Diffuse faint pigment network pattern Irregular and cloudy edges and Blotchy pigmentation	Biopsy not done.
BLAISE	Erythematous linear individual and confluent papules	Erythematous background Yellow structures	Lichenoid infiltrate of lymphocytes and mononuclear cells Spongiosis, necrotic keratinocytes

BLAISE – Blaschko-Linear AcquiredInflammatory Skin Eruption

Table 4: Comparison of current study to previous studies.

Variables	**Das A et al [12]**	**Taieb a et al. [13]**	**Saraswathy p et al [14]**	**Our Case series**
Linear dermatosis cases studied	136	18	90	28
Most common cases	Verrucous epidermal nevus	Lichen striatus	Lichen striatus	Lichen striatus, Linear LP
Age at presentation (range)	15.58 ± 14.94 years	6 months – 14 years	1- 30 years	17.92± 7.1 years
Male to female ration	1.32:1	1:1	10:11	0.75:1
Most common site	legs	trunk	extremities	Extremities

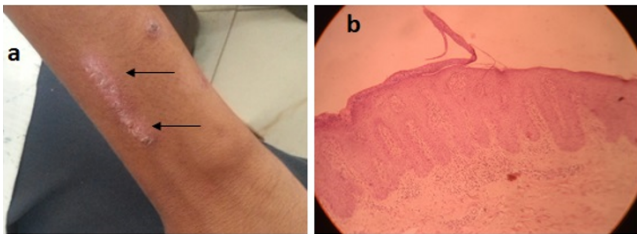

Figure 5: Linear psoriasis clinical and histopathology images;**a:** Clinical image showing linear well defined erythematous scaly plaque over right forearm; **b:** HPE (10x), showing Hyperkeratosis, regular elongated rete ridges, dilated torturous capillaries in thinned out dermal papillae, few inflammatory infiltrate

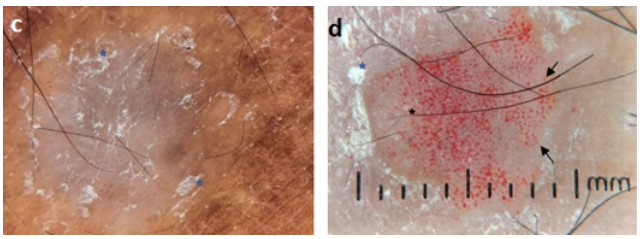

Figure 6: Linear psoriasis dermoscopy images; **c:** Dermoscopy showing silvery white shiny scales (Blue star); **d:** On removal of scales, regular red dots (black arrow) and globules (black star) in a pinkish erythematous background with scales at periphery.

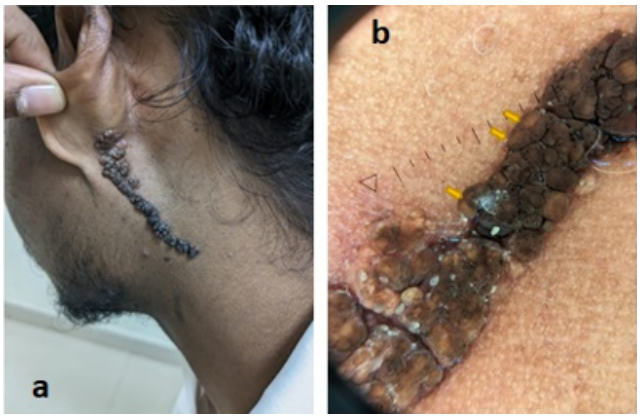

Figure 7: Verrucous epidermal nevus clinical and dermocopy images; **a:** Clinical image showing linear verrucous plaque behind the ear; **b:** Dermoscopy showing -Brown exophytic structures, Cerebriform pattern in the form of ridges and fissures. Brown dots and globules. Brown ring with hypopigmented center (yellow arrows)

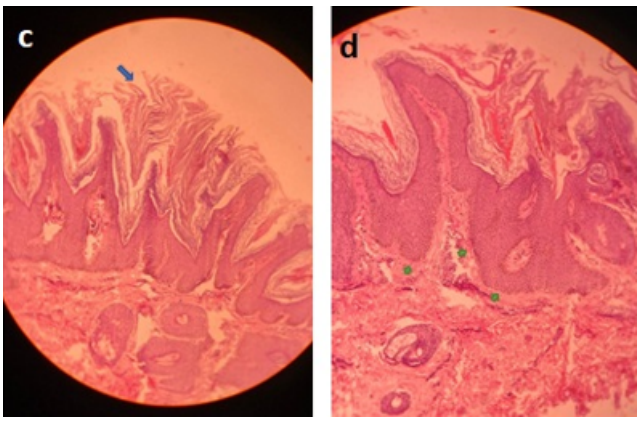

Figure 8: Verrucous epidermal nevus histopathology images; **c:** HPE Low power view (4x), showing hyperkeratosis (blue arrow), papillomatosis; **d:** HPE high power view (40x), showing hyperkeratosis, papillomatosis with increased pigmentation in the basal layer (green arrow)

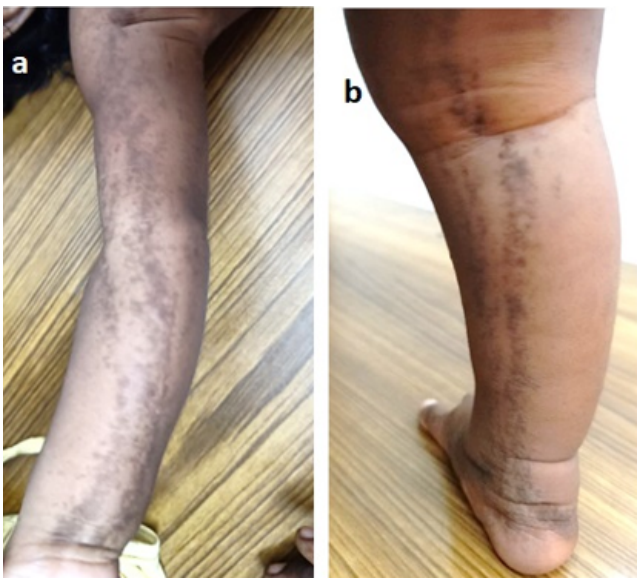

Figure 9: Epidermal nevus clinical images;**a:** Clinical image showing linear pigmented papules coalescing to form plaques, over forearm of 1 year old child; **b:** Clinical image showing linear pigmented papules and macules coalescing to form plaque in the posterior aspect of legs in the same child.

somatic mutation, half-chromatid mutation,[2] chromosomal non-disjunction or chimerism can result in these lines.[14] The anatomic equivalent of Blaschko's lines have also been reported over the teeth as well as in the eyes.[17]

The earlier the mutation, the more widely dispersed and more intimately mixed are the mosaic clones and, consequently, longer are the lines of migration. The pattern of cutaneous mosaicism also varies according to the cell-type that is affected.[18] However, these dermatoses are acquired, implying an initial immune tolerance to

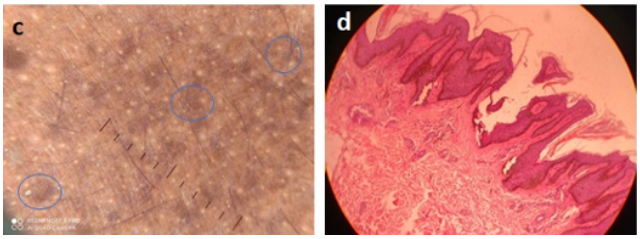

Figure 10: Epidermal nevus dermoscopy and histopathology images; **c:** Dermoscopy showing Globular pigment pattern (blue circle); **d:** HPE 10x view- showing compact hyperkeratosis, papillomatosis with few broad, flat rete ridges with increased pigment in the basal layer

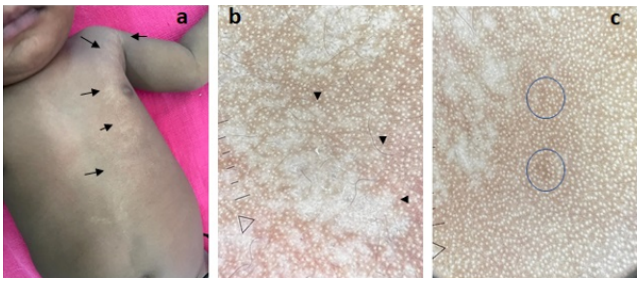

Figure 11: Hypomelanosis of Ito clinical and dermoscopy image, Hypoigmented macules and patch in whorls and streaks over the trunk extending to arms (black arrow); **b,c:** Dermoscopy showing – Diffuse faint pigment network pattern, irregular and cloudy edges (black arrow head) and blotchy pigmentation (blue circles)

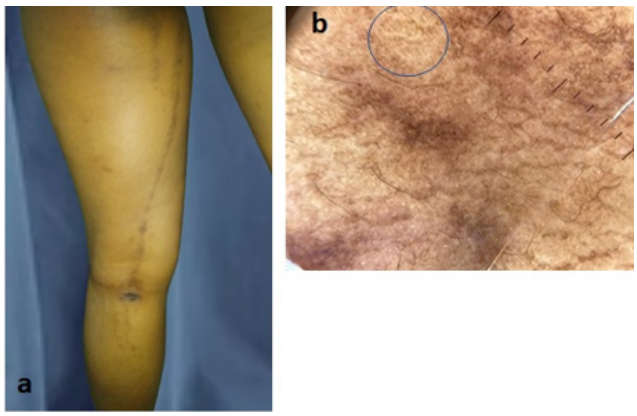

Figure 12: BLAISE clinical and dermoscopy images; **a:** Clincal image showing erythematous linear individual and confluent papules; **b:** Dermoscopy showing yellow structures in a erythematous back ground.

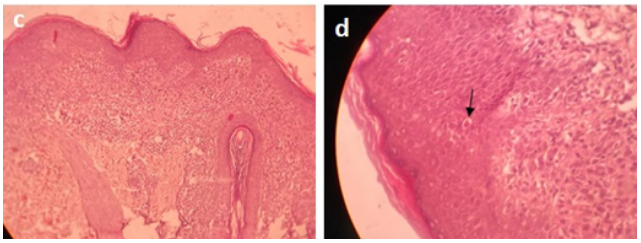

Figure 13: BLAISE histopathology images, **c:** HPE low power view (10x view) showing lichenoid infiltrate consisting of mononuclear cells in the DEJ, surrounded on either side by acanthotic collarette **d:** high power view (40x) showing apoptotic keratinocytes just above DEJ (black arrow); DEJ- Dermoepidermal Junction

these mosaic cells. The dermatosis occurs when the immunotolerance to the mosaic cells are broken resulting in autoimmune response to these cells. Acquired events such as viral infection might be the underlying initiating event in expression of novel membrane antigen by these mosaic cells leading to inflammatory reaction. [13]

Causes of other linear dermatosis includes lesions following, blood vessels or lymphatics; lesions due to Koebner phenomenon (KP) and autoinoculation; lesions due to external factors; and lesions due to infestations such as cutaneous larva migrans and scabies (burrows). [19]

Numerous congenital and acquired dermatological conditions exhibit a pattern along Blaschko's lines, including X-linked dominant skin disorders, epithelial naevi, and pigmentary disorders. These dermatoses are categorized into three groups: genodermatoses, congenital and/or naevoid conditions, and acquired conditions. Among these, naevoid skin lesions are particularly prevalent, manifesting either at birth or later in life. The term 'naevoid' pertains to mosaic forms of inherited skin conditions that adhere to these lines, exemplified by conditions such as naevoid psoriasis, [20] epidermal nevus and intricate nevi of the connective tissue

In our examination, lichen striatus and linear lichen planus (LP) have emerged as more prevalent conditions contributing to 57.1% of cases, with a notable female predominance and unilateral distribution on the extremities which aligns with established trends documented in the literature. [12] The majority of patients, accounting for 64.3%, were asymptomatic, with anxiety and cosmetic concerns being the primary reasons for hospital visits. Itching was reported by only 28.5% of the patients.

Among the examined cases, only one patient exhibited a positive family history, implying that these disorders predominantly arise due to sporadic mutations. The mean age at presentation was 17.92± 7.1 years, indicating the concern regarding the lesions especially among adolescents. The proximal-to-distal progression of the lesion aligned with the embryological migration of cutaneous cells from

the dorsal midline along the lateral walls to ultimately reach the corresponding ventral midline.[21] Mongolian spots were noted in a case of hypomelanosis of Ito, an association documented in the literature.[22]

An interesting patient discussed includes the 27-years old female who, presented with features of both blaschkitis.[23] such as the onset in adulthood, erythematous, pruritic skin papules and lichen striatus including distribution along the extremities and the presence of a band-like inflammatory infiltrate, suggesting the diagnosis of Blaschko-linear acquired inflammatory skin eruption (BLAISE) was noted.[24]

The histopathological diagnosis, acknowledged as the gold standard, was meticulously juxtaposed with clinical and dermoscopic diagnoses, with the outcomes presented in Table 2. The diagnosis of BLAISE requires histopathological analysis for confirmation. Noteworthy is the substantial enhancement in diagnostic accuracy achieved through dermoscopy, a non-invasive analytical method. The clinical-histopathological correlation was observed in 64.2% of cases, while dermoscopy exhibited an even higher correlation in 92.8% of cases. This discernible improvement of approximately 30% underscores the valuable contribution of dermoscopy in augmenting diagnostic precision. The summary of relationship between clinical, dermoscopic and histopathological features are given in Table 3.

In a comparative analysis of study variables with findings from similar studies, previous investigations on linear dermatosis have shown comparable results which was represented in Table 4. Das et al. reported a mean age group of 15.58 ± 14.94, identifying Verrucous Epidermal Nevus as the most prevalent presentation, followed by linear LP. In our study, the mean age was 17.92 ± 7.1 years, with a predominance of LP and Lichen Striatus, followed by psoriasis and VEN. A slight female predominance was observed in the study conducted by Saraswathy et al. Additionally, the extremities were consistently identified as the predominant site in these studies, with the exception of Taieb et al.'s investigation, where the trunk was noted as the predominant site.

The spectrum is continuously expanding and newer diseases (eosinophilic cellulites, linear scleroderma and erythematous exanthem of scarlet fever) have been included in this category.[25] In these polygenic inflammatory disorders, there exists a sharp demarcation between involved and uninvolved skin. The comparative analysis of two cell populations exposed to identical environmental conditions and possessing the same genetic background, except for the mosaic gene, through additional genetic studies, may facilitate the identification of precise genetic loci accountable for these manifestations

5. Conclusion

This case series highlights the various linear dermatosis along the lines of Blaschko along with their demographic, clinical, dermoscopic and histopathological features. While the distribution pattern of linear dermatoses by itself serves as a valuable diagnostic tool, achieving enhanced diagnostic accuracy often necessitates correlation with associated clinical symptoms, dermoscopy, and histopathological findings- an emphasis that cannot be overstated.

6. Limitation

Small sample size, biopsy was not done in few cases, Immunohistochemical analysis of biopsy specimen was not done.

7. Source of Funding

None.

8. Conflicts of Interest

The authors declare no conflicts of interest.

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