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Case Report

Dermatology Section

Acral Acanthosis Nigricans with Concurrent Vitamin B12 Deficiency in an Indian Patient: An Atypical Presentation

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ABSTRACT

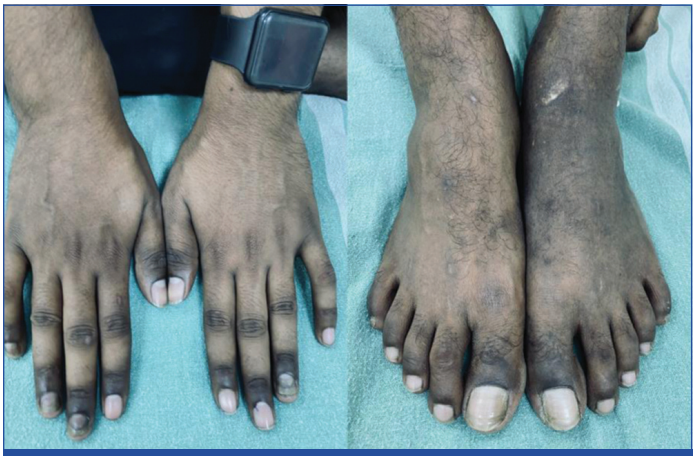
Acanthosis Nigricans (AN) is characterised by velvety, papillomatous, brownish-black, hyperkeratotic plaques, typically on the intertriginous areas and neck. It is more commonly seen in the African American descent, rarely occurs in the Indian population. The present case includes 28-year-old male, who presented to the Outpatient Department with asymptomatic hyperpigmention over skin of both feet and knuckles of both hands since three months. The distribution pattern over the knuckles was suggestive of vitamin B12 deficiency however the atypical distribution over the feet leads to suspicion of a differential diagnosis of lichen planopigmentosus, vitamin B12 deficiency and acral AN. Dermoscopy was done to aid in the diagnosis and revealed linear crista cutis and sulcus cutis which are features suggestive of AN. On investigation, serum vitamin B12 levels were below 100 µg/mL and histologic sections showed hyperkeratosis with papillomatosis and mild acanthosis. The patient was treated solely with 1500 mcg mecobalamine daily for 10 days and followed-up. The dermoscopic and histopathological findings were consistent with the diagnosis of acral AN and thus a final diagnosis of acral AN superimposed with vitamin B12 deficiency was made. This case is being reported due to its rare occurrence in the Indian population, the atypical clinical presentation of AN in form of macules and to highlight dermoscopy as an essential non invasive tool aiding in the diagnosis. The diagnosis of acral AN should not be overlooked despite the finding of low serum vitamin B12 levels in such a case and the authors wish to create awareness among the clinicians to investigate the patient further.

Keywords: Dermoscopy, Hyperpigmentation, Pigmentary disorders

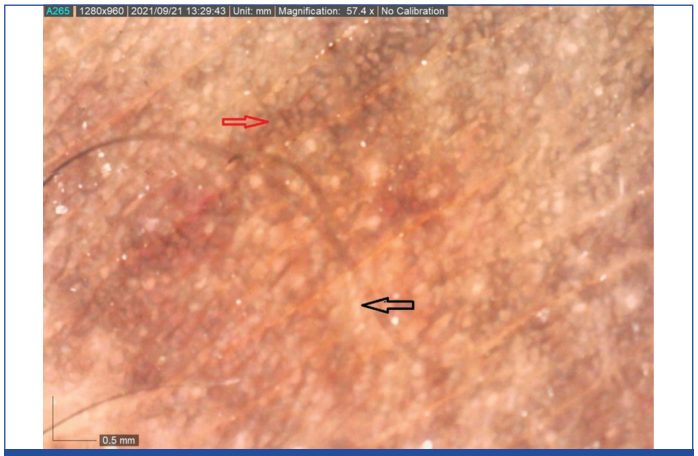
CASE REPORT

A 28-year-old male, apparently healthy and moderately built, presented to the Outpatient Department with asymptomatic hyperpigmention over skin of bilateral feet and bilateral knuckles since three months. The pigmentation started over medial side of left foot initially and then progressed to involve other sites. Patient had no history of occupational exposure to coal tar, chemicals or dyes. No history of any previous medications prior to onset of lesions or any significant family history. On examination, multiple ill-defined hyperpigmented macules, few of which coalesced to form large macules were present on the dorsum of the feet, metatarsophalangeal joints and metacarpophalangeal joints in a bilaterally symmetrical manner [Table/Fig-1]. The 3rd, 4th and 5th fingernails of right hand and fourth fingernail of left hand showed subungual hyperkeratosis and onycholysis. Mucocutaneous examination of other sites revealed no abnormalities. General physical examination was normal and patient's Body Mass Index (BMI) was 22.03 kg/m^2. There were no systemic features suggestive of diabetes or other endocrinopathies.

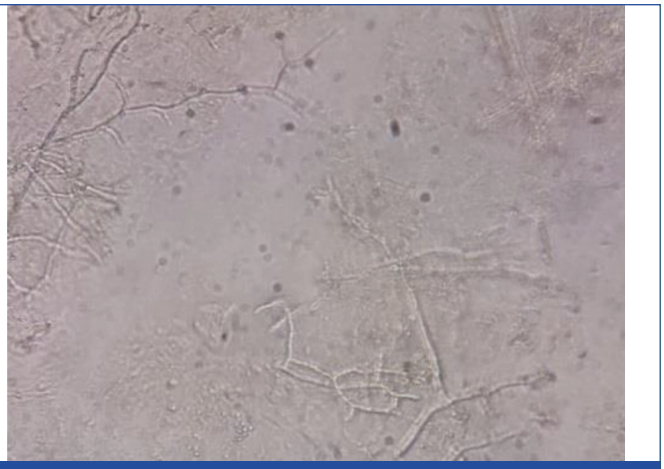
Dermoscopy was done due to the atypical distribution of the lesions considering a differential diagnosis of lichen planopigmentosus, B12 deficiency and acral AN. Dermoscopic examination revealed linear crista cutis and sulcus cutis which was suggestive of AN [Table/Fig-2]. KOH examination was positive confirming the diagnosis of onychomycosis [Table/Fig-3]. Complete blood count with peripheral smear, fasting and postprandial blood sugar, thyroid profile and routine urine analysis were within normal limits. Serum insulin level was within normal limits. Ultrasonography of whole abdomen revealed no abnormalities. Serum B12 levels were below 100 µg/mL. Skin biopsy was performed and haematoxylin and eosin stained histologic sections showed orthokeratotic hyperkeratosis, acanthosis along with papillomatosis. The valley between the papillae is filled with keratotic material [Table/Fig-4,5]. Patient was treated solely with 1500 mcg mecobalamine daily for 10 days and followed-up. No other oral or topical medication was prescribed at this stage. The hyperpigmented macules on metacarpophalangeal joint and metatarsophalangeal joints showed significant improvement



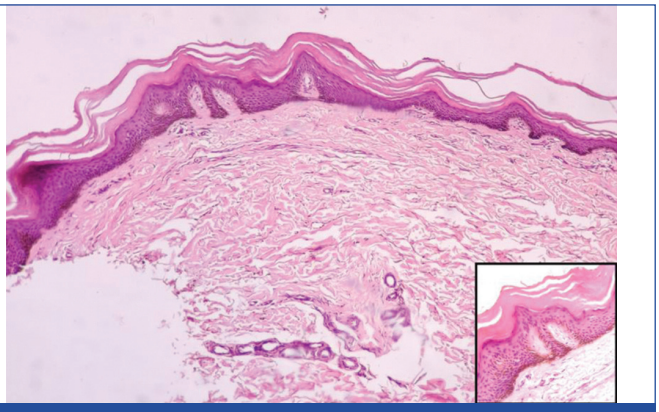
[Table/Fig-1]: Hyperpigmented macules on dorsal surface of hands and feet, predominantly over metatarsophalangeal joints and metacarpophalangeal joints.



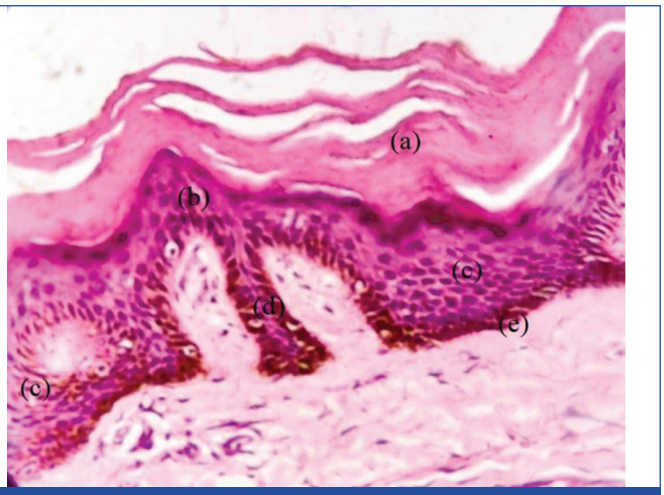
[Table/Fig-2]: Dermoscopy showing linear crista cutis (yellow arrow) and sulcus cutis (black arrow) (Dino-lite AM4515ZT, polarizing, 57X magnification).



[Table/Fig-3]: Potassium hydroxide (KOH) mount of nail clipping showing refractile, branching fungal hyphae in dermatophytic infection (40X magnification).



[Table/Fig-4]: Skin biopsy, haematoxylin and eosin stain, 10X magnification showing hyperkeratosis with papillomatosis and the valley between the papillae is filled with keratotic material and showing mild acanthosis (Inset-Skin biopsy, haematoxylin and eosin stain, 40X magnification).

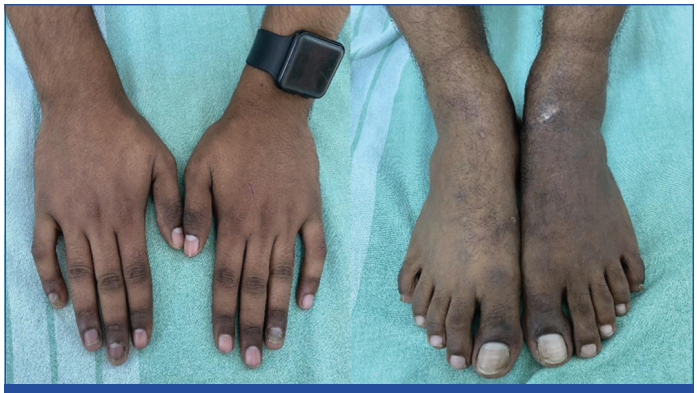


[Table/Fig-5]: Skin biopsy showing: a) orthokeratotic hyperkeratosis; b) thinned out epidermis; c) acanthosis; d) papilomatosis; e) basal layer melanosis (H&E;40X).

in the pigmentation over a short duration of 10 days [Table/Fig-6]. The dermoscopic and histopathological findings were consistent with the diagnosis of AN and thus a final diagnosis of acral AN superimposed with vitamin B12 deficiency was made.

DISCUSSION

AN is characterised by velvety, papillomatous, brownish-black, hyperkeratotic plaques, typically on the intertriginous areas and neck [1]. AN commonly affects neck, axillae, groin, inner aspects of the thighs and is often routinely encountered in daily dermatological practice [2]. Schwartz RA has classified AN into benign, obesity-associated, syndromic, malignancy-associated, unilateral, drug-induced, mixed-type and acral types [2]. It is often associated with hyperinsulinemia,



[Table/Fig-6]: Improvement seen after treatment with 1500 mcg of mecobalamine daily for 10 days.

insulin resistance, benign endocrinopathies, heritable diseases and even malignancies [3]. Histopathological findings characteristically show papillomatosis and hyperkeratosis [4].

Acral AN is more commonly seen in patients of African American descent. Acral AN (also known as acral acanthotic anomaly) and the lesions are usually localised to the knee, ankle, phalangeal joints and tarsophalangeal joints [5,6]. The occurrence of acral AN in Indian population is a rare phenomenon in itself and to the best of the author's knowledge, the review of literature has revealed only two such cases from India [1,6]. One of the reported cases of acral AN in Indian population was of a 40-year-old female along with scleroderma and the other patient was a 28-year-old female without any other systemic involvement or endocrinopathy [1,6]. Although acral type of AN is not commonly associated with malignancy, recent case reports have demonstrated an association with gastric adenocarcinoma and Hodgkin's lymphoma, thereby warranting a thorough workup of the patient [7,8].

The exact aetiology of AN is unclear, but it is most commonly associated with insulin resistance. Increased circulating insulin leads to increase in circulating Insulin like Growth Factor (IGF) which causes keratinocyte and dermal fibroblast proliferation that is responsible for AN [9]. Other factors that have been implicated in the pathogenesis of AN include obesity, endocrine dysfunction, malignancy, association with autoimmune diseases and medications such as systemic glucocorticoids, diethylstilbestrol, combined oral contraceptive pill, growth hormone therapy and oestrogen [10].

Diagnosis of AN is usually clinical and histopathology is rarely needed, for confirmation. However, the emergence of dermoscopy in the recent years has aided in providing a non invasive and accurate diagnostic tool for cases requiring further evaluation to confirm diagnosis, as in this case. Cutaneous pigmentation is one of the most strikingly variable phenotypes in humans, therefore making pigmentatory disorders manifest in a multitude of forms [11]. This case presented only with asymptomatic hyperpigmented macules at acral sites which is not typical clinical picture of AN, however the dermoscopic findings of crista cutis and sulcus cutis led to the suspicion of acral AN. Common dermoscopy findings in AN are crista cutis, sulcus cutis, papillary projections, hyperpigmented dots, crypts, and blotching; which can all be correlated with histopathological features [4]. This stresses the importance of dermoscopy as a non invasive diagnostic tool as skin biopsy is not a routine procedure for such cases.

Diagnostic work-up in patients of AN comprises of fasting lipid profile, fasting glucose, fasting insulin levels, haemoglobin, thyroid profile and radiological investigations (like chest X-ray PA view, ultrasonography whole abdomen and magnetic resonance imaging/computerised tomography) to rule out malignancy associated AN.

Treatment of AN is challenging and the mainstay of therapy aims at treating the underlying cause, such as controlling blood glucose

levels through exercise and diet, treating the insulin resistance or treating the malignancy in cases of malignancy associated AN [12]. AN associated with insulin resistance can be treated with drugs such as metformin and rosiglitazone which are insulin-sensitising agents [10].

Topical treatments include keratolytics, like topical retinoids, vitamin D3 analogues, urea and salicyclic acid. Physical modalities such as long pulsed alexandrite lasers, dermabrasion CO_2 ablation and chemical peels have also been tried. All treatment methods have shown variable success [13].

CONCLUSION(S)

The present case presented with hyperpigmented macules at acral sites instead of the routinely encountered plaques over flexures with concurrent serum vitamin B12 deficiency. This case is being resported due to its rare occurrence in the Indian population, the atypical clinical presentation in the form of macules and to highlight dermoscopy as an essential non invasive tool aiding in the diagnosis. The diagnosis of acral AN should not be overlooked despite the finding of low serum vitamin B12 levels in such a case and the authors wish to create awareness among the clinicians to investigate the patient further.

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