

## Response of Acitretin in Greither's Disease: A Rare Case Report

Sir,  
Palmoplantar keratodermas (PPKs) are a diverse group of disorders characterized by hyperkeratosis of the palms and soles, usually distinguishable by the mode of inheritance and by associated clinical findings.<sup>[1]</sup> In 1952, Greither described diffuse non-epidermolytic type of PPK with progressive extension of keratoderma to dorsa of hands and feet to which he termed it as "keratosis extremitatum hereditaria progrediens."<sup>[2]</sup> We report a case of Greither's disease (GD) in an 8-year-old male child, diagnosed clinically and histopathologically who responded well to oral acitretin therapy.

An 8-year-old male child born of non-consanguineous marriage presented with thickening and fissuring of palms and soles associated with raised lesions over knuckles, elbows, knees, and ankles since the age of 4 years. Initially, the thickening was noted as small raised lesions over finger tips and plantar surface of great toe which gradually progressed to diffuse thickening of the palms and soles with extension of lesions to the dorsum of hands and feet over a period of 4 years. There was no history of excessive sweating. None of the family members were affected. Cutaneous examination revealed diffuse keratoderma of the palms and soles with erythematous border extending to dorsum of bilateral hands and bilateral feet [Figure 1a-d]. Hyperkeratotic plaques were seen on knuckles, bilateral elbow joints, knee joint, lateral malleoli [Figure 2a-d]. Hair, nails, and teeth were normal. Based on clinical presentation, differential diagnoses of GD and Mal de Meleda syndrome were considered. All hematological investigations including serum lipid profile were normal. Biopsy taken from lesion over sole revealed hyperkeratosis, parakeratosis, acanthosis of epidermis with hypergranulosis, suggestive of PPK [Figure 3a and b]. Based on clinical

presentation and histopathological findings, a diagnosis of GD was reached. Electron microscopy and mutation analysis was not done in our case due to lack of financial resources. He was started on acitretin at a dose of 25 mg thrice a week and emollient containing urea and lactic acid. There was moderate [Figure 4a and b] and marked [Figure 4c and d] improvement in transgradient PPK after 2 and 3 months of therapy with acitretin, respectively. There was marked resolution of hyperkeratotic plaques over the knuckles [Figure 5a], elbow joints [Figure 5b], knee joints [Figure 5c], lateral malleoli [Figure 5d] after 2 months of acitretin therapy. During treatment with acitretin, hematological investigations were within normal limits. Patient was managed with maintenance dose of acitretin in the dose 25 mg twice per week for 4 months, during which no relapse was observed. Thereafter, he was advised regular use of emollient containing urea and lactic acid.

GD has autosomal dominant inheritance with variable penetrance and mutations in the gene encoding keratin 1.<sup>[3,4]</sup> It is characterized by diffuse transgradient PPK with hyperkeratotic erythematous papules and plaques over the achilles tendons, knees, and elbows. It may be rarely associated with nail changes, palmoplantar hyperhidrosis, and amputation of digits or blistering.<sup>[1,5]</sup> Histopathological findings are nonspecific and ill defined.<sup>[1]</sup> However, Grilli *et al.* had described most striking findings on histopathology as round, focal areas of orthokeratosis located on depressed areas of the epidermis.<sup>[3]</sup> Beylot-Barry *et al.* showed aggregated tonofilaments around the nucleus with desmosomes and cell-cell junctions showing an imbricated pattern, without true clump formation on electron microscopy.<sup>[6]</sup> The closest differential diagnosis of GD is Mal de Meleda syndrome. Mal de Meleda

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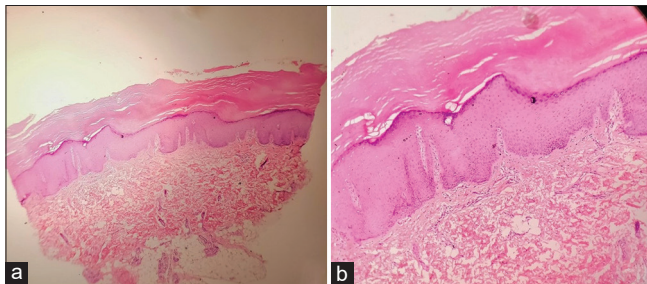
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**Figure 1:** (a-d) Diffuse keratoderma of the palms and soles with erythematous border (a and b) extending to dorsum of bilateral hands and bilateral feet (c and d)



**Figure 3:** (a and b) Biopsy taken from lesion over sole revealed hyperkeratosis, parakeratosis, acanthosis of epidermis with hypergranulosis, suggestive of PPK

(Keratosis Palmoplantaris transgradiens of Siemens) is autosomal recessive type of transgradient PPK, characterized by yellow waxy PPK with well demarcated erythema, palmoplantar hyperhidrosis, conical tapering at fingernails, nail changes, lingua plicata, syndactyly, reduced mobility of hands and feet, erythema of nose, corneal lesions.<sup>[1,7]</sup> The nosological situation of this keratoderma is under scrutiny whether it is a separate entity or just an extensive variant of the Unna-Thost type.<sup>[8]</sup>

The treatment modalities that have been tried are keratolytic agents such as salicylic acid, topical steroids in combination with keratolytics, propylene glycol, and systemic retinoids like acitretin. Acitretin, a synthetic retinoid acts at cytosolic proteins and intranuclear receptors. Its metabolites activate

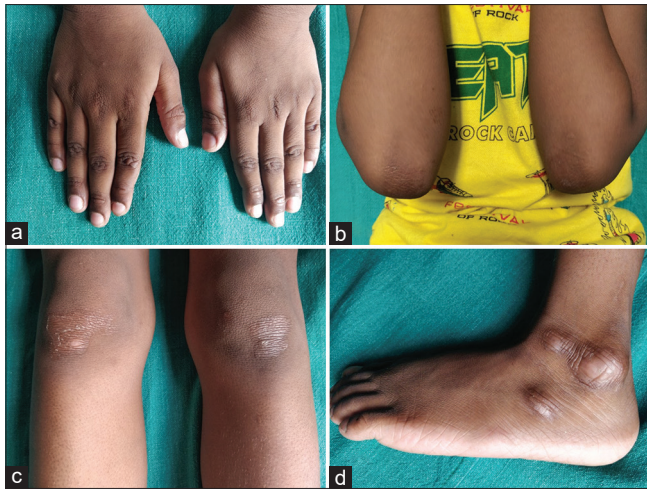


**Figure 2:** (a-d) Hyperkeratotic plaques were seen on knuckles (a), bilateral elbow joints (b), knee joints (c), lateral malleoli (d)



**Figure 4:** (a-d) Moderate (a and b) and marked (c and d) improvement in transgradient palmoplantar keratoderma after 2 and 3 months of therapy with acitretin respectively

the nuclear retinoic acid receptors (RARs) without binding to it, leading to alteration of gene transcription through response elements which is responsible for its antiproliferative and anti-inflammatory effects. It normalizes epidermal cell proliferation, differentiation, and cornification in psoriasis and other disorders of cornification.<sup>[9]</sup> It is used in low dose (25–35 mg/day or thrice weekly) for treatment to maintain the balance between hyperkeratinization and local residual tenderness. The benefits and long-term risks, with regard to teratogenicity, liver function, hyperlipidemia, and bone remodeling in children have to be carefully weighed.<sup>[10]</sup> There is paucity of literature describing this type of PPK and its management from India. Thus, we report a non-familial case of GD in an 8-year-old male



**Figure 5: (a-d) Marked resolution of hyperkeratotic plaques over the knuckles (a), elbow joints (b), knee joints (c), lateral malleoli (d) after 2 months of acitretin therapy**

child treated with oral acitretin. Excellent response was observed after 2 months of therapy in the form of decrease in thickening over palms and soles.

### **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.

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Nil.

### **Conflicts of interest**

There are no conflicts of interest.

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