Mutilating Keratoderma with Concomitant Alopecia and Keratoses Follicularis Spinulosa Decalvans: X-Linked Olmsted Syndrome and its Response to Isotretinoin

Abstract

We report a case of mutilating keratoderma with alopecia and keratoses follicularis spinulosa decalvans (KFSD), which was initially diagnosed as ectodermal dysplasia and Olmsted syndrome but was revisited as a case of X-linked Olmsted (XLO) syndrome. We focus on this uncommon entity (XLO) to highlight the differentials of alopecia with palmoplantar keratoderma.

Keywords: *Keratoderma, X linked Olmsted, olmsted syndrome*

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Introduction

Though PPK is a relatively common disorder in tertiary pediatric centers, mutilating keratoderma is decidedly uncommon.[1] Among the diffuse palmoplantar keratoderma (PPK), Olmsted and Vohwinkel syndrome are characterized by mutilating PPK. Olmsted syndrome in turn can have X-linked (*MBTPS2* mutation) and autosomal dominant (AD) (*TRPV3* mutation) inheritance. PPK with associated alopecia and keratosis follicularis apinolusus decalvans (KFSD) is suggestive of the X-linked Olmstead (XLO) syndrome.[2]

Case Report

A 6-year-old boy born to non-consanguineous marriage presented with thickened keratotic plaques over both hands and feet. The lesions started at 3 years of age and gradually progressed leading to fissures and flexion deformity of digits. The patient was initially diagnosed as ectodermal dysplasia and Olmsted syndrome at two different centres and referred to us for opinion. On examination, the patient had diffuse alopecia with follicular prominences, thin and sparse eyebrows, and pits over the malar eminence [Figure 1a and b]. All 20 nails were dystrophic and subungual hyperkeratosis was present. None of his siblings (3 sisters and 2 brothers) had similar lesions. Histopathological examination of the lesional skin of the palm revealed hyperkeratosis, acanthosis, and perivascular inflammatory dermal infiltrate, whereas the papular lesions revealed a histology suggestive of keratosis pilaris. Based on these findings, a diagnosis of XLO syndrome was made. Tests before initiation of retinoids were done including a baseline complete blood count and chemistry panel which included liver function tests, fasting triglyceride, and cholesterol levels, as well as baseline radiographs of lateral cervical, lumbar, and thoracic spine. Following this, saline compresses and topical salicylic acid 6% with oral isotretinoin (0.5 mg/kg) was initiated and there was marked improvement in PPK at 1-month follow up [Figure 2a-d]; the dose was subsequently reduced by 5 mg every alternate day for a month.

Discussion

The clinical scenario of mutilating PPK with alopecia can have various causes [Table 1]. The presence of keratosis pilaris helped in narrowing down the diagnosis to XLO and PPK congenital alopecia syndrome. The latter has an AD/AR inheritance and additionally has pseudoainhum.[3] In our case, the presence of KFSD [Figure 1] in a male child helped to arrive at the diagnosis of XLO syndrome.

Of the various genotypes of Olmsted syndrome, the X-linked variant is uncommon and the inheritance may be

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Table 1: An elucidation of disorders of PPK with alopecia[2,3,4,8,9]

	X-linked Olmsted syndrome	Vohwinkel syndrome	Hidrotic ectodermal dysplasia	Palmoplantar congenital alopecia syndrome
Palmoplantar keratoderma	a. Diffuse b. Transgradient c. Thick hyperkeratotic	"Honey Comb" (Star shaped) Appearance (associated with hearing loss)	Diffuse Palmoplantar Hyperkeratosis	a. PPK involving fingertips and borders of the hands and feet b. Pseudo-ainhum
Hair	a. Lost b. Follicular papules c. KFSD - pits on cheeks and eyebrows d. Atrichia of eyelashes	Normal	a. Patchy alopecia b. Coarse, brittle, pale hair	a. Diffuse atrichia of eyelashes b. Keratosis pilaris including ulerythema ophryogenes
Nails	Subungal hyperkeratosis	Normal	Dystrophy	Mild dystrophy
Teeth	Normal	Normal	Normal	

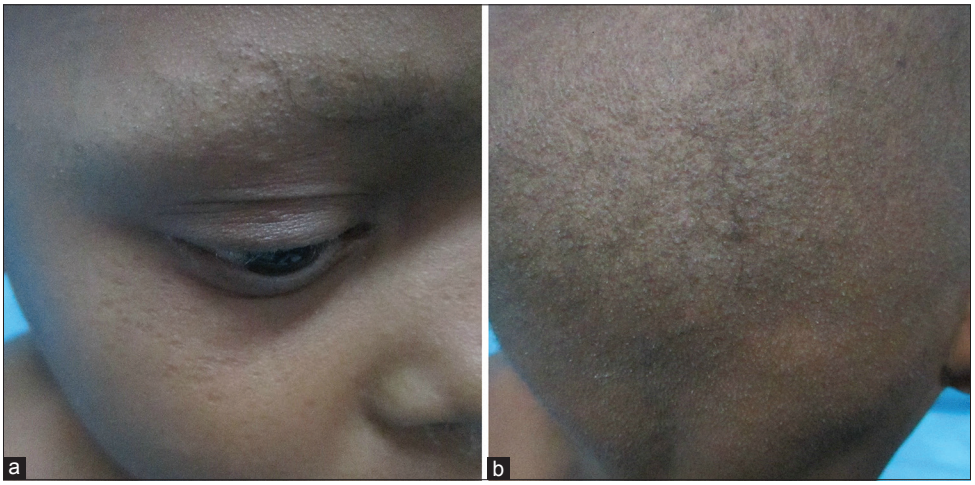

Figure 1: (a) Atrichia of eyelashes and eyebrows, follicular papules, and pits on malar prominences. (b) Follicular papules on scalp with alopecia

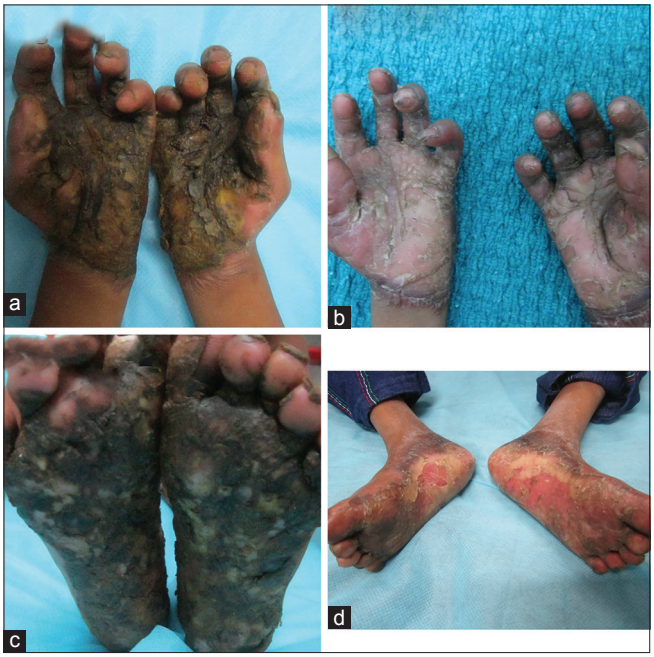

Figure 2: (a) Mutilating transgradient keratoderma restricted to palm. (b) Posttreatment 1 month. (c) Mutilating keratoderma of soles. (d) Post-isotretinoin therapy marked improvement in PPK

either XLR or XLD.[4] XLO is linked to a missense mutation in *MBTPS2* gene.[2] Thus, when confronted with a case of mutilating PPK with alopecia, the presence of KFSD can help to narrow down the diagnosis to XLO diagnose correctly.

It is difficult to differentiate OS caused by *TRPV3* and *MBTPS2* mutations despite the mode of inheritance. This is because there is clinical variability observed in patients from the same family or unrelated patients harbouring the same mutation, suggesting the implication of modifier genes, epigenetics, and/or environmental factors. However, XLO syndrome has been linked to the *MBTPS2* mutations, which is seen in IFAP syndrome (ichthyosis follicularis with atrichia and photophobia). Thus, the clinical features mimic this syndrome.[2] In line with the X-linked inheritance, only male patients present with full clinical disease features, whereas female carriers of *MBTPS2* mutations were either phenotypically normal or showed rather mild and asymmetric symptoms. On the contrary, with *TRPV3* mutations, there is profound clinical heterogeneity and the patients can present either with typical OS hallmarks or incomplete phenotype with atypical features. It can be rarely associated with erythromelalgia.[4]

A recent review opined that, of all the cases reported of OS, only 14 patients with different genetic background (Chinese, Indian, Iranian, Arabic, Caucasian) were found to have AD inheritance, and because of the marked variation in genotype phenotype correlations with the TRPV3 mutations it is difficult to arrive at a consensus regarding its clinical features.[5] Hence, it is difficult to delineate the clinical difference between the XLO syndrome (*MBTPS2* mutation) and the AD variant (*TRPV3* mutation), however, the male affliction is characteristic of XLO syndrome, as seen in our case.

There is no satisfactory treatment for XLO, however, symptomatic relief of the PPK using salicylic acid, retinoids, urea, and topical steroids have been tried. In our case, we administered oral isotretinoin as its action is directed against the major components of the disorder, i.e., PPK and KFSD with appreciable improvement in the morphology.[6]

Though there is no previous report of use of isotretinoin in this disorder, there are studies that have used isotretinoin in pediatric PPK disorders including Papillon-Lef èvre syndrome.[7] Before initiating the treatment, some tests are warranted and the drug should be stopped before the growth spurt occurs.[8] The profound improvement in our case, suggests that isotretinoin is a simple and safe modality in cases of mutilating PPK.

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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Conflicts of interest

There are no conflicts of interest.

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