

Variant of Vohwinkel's syndrome

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ABSTRACT

A 28-year-old female born to consanguineous parents, presented with progressive palmoplantar keratoderma since the age of six months and a constricting band on right fourth finger of one year duration. There was history of similar complaints being present in two other family members. Associated clinical findings included starfish-shaped cornified plaques on knuckles, resorption of distal phalanges and keratotic plaques on elbows, groins and knees. The patient was mentally sound and had normal audiometry. Biopsy from hyperkeratotic plaque showed hyperkeratosis, parakeratosis, increased granular layer and papillomatosis. Gene mapping for loricrin mutation was found to be negative.

Key Words: Keratoderma, Palmoplantar, Vohwinkel's syndrome

INTRODUCTION

Keratoderma hereditaria mutilans (KHM) was first described by Vohwinkel in the German literature in 1929.^[1] This palmoplantar keratoderma is thought to be an autosomal dominant genodermatosis with defective epidermal differentiation and is quite rare.^[2] A triad of clinical features is essentially pathognomonic for Vohwinkel's syndrome and this includes diffuse "honeycomb-like" thickening of palms and soles, "starfish-shaped" keratotic plaques on the dorsum of hands and feet and fibrous constricting bands (pseudo-ainhum) at the interphalangeal joints of hands and feet.^[2,3] The disease is seen in early childhood and has a familial tendency.^[3] Associated findings with the disease are cicatricial alopecia,^[4] ichthyosiform dermatoses, high-tone acoustic impairment, deaf mutism, spastic paraplegia and myopathy, knuckle pads and nail anomalies.^[5] The hyperkeratosis in patients with KHM is difficult to treat.

CASE REPORT

A 28-year-old female born to consanguineous parents presented with progressive thickening of palms and soles since the age of six months and a constricting band on the proximal interphalangeal joint of the right fourth finger of one year duration. There was no history of deaf mutism, mental retardation, spastic paralysis or myalgias, cicatricial alopecia, ichthyosiform dermatoses or autoamputation of digits. Two of her second-degree relatives had similar problems [Figure 1]. Physical examination revealed that the volar aspect of the constricting band was opened and cracked [Figure 2]. Associated with the keratoderma, the patient also had "starfish-shaped" cornified plaques on the knuckles, resorption of distal phalanges and keratotic papules and plaques on the elbows, groin, knees and feet [Figure 3].

Biopsy of hyperkeratotic papules showed

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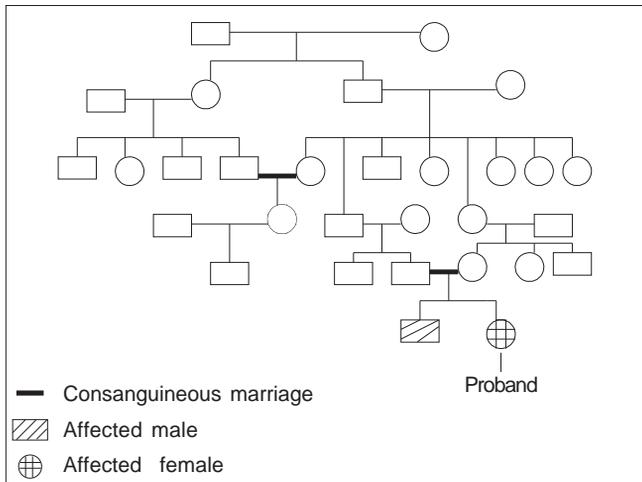


Figure 1: Pedigree chart



Figure 2: Keratoderma showing constricting band at the proximal interphalangeal joint of the right fourth finger



Figure 3: Ketatotic plaques on the dorsa of the feet

hyperkeratosis, parakeratosis, increased granular layer and papillomatosis. X-ray of both hands showed acral osteolysis. Audiometry revealed hearing in both ears

to be within normal limits. To identify an underlying mutation in the loricrin gene in this patient, genomic DNA was isolated from peripheral blood lymphocytes of the proband using PureGene® DNA isolation kit. The entire loricrin gene was polymerase chain reaction amplified from genomic DNA and sequenced directly in an ABI Prism 310 automated sequencer, using the ABI prism big dye terminator cycle sequencing ready reaction kit, following purification with centriflex gel filtration cartridges. Gene mapping for loricrin mutation was found to be negative.

DISCUSSION

There are thought to be two different forms of Vohwinkel's syndrome. The type that is associated with sensorineural hearing loss is thought to result from a mutation of GJB2 gene that codes for the gap junction protein, connexin 26.^[6] Cases of connexin 26 mutations causing autosomal dominant palmoplantar keratoderma with deafness but without other clinical features of Vohwinkel's syndrome have also been reported.^[7] The other clinical variant of Vohwinkel's syndrome associated with generalized ichthyosis without deafness is caused by mutations of the gene encoding loricrin.^[8]

The differential diagnosis of Vohwinkel's syndrome includes other types of hereditary keratodermas that may be associated with autoamputation of the digits. These are Olmsted's syndrome, acral keratoderma of Sybert, Mal de meleda and palmoplantar keratoderma of Gamborg Nielsen.^[9]

Vohwinkel's syndrome has variable expression and treatment should focus on palliation of the keratoderma and prevention of autoamputation. Surgical release of the constricting bands may be used to prevent autoamputation. Treatment options for keratoderma include keratolytics and retinoids. Etretinate and isotretinoin have been used successfully in several patients with Vohwinkel's syndrome to reverse both the keratoderma and pseudoainhum; however, the condition recurred once the medication was discontinued.^[2,3,10,11]

Our patient had neither ichthyosis nor deafness. There

was no evidence of mutation in the loricrin gene. So this may be considered as a new variant of Vohwinkel's syndrome. As our patient was in the reproductive age she refused any treatment with systemic retinoids. However, keratolytics were tried with partial benefit.

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REFERENCES

1. Vohwinkel KH. Keratoderma hereditarium medians. Arch Dermatol Syphil 1929;158:354-64.
2. Camisa C, Rossana C. Variant of Keratoderma hereditaria mutilans (Vohwinkel's syndrome). Treatment with orally administered isotretinoin. Arch Dermatol 1984;120:1323-8.
3. Chang Sing Pang AF, Oranje AP, Vuzevki VD, Stolz E. Successful treatment of keratoderma hereditaria mutilans with an aromatic retinoid. Arch Dermatol 1981;117:225-8.
4. Gibbs RC, Frank SB. Keratoderma hereditaria mutilans (Vohwinkel): Differentiating features of conditions with constriction of digits. Arch Dermatol 1966;94:619-25.
5. Wirz F. Keratoma hereditarium mutilans. Arch Dermatol Syphil 1930;159:311-2.
6. Maestrini E, Korge BP, Ocana-Sierra J, Calzolari E, Cambiaghi S, Scudder PM, *et al.* A missense mutation in connexin 26, D66H, causes mutilating keratoderma with sensorineural deafness (Vohwinkel's syndrome) in three unrelated families. Hum Mol Genet 1999;8:1237-43.
7. Richard G, White TW, Smith LE, Bailey RA, Compton JG, Paul DL, *et al.* Functional defects in a family with deaf mutism and palmoplantar keratoderma. Human Genet 1998;103:393-9.
8. Maestrini E, Monaco AP, McGrath JA, Ishida-Yamamoto A, Camisa C, Hovnanian A, *et al.* A molecular defect in loricrin, the major component of the cornified cell envelope, underlies Vohwinkel's syndrome. Nat Genet 1996;13:70-7.
9. Peris K, Salvati EF, Torlone G, Chimenti S. Keratoderma hereditaria mutilans (Vohwinkel's syndrome) associated with congenital deaf mutism. Br J Dermatol 1995;132:617-20.
10. Wereide K. Mutilating palmoplantar keratoderma successfully treated with etretinate. Acta Derm Venerol 1984;64:566-9.
11. Rivers JK, Duke EE, Justus DW. Etretinate: Management of keratoma hereditaria mutilans in four family members. J Am Acad Dermatol 1985;13:43-9.

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