Resolution of pseudoainhum with acitretin therapy in a patient with palmoplantar keratoderma and congenital alopecia

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Key words: acitretin; congenital alopecia; palmoplantar keratoderma; pseudoainhum.

INTRODUCTION

We report on a patient with palmoplantar keratoderma (PPK) and congenital alopecia (CA) who presented with pseudoainhum and resultant constricted hand mobility. With several months of treatment with acitretin, 25 mg daily, the patient's pseudoainhum resolved, with improvement in hyperkeratosis. We therefore post acitretin as an option for treatment of pseudoainhum, a condition for which reconstructive surgery is considered the conventional treatment.[1]

Abbreviations used:

CA: congenital alopecia
PPK: palmoplantar keratoderma

CASE REPORT

A 46-year-old woman with a history of complex partial epilepsy status post—left anterior temporal lobectomy presented to our clinic with hyperkeratosis of the bilateral hands and feet, progressive since the first year of life. She reported previous trials of topical steroids, salicylic acid, urea, imiquimod and Vaseline throughout her life for hyperkeratosis without improvement. Her chief complaint was the painful fissures that occasionally developed. The patient had otherwise developed normally, with vision and hearing within normal limits. Her mother reported that before the development of hyperkeratosis, around 3 months of age, she had seizures followed by loss of all her scalp and eyebrow hair. Her seizures were accompanied by facial flushing. She also reported a history of hypohidrosis. No other family members, including the patient's parents or 2 children, were affected.

Physical examination was notable for desquamation, hyperkeratosis (most noted around the proximal nail fold), horizontal ridging of the nails, and mild erythema on the dorsal aspect of fingers, with hyperkeratotic plaques at the pressure points of the plantar feet, without toenail involvement (Figs 1 and 2). Alopecia of the scalp, eyebrows, eyelashes, and pubic area was noted, with follicular plugging visible on scalp. After not responding to a trial of emollients, urea and betamethasone ointment, the patient returned for follow-up 5 months later. She reported having a great deal of difficulty moving her fingers over the preceding months. Physical examination found pseudoainhum of her third digit on her right hand (Fig 3). The patient was started on 25 mg (0.3 mg/kg) of acitretin daily. She returned 2 months later with resolution of pseudoainhum and marked improvement in hyperkeratosis (Fig 4). She deferred genetic testing.

DISCUSSION

We present this case not only as an example of a rare condition but also as a report of successful treatment of pseudoainhum with acitretin. The combination of PPK and hypotrichosis (also referred to as congenital alopecia or CA), as found in our patient, can be observed in various well-defined genodermatoses, which are differentiated on the basis of specific additional manifestations and genetic findings.[2-7]

Stevanović[2] in 1959 first described a 4-generation family presenting with hypotrichosis (CA) and PPK. Since then, variants of the condition, including

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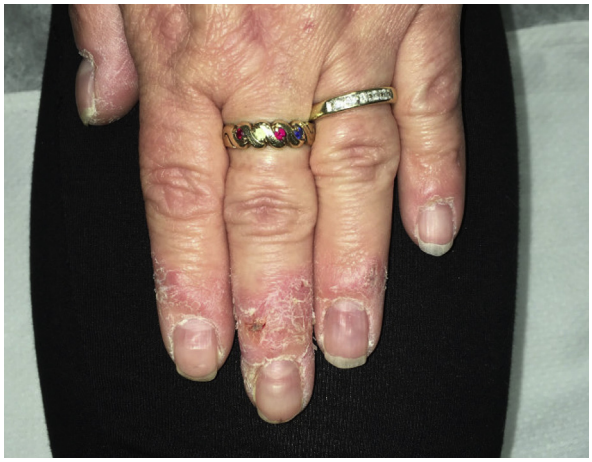

Fig 1. Initial presentation. Desquamation, hyperkeratosis (most noted around the proximal nail fold), horizontal ridging of the nails, and mild erythema on the dorsal aspect of fingers.

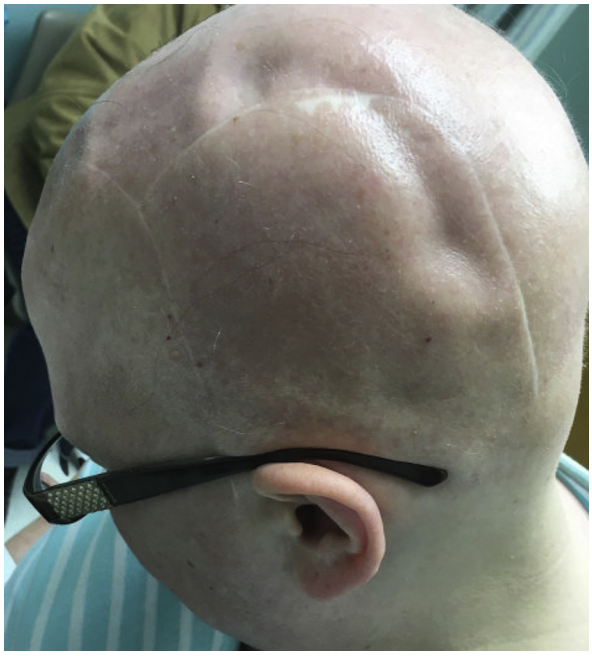

Fig 2. Initial presentation. Alopecia of the scalp.

cataracts-alopecia-sclerodactyly, Vohwinkel disease with CA universalis, Alves syndrome, and keratoderma—hypotrichosis—leukonychia totalis, have been described in multiple families.[3-6] Castori et al[7] reported a case of a 10-year-old girl with generalized atrichia and a severe form of PPK causing pseudoainhum, sclerodactyly, and contractures. As in our patient, the patient's mother reported that she had been born with scalp hair and eyebrows, which was subsequently lost around 1 month of age.[7] Other similarities include preservation of hair follicle openings, hyperkeratosis particularly evident around

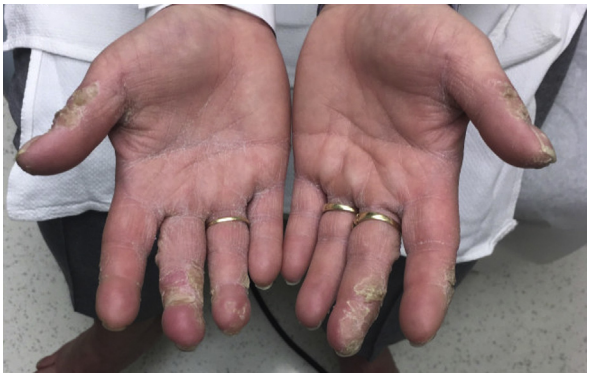

Fig 3. Pseudoainhum of third digit on the right hand.

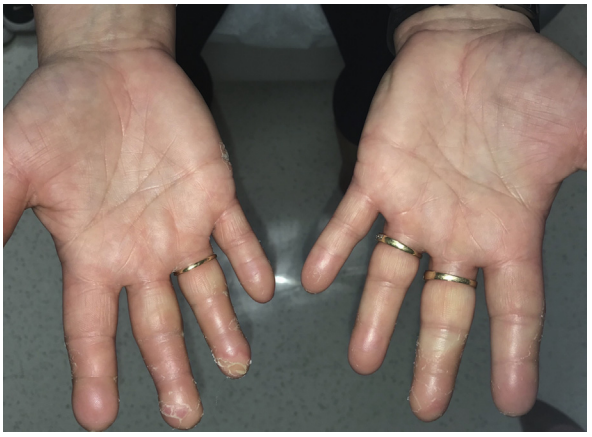

Fig 4. Resolution of pseudoainhum after acitretin therapy.

nails, pseudoainhum, and hyperkeratosis at feet pressure points.[7] The coding regions of *GJB2* and *LOR*, responsible for various forms of Vohwinkel syndrome, were sequenced in this patient, and neither showed a causal mutation.[7]

Although the combination of PPK and CA/hypotrichosis/atrichia may be observed in various ectodermal dysplasias and keratinization disorders, including Clouston syndrome (which can include pseudoainhum), HOPP syndrome, keratosis follicularis spinulosa decalvans, KID syndrome (keratitis-ichthyosis-deafness), odonto-onycho-dermal dysplasia, Lelis syndrome, Olmsted syndrome, and Schöpf-Schulz-Passarge syndrome, the above patients (and our patient) all lack features characteristic of these disorders.[7] A previous review identifying 18 cases of PPK-CA found that the same disorder was present in more than 1 family member.[7] In other cases, only a single family member was affected, making the inheritance pattern unclear.[7] The genetics of PPK-CA remain unknown.[2-7]

Over the last several years, animal experiments have related alterations in the expression of certain connexin subtypes to epileptogenesis, and there are

several reports of patients with Vohwinkel syndrome reported to also have a history of cryptogenic partial epilepsy, postulated to be related to the role of connexin 26 in neuronal migration.[8] Cambiaghi et al[9] reported a case of a girl having seizures shortly after birth, followed by universal alopecia at 4 months of age and PPK at 10 years of age, with later development of pseudoainhum, similar to our patient.[9] It is not known in our patient if the mutation leading to the development of her dermatologic manifestations is also associated with her history of epilepsy.

We present, to our knowledge, the first case of an individual with pseudoainhum caused by PPK-CA successfully treated with acitretin, a monoaromatic second-generation retinoid, which down regulates gene transcription leading to antiproliferative, antiinflammatory, and antikeratinizing effects.[1] There is one report in the literature of resolution of pseudoainhum in a patient with Camisa syndrome, an ichthyosiform variant of Vohwinkel syndrome, after treatment with acitretin.[1] The patient was continued on acitretin for 6 months with near normalization of ichthyosis and reversal of pseudoainhum.[1] After discontinuing treatment for 1 year, the ichthyosis relapsed with lesser severity, but the pseudoainhum did not.[1] There are also reports of 2 families whose pseudoainhum caused by Vohwinkel syndrome resolved with etretinate therapy, with normalization of digital blood circulation.[10] We therefore post acitretin as an option for treatment of pseudoainhum, a condition for which reconstructive surgery is considered the conventional treatment.[1]

REFERENCES

1. Kura MM, Parsewar S. Reversal of pseudo-ainhum with acitretin in Camisa's syndrome. *Indian J Dermatol Venereol Leprol*. 2014;80(6):572-574.
2. Stevanović DV. Alopecia congenita: the incomplete dominant form of inheritance with varying expressivity. *Acta Genet Stat Med*. 1959;9:127-132.
3. Wallis C, Ip FS, Beighton P. Cataracts, alopecia, and sclerodactyly: a previously apparently undescribed ectodermal dysplasia syndrome on the island of Rodrigues. *Am J Med Genet*. 1989;32:500-503.
4. Bhatia KK, Chaudhary S, Pahwa US, Mehrotra GC. Keratoma hereditaria mutilans (Vohwinkel's disease) with congenital alopecia universalis (atrichia congenita). *J Dermatol*. 1989;16:231-236.
5. Stratton RF, Jorgenson RJ, Krause IC. Possible second case of tricho-oculo-dermo-vertebral (Alves) syndrome. *Am J Med Genet*. 1993;46:313-315.
6. Başaran E, Yilmaz E, Alpsoy E, Yilmaz GG. Keratoderma, hypotrichosis and leukonychia totalis: a new syndrome? *Br J Dermatol* 1995;133:636-638.
7. Castori M, Valiante M, Ritelli M, et al. Palmoplantar keratoderma, pseudo-ainhum, and universal atrichia: a new patient and review of the palmoplantar keratoderma-congenital alopecia syndrome. *Am J Med Genet A*. 2010;152A:2043-2047.
8. Serrano Castro PJ, Naranjo Fernandez C, Quiroga Subirana P, Payan Ortiz M. Vohwinkel Syndrome secondary to missense mutation D66H in GJB2 gene (connexin 26) can include epileptic manifestations. *Seizure*. 2010;19(2):129-131.
9. Cambiaghi S, Barbareschi M, Tadini G. Ichthyosis follicularis with atrichia and photophobia (IFAP) syndrome in two unrelated female patients. *J Am Acad Dermatol*. 2002;46:S156-S158.
10. Rivers JK, Duke EE, Justus DW. Etretinate: management of keratoma hereditaria mutilans in four family members. *J Am Acad Dermatol*. 1985;13(1):43-49.