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Isotretinoin Treatment in Acrokeratosis Verruciformis of *Hopf*

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Abstract

Observation: Acrokeratosis verruciformis of Hopf (AV) is a rare autosomal dominant or sporadic genodermatosis characterized by multiple, flat-topped, verrucous, skin-colored papules on the dorsal aspects hands and feet, elbows and knees. Lesions usually manifest at birth or during childhood and closely resemble verruca plana and acral lesions of Darier disease. We present a case of sporadic AV in a 39-year-old woman who presented with about 25-year history of progressive, flat, warty papules localized to the dorsum of the her hands and feet. She had been previously misdiagnosed as Darier disease. We started oral isotretinoin treatment and observed a moderate response. We reported this case with review of the literature to remind this rare disease and to suggest oral isotretinoin as an alternative treatment choice.

Introduction

Acrokeratosis verruciformis of *Hopf* (AV) is a rare genodermatosis characterized by multiple, flat-topped, verrucous, skin-coloured papules on the dorsum of the hands and feet, elbows and knees [**1, 2, 3, 4**]. The nails may be whitish and thickened, and have longitudinal ridges breaking at the distal edge [**2**].

We present a case of sporadic AV in a 39-year-old woman managed with oral isotretinoin who had been previously misdiagnosed as *Darier* disease.

Case Report

A 39 year-old woman presented with about 25-year history of slightly pruritic lesions on the hands and feet (**Figure 1**). There was not family history of similar lesions. She did not any systemic disease. She previously had been treated with clobetasol 17 propionate 0.05 % cream with diagnosis of Darier disease in different center, but the lesions had no regressed. Physical examination revealed 1-4 mm, skin-colored, verrucous, flat-topped, hyperkeratotic papules over the dorsal hands,

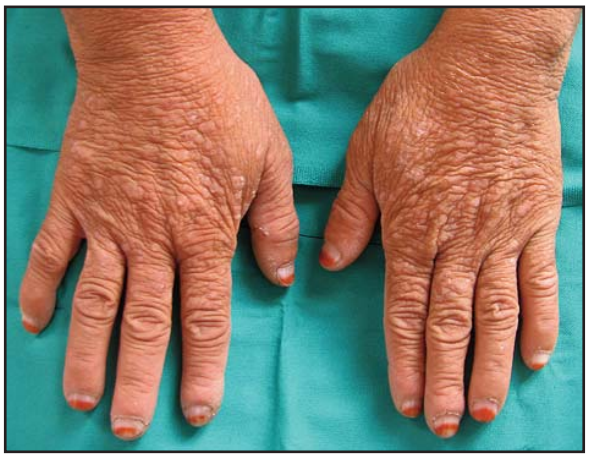

Figure 1. Warty papules over the dorsal aspects of her hands (before the treatment)

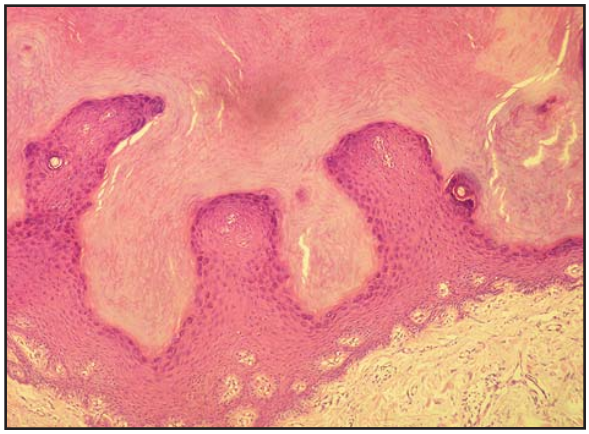

Figure 2. The epidermis shows marked hyperkeratosis, acanthosis, and papillomatosis. An increase in thickness of the granular layer. (H&E, x200)

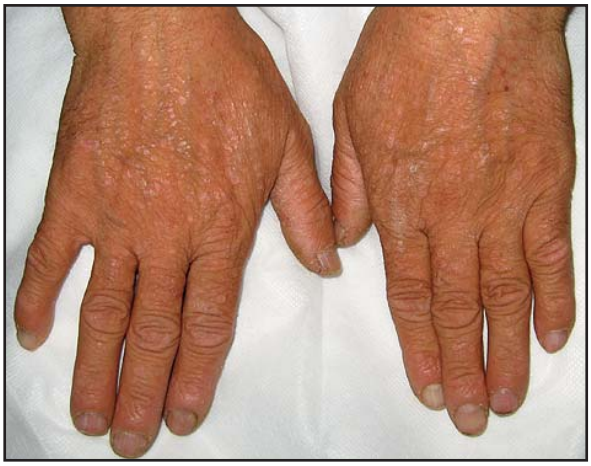

Figure 3. Appearance of papules (during the third months of the treatment)

wrists, feet, and ankles and longitudinal ridges breaking at the distal edge in her nails. There was no palmar involvement. The remaining physical and laboratory investigations were normal. Skin biopsy was revealed marked hyperkeratosis with acanthosis, papillomatosis and hypergranulosis. The dermis was infiltrated with a few inflamatory cells surrounding the superficial vessels (**Figure 2**). Both clinical and laboratory findings were compatible of acrokeratosis verruciformis of *Hopf*. Initial, 3 months topical retinoid therapy was failed. So she had pregnancy plan for two years later, we didn't start acitretin. Oral isotretinoin at 0.5 mg/kg (30 mg/day) was started. The papules had moderately disappeared, and roughness and thickness of the skin had decreased during the treatment (**Figure 3**). Treatment was continued for three months and then stopped because of severe dryness side effect. The lesions reappeared after the treatment.

Discussion

Acrokeratosis verruciformis of *Hopf* was firstly described by *Hopf* in 1931. Although the lesions are usually present at birth, the disease may also appear any times of life [**2**]. The disease is inherited in autosomal dominant, but sporadic cases also occur [**1, 2, 5, 6**]. Our case was considered sporadic due to lack of similar complaints in her family.

Skin biopsy is required to confirm the diagnosis. Histological examination of AV usually demonstrates considerable hyperkeratosis, an increase in thickness of the granular layer, mild regular acanthosis and variable "church spire" papillomatosis. No parakeratosis, dyskeratosis or viral cytopathic changes is seen [**1, 2, 3**].

The differential diagnosis of AV includes *Darier* disease, verruca plana, epidermodysplasia verruciformis, and stucco keratoses. Acrokeratosis verruciformis can be easily distinguished from other diseases through its histopathological features and clinical distribution of lesions [**1, 2, 7**].

The relationship between AV and *Darier*'s disease has not been made exactly clear yet. While some authors have been suggesting that both diseases are entirely different diseases, the others have been claiming that these are diverse types of the same disease [**1, 7, 8, 9**]). AV shows excessive but normal keratinization, whereas in *Darier*'s disease keratinization is changed and defective [**2, 3, 8**]. Opposite to *Darier*'s disease, AV does not display seborrheic regions and mucous membranes [**1, 2**]. AV like acral lesions can be seen in Darier's disease and these lesions may precede, appear with, or follow the development of *Darier*'s lesions in other regions [**1**]. For this reason, it should be considered a patient admitted to the clinic with AV like lesions can be a patient of *Darier*'s disease and other lesions can appear later. AV and *Darier* disease can be distinguished by histology. Acantholysis, parakeratosis and dyskeratosis are found *Darier* disease but there isn't in AV [**1, 4**].

Acrokeratosis verruciformis of *Hopf* have been reported coexisted with some disease such as nevoid basal cell carcinoma syndrome, *Darier*

disease, and ichthyosis vulgaris in the literature [**7, 10, 11**]. Furthermore, transformation to squamous cell carcinoma has been reported [**12**].

There is no completely curative treatment for AV. Topical retinoids and keratolytics, superficially ablative therapies such as peels, CO_2 or Nd:YAG laser, or cryotherapy, and acitretin can be used. Recurrence is quite frequent after the treatment [**1, 2, 3, 4**].

We have not seen use of isotretinoin in the treatment of AV in the literature so far. We observed moderately decrease the papules, and roughness and thickness of the skin during the treatment. As in other treatments, recurrence was observed also in our case after isotretinoin was stopped.

We offer that using oral isotretinoin in treatment of AV rather than acitretin especially women patients in reproductive age, because the teratogenic risk time after the end of isotretinoin treatment is much shorter than that of asitretin treatment. Recurrence is almost rule after current treatments, therefore, researches about new therapy modalities for AV are require. It is proposed to remind AV at differential diagnosis in the patience with skin-coloured, flat, warty papules localized to the dorsum of the hands and feet.

In conclusion, we reported this case with review of the literature to remind this rare disease especially in differential diagnosis of *Darier* disease and to suggest oral isotretinoin as an alternative treatment choice for AV treatment.

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