Confluent and Reticulated Papillomatosis Successfully Treated with Minocycline

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Confluent and reticulated papillomatosis (Gougerot and Carteaud) is a rare but clinically distinct dermatosis of which the etiology is unknown.

We report 2 cases. One case is a 16-year-old boy who had a hyperpigmented reticulated eruption on the trunk and both arms and the other case is a 33-year-old man who had a similar eruption on the chest and back. The former, with previous treatment with oral and topical antifungal agent in another clinic didn’t show any improvement and the latter case, with initial treatment of itraconazole did not improve his skin lesion. The rashes of two patients virtually disappeared with administration of minocycline. These observations indicate that the role of microorganisms sensitive to minocycline or anti-proliferative effect of minocycline could be presumed. (Ann Dermatol 12(1) 33–37, 2000).

Key Words: Confluent and reticulated papillomatosis, Minocycline

Confluent and reticulated papillomatosis is one of three related cutaneous disorders of unknown etiology first described by Gougerot and Carteaud in 1927. The other two morphologic variants are nummular and confluent papillomatosis and generalized punctate papillomatosis. These three variants share the features of asymptomatic, scaly pigmented papules and plaques and papillomatosis histopathologically. Because the etiology of confluent and reticulated papillomatosis is unclear, a variety of treatments have been attempted.

We present two cases of confluent and reticulated papillomatosis that initially did not improve with antifungal agents and were successfully treated with minocycline.

CASE REPORT

CASE 1- A 16-year-old boy presented with a 1 year history of itchy pruritic eruptions on his trunk and both arms (Fig. 1). His medical and family histories were unremarkable. He was treated with oral antifungal agents and topical treatment under the impression of tinea versicolor for 1 month, but his skin lesions did not improve. During winter time, his skin lesion slightly improved without any treatment. In the spring, the skin lesion was aggravated again and he visited our clinic. Physical examination revealed brownish reticulated patches on the trunk and both arms. Direct microscopic examination of the skin scales in potassium hydroxide (KOH) showed no yeasts and hyphae. The results of routine laboratory studies, including complete blood cell count, urinalysis, erythrocyte sedimentation, liver function tests, blood urea nitrogen, and serum cholesterol and triglyceride levels, were within normal limits. Histopathologic examination of the skin biopsy specimen from the lesion of the lower abdomen demonstrated epidermal changes with hyperkeratosis, increased basal pigmentation, papillomatosis, and mild acanthosis.
Sparse upper dermal perivascular mononuclear cell infiltrates were also noted. Fungal elements were not present in sections stained with Periodic acid-Schiff stain (Fig. 2).

The clinical and histopathologic findings were consistent with confluent and reticulated papillomatosis. Because of failure of the previous treatment with antifungal agent, a therapeutic trial of minocycline (100 mg twice a day) was started. He was treated with minocycline for a total 8 weeks and it was discontinued without tapering. Within 2 weeks the eruption had virtually disappeared. After 1 month of additional therapy, the confluent and reticulated papillomatosis cleared completely (Fig. 3). Follow up examination at 7 months after discontinuation of therapy revealed no evidence of recurrence.

CASE 2-A 33-year-old man had hyperpigmented confluent and reticulated patches on the chest and back. During the past year, his skin lesion had been aggravated in the summer and improved in the winter. He had not been received any treatment. Wood's lamp examination and direct smear for fungus were negative. A skin biopsy was not done. We began to treat him with daily itraconazole 200 mg for 1 week and topical bifonazole spray for 1 month. These were no improvement, so a trial with oral minocycline, 100 mg twice a day, was started. After 1 month of therapy, the skin lesions of confluent and reticulated patches had cleared almost completely. Skin lesions have not recurred since 9 months after minocycline treatment.

DISCUSSION

Confluent and reticulated papillomatosis is an uncommon condition that was described in 1927 by Gougerot and Carteaud as "unnamed pigmented papillomatosis". Initial lesions of confluent and reticulated papillomatosis are 1 to 2 mm erythematous papules that typically occur on the intermammary, interscapular, and epigastric regions. Subsequently the individual lesions enlarge to 4 to 5 mm and develop a brown hue. Continued radial spread results in confluence on the central trunk and a reticulated pattern peripherally. Eventually the chest, neck, shoulder, and back are involved. The
mucous membranes are spared. It progresses chronically and may become worse in the summer, although spontaneous resolution is also possible. The typical onset is during puberty, and females are affected more frequently than males; although some authors found no evidence in recent literature as suggested by earlier publications. There are two familial cases in the literature.

The differential diagnosis of confluent and reticulated papillomatosis includes acanthosis nigricans, pseudoacanthosis nigricans, pseudoatrophoderma of colli, tinea versicolor, amyloidosis cutis, ictyosis, Darier's disease, flat wart, and other two variants of cutaneous papillomatosis, namely nummular and confluent papillomatosis and generalized punctate papillomatosis.

Acanthosis nigricans is similar to confluent and reticulated papillomatosis morphologically with thicker, velvety hyperpigmented papules and plaques in a confluent pattern, but the involvement of intriginous areas, most often the neck and axillae, differs from the pattern of confluent and reticulated papillomatosis. Histologically, there is no distinction between acanthosis nigricans and confluent and reticulated papillomatosis. Whether these are truly different diseases or different patterns of the same disease remains unknown. Pseudoacanthosis nigricans, probably a variant of benign acanthosis nigricans, is characterized by onset with obesity and disappearance with weight loss. Pseudoatrophoderma of colli is inherited with autosomal dominant pattern.

It shows hypopigmentation and atrophy alternating with areas hyperpigmentation and scale often the neck and upper trunk. Tinea versicolor can mimic confluent and reticulated papillomatosis and often has a grey or brown scale clinically similar to confluent and reticulated papillomatosis. It differs from confluent and reticulated papillomatosis with positive KOH examination of the biopsy specimen that demonstrates hyphae of Malassezia furfur and the histopathologic finding that does not show papillomatosis. Amyloidosis cutis was considered by several authors to be a possible cause of confluent and reticulated papillomatosis. Although macular amyloidosis may clinically mimic early confluent and reticulated papillomatosis, the histologic findings differentiate these entities. The other two variants of confluent and reticulated papillomatosis are rare and may be under-reported.

Histologic findings of confluent and reticulated papillomatosis are hyperkeratosis, sometimes with focal parakeratosis, atrophy of stratum granulosum, hyperpigmentation of the basal cell layer, acanthosis, and papillomatosis. At times, there is also a perivascular or periadnexal mononuclear cell infiltrate that may be associated with dermal edema. Electron-microscopic findings vary from authors to authors. Sonnichsen et al. and Groh et al. found destruction of desmosomes and tonofilaments and Lee et al. noted an increase in the number of transitional cells between the strata granulosum and corneum. The pathophysiology of this disorder is unknown, although two prominent theories are suspected. One is abnormal host response to Pityrosporum orbiculae and abnormal keratinization. Other suggestions include photosensitivity, genetic predisposition, amyloidosis cutis, and endocrinopathy. The causative role of Pityrosporum orbiculae in the pathogenesis is controversial. The clinical resemblance of confluent and reticulated papillomatosis to tinea versicolor falls into confusion, and Pityrosporum orbiculae occasionally can be found in the lesions. The mere presence of spores in the patients does not necessarily prove a casual relationship. Furthermore, treatment with antifungal agents is not effective in the majority of cases. A bacterial cause of confluent and reticulated papillomatosis has never been documented. But the frequent onset of confluent and reticulated papillomatosis in adolescents or young adults, the occasional association with obesity, and the predilection for seborrheic areas of the trunk suggest an association with sebum production or an alteration of sebum by resident bacteria. Recently a defect in keratinization was suggested on the basis of findings that the transitional cell layer between stratum corneum and stratum granulosum was increased to three or four layers in patients with confluent and reticulated papillomatosis.

The treatment modalities proposed in this condition are numerous as like keratolytics such as urea cream or salicylic acid, ketoconazole, topical 2.5% selenium sulfide lotion and 20% sodium thiosulfate and so forth and their success is variable. But the majority of patients with confluent and reticulated papillomatosis often do not respond well to these treatments.

The response of confluent and reticulated papil-
lomatosi to cycline antibiotics was first proposed by Carteaud\textsuperscript{18} (using furacyleline) in 1965 and further success have been confirmed by other authors\textsuperscript{15,18,21}. We also experienced a remarkable effect with minicycline. The mechanism of action of minicycline in confluent and reticulated papillomatosis remains obscure. Minicycline has been found to reduce free fatty acids in sebum\textsuperscript{10}, prevent lipid oxidation and superoxide scavenging\textsuperscript{10}, suppress leukocyte chemotaxis\textsuperscript{16} and also to block protein and DNA synthesis\textsuperscript{22}. Recently Poiskitt and Wilkinson\textsuperscript{30} suggested that the latter two mechanisms may be responsible for its effectiveness in confluent and reticulated papillomatosis on the basis that it showed more epidermal proliferative than inflammatory features. Another hypothesis is proposed by Katayama et al\textsuperscript{1}, that bacterial factors such as staphylococcus-derived toxins may play a role in keratinizing disorders such as confluent and reticulated papillomatosis.

In 1954 Meischer\textsuperscript{22} first proposed that confluent and reticulated papillomatosis was a disorder of keratinization after the successful treatment with vitamin A for one case of confluent and reticulated papillomatosis. Other authors also have reported satisfactory clearing of confluent and reticulated papillomatosis with tretinoin cream\textsuperscript{23}, etretinate\textsuperscript{3,24} and isotretinoin\textsuperscript{25}. But teratogenic side effect of etretinate and isotretinoin is a serious problem among other things. Furthermore confluent and reticulated papillomatosis is more prevalent in young females. So we suggested that minicycline should be considered as a first-choice therapeutic agent in patients with confluent and reticulate papillomatosis because minicycline is safe, economic and effective, although our study was neither controlled nor double-blinded. But further study for overall dosage of minicycline and treatment duration is required.

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