Confluent and Reticulate Papillomatosis Treated With Minocycline and Tazarotene

Hui-Wen Tseng, MD, MOH; Hui-Hwa Tseng, MD; Chieh-Shan Wu, MD

Practice Points

- Confluent and reticulate papillomatosis is diagnosed based on clinical findings (ie, scaling brown macules and patches that appear reticulate and show signs of papillomatosis) and typical distribution (eg, involvement of the upper trunk and neck) as well as negative fungal staining of scales and no response to antifungal treatment.
- Confluent and reticulate papillomatosis can manifest with mild pruritus, but typically there are no symptoms.
- Minocycline is the most effective treatment of confluent and reticulate papillomatosis.

Confluent and reticulate papillomatosis (CRP) (also known as Gougerot-Carteaud syndrome) is a rare disorder that usually presents sporadically, with onset typically occurring in young adulthood. We present 2 cases of CRP with typical clinical manifestations of scaly, dull, brownish, confluent and reticulate macules and patches. On examination using a potassium hydroxide (KOH) preparation and Periodic acid–Schiff (PAS) stain, both patients' lesions were negative for fungal elements; in patient 2, bacteria colonies accumulated in follicular orifices without perifollicular inflammation in the dermis. Both patients responded well to treatment with oral minocycline and topical tazarotene and showed clearance of CRP lesions at 12- and 8-month follow-up, respectively.

Cutis. 2013;91:194-197.

Confluent and reticulate papillomatosis (CRP) (also known as Gougerot-Carteaud syndrome) is a rare disorder that was first described in 1927.[1] The occurrence of CRP is mostly sporadic, with onset typically occurring in young adulthood. The clinical findings of CRP include scaly, dull, brownish macules and patches in a reticulate pattern and papillomatosis on the upper trunk and neck. Lesions typically respond well to treatment with minocycline. We present 2 patients with CRP based on classic clinical and histopathologic findings.

From Kaohsiung Veterans General Hospital, Taiwan. Drs. Hui-Wen Tseng and Wu are from the Department of Dermatology, and Dr. Hui-Hwa Tseng is from the Departments of Pathology and Laboratory Medicine. Dr. Hui-Wen Tseng also is from the Department of Nursing, College of Health and Nursing, Meiho University, Pingtung, Taiwan.

The authors report no conflict of interest.

Correspondence: Hui-Wen Tseng, MD, MOH, 386 Ta-Chung 1st Rd, Kaohsiung, Taiwan 81362 (hwtseng@vghks.gov.tw).

Case Reports

Patient 1—A 22-year-old man presented with a large area of extensive scaly, velvety, dull, brownish, confluent macules and patches on the neck and trunk of 4 years' duration (Figure 1). The patient reported no initial erythematous changes or itching. The lesions were refractory to topical antifungals that were used when he initially was believed to have pityriasis versicolor. The brownish patches initially appeared in the inframammary area and then spread to the abdomen, flanks, infra-axillary area, back, and neck. The lesions formed a reticulate pattern at the periphery and persisted year-round. The patient reported mild itching in the winter when his skin became dry. The lesions were not exacerbated by hot humid weather and did not subside in the winter. Urea cream was effective in relieving the patient's dry itchy skin but did not clear the lesions.

The patient presented in the summer. Examination of skin scrapings using a potassium hydroxide (KOH) preparation showed no fungal hyphae. A biopsy of an abdominal lesion showed hyperkeratosis, mild acanthosis, and undulation of the epidermis (Figure 2). Mild

perivascular mononuclear inflammatory cell infiltration was observed in the superficial dermis; pathology of the subcutaneous tissue was unremarkable. Periodic acid–Schiff (PAS) stain showed no fungal hyphae in the corneal layer.

Clinical and pathological features were indicative of CRP. Treatment with oral minocycline hydrochloride (100 mg twice daily) and tazarotene cream 0.1% (once daily) was prescribed. The lesions partially subsided 1 week following initiation of treatment and were mostly faded at 4 weeks. After 8 weeks of treatment with minocycline, only residual, focal, irregular-shaped, brownish patches on the lower abdomen were noted. At his 12-month follow-up, the patient reported no recurrence of the lesions.

Patient 2—A 27-year-old woman presented with dull, brownish, velvety patches on the abdomen and the inguinal, inframammary, and axillary areas that had progressively enlarged over 2 years (Figure 3). The cutaneous manifestations and characteristics were similar to those observed in patient 1.

At 14 years of age, the patient was diagnosed with papillary carcinoma in situ of the thyroid, which was treated via a subtotal thyroidectomy and partial parathyroidectomy. She was prescribed levothyroxine sodium and was euthyroid with no recurrence. The patient did not receive treatment of the lesions prior to presentation. Examination via a KOH preparation revealed no fungal hyphae. The pathologic features of a skin biopsy of an abdominal lesion were similar to those observed in patient 1 (Figure 4); PAS stain showed no fungal hyphae.

Interestingly, we found gram-positive cocci that had accumulated in the corneal layer of the follicular orifices. A diagnosis of CRP was made, and the patient was prescribed minocycline hydrochloride (100 mg twice daily) and tazarotene cream 0.1% (once daily) for 2 weeks. She discontinued the minocycline on her own later because she was undergoing treatment of a Bartholin gland infection, but she continued once-daily treatment with topical tazarotene. At her 8-month follow-up, the patient reported total clearance of the lesions with no recurrence.

Comment

Confluent and reticulate papillomatosis is a rare disorder of sporadic occurrence and has been reported in all racial groups. It can occur in both genders as well as in all age groups but most commonly presents in young adults.[2]

The initial clinical manifestations of CRP include 1- to 2-mm, brownish, scaly macules or hyperkeratotic papules that can enlarge up to 4 to 5 mm in diameter. The lesions form confluent patches centrally and a reticular pattern peripherally. Early lesions can sometimes be erythematous but commonly are dull brown. Confluent and reticulate papillomatosis normally manifests without symptoms but sometimes can be mildly pruritic. Lesions usually arise on the trunk, initially in the inframammary and/or epigastric areas, and then extend to the chest, particularly the intermammary area; back; and abdomen. Confluent and reticulate papillomatosis also can occur in the infrascapular or interscapular regions and spread to the shoulders, nape, and/or buttocks.[2] Other unusual locations that have been reported include the forehead,[3] pubic area, hand, elbow, knee,[4] and popliteal fossa.[5]

Confluent and reticulate papillomatosis was diagnosed in both of our patients based on the characteristic

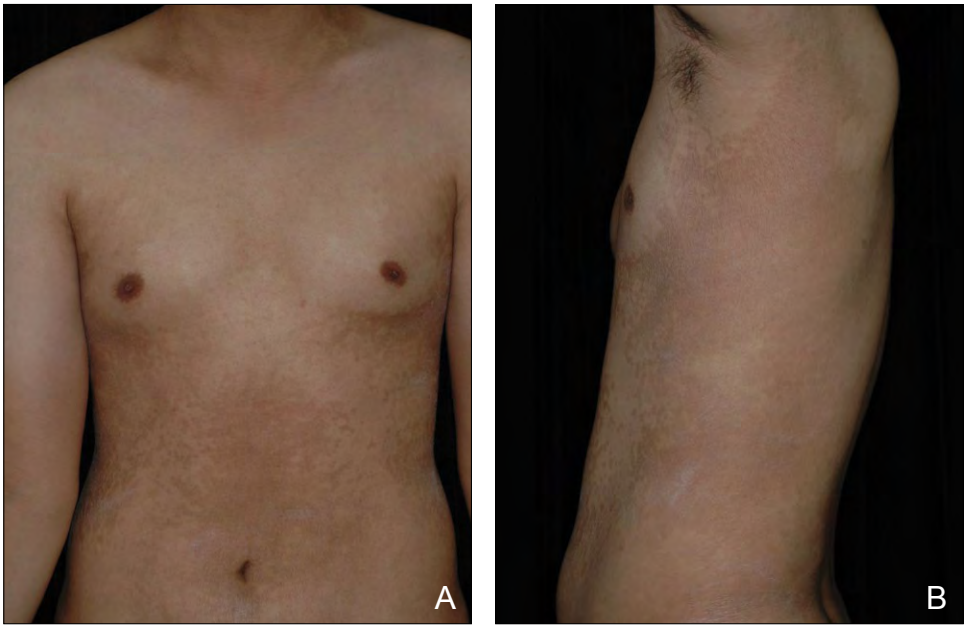

Figure 1. Confluent and reticulate scaling with brownish macules and patches on the neck, trunk, and back (A and B).

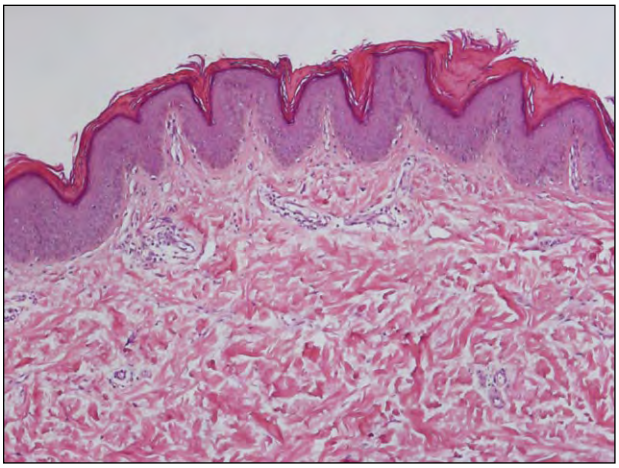

Figure 2. Epidermal undulation with hyperkeratosis, mild acanthosis, and mild perivascular infiltration of mononuclear inflammatory cells (H&E, original magnification ×100).

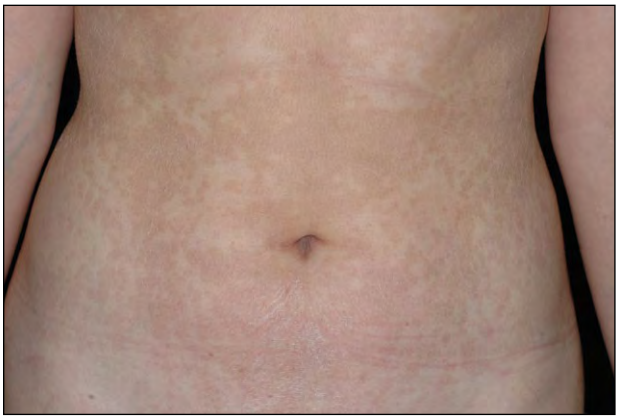

Figure 3. Confluent and reticulate scaling with brownish papules and patches on the abdomen.

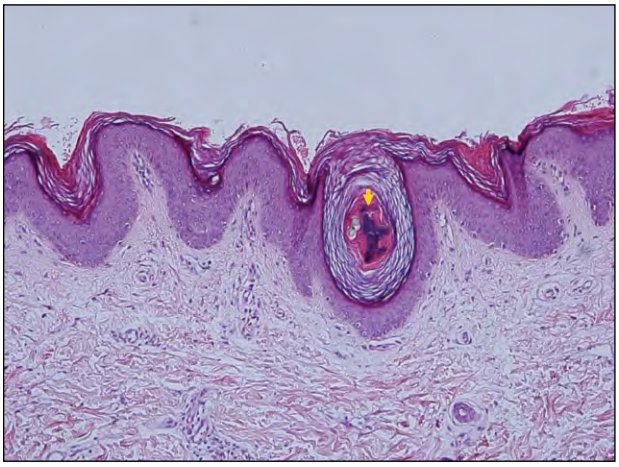

Figure 4. Epidermal undulation with hyperkeratosis, minimal acanthosis, and mild perivascular infiltration of mononuclear inflammatory cells. Bacterial colonies mixed with keratins and vellus hairs in the hair follicular orifice also were observed (arrow)(H&E, original magnification ×100).

clinical pattern and distribution, supportive histology, and dramatic response to treatment with minocycline and tazarotene. Davis et al[6] proposed the following criteria for diagnosis of CRP: (1) clinical findings that include scaling brown macules and patches that appear reticulate and show signs of papillomatosis; (2) involvement of the upper trunk and neck; (3) negative fungal staining of scales; (4) no response to antifungal treatment; and (5) excellent response to treatment with minocycline.

Histology of CRP lesions typically demonstrates hyperkeratosis, papillomatosis, and acanthosis with a mild to moderate increase in the deposition of pigmentation (melanin). A characteristic feature of CRP is bulbous epidermal rete ridges that protrude slightly into the papillary dermis with pigment at their bases. Mutasim[7] described the diagnosis of confluent and reticulated papulosquamous eruption in cases with lesions that demonstrated clinical characteristics and responded well to treatment with minocycline but without papillomatosis. Atasoy and Aliağaoğlu[8] claimed that papillomatosis in histology is characteristic of CRP but is not diagnostic. Papillomatosis may be seen in fully developed lesions, but it may be subtle in early or late lesions.

Acanthosis nigricans (AN), one of several differential diagnoses, is similar to CRP in cutaneous and histologic characteristics; however, the clinical distribution and etiology differ. The clinical features of AN are darker, thicker, more velvety plaques that typically involve the intertriginous area.[2] Hamilton et al[9] concluded that CRP was a separate disease entity because most patients with CRP were healthy without endocrinopathy or malignancy, which often are associated with AN.

Clinical manifestation of CRP resembles pityriasis versicolor but without evidence of fungal elements. The diagnostic examinations for fungal infection include KOH examination of skin scrapings using light microscopy, fluorescence by Wood light, and PAS stain or Gomori methenamine-silver stain of skin biopsy specimens.[6] In one patient with CRP lesions, heavy yeasts were found via KOH examination of skin scrapings, but he failed to respond to antifungal treatment.[10]

The late stage of prurigo pigmentosa is similar to CRP with reticulate hyperpigmentation present clinically and epidermal acanthosis and hyperkeratosis observed pathologically. The initial inflamed pruritic stage (ie, pruritic urticarial papules or vesicles in a reticulate pattern on the neck and trunk) of prurigo pigmentosa is not seen in cases of CRP. Prurigo pigmentosa also responds to minocycline treatment.[11]

Minocycline has been recommended as the most effective treatment of CRP.[2,5,6,10,12-14] Various oral antibiotics including azithromycin,[4,15] clarithromycin, erythromycin, fusidic acid,[13] doxycycline, tetracyclines,[16]

roxithromycin,[17] and cefdinir[14] also have been successful in treating CRP. The effect of antibiotics might be predominantly anti-inflammatory; however, no bacteria, even in the role of colonizers, were identified in the lesion sites or biopsied specimen before.[2] One report has linked the presence of the actinomycete *Dietzia* species in the skin of patients with CRP.[18]

Confluent and reticulate papillomatosis also responds to treatment with retinoids and vitamin D derivatives, such as oral isotretinoin,[19] etretinate, and acitretin, as well as topical tretinoin,[20] tazarotene,[21] and calcipotriol.[22] This evidence suggests that CRP is a disease of keratinization. Most patients show no response to antifungal treatment; therefore, a poor response to antifungal therapy may provide a clue to the diagnosis of CRP.[6] The debate on the etiology of CRP has lasted for decades and continues without a definite conclusion.

Conclusion

We describe 2 patients who fulfilled the diagnostic criteria for CRP. In both patients, the location and reticulate pattern of the lesions were distinctive of CRP and irregular undulation was observed in the epidermis. The papillomatosis was subtle, was not clinically striking, and was mild and irregular on histopathologic analysis. In both patients, the lesions completely resolved after treatment with oral minocycline and topical tazarotene, with disease-free intervals of 12 and 8 months, respectively. In patient 2, we found bacteria colonies accumulated in the follicular orifices without perifollicular inflammation in the dermis on histopathology; this finding was uncommon. It is uncertain if this finding is attributed to the normal flora of skin or the pathogenesis of CRP; further investigation is warranted.

REFERENCES

1. Gougerot H, Carteaud A. Papillomatose pigmentee innominee. *Bull Soc Fr Dermatol Syphiligr.* 1927;34:719-721.
2. Scheinfeld N. Confluent and reticulated papillomatosis: a review of the literature. *Am J Clin Dermatol.* 2006;7:305-313.
3. Kim BS, Lim HJ, Kim HY, et al. Case of minocycline-effective confluent and reticulated papillomatosis with unusual location on forehead. *J Dermatol.* 2009;36:251-253.
4. Atasoy M, Aliağaoğlu C, Erdem T. A case of early onset confluent and reticulated papillomatosis with an unusual localization. *J Dermatol.* 2006;33:273-277.
5. Lee D, Cho KJ, Hong SK, et al. Two cases of confluent and reticulated papillomatosis with an unusual location. *Acta Derm Venereol.* 2009;89:84-85.
6. Davis MD, Weenig RH, Camilleri MJ. Confluent and reticulate papillomatosis (Gougerot-Carteaud syndrome): a minocycline-responsive dermatosis without evidence for yeast in pathogenesis. a study of 39 patients and a proposal of diagnostic criteria. *Br J Dermatol.* 2006;154:287-293.
7. Mutasim DF. Confluent and reticulated papillomatosis without papillomatosis. *J Am Acad Dermatol.* 2003;49:1182-1184.
8. Atasoy M, Aliağaoğlu C. Is confluent and reticulated papillomatosis without papillomatosis early or late stage of confluent and reticulated papillomatosis? *J Cutan Pathol.* 2006;33(suppl 2):52-54.
9. Hamilton D, Tavafoghi V, Shafer JC. Confluent and reticulated papillomatosis of Gougerot and Carteaud. its relation to other papillomatoses. *J Am Acad Dermatol.* 1980;2:401-410.
10. Fuller LC, Hay RJ. Confluent and reticulate papillomatosis of Gougerot and Carteaud clearing with minocycline. *Clin Exp Dermatol.* 1994;19:343-345.
11. Böer A, Misago N, Wolter M, et al. Prurigo pigmentosa: a distinctive inflammatory disease of the skin. *Am J Dermatopathol.* 2003;25:117-129.
12. Montemarano AD, Hengge M, Sau P, et al. Confluent and reticulated papillomatosis: response to minocycline. *J Am Acad Dermatol.* 1996;34(2, pt 1):253-256.
13. Jang HS, Oh CK, Cha JH, et al. Six cases of confluent and reticulated papillomatosis alleviated by various antibiotics. *J Am Acad Dermatol.* 2001;44:652-655.
14. Yamamoto Y, Kadota M, Nishimura Y. A case of maxacalcitol-resistant confluent and reticulated papillomatosis successfully treated with minocycline. *J Dermatol.* 2006;33:223-224.
15. Atasoy M, Ozdemir S, Aktaş A, et al. Treatment of confluent and reticulated papillomatosis with azithromycin. *J Dermatol.* 2004;31:682-686.
16. Angeli-Besson C, Koeppel MC, Jacquet P, et al. Confluent and reticulated papillomatosis (Gougerot-Carteaud) treated with tetracyclines. *Int J Dermatol.* 1995;34:567-569.
17. Ito S, Hatamochi A, Yamazaki S. A case of confluent and reticulated papillomatosis that successfully responded to roxithromycin. *J Dermatol.* 2006;33:71-72.
18. Natarajan S, Milne D, Jones AL, et al. Dietzia strain X: a newly described Actinomycete isolated from confluent and reticulated papillomatosis [published correction appears in *Br J Dermatol.* 2005;153:1092]. *Br J Dermatol.* 2005;153:825-827.
19. Lee MP, Stiller MJ, McClain SA, et al. Confluent and reticulated papillomatosis: response to high-dose oral isotretinoin therapy and reassessment of epidemiologic data. *J Am Acad Dermatol.* 1994;31(2, pt 2):327-331.
20. Schwartzberg JB, Schwartzberg HA. Response of confluent and reticulate papillomatosis of Gougerot and Carteaud to topical tretinoin. *Cutis.* 2000;66:291-293.
21. Bowman PH, Davis LS. Confluent and reticulated papillomatosis: response to tazarotene. *J Am Acad Dermatol.* 2003;48(suppl 5):S80-S81.
22. Carrozzo AM, Gatti S, Ferranti G, et al. Calcipotriol treatment of confluent and reticulated papillomatosis (Gougerot-Carteaud syndrome). *J Eur Acad Dermatol Venereol.* 2000;14:131-133.