Familial Confluent and Reticulate Papillomatosis Successfully Treated With Minocycline

Joung Soo Kim, MD; Jun Oh Paek, MD; Ho Song Kang, MD; Hee Joon Yu, MD, PhD

Practice Points

- Confluent and reticulate papillomatosis (CRP) is an idiopathic disorder characterized by persistent patches and plaques that are centrally confluent and peripherally reticulate.
- Although it mainly occurs sporadically, familial cases have been described.
- Several reports have noted that CRP responds to variable treatments, and minocycline has been reported as effective in the treatment of CRP, seemingly due to its antimicrobial and anti-inflammatory activity.

Confluent and reticulate papillomatosis (CRP) is an idiopathic disorder characterized by persistent patches and plaques that are centrally confluent and peripherally reticulate. Although CRP primarily occurs sporadically, there may be a familial predisposition to the development of CRP. Minocycline has been reported as effective in the treatment of CRP, seemingly due to its antimicrobial and anti-inflammatory activity. We describe a case of familial CRP involving 2 brothers who were successfully treated with minocycline.

Cutis. 2014;93:199-203.

Confluent and reticulate papillomatosis (CRP) is an idiopathic disorder characterized by persistent patches and plaques that are centrally confluent and peripherally reticulate. Although it mainly occurs sporadically, a few familial cases have been described.[1] We report a case of familial CRP that presented in 2 brothers who were successfully treated with minocycline.

From the Department of Dermatology, Hanyang University Guri Hospital, South Korea.
The authors report no conflict of interest.
Correspondence: Hee Joon Yu, MD, PhD, Department of Dermatology, Hanyang University Guri Hospital, Guri, Gyeonggi-do, 471-701, South Korea (yuhjoon@hanyang.ac.kr).

Case Reports

Patient 1—A 16-year-old adolescent boy presented with a 12-month history of nonpruritic brownish patches forming confluent plaques in the center and a reticulate network at the periphery. The eruption first appeared on the neck and progressed to both axillae, the trunk, and the crus (Figure 1A). Direct microscopic examination of the scales in potassium hydroxide (KOH) showed no yeast and hyphae. No fluorescence was observed on Wood lamp examination. Routine laboratory tests, including complete blood cell count, blood chemistry analysis, and urinalysis, were within reference range. On histopathologic examination, a specimen from the lower abdomen showed mild hyperkeratosis, papillomatosis, and focal acanthosis, as well as fungal elements, such as *Malassezia* spores in the stratum corneum. A discrete perivascular lymphocytic infiltrate was present in the papillary dermis (Figures 2A and 2B), but periodic acid–Schiff (PAS) staining was negative for fungal hyphae. The patient was diagnosed with CRP and was treated with minocycline 200 mg (2.5 mg/kg) daily. After 9 weeks of treatment, the lesions were almost completely clear and have been in satisfactory condition for 3 years (Figure 1B).

Patient 2—At the same time, a 17-year-old adolescent boy who was the brother of patient 1 presented with a similar eruption of nonpruritic brownish patches and plaques of 7 months' duration.

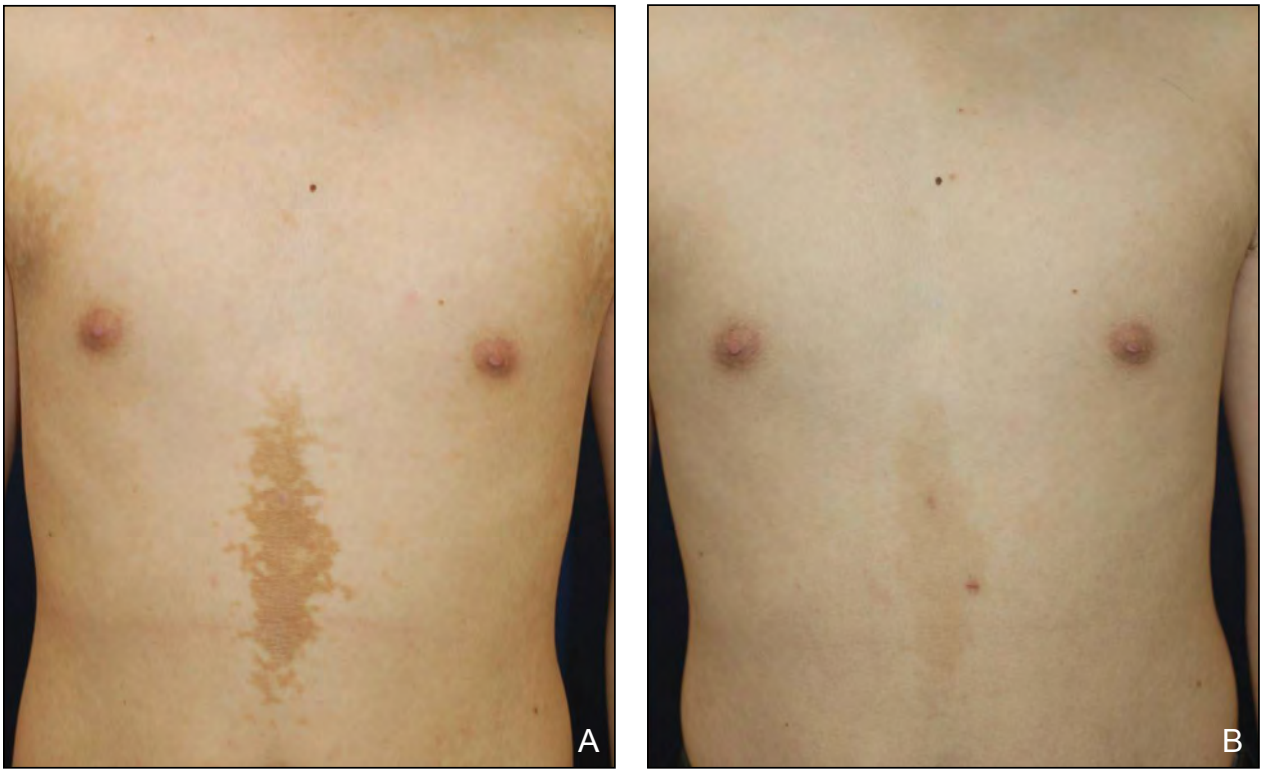

Figure 1. Hyperpigmented central confluent and peripheral reticulate brownish patches in the epigastric area (A). Nine weeks after minocycline treatment, the skin lesions were mostly resolved (B).

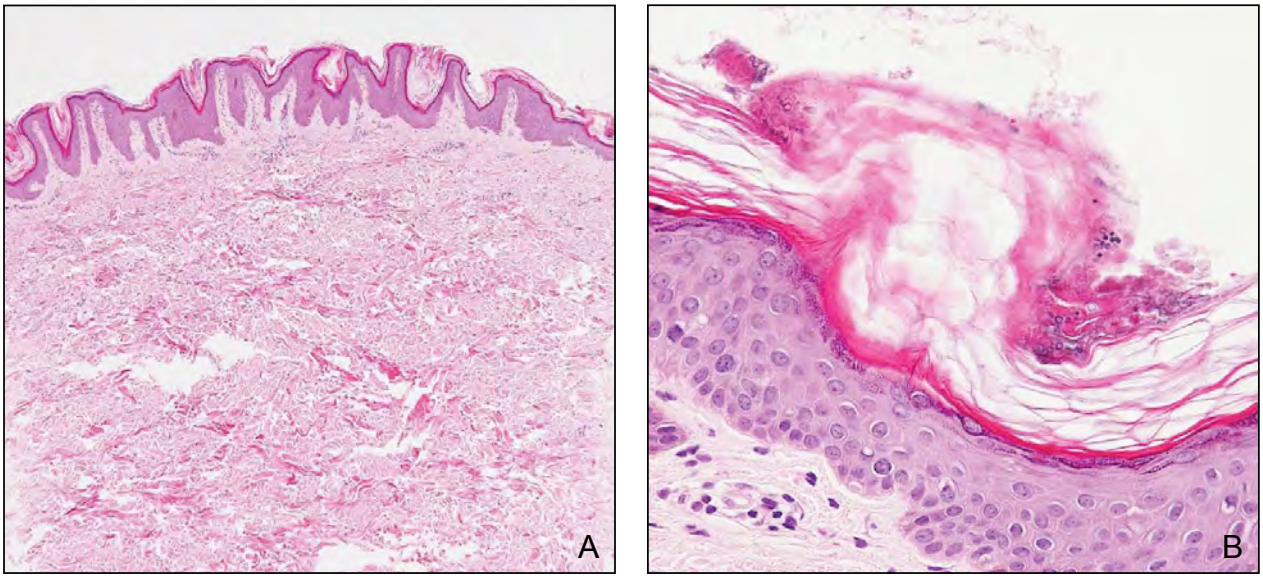

Figure 2. Skin biopsy findings showed epidermal change with hyperkeratosis, papillomatosis, and mild acanthosis (A)(H&E, original magnification ×40). *Malassezia* spores were observed in the stratum corneum (B)(H&E, original magnification ×400).

The eruption first appeared on the neck and progressed to both axillae and the trunk (Figure 3A). A KOH preparation was negative for fungal organisms on direct microscopy. No fluorescence was observed on Wood lamp examination, and routine laboratory tests were within reference range. A skin biopsy specimen from the lower abdomen showed findings similar to patient 1, including fungal elements

such as *Malassezia* spores, and PAS staining also was negative for fungal hyphae. A diagnosis of CRP was made, and he was treated with minocycline 200 mg (2.5 mg/kg) daily. After 9 weeks of treatment, the lesions showed much improvement and have been in satisfactory condition for 3 years (Figure 3B).

Comment

Confluent and reticulate papillomatosis is an uncommon condition that was described in 1927 by Gougerot and Carteaud[2] as unnamed pigmented papillomatosis. Clinically, CRP lesions initially appear as 1- to 2-mm erythematous macules that typically occur on the intermammary, interscapular, and epigastric regions. Subsequently, lesions can enlarge to 4 to 5 mm and develop a brownish hue. Continued radial spread results in confluence on the central trunk and a reticulate pattern peripherally. Eventually the chest, neck, shoulders, and back are involved. The cheeks, pubic area, and forehead rarely are affected.[1,3]

The pathophysiology of CRP is unknown, though 2 prominent theories suggest an abnormal host response to *Malassezia* or abnormal keratinization. *Malassezia* spores occasionally can be found when scraping from a CRP lesion in a KOH mount.[1] Topical antifungals sometimes are effective in treating CRP,[4] but the causative role of *Malassezia* in the pathogenesis is controversial. The mere presence of *Malassezia* spores in patients might be the result of tinea versicolor being confused with CRP. Abnormal keratinization may play a role in the pathogenesis of CRP because the transitional cell layer between the stratum corneum and stratum granulosum increases to 3 or 4 layers in some patients.[5] Confluent and reticulate papillomatosis also responds to treatment with retinoids and vitamin D derivatives, which are therapies for diseases of keratinization.[6] However, this theory does not explain resolution of CRP with antibacterial treatment, which does not directly affect keratinization. Other suggestions include a reaction to bacterial infection, photosensitivity, endocrinopathy, amyloidosis cutis, and genetic predisposition.[1]

Although there is no proof of a genetic cause for CRP at this time, there may be a familial predisposition

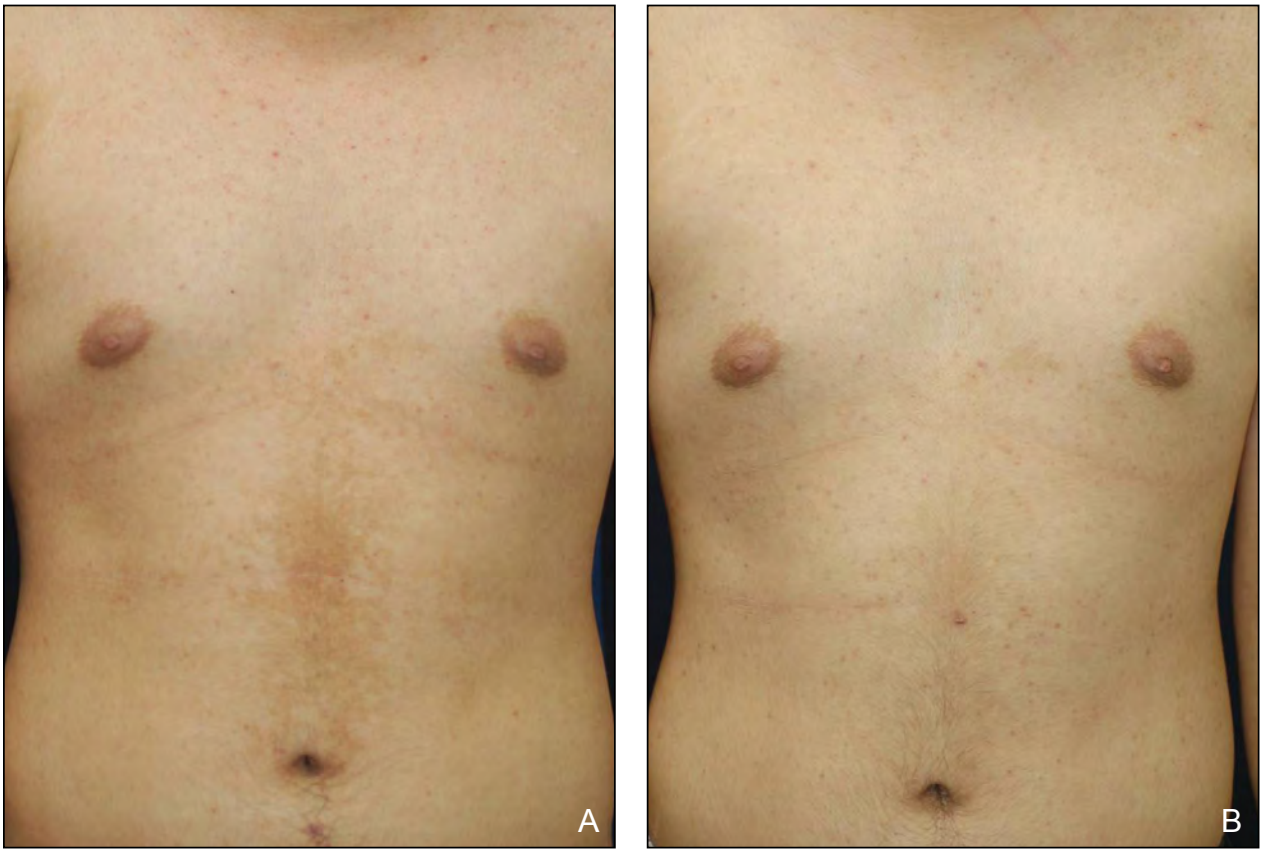

Figure 3. Hyperpigmented central confluent and peripheral reticulate brownish patches in the epigastric area (A). Nine weeks after minocycline treatment, the skin lesions were much improved (B).

to the development of CRP, at least in some families, as suggested by our cases. Five other reports in the literature describe CRP occurring among multiple family members (Table).[7-11] In one report, 2 of 3 patients had confirmed tinea versicolor with positive KOH scrapings, while the skin specimen was negative with PAS staining.[11] The presence of tinea versicolor may be coincidental, but it is the only known report describing family members having both CRP and tinea versicolor.

In our patients, the yeast forms of *Malassezia* were observed in the skin specimens, and the differential diagnosis of tinea versicolor was considered. However, KOH examination was negative for fungal organisms, and no fluorescence was seen on Wood lamp examination. In addition, PAS staining also was negative for fungal hyphae. Thus tinea versicolor was ruled out.

Treatment of CRP with tetracycline antibiotics was first proposed by Carteau[12] in 1969, and further successes have been confirmed in the literature.[13] Minocycline has been shown to be effective in patients with CRP who did not respond to treatment with isotretinoin or erythromycin.[14] Minocycline has been found to reduce free fatty acids in sebum, prevent lipid oxidation, and suppress leukocyte chemotaxis.[13] Poskitt and Wilkinson[15] also suggested that minocycline's ability to block protein and DNA synthesis, which was responsible for reduced epidermal proliferation, might contribute to its effectiveness in treating CRP. Additionally, an in vitro study showed that minocycline suppresses the production of IL-1α, IL-6, and tumor necrosis factor α, which affect epidermal keratinization.[16]

Supporting the concept that CRP is a disease of keratinization, retinoids (eg, isotretinoin, etretinate) have been shown to effectively treat CRP.[1,6,17] A variety of other antibacterial agents also have shown to be effective treatments of CRP.[1] Several reports have noted that CRP responds to minocycline, clarithromycin, erythromycin, azithromycin, and roxithromycin.[18,19] These antibiotics seem to produce therapeutic effects by eliminating the bacterial agents that induce inflammation and an epidermal proliferative change. Our patients were treated with minocycline 200 mg daily. After 9 weeks of therapy, the CRP skin lesions had almost cleared, and no recurrence was noted at 3 years' follow-up.

Conclusion

Confluent and reticulate papillomatosis is a dermatologic entity with an unknown etiology. Although

Cases of Familial Confluent and Reticulate Papillomatosis

Reference (Year)	Relationship and Age of Patients	Treatment	Progress
Baden[7] (1965)	2 sisters: 41 y and 44 y; daughter/niece: 11 y	Topical hydroquinone, topical sulfur, salicylic acid cream	Persistent
Henning and de Wit[8] (1981)	Mother: 44 y; daughter: 15 y; son, 18 y	Topical urea, tretinoin	Persistent
Schwartzberg and Schwartzberg[9] (2000)	2 brothers: both 17 y	Topical tretinoin	Cleared
Inalöz et al[10] (2002)	2 brothers: 21 y and 27 y	NA	NA
Stein et al[11] (2005)	2 sisters: 13 y and 18 y; brother: 16 y	Minocycline	Cleared
Current cases	2 brothers: 16 y and 17 y	Minocycline	Cleared

Abbreviation: NA, not available.

eminently treatable, there is no standard therapy for CRP. Continued interest in this condition may elucidate its true cause and the most effective treatment.

REFERENCES

1. Scheinfeld N. Confluent and reticulated papillomatosis: a review of the literature. *Am J Clin Dermatol*. 2006;7:305-313.
2. Gougerot H, Carteaud A. Papillomatose pigmentee innominee. *Bull Soc Fr Dermatol Syph*. 1927;34:719-721.
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. Hamaguchi T, Nagase M, Higuchi R, et al. A case of confluent and reticulated papillomatosis responsive to ketoconazole cream. *Nihon Ishinkin Gakkai Zasshi*. 2002;43:95-98.
5. Jimbow M, Talpash O, Jimbow K. Confluent and reticulated papillomatosis: clinical, light and electron microscopic studies. *Int J Dermatol*. 1992;31:480-483.
6. Solomon BA, Laude TA. Two patients with confluent and reticulated papillomatosis: response to oral isotretinoin and 10% lactic acid lotion. *J Am Acad Dermatol*. 1996;35:645-646.
7. Baden HP. Familial cutaneous papillomatosis. *Arch Dermatol*. 1965;92:394-395.
8. Henning JP, de Wit RF. Familial occurrence of confluent and reticulated papillomatosis. *Arch Dermatol*. 1981;117:809-810.
9. Schwartzberg JB, Schwartzberg HA. Response of confluent and reticulate papillomatosis of Gougerot and Carteaud to topical tretinoin. *Cutis*. 2000;66:291-293.
10. Inalöz HS, Patel GK, Knight AG. Familial confluent and reticulated papillomatosis. *Arch Dermatol*. 2002;138:276-277.
11. Stein JA, Shin HT, Chang MW. Confluent and reticulated papillomatosis associated with tinea versicolor in three siblings. *Pediatr Dermatol*. 2005;22:331-333.
12. Carteau A. Un cas de papillomatose papuleuse confluente et reticulee de Gougerot and Carteaud, completement blanchie par antibiotques. *Bull Soc Fr Dermatol Syphiligr*. 1969;76:112-113.
13. Lee SY, Choi JH, Sung KJ, et al. Confluent and reticulated papillomatosis successfully treated with minocycline. *Ann Dermatol*. 2000;12:33-37.
14. Wiesenborn A, Hengge U, Megahed M. Confluent and reticulated papillomatosis. Gougerot-Carteaud disease [in German]. *Hautarzt*. 2004;55:976-978.
15. Poskitt L, Wilkinson JD. Clearance of confluent and reticulate papillomatosis of Gougerot and Carteaud with minocycline. *Br J Dermatol*. 1993;129:351-353.
16. Célérier P, Litoux P, Dréno B. In vitro modulation of epidermal inflammatory cytokines (IL-1α, IL-6, TNF-α) by minocycline. *Arch Dermatol Res*. 1996;288:411-414.
17. Baalbaki SA, Malak JA, al-Khars MA. Confluent and reticulated papillomatosis. treatment with etretinate. *Arch Dermatol*. 1993;129:961-963.
18. 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.
19. Ito S, Hatamochi A, Yamazaki S. A case of confluent and reticulated papillomatosis that successfully responded to roxithromycin. *J Dermatol*. 2006;33:71-72.