

## BRIEF ARTICLE

## Successful Treatment of Confluent and Reticulated Papillomatosis with Minocycline Topical 4% Foam

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### ABSTRACT

This report discusses the use of a novel treatment method for Confluent and Reticulated Papillomatosis (CRP) in a middle-aged African American woman. The patient was hesitant to begin oral antibiotics, namely oral minocycline, due to safety concerns of all oral medications. The patient was placed on minocycline topical 4% foam, recently approved by the FDA, for the course of one month. Concluding her therapy, we observed a complete resolution of plaques with residual hyperpigmentation. In the literature, topical minocycline has been reported to treat more common dermatologic conditions, such as rosacea and acne vulgaris. To date, this is the first report on the usage of topical minocycline for the treatment of CRP.

### INTRODUCTION

Confluent and reticulated papillomatosis was first recognized in 1927 by Henri Gougerot and Alexandre Carteaud as *papillomatose pigmentée innominée*, and subsequently *papillomatose pigmentée confluente et reticulée*.<sup>1,2</sup> In 1937, the first reported case in the United States was reported by Fred Wise and Wilbert Sachs, who renamed the condition Confluent and Reticulated Papillomatosis (CRP).<sup>3,4</sup> CRP is an uncommon dermatosis with many proposed etiologies, including a disorder of keratinization, a reaction to *Malassezia*, an outbreak in relation to an endocrinopathy, a response to bacterial infection, a response to UV light, a genetic factor, and a process involving amyloidosis.<sup>5</sup> Under both light and electron microscopy, CRP is found to affect the epidermis through disordered and hyperproliferative keratinization.<sup>6</sup>

CRP typically presents as papules or plaques, approximately 3-5 mm in diameter, which merge centrally in a confluent pattern and scatter peripherally in a reticular pattern.<sup>7</sup> Populations in which lesions occur most commonly are young adults, although it has been reported to affect all races and ages worldwide, with an unidentifiable preference for gender.<sup>5,8</sup> Typically, lesions initially occur near the inframammary folds and epigastric skin. They can extend to the center of the chest, and both the upper and lower back and abdomen.<sup>9</sup> The following is diagnostic criteria for CRP proposed by Davis et al, which has been consistent across existing literature on CRP case series: (i) clinical findings include brown, scaly patches and macules, at least parts of which display reticulation and papillomatosis; (ii) the rash involves the upper trunk and neck; (iii) negative fungal staining of scales; (iv) no response to

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antifungal treatment; and (v) an excellent response to oral minocycline.<sup>10,11</sup>

Successful treatment of CRP can be difficult, as lesions have been noted to recur months after treatment depending on the treatment modality.<sup>12</sup> The preferred treatment of CRP consists of oral minocycline, which has been shown to be the most effective against CRP, 50-100 mg twice daily. Minocycline, like all tetracyclines, works to prevent protein synthesis by attaching to the 30s ribosomal subunit in bacteria. Minocycline also prevents the migration, and therefore the role of neutrophils in inflammatory processes. It possesses both anti-inflammatory and immunomodulatory effects, but it's unclear how these qualities treat atypical keratinization.<sup>9</sup> However, minocycline as a preferred method of treatment comes with concerns of adverse effects such as drug toxicity, drug-induced lupus, and abnormal skin pigmentation at the site of pre-existing lesions.<sup>11</sup> Furthermore, minocycline is not recommended for use in pregnant women.<sup>9</sup> Of late, oral azithromycin has been proven to be effective in treating CRP, and the medication is safe for use during pregnancy.<sup>13</sup> Other oral treatment methods for CRP have been cited in the literature, including clarithromycin and erythromycin.<sup>14,15</sup> Topical treatments have been reported for use in the treatment of CRP, including retinoids, tazarotene, urea, calcipotriol, and tacrolimus.<sup>16,17,18,19,20</sup> A limitation in using topical treatment is the inability to reach the affected area for application, especially if CRP is located on the back.<sup>11</sup> Recurrences have been reported with the use of antifungals such as ketoconazole, tolnaftate, and itraconazole.<sup>21</sup> A recent systematic review of treatment outcomes in CRP found that minocycline was the most frequently used tetracycline across the literature, achieving complete

resolution in 61% of 114 cases and partial resolution in 21.1% of cases within 51.0 days. Oral antibiotics such as amoxicillin and azithromycin were used in 26 cases, reaching complete resolution or partial resolution of CRP within 57.9 days in 92.3% of cases. Oral and topical antifungals fared poorly, with the majority of patients (62.5% of 56 cases) reporting no improvement in appearance. Oral and topical retinoids resulted in complete or partial resolution in 73.3% of the 19 cases within 68.8 days. Combination therapy with minocycline and other topical agents was used in 25 cases, 9 of which reached complete resolution (36%) and 8 of which reported no improvement (32%). Adverse effects such as fatigue, gastrointestinal symptoms, and cheilitis were reported with combination therapies.<sup>22</sup> Further reviews have found the use of minocycline or azithromycin to yield positive results with a marked response, defined as a 50% improvement in appearance, against CRP.<sup>11</sup>

Overall, antibiotics such as oral minocycline have proven to be the most efficacious against CRP. Antibiotics that boast both antibacterial and anti-inflammatory properties, such as tetracyclines, yield the greatest results.<sup>9</sup> Future directions for the treatment of CRP include topical minocycline. Approved by the FDA in 2019, minocycline topical 4% foam has been cited in the literature to treat acne vulgaris and rosacea.<sup>23</sup> Currently, there is no existing literature on the usage of topical minocycline for the treatment of CRP.

## CASE REPORT

A 51-year-old African American woman with a past medical history of a rash for the past eight months presented with reticulated brown plaques overlying the midline of the

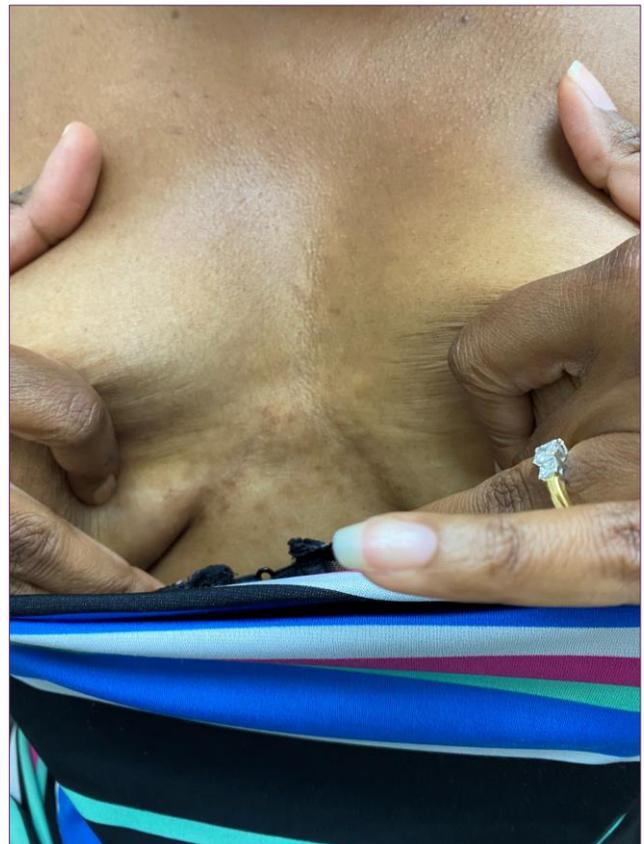
chest and extending underneath the inframammary folds (Figure 1).



**Figure 1.** CRP on the midline of the patients' chest before treatment with minocycline topical 4% foam.

CRP was diagnosed clinically. The patient was reluctant to take oral antibiotics, namely oral minocycline, due to her concerns regarding the safety of all oral medications. The patient was prescribed minocycline topical 4% foam, to be applied once a day over the affected area for one month. Follow-up with the patient approximately one month after her initial visit showed resolution of plaques with significant improvement (Figure 2). On follow-up with the patient approximately 2 months after initial diagnosis, she reported that the rash cleared completely after one month of continuous application of topical medicine. Two weeks after suspending use, the rash on her chest returned. She reports using the topical minocycline intermittently. The rash cleared

within 4-5 days of use; however it recurred soon after stopping treatment.



**Figure 2.** After treatment with minocycline topical 4% foam. Significant improvement with resolution of plaque and decreased hyperpigmentation.

## DISCUSSION

CRP is a relatively rare dermatosis with unknown etiology. The chronic nature of CRP is demonstrated by its recurrence rate with pharmacologic treatments other than monotherapy with oral minocycline, with antifungals, combination therapies, and retinoids either yielding poor results or lacking sufficient evidence due to study limitations (small sample sizes, uncontrolled trials).<sup>22</sup> The most successful treatment in the literature to date is oral minocycline, 50 - 100 mg a day. However, there is increasing concern regarding bacterial resistance due to the overuse of antibiotics. Although

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topical minocycline is still an antibiotic, the risks conferred with oral antibiotics for treatment of dermatoses are greater due to increased likelihood of systemic side effects, decreased concentration of antibiotic at the preferred site on skin, antibiotic resistance selection in gut microbiota, and generally less drug usage to achieve the desired effect.<sup>24</sup> There is a generalized pervasive aversion to the utilization of oral medications in dermatology from the patient's perspective, due in part to these factors.

## CONCLUSION

While further research is necessary on the topic, minocycline topical 4% foam offers a new alternative to long-term oral antibiotics in treating a recurrent, chronic disease.

**Conflict of Interest Disclosures:** None

**Funding:** None

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