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Treatment outcomes in confluent and reticulated papillomatosis: A systematic review

To the Editor: Confluent and reticulated papillomatosis (CARP) is a rare dermatosis characterized by persistent, hyperpigmented, reticulated papules and plaques.[1] Various treatment options including antibiotics, antifungals, and retinoids have been reported[2]; however, no well-established guidelines or consensus statements exist for the management of CARP. The aim of this systematic review was to summarize CARP treatment options and their outcomes.

MEDLINE and Embase in OVID were searched on July 1, 2020, by using variations of the keywords "confluent and reticulated papillomatosis" and "Gougerot-Carteaud syndrome" (Supplementary Material available on Mendeley at https://doi.org/10.17632/s6p2cbk8kx.1). After screening, 70 studies consisting of 192 patients (mean age, 22.5 years; 53.1% male) and 278 treatment regimens, because some patients received multiple therapies, were included (Table I, Fig 1).

Oral tetracyclines were the most commonly reported drug class used as monotherapy (44.6%; n = 124/278), achieving complete resolution (CR) in 59.7% (n = 74/124) and partial resolution (PR) in 22.6% (n = 28/124) of cases, with a mean resolution period of 51.8 days. Specifically, minocycline was the most frequently used tetracycline (91.9%; n = 114/124), achieving CR in 61.4% (70/114) and PR in 21.1% (n = 24/114) of cases within 51.0 days. Other oral antibiotics (amoxicillin and azithromycin) were administered in 9.4% (n = 26/278) of cases, achieving CR or PR within 57.9 days in 92.3% (n = 24/26) of cases.

Oral and topical antifungal treatments achieved CR or PR within 31.6 days in 30.4% (n = 17/56) of cases; however, the majority of patients (62.5%; n = 35/56) did not notice any improvement. Oral and topical retinoid monotherapy resulted in CR or PR in 73.7% (n = 14/19) of cases within 68.8 days. Additionally, topical vitamin D derivatives, despite being uncommon treatment interventions, resulted in CR or PR in 85.7% (n = 6/7) of cases within 42.6 days.

Combination therapies, most commonly minocycline and various topical agents, were used in 9.0% (n = 25/278) of cases. Although CR was achieved in 36.0% (n = 9/25) within 58.8 days, no improvement occurred in 32.0% (n = 8/25) of cases. Treatment-related adverse events were reported in 1.6% (n = 3/192) of patients and included fatigue (minocycline and topical tretinoin), gastrointestinal symptoms (minocycline and topical lactic acid), and cheilitis (treatment unreported).

Many theories have postulated the role of bacterial or fungal infection in CARP.[3] We found that minocycline, a tetracycline derivative, was the most commonly used. Because minocycline inhibits the migration and function of neutrophils,[2] its anti-inflammatory and immunomodulatory effects may explain its effectiveness in treating CARP. In addition to the bacterial etiology, clinical resemblance between CARP and tinea versicolor has led researchers to propose the role of *Malassezia* species in CARP pathogenesis.[4] However, the majority of patients (62.5%; n = 35/56) in this review did not experience any improvement with antifungals. It is possible that patients who responded to antifungals had tinea versicolor or that their CARP cleared spontaneously and not in response to a specific agent.

A few limitations of this systematic review should be taken into consideration, including lack of high-quality randomized controlled trials, prospective studies, inaccessible full texts, and non-English studies. Additionally, the majority of the studies did not report adverse events, making the safety of treatments difficult to assess. Despite these limitations, our findings provide useful information to guide the clinical management of CARP. Although minocycline monotherapy yielded the highest reported CARP resolutions, further studies with large sample size are needed to confirm our findings.

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Table I. Outcomes of treatments used for confluent and reticulated papillomatosis*

Treatment class	Treatment	Number of times used	Worsening (number of times)	No resolution (number of times)	Resolution NR, number of times	Partial resolution, number of times	Complete resolution, number of times	Resolution period, days†
Tetracycline or its derivatives monotherapy	Minocycline	114	2	2	16	24	70	51.0
	Doxycycline	9	—	—	2	3	4	73.0
	Tetracycline‡	1	—	—	—	1	—	NR
	Total	124	2	2	18	28	74	51.8
Other oral antibacterial monotherapy	Amoxicillin	2	—	—	—	—	2	150.0
	Azithromycin	12	—	—	—	1	11	43.0
	Erythromycin	7	—	2	—	1	4	30.0
	Clarithromycin	1	—	—	—	—	1	NR
	Oral fusidic acid	3	—	—	—	—	3	NR
	Roxithromycin	1	—	—	—	1	—	60.0
	Total	26	—	2	—	3	21	57.9
Antifungal monotherapy	Topical ketoconazole	4	—	1	—	2	1	18.5
	Topical itraconazole	4	—	1	1	2	—	28.0
	Topical selenium sulfide	8	—	3	—	1	4	35.0
	Topical econazole	1	—	1	—	—	—	—
	Topical clotrimazole	1	—	1	—	—	—	—
	Topical tolnaftate	1	—	—	—	1	—	14.0
	Topical sodium thiosulphate solution	1	—	—	—	1	—	21.0
	Topical selenium sulfide and topical ketoconazole	1	—	1	—	—	—	—
	Topical sodium thiosulfate and topical selenium sulfide	1	—		—	—	1	28
	Topical miconazole and topical ketoconazole	1	—	1	—	—	—	—
	Oral ketoconazole	4	—	4	—	—	—	—
	Oral griseofulvin	1	—	1	—	—	—	—
	Oral and topical antifungal combination	13	1	11	—	—	1	90.0
	Antifungal‡	15	1	10	1	—	3	NR
	Total	56	2	35	2	7	10	31.6
Retinoid monotherapy	Oral isotretinoin	6	—	1	—	1	4	150.0
	Topical isotretinoin	1	—	—	—	1	—	NR
	Oral acitretin	2	—	1	—	1	—	42
	Topical tretinoin	3	—	1	1	1	—	NR
	Topical tazarotene	3	—	—	—	—	3	75.0
	Oral etretinate	1	—	—	—	—	1	28.0
	Topical retinoic acid	1	—	—	—	—	1	NR
	Topical tretinoin and oral isotretinoin	1	—	—	—	—	1	60.0
	Topical retinoid‡	1	—	—	1	—	—	NR
	Total	19	—	3	2	4	10	68.8

Vitamin D derivatives monotherapy	Topical calcipotriol	5	—	1	—	1	3	27.0
	Topical tacalcitol	1	—	—	—	1	—	42.0
	Topical vitamin D3[‡]	1	—	—	—	1	—	90.0
	Total	7	—	1	—	3	3	42.6
Other therapy	Oral norethynodrel mestranol	2	—	—	—	—	2	60.0
	Topical methylprednisolone aceponate cream	1	—	—	—	—	1	28.0
	Topical steroids	1	—	1	—	—	—	
	Oral or topical vitamin A	4	—	1	—	3	—	240.0
	Oral low-dose estrogen/progestin combination	1	—		—	—	1	180.0
	Cryotherapy with liquid nitrogen	1	—	1	—	—	—	
	Oral highly active antiretroviral therapy (HART)	1	—		—	—	1	35.0
	Topical salicylic acid	5	—	3	2	—	—	
	Topical lactic acid	2	—	2	—	—	—	
	Topical mupirocin	1	—	—	—	—	1	30.0
	Topical pyrithione zinc	1	—	1	—	—	—	
	Topical tacrolimus	1	—	—	—	—	1	60.0
	Total	21	—	9	2	3	7	90.4
Combination therapy	Minocycline and topicals (ie, topical ketoconazole, lactic acid, topical tretinoin, alcohol swabs, ammonium lactate lotion, topical calcipotriol, and topical tazarotene)	11	—	1	1	6	3	63.0
	Topical retinoids (ie, retinoic acid or topical tretinoin) and other topicals (ie, topical hydroquinone, urea-containing emollients, selenium sulfide)	4	—	1	—	—	3	45.0
	Oral retinoids (ie, isotretinoin) and other topicals (ie, lactic acid or lactinol lotion)	3	—	1	—	—	2	85.0
	Topical steroids and antifungals (topical or oral)	3	—	3	—	—	—	—
	Topical antibiotic ointment and fractional CO_2 laser	1	—		—	—	1	30
	Topical urea-containing emollients and others topicals (corticosteroid or antifungal)	2	—	2	—	—	—	—
	Oral fusidic acid and topical betamethasone valerate	1	—	—	—	1	—	—
	Total	25	—	8	1	7	9	58.8

NR, Not reported.
*A dash indicates 0 times.
[†]Average time in days to reach partial or complete resolution after starting treatment.
[‡]Specifics not reported.

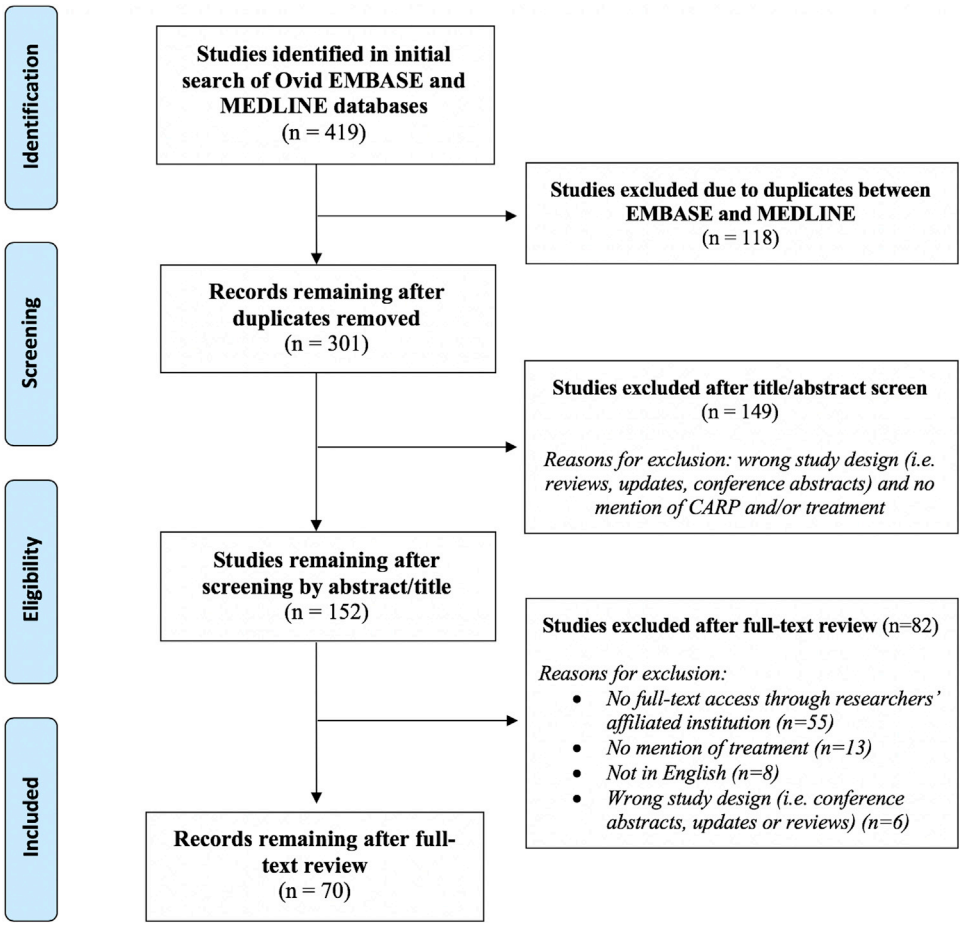

Fig 1. Flow diagram of the literature screening using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Adapted from http://prisma-statement.org. *CARP,* Confluent and reticulated papillomatosis.

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Quality of life in hidradenitis suppurativa: A cross-sectional study of a pediatric population

To the Editor: Adult patients with hidradenitis suppurativa (HS) experience increased rates of depression and an appreciably reduced quality of life (QoL).[1,2] Although the impacts of HS on QoL have been well characterized in adults, we sought to characterize QoL in pediatric patients with HS and their caregivers.

A cross-sectional study was conducted from 2018 to 2019 evaluating QoL measures in pediatric patients (12-17 years of age) with HS by using validated surveys in English and Spanish. Appropriate permissions were obtained for all surveys, and the study was approved by our institutional review board. Surveys included (1) the Skindex-Teen questionnaire, a dermatology-specific QoL questionnaire for patients ages 12 to 17 years, (2) the Patient Health Questionnaire−2 (PHQ-2), a depression screening tool, and (3) and the Family Dermatology Life Quality Index, a survey assessing QoL in family members of patients with skin disease. For each survey, a higher score indicates a more profound impact on QoL or mental health.

Twenty-five pediatric patients with HS participated in the study. Patient characteristics are detailed in Table I. Patients with a greater Hurley stage of disease (indicating more severe HS) had a higher average Skindex-Teen score, suggesting that patients with greater disease severity trended toward having worse QoL (see Table I). The average score of the Skindex-Teen survey was 45.7 (range, 0-84). Fig 1 describes the patients' mean responses to the questions of this survey. On average, the greatest negative impacts on QoL were regarding the appearance of the involved skin and feeling frustrated by their HS. On the PHQ-2, 32% of participants had positive screening results for depression (score of ≥3). The average score on the Family Dermatology Life Quality Index was 9.9 (range, 0-30). Based on this survey, caregivers' lives were most affected by the time spent caring for their child with HS and the personal emotional distress related to their child's condition.

Table I. Patient demographics

Characteristics	Value
Number of participants	25
Age, y, mean (range)	15.3 (12-17)
Sex, % (n/total)	Female: 76 (19/25)
	Male: 24 (6/25)
Race, % (n/total)	Hispanic: 66.7 (16/24)
	White: 16.7 (4/24)
	Black: 12.5 (3/24)
	Asian: 4.2 (1/24)
BMI percentile, median (range)	98 (59-99)
Hurley stage, % (n/total)	
I	33 (8/24)
II	54 (13/24)
III	13 (3/24)
Skindex-Teen QoL score by Hurley stage, mean	
I	42.6
II	49.8
III	53.7

BMI, Body mass index; *QoL,* quality of life.

Our results show the profound effect that HS has on QoL in pediatric patients and their caregivers. Although our study did not have a control group for direct comparison, it is helpful to put the findings in context. The negative impact on QoL in pediatric patients with HS on the Skindex-Teen questionnaire was more than double that of pediatric patients with psoriasis (45.7 vs 21.1).[3] The rate of positive screening results for depression (32%) was greater than double that of a general adolescent population (12%).[4] The QoL impact on caregivers was overall similar to that of patients with other inflammatory dermatologic conditions.[5]

Our results suggest a negative impact on QoL in pediatric patients with HS. Our finding that, as disease severity progresses, so does the negative impact on QoL underscores the importance of the early diagnosis and treatment of HS to potentially prevent disease progression and limit the negative impact on QoL. Given the high rates of depression found in our study, practitioners may even consider screening pediatric patients with HS for depression with the simple, 2-question PHQ-2 survey. Our findings should be taken in the context of its limitations: a small sample size, lack of control group, and a single-center study.