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ORIGINAL PAPER

Clinical factors and hair care practices influencing outcomes in central centrifugal cicatricial alopecia

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Abstract

Central centrifugal cicatricial alopecia (CCCA) is the most common form of primary scarring alopecia in women of African descent, negatively impacting their quality of life. Treatment is often challenging, and we usually direct therapy to suppress and prevent the inflammation. However, factors affecting clinical outcomes are still unknown. To characterize medical features, concurrent medical conditions, hair care practices, and treatments used for patients with CCCA and assess their relationship with treatment outcomes. We analyzed data from a retrospective chart review of 100 patients diagnosed with CCCA who received treatment for at least one year. Treatment outcomes were compared with patient characteristics to determine any relationships. P-values were calculated using logistic regression and univariate analysis with 95% CI $P < 0.05$ was considered significant. After one year of treatment, 50% of patients were stable, 36% improved, and 14% worsened. Patients without a history of thyroid disease ($P = 0.0422$), using metformin for diabetes control ($P = 0.0255$), using hooded dryers ($P = 0.0062$), wearing natural hairstyles ($P = 0.0103$), and having no other physical signs besides cicatricial alopecia ($P = 0.0228$), had higher odds of improvement after treatment. Patients with scaling ($P = 0.0095$) or pustules ($P = 0.0325$) had higher odds of worsening. Patients with a history of thyroid disease ($P = 0.0188$), not using hooded dryers (0.0438), or not wearing natural hairstyles ($P = 0.0098$) had higher odds of remaining stable. Clinical characteristics, concurrent medical conditions, and hair care practices may affect clinical outcomes after treatment. With this information, providers can adjust proper therapies and evaluations for patients with Central centrifugal cicatricial alopecia.

Keywords Hair loss · Scarring alopecia · Central centrifugal cicatricial alopecia · CCCA

Introduction

Central centrifugal cicatricial alopecia (CCCA) is a progressive form of lymphocyte-predominant scarring alopecia that negatively impacts the quality of life of those affected. It is the most common form of primary scarring alopecia in women of African descent [1]. Although etiology remains uncertain, the pathogenesis of CCCA is characterized by inflammation of the lower infundibulum with subsequent progression to fibrosis. Premature desquamation of the inner root sheath is a dependable histopathologic finding in CCCA [2, 3]. This finding corresponds well to certain genetic mutations in the PADI3 gene that have been identified in patients with CCCA [4]. Hairstyles and hair care practices have long been suspected in the development of CCCA, but the available evidence is conflicting [5]. Clinically, it presents with scarring at the vertex or crown of the scalp that tends to spread centrifugally. Patients often complain of pruritus, scalp tenderness, or dysesthesias; however, others can be asymptomatic. Effective, safe medical therapy is often challenging. Treatment of CCCA is directed at suppressing and preventing the inflammation, thus slowing down and hopefully aborting scarring. Several studies have shown the possible connection between CCCA and type 2 diabetes mellitus, bacterial skin infections, and tinea capitis [6, 7]. However, it has remained unclear if clinical characteristics, associated comorbidities, or hair care practices impact outcomes in CCCA.

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The present study aims to characterize medical features, concurrent medical conditions, hair care practices, and treatments used for patients with CCCA and correlate them with their treatment outcomes. For this purpose, we conducted a retrospective chart review of CCCA patients seen at a specialty alopecia clinic.

Methods

Approval was obtained from the Wake Forest School of Medicine Institutional Review Board before conducting this retrospective chart review. A total of 994 medical records of patients seen by the Department of Dermatology from January 2014 to December 2019 were reviewed. Inclusion criteria for the study were patients between the ages of 18 and 85 with a diagnosis of CCCA, either biopsy-proven or clinical, who received treatment for at least one year. Additionally, only medical records that included a complete standard intake hair questionnaire and sequential photographs were utilized for the study. One hundred medical records met the inclusion criteria. Clinician documentation and photographs at baseline and after treatment were used to evaluate treatment outcomes. Treatment outcomes were assessed by the research team after the first year of therapy. According to their Central Scalp Photography Scale in African American women [8], they were classified as improved, stable, or worsened. Patients with increased hair density in post-treatment photographs were classified as improved. Patients with no change in hair density were classified as stable, and patients with a decrease in hair density in similar post-treatment photographs were classified as worsened. In addition, treatment outcomes were compared with patient characteristics to determine any relationships. The patient characteristics evaluated in this study include duration of disease, stage of disease, types of symptoms, co-morbid conditions, hair care practices, hair styling history, exam findings, prior treatments, and treatments after the initial visit. P-values were calculated using logistic regression with 95% CI $P < 0.05$ was considered significant. Treatment outcomes were also compared with treatments started after the initial visit to identify any association between specific treatments on outcomes. P-values were calculated using univariate analysis with 95% CI $P < 0.5$ was considered significant.

Results

Patient characteristics and comorbidities

A total of 100 patient records were included in this review. (Tables 1, 2 and 3) The average age was 49.93 ± 12.12 years, ranging from 26 to 74 years. The average and range for the duration of hair loss and symptoms were 6.84 ± 0.49 and 0.5–25 years, respectively. Age at the time of presentation was not found to significantly affect the odds of improving, remaining stable, or worsening after treatment ($P = 0.0922$, 0.1125, 0.4067, respectively). Most patients and providers (73%) reported similar disease duration on the intake hair questionnaire and during the clinical encounter. A minority of patients reported a longer or shorter duration than the provider obtained during the clinical encounter, 14% and 13% respectively. Of the co-morbid conditions, seborrheic dermatitis was the most common condition (39%), followed by anemia (30%), thyroid disease (16%), and diabetes mellitus (13%). Data analysis of treatment outcomes showed that patients without a history of thyroid disease ($P = 0.0422$), and patients using metformin for diabetes control ($P = 0.0255$) had higher odds of improvement after treatment. Patients with a history of thyroid disease had higher odds of remaining stable after treatment ($P = 0.0188$).

Hair care practices

History of relaxer use was the most documented hairstyle (72%), followed by natural hair (69%). Almost half of patients (49%) had used relaxers and then transitioned to natural hair. Some patients used relaxers exclusively (23%) or natural hairstyles exclusively (19%). There were 42% with a history of braids, 42% with a history of hair dye use, and 30% used wigs. Over half (56%) of patients reported a history of sitting under a hooded dryer. Most patients washed their hair either once (34%) or twice (43%) per month. Data analysis of treatment outcomes showed that patients using hooded dryers ($P = 0.0062$), and those wearing natural hairstyles ($P = 0.0103$) had higher odds of improvement after treatment. Patients not using hooded dryers ($P = 0.0438$) or not wearing natural hairstyles ($P = 0.0098$) had higher odds of remaining stable after treatment.

Clinical features

On presentation, 2% of patients were stage 0 on the central scalp scale, 22% stage 1A/1B, 35% stage 2A/2B, 27% stage 3A/3B, 7% stage 4A/4B, and 7% stage 5A/5B. The stage at presentation was not found to have any significant effect on the odds of improving, remaining stable, or worsening ($P = 0.123$, 0.8148, 0.4083, respectively). Most patients (70%) reported symptoms. The most common experienced symptom was pruritus (90%, n = 63), followed by pain/tenderness (84%, n = 60) and burning (24.3%, n = 17). Besides cicatricial alopecia, 48% of patients had no other signs at physical examination. In patients demonstrating additional exam findings, the most common were scaling (37%), followed by erythema (16%), dyspigmentation (13%), and pustules (6%). Patients having no other physical signs besides cicatricial alopecia showed higher odds of improvement after

Table 1 Clinical and demographic characteristics (n = 100)

Characteristic	n (%) or mean
Average age (years) at onset (SD; range)	49.93 (± 1.212; 26–74)
Average disease duration on patient questionnaire (years ± SD)	6.840 ± 0.4993
Average disease duration on clinical history (years ± SD)	6.520 ± 0.4684
Symptoms duration (years ± SD)	4.235 ± 0.4483
Symptoms	
Presence of symptoms	70 (70%)
Pruritus	63 (90%)
Pain/Tenderness	60 (85.7%)
Burning	17 (24.3%)
Tingling	0 (0%)
Clinical findings	
Scaling	37 (37%)
Erythema	16 (16%)
Dyspigmentation	13 (13%)
Pustules	6 (6%)
No other clinical findings besides alopecia	48 (48%)
Previous use of treatment	42 (42%)
Topical corticosteroids	23 (54.8%)
Intralesional corticosteroids	19 (45.2%)
Topical minoxidil	18 (42.9%)
Doxycycline	6 (14.3%)
Treatments started after initial visit	100 (100%)
Topical corticosteroids	97 (97%)
Intralesional corticosteroids	78 (78%)
Topical Minoxidil	46 (46%)
Doxycycline	18 (18%)
Treatment outcome	
Stabilized	50 (50%)
Improved	36 (36%)
Worsened	14 (14%)
Insured coverage	
Commercial	75 (75%)
Medicare	20 (20%)
Medicaid	4 (4%)
Uninsured	1 (1%)

treatment (P = 0.0228). Patients with scaling (P = 0.0095) or pustules (P = 0.0325) on the physical exam were correlated with higher odds of worsening after treatment.

Therapies

Many patients (42%) reported treatments for CCCA before the first visit. The most common prior treatment among these patients was topical steroids (54.8%, n = 23), followed by intralesional steroids (45.2%, n = 19), topical minoxidil (42.9%, n = 18), and doxycycline (14.3%, n = 6). All patients received treatment after the initial provider encounter. Most patients used a combination of therapies. The most common treatments begun after inital encounter were topical steroids (97%), intralesional steroids (78%), topical minoxidil (46%), and oral doxycycline (18%). After one year of treatment, 50% of patients were stable, 36% improved, and 14% worsened. 43.5% (n = 20) of patients treated with topical minoxidil improved, 41.3% (n = 19) of patients remained stable, and 15.2% (n = 7) worsened. Close to half, 49.5% (n = 48), of patients treated with topical steroids remained stable, 36.1% (n = 35) improved, and 14.4% (n = 14) worsened. Just under half, 47.4% (n = 37), of patients treated with intralesional steroids remained stable, 38.5% (n = 30) improved, and 14.1% (n = 11) worsened. Half, 50% (n = 9) of the patients treated with doxycycline improved, 38.9% (n = 7) remained stable, and 11.1% (n = 2) worsened (Fig. 1). No specific treatments

Table 2 Hair care practices and styling

Hair care practices and styling	n (%)
Hair styling	
Relaxer use	72 (72%)
Natural hair	69 (69%)
Braids	42 (42%)
Hair weaves	30 (30%)
Jheri curl perm	5 (5%)
Hair color	42 (42%)
Twists/locs	6 (6%)
Texturizer	3 (3%)
Wig use	28 (28%)
Hair roller	7 (7%)
Hair care practices	
Hooded dryer use	56 (56%)
Scalp oil use	17 (17%)
Scalp grease/pomade use	6 (6%)
Shampoo frequency	
Once weekly	34 (34%)
Twice weekly	11 (11%)
Once every 2 weeks	43 (43%)
Once every 3 weeks	5 (5%)
Once a month	13 (13%)

were found to have a significant association with treatment outcomes. (Table 4).

Discussion

CCCA treatment remains a challenge, and factors impacting outcomes remain a mystery. Typical therapies aim to suppress and prevent inflammation. However, CCCA can often occur without signs of inflammation, and even clinically unaffected sites can show histological evidence of disease [9–11]. It has remained unclear if specific clinical characteristics, associated comorbidities, hair care styles, or practices would impact outcomes in CCCA. In the present article, we investigated whether these factors would correlate with the odds of improving, remaining stable, or worsening after one year of treatment.

Age and stage at the presentation did not affect the odds of response to treatment. Although previous studies have shown that the natural progression of CCCA is strongly associated with the duration of hair loss [7], some patients may benefit from treatment independent of the years or stage of the disease. Of comorbidities, the most common associated condition was seborrheic dermatitis. Our findings converge with previous results [7, 12] showing a high frequency of seborrheic dermatitis in our population. This could be due to long periods of hairstyle retention, leading to infrequent shampooing, a typical hair care practice amongst women of African descent. We found that patients without a history of thyroid disease had higher odds of improving. Patients with a history of thyroid disease had higher odds of remaining stable after treatment. This may be explained by the fact that thyroid disease can cause diffuse hair loss. One way to overcome hair loss secondary to thyroid disease is optimizing the treatment of thyroid disease and keeping thyroid hormones at normal levels. However, our study did not investigate how control of thyroid disease would impact treatment outcomes in CCCA, making this an area of interest for further investigation in future studies. Multiple studies have reported an association between CCCA and diabetes mellitus. A survey by Kyei et al. reported an increased prevalence of Type 2 Diabetes Mellitus among 326 African Americans with CCCA [12]. Olsen saw an association between diabetes

Table 3 Clinical characteristics and hair practices predicting treatment outcomes in CCCA

	Odds ratio	95% wald confidence limits		P-value
Stable disease				
History of thyroid disease	4.725	1.294	17.251	0.0188
History of hooded dryer	382	150	974	0.0438
History of natural hair	262	95	723	0.0098
Worsened disease				
Scaling	5.540	1.520	20.198	0.0095
Pustules	7.783	1.187	51.032	0.0325
Improved disease				
Taking metformin for diabetes control	6.593	1.260	34.486	0.0255
No history of thyroid disease	4.749	1.057	21.345	0.0422
History of natural hair	4.652	1.437	15.061	0.0103
History of hooded dryer	4.565	1.540	13.534	0.0062
No other clinical findings besides alopecia	3.170	1.174	8.560	0.0228

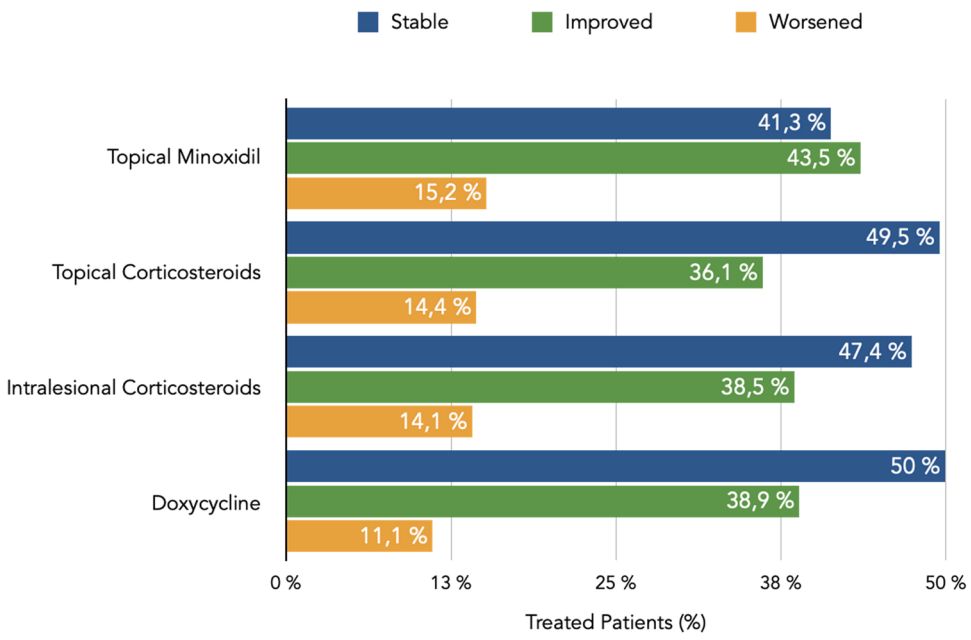

Fig. 1 Treatments prescribed for patients after initial visit

Table 4 Specific therapy and treatment outcomes evaluation (univariate analysis)

Treatments	P-values
Topical corticosteroids	0.2590
Intralesional corticosteroids	0.7368
Topical minoxidil	0.5870
Doxycycline	0.3930

and late-stage CCCA [13]. Coogan et al. reported type 2 diabetes mellitus increased the risk of developing CCCA [6]. On the other hand, Narasimman M et al. did not see a significant association with Diabetes Mellitus in 74 CCCA cases and 96 controls [14]. Interestingly, in our study, diabetes was the least common co-morbid condition and was not found to impact the treatment outcome. Previous findings regarding diabetes may differ from our results due to larger sample sizes in former studies. Although diabetes did not predict outcomes in our research, it was interesting that the use of metformin and insulin significantly impacted the treatment outcome. Our results indicate patients using metformin to treat Type 2 Diabetes Mellitus had higher odds of improving. A case report by Araoye et al. reported regrowth of hair using topical metformin in two patients [15]. Metformin works to activate AMPK, an enzyme encoded by the gene PRKAA2. One-third of patients with CCCA have been found to under-express this gene. Patients with CCCA have also been found to have an up-regulation of genes responsible for fibroblast activity [16]. A reduction in AMPK activity has been implicated in the pathogenesis of fibroproliferative conditions. The increase of AMPK activity with metformin may explain our finding of improvement in patients using metformin to treat Type 2 Diabetes Mellitus.

Hairstyles and care practices have long been suspected in CCCA, but the available evidence is conflicting [5]. Traction hairstyles, like cornrows, braids with extensions, and hair weaves, are commonly utilized by women of African descent [3]. Natural hairstyles are another option that may or may not induce traction. Our study defined any hairstyle using unrelaxed hair, including loose cornrows and braids underneath wigs, as a natural hairstyle. A study evaluating the histologic findings of women without alopecia or scalp inflammation who engaged in traumatic hairstyles within the past month found that peri-infundibular lymphocytic inflammation and concentric infundibular fibrosis were present in all patients [17]. Our findings indicate that patients wearing natural hairstyles had higher odds of improving while patients not wearing natural hairstyles had higher odds of staying stable with treatment. Narasimman M et al. saw an association between using chemical relaxers and developing CCCA [14]. In addition, Gathers reported that natural hairstyles without chemicals and heat before age 20 decreased the odds of developing CCCA by 86% [18]. This aligns with the findings in our study, indicating that providers can encourage patients to utilize natural hairstyles with minimal traction. Various forms of heat (hooded dryers, hand dryers, hot combs, etc.) are common among women of African descent to achieve different hairstyles [3]. In this study, we examined the effect that hooded dryers may have on the outcome of CCCA. Our findings indicate that patients who used hooded dryers had higher odds of improving, while

patients who did not use hooded dryers had higher odds of being stable. It is unclear why hooded dryers might predict stable or improved CCCA, but this may be a surrogate measure of decreased hair manipulation after styling since hairstyles with a hooded dryer are often set and left for weeks until the next manipulation. No prior studies evaluate the effect of hooded dryers on the development of CCCA. Still, studies have shown that using hot combs is not associated with the development of CCCA.

Clinical findings can vary in patients with CCCA [19]. Due to the scarring nature of the disease, the absence of follicular ostia is paramount and seen even in the early stages. Signs of inflammation like scaling and erythema are common findings. Pustules can also be seen early in disease onset [20]. In our study, scaling and pustules significantly impacted treatment outcomes. Patients with these signs on the exam had higher odds of worsening after treatment; meanwhile, patients without them had higher odds of improving. Scaling and pustules may indicate a more severe disease process and explain why patients are likely to worsen even with treatment. Although we did not find any significant association with clinical outcomes for a specific type of treatment, 86% of patients following medical treatment had at least stabilization, and in some cases, improvement, of their condition after one year. That finding reinforces the importance of medical treatment to halt the disease progression.

To the best of our knowledge, this is the most extensive study to evaluate treatment outcomes in a group of patients with CCCA. Our findings provide valuable insights for providers. For example, CCCA patients with pustules, scaling, and thyroid disease may have a worse outcome; meanwhile, patients using natural hairstyles may bode for a good result. With this information, providers can adjust proper treatments and assessments for patients with worsening factors. As understanding the physiologic causes of CCCA is slowly uncovered in the coming years, optimizing treatment outcomes will increase the quality of care provided to patients with this condition. However, our study has limitations—a retrospective design subjecting it to misclassification bias. The sample size was also small, which limited the analysis. The small sample size is compared with many variables, leading to wide confidence intervals. Because the authors determined treatment outcomes, observer bias must be considered. The lack of histologic confirmation, in some cases, could be a limitation. However, it is essential to note that CCCA is often diagnosed clinically. This allows the study to reflect current clinical practices. Future studies with a larger sample size analyzed by blinded investigators would help interpret our preliminary findings better.

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Author contributions Vanderbilt University School of Medicine had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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Data Availability The data that support the findings of this study are available from the corresponding author, [AJM], upon reasonable request.

Declarations

Conflict of interest Conflict of Interest Disclosures. Dr McMichael reported being a consultant for Almirall, Arcutis, Concert, Revian, UCB, Lilly, Pfizer, Galderma, Incyte, and Procter & Gamble; reported performing research for Incyte and Procter & Gamble; reported receiving grants from Procter & Gamble, Concert, and Incyte; and reported receiving personal fees from UpToDate outside the submitted work. No other disclosures were reported.

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