Central Centrifugal Cicatrical Alopecia: An Update

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OBJECTIVES

Central Centrifugal Cicatricial Alopecia

• Update of Clinical Subtypes
• CCCA in Male Patients
• Comorbidities in Patients with CCCA
• Delphi Consensus Therapeutic Recommendations
Nomenclature

Hot Comb Alopecia
LoPresti et al. described 51 African American women who straightened their hair with a hot comb and petrolatum with vertex alopecia that expanded peripherally.

CCCA
North American Hair Research Society used the descriptive term CCCA. Group agreed follicular degeneration is due to a primary insult against the hair follicle and is not just a consequence of an adjacent process.

Follicular Degeneration Syndrome
Sperling and Sau studied 10 African American women with central scarring alopecia who did not use hot comb and petrolatum for hair straightening. Hypothesized that the inner root sheath degenerates prematurely, leading to migration of the hair shaft through the outer root sheath. Injury was due to external injury from chemicals applied and hairstyles.
Central Centrifugal Cicatricial Alopecia

- Chronic progressive alopecia primarily in women of African descent
- Hair loss in the crown or vertex of the scalp with symmetric expansion with active disease at periphery
- Occult vertex breakage may be a presenting and early sign of CCCA

Central Centrifugal Cicatricial Alopecia

• Symptoms in 70% of subjects (n=100) ranging from itching (90%), pain/tenderness (84%), burning (24%), and/or soreness when present
• Characterization of severity of symptoms may serve as a marker of active disease (scale 0/10 - 10/10)
• Additional findings may include scaling (37%), erythema (16%), dyspigmentation (13%), pustules (6%)

Onsmudi et al. Arch Dermatol Research. 2023
Central Centrifugal Cicatricial Alopecia

- Likely responsible for more cases of scarring alopecia than all other form in Blacks with prevalence 2.7% to 5.7%
- Mean age 36 years in women with earliest report at age 14
- Infrequently reported in men

Central Scalp Photography Scale (Olsen Scale)
Misdiagnosis
Misdiagnosed as
Androgenetic Alopecia
Alopecia Areata
Other Scarring Alopecia

Delay in Diagnosis
Early CCCA treatment may prevent permanent hair loss and promote hair regrowth

Inadequate Treatment
Misdiagnosis may lead to inadequate treatment, as scarring and non-scarring alopecia require different therapeutic regimens

Psychosocial Burden
Misdiagnosis and inadequate treatment can worsen the psychosocial burden and poor quality of life outcomes in CCCA

What happens when CCCA does not have a typical presentation?

Central Centrifugal Cicatricial Alopecia - Subtypes

- CCCA nomenclature may drive clinical diagnosis
- However, atypical presentations have been noted clinically by the authors and reported in the literature
- This scoping review sought to characterize the distribution of hair loss in published cases of adult patients with CCCA
Central Centrifugal Cicatricial Alopecia - Subtypes

Methods
- Textbooks
- Case Reports
- Case Series
- Clinical Research Studies

Eligible Studies
1. Described the alopecia pattern or had scalp photographs
2. Adults (>18 years)
3. Clinical diagnosis with or without histopathological evidence
Central Centrifugal Cicatricial Alopecia Subtypes

**Atypical**
Hair loss distribution other than only symmetric, vertex involvement

**Classic Variation**
Symmetric, vertex involvement with frontal, temporal, parietal, and/or occipital involvement

**Distinct Subtype**
Patchy, occipital, parietal, frontal, temporal, and/or trichorrhexis without symmetric, vertex involvement

**Publications:** 99

**CCCA Cases:** 281

**Classic:** 203 (72%)

**Atypical:** 78 (28%)
Central Centrifugal Cicatricial Alopecia
Distinct Subtypes

- Patchy (8%)
- Occipital (0.4%)
- Parietal (3%)
- Temporal (0.7%)
- Frontal (0.7%)
- Trichorrhexis (6%)
Central Centrifugal Cicatricial Alopecia - Subtypes


All Photographs are Biopsy-Confirmed CCCA Patients
Central Centrifugal Cicatricial Alopecia
Frontal, Parietal, Temporal Subtypes

53 yr old AA F
Biopsy Proven

79 yr old AA F
Biopsy Proven

Central Centrifugal Cicatricial Alopecia
Patchy Subtype

48 yr old AA F
Clinical Diagnosis

43 yr old AA M
Biopsy Proven

Central Centrifugal Cicatricial Alopecia
Frontal and Bitemporal Subtypes

75 yr old AA F
Biopsy Proven

Central Centrifugal Cicatricial Alopecia
Classic with Occipital and Occipital Subtypes

49 yr old AA F
Biopsy Proven

35 yr old AA M
Clinical Diagnosis

Central Centrifugal Cicatricial Alopecia
Trichorrhexis Subtype

31 yr old AA F
Clinical Diagnosis

43 yr old AA F
Clinical Diagnosis

Central Centrifugal Cicatricial Alopecia Classic with Temporal accentuation and Trichorrhexis

58 yr old AA F
Clinical Diagnosis

Nonclassical clinical subtypes of CCCA may present similarly to other types of alopecia creating a diagnostic challenge.

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Differential</th>
<th>Differential</th>
<th>Differential</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patchy</strong></td>
<td>Alopecia Areata</td>
<td>Tinea Capitis</td>
<td>Syphilitic Alopecia</td>
</tr>
<tr>
<td><strong>Temporal</strong></td>
<td>Traction Alopecia</td>
<td>Female Pattern Hair Loss</td>
<td>Discoid Lupus Erythematous</td>
</tr>
<tr>
<td><strong>Frontal/ Parietal</strong></td>
<td>Frontal Fibrosing Alopecia</td>
<td>Lichen Planopilaris</td>
<td>Traction Alopecia</td>
</tr>
</tbody>
</table>
Central Centrifugal Cicatricial Alopecia - Subtypes

Nearly one third
CCCA typically presents classically but nearly one third of published CCCA cases had distinct distributions

Diagnostic challenge
CCCA may present similarly to other types of alopecia. Trichoscopy and histopathology are encouraged for accurate diagnosis

Nomenclature is limited
CCCA nomenclature does not always reflect clinical presentation and there may be a gap in reporting atypical alopecic distributions

Future research
Validated severity scales inclusive to all clinical presentations of CCCA should be developed
Central Centrifugal Cicatricial Alopecia - Subtypes

Study Limitations

• Unable to access all potentially eligible sources and data
• Some studies did not have corresponding scalp photography, making it challenging to clarify vague data
• Photos limited by quality, dimensions, and inclusion of scalp quadrants to determine their assessment
• Unknown if patients had concurrent types of alopecia or trichoscopy findings that may have aided in diagnostic accuracy
Central Centrifugal Cicatricial Alopecia In Male Patients

CCCA is rarely reported in **males** and investigated demographics, medical histories, and clinical findings in men.

Chart review of males at Penn Dermatology outpatient clinics (2012-2022) Biopsy-confirmed CCCA or Cicatricial Alopecia - Unspecified” as identified by ICD-9 and 10 codes.
Demographics

- Patients primarily Black or African American (n=15/17)
- Mean age 43 years (age 30 – 72 years)

Medical History

- 76.5% symptomatic (most commonly pruritus)
- 82.4% did not report hair care practices such as use of hot tools, chemical processing, tight braids, or locs
- 47.1% with FH of alopecia
- None had diagnosis of T2DM
- 3 cases had history of latent TB

Clinical Findings

- 8 cases with distinct distribution of scalp alopecia
- 29.4% had an overlapping diagnosis on scalp biopsy: 2 androgenetic alopecia, 2 lichen planopilaris, 1 lichen simplex chronicus

Central Centrifugal Cicatricial Alopecia in Males

Subtypes

- 8 Classic
- 3 Occipital
- 2 Patchy
- 2 Posterior Vertex
- 1 Diffuse
- 1 Undetermined

Only 8/17 cases presented with the classical subtype.
Central Centrifugal Cicatricial Alopecia in Males

- CCCA may be unrecognized and underdiagnosed in males due to atypical presentations
- Variations in presentation can be clinically misdiagnosed (e.g. AGA)
- Scalp biopsy may be warranted even when diagnosis is thought to be clinically apparent
- Some similarities between males and females, but risk factors may be distinct (e.g. investigate TB infections in males with CCCA)
Central centrifugal cicatricial alopecia in males severity and time to diagnosis

Tiaranessa K. Jackson MPH a, Yacine Sow BA a, Katherine Omueti Ayoade MD, PhD c, John T. Seykora MD, PhD c d, Susan C. Taylor MD c, Temitayo Ogunleye MD c

Accepted for publication
Earl diagnosis and treatment slow or halt disease progression and prevent permanent damage to hair follicles.

This study investigated alopecia severity and the time to biopsy-confirmed diagnosis among males with CCCA.
91.7% had a severity grade of 3 or greater (severity was independently assessed by 2 dermatologists using the “Central Scalp Alopecia Photographic Scale”)

On average, it took 6.4 years for patients to receive a diagnosis of CCCA after the onset of scalp symptoms and/or hair loss (CCCA onset was defined as the patient reported start time of hair loss and/or scalp symptoms using chart review)

72.7% were diagnosed >1 year after onset of CCCA

45.4% were diagnosed >5 years after onset

For patients with alopecia areata: 72.4% of patients received their diagnosis within a year after onset of symptoms, and the mean time from onset of symptoms to diagnosis was 1 year

Males with CCCA experience significant diagnostic delay and present to dermatology with late-stage alopecia

Small sample size of 12
Central Centrifugal Cicatricial Alopecia - Diagnosis

- Reason for performing a scalp biopsy is to confirm the diagnosis and to identify multiple diagnoses.
- Use a dermatoscope to select the site for biopsy which yields higher diagnostic results on pathology.
- Peripilar gray/white halo that is a specific and sensitive dermatoscopic sign for CCCA.
- White patches represent follicular dropout and follicular scarring.
- Hair shaft variability with diminished terminal-to-vellus ratio.
- Pinpoint white dots.

Central Centrifugal Cicatricial Alopecia - Diagnosis

- CCCA is associated with a CD4-predominant perifollicular lymphocytic inflammatory infiltrate in contrast to both LPP and FFA which are CD8-predominant lymphocytic infiltrates.
- Premature desquamation of the inner root sheath
- Lamellar perifollicular fibrosis
- Eccentric thinning of ORS
- Reduced follicular density
- Polytrichia
A 22-item survey of dermatology patients with biopsy confirmed CCCA, the average CCCA-QLI score was 53.31.

• Subjective symptoms and objective signs indicated significantly impaired QoL
• The subjective concerns that brought the most distress to our population were:
  • “I am sad about the appearance of my hair”
  • “I tend to hide my scalp with hats or bandanas”
  • “I cannot forget I have this hair problem”
Central Centrifugal Cicatricial Alopecia
Quality of Life

The risk of psychiatric comorbidity for patients with CCCA was found to be similar to psoriasis and alopecia areata, which are diseases with known psychiatric comorbidities.

- These findings suggest that CCCA patients may benefit from psychological screening and interventions.
- Dermatologists caring for patients with CCCA should provide appropriate resources to better support patients with this diagnosis.
Women with CCCA had a 4-fold increased likelihood of prediabetes or diabetes, when compared to race-, and sex-matched controls. Clinicians should caution women with diabetes that they may have an increased risk of CCCA and consider screening. Average CCCA severity grade in the T2DM or prediabetes group was 3.16 vs 2.57 in the control group (p = 0.043).
Central Centrifugal Cicatricial Alopecia - Associations

- Women with CCCA had a nearly 3-fold increased likelihood of a history of breast cancer, when compared to race-, age-, and sex-matched controls.
- The association may be due to several unknown genetic or environmental factors, but this association may also be due to a shared mutation in PADI3.

- Women with CCCA have nearly 5 times increased odds of having uterine leiomyomas compared with race-, age-, and sex-matched controls.

Onsmudi et al. Arch Dermatol Research. 2023
CCCA- Associations

- Utilized the NIH “All of Us” research program database to investigate comorbidities
- n=201 CCCA cases
- n=201 age-, race-, ethnicity-, and gender-matched controls
- CCCA patients have significantly increased risk of metabolic dysfunction, atopic, autoimmune, metabolic, and psychiatric comorbidities

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperlipidemia</td>
<td>↑ 5.20</td>
</tr>
<tr>
<td>Hypertension</td>
<td>↑ 8.62</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>↑ 5.66</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>↑ 6.03</td>
</tr>
<tr>
<td>Asthma</td>
<td>↑ 3.55</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>↑ 4.94</td>
</tr>
<tr>
<td>Autoimmune condition</td>
<td>↑ 4.92</td>
</tr>
<tr>
<td>Depression</td>
<td>↑ 3.23</td>
</tr>
<tr>
<td>Anxiety</td>
<td>↑ 5.37</td>
</tr>
</tbody>
</table>

Joshi TP. Comorbidities in patients with central centrifugal cicatrical alopecia: A case controlled study. [https://doi.org/10.1111/ijd.16932](https://doi.org/10.1111/ijd.16932)
Central Centrifugal Cicatricial Alopecia

Treatment

• No published case-controlled studies
• No FDA approved treatment
• NAHRS (n=529) study NO association with
  • Relaxer, texturizer or hot comb use
  • Braids with extensions, weaves or tracts
  • History of seborrheic dermatitis
  • Reaction to a hair care product
  • Bacterial infection
• **Hair care practices are not causative** and treatment recommendations based solely on hair style modification are insufficient
• PADI-3 gene mutation in 25% in a study population

Central Centrifugal Cicatricial Alopecia

Treatment

- Patients with a history of thyroid disease and those using metformin for DM had higher odds of improvement after treatment
- Patients using hooded dryers and those wearing natural hairstyles had higher odds of improvement after treatment
- Patients with scaling or pustules had higher odds of worsening

- Age and stage at presentation was not found to have any significant effect on the odds of improving, remaining stable, or worsening
- Some patients may benefit from treatment independent of the years of stage of the disease

Onsmudi et al. Arch Dermatol Research. 2023
Central Centrifugal Cicatricial Alopecia Treatment

Dermatologists must avoid a “nothing can be done mentality”

- Review study of 71 cases of hair regrowth
- Among scarring alopecias, FFA had the most published cases of regrowth
- Treatments varied widely between and within each subtype
- Most commonly reported treatments were topical metformin for CCCA, light therapy for LPP, 5αRI for scalp FFA, intralesional triamcinolone for eyebrow FFA

Central Centrifugal Cicatricial Alopecia Treatment

**Objective**
To develop consensus statements for appropriate therapies in adults with CCCA and establish a framework to guide clinical practice.

**Methods**
3 round modified-Delphi of 21 US board-certified dermatologists with hair and scalp expertise January – March 2023

**Gap**
No established guidelines exist for the treatment of CCCA

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[Reference]
Central Centrifugal Cicatricial Alopecia Treatment Delphi Consensus Recommendations

20 total statements met strong consensus (≥75%)

2 statements met moderate consensus (≥55% but < 75)

70 statements did not meet consensus (<55%

Central Centrifugal Cicatricial Alopecia Treatment Delphi Consensus Recommendations

**Table I. Delphi consensus recommendations**

<table>
<thead>
<tr>
<th>Statements meeting strong consensus</th>
<th>Delphi round for consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>High potency topical corticosteroids (alone or in combination) for at least 4 weeks then tapered to maintenance dose of 2-5x weekly</td>
<td>1</td>
</tr>
<tr>
<td>A high potency topical corticosteroid scalp (alone or in combination) as a maintenance dose.</td>
<td>2</td>
</tr>
<tr>
<td>A high potency topical corticosteroid (alone or in combination) as a maintenance dose.</td>
<td>1</td>
</tr>
<tr>
<td>Topical minoxidil 5% or greater as adjunct treatment in adults with CCCA.</td>
<td>3</td>
</tr>
<tr>
<td>Topical minoxidil 5% or greater or oral minoxidil as adjunct therapy (oral dose unspecified)</td>
<td></td>
</tr>
</tbody>
</table>

*Statement combines 2 therapeutic options.*

Central Centrifugal Cicatricial Alopecia Treatment
Delphi Consensus Recommendations

Table II. Delphi consensus recommendations—systemic

<table>
<thead>
<tr>
<th>Statements meeting strong consensus (n)</th>
<th>Delphi round for consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral doxycycline (or other tetracyclines or in combination) up to 6 months in patients with active disease (DISAGREEMENT)*†</td>
<td>3</td>
</tr>
<tr>
<td>Oral antibiotics are appropriate for CCCA. (DISAGREEMENT)†</td>
<td>2</td>
</tr>
<tr>
<td>Systemic corticosteroids are NOT appropriate (DISAGREEMENT)†</td>
<td>3</td>
</tr>
</tbody>
</table>

**CCCA,** Central centrifugal cicatricial alopecia

*Statement met strong consensus during peer discussion in round 3.
†CONSSENSUS DISAGREEMENT = strong consensus followed by discussion and clarification in round 3.
## Central Centrifugal Cicatricial Alopecia Treatment Delphi Consensus Recommendations

### Table III. Delphi consensus recommendations

<table>
<thead>
<tr>
<th>Statements meeting strong consensus</th>
<th>n</th>
<th>Delphi round for consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intralesional triamcinolone acetate prescribed (alone or in combination)</td>
<td>18/21</td>
<td>1</td>
</tr>
<tr>
<td>Intralesional triamcinolone acetate as maintenance therapy for active disease</td>
<td>16/20</td>
<td>2</td>
</tr>
<tr>
<td>It is appropriate to limit the maximum dose of intralesional corticosteroids to an adult with CCCA is up to 20 mg in 1 session</td>
<td>17/20</td>
<td>2</td>
</tr>
<tr>
<td>The maximum dose of intralesional corticosteroids should be limited to 20 mg in 1 session</td>
<td>15/16</td>
<td>3</td>
</tr>
<tr>
<td>Hair transplantation should be avoided in patients with active scalp inflammation</td>
<td>20/21</td>
<td>1</td>
</tr>
<tr>
<td>Hair transplantation may improve patients with active scalp inflammation for at least 1 yr before hair transplant</td>
<td>14/16</td>
<td>3</td>
</tr>
<tr>
<td>There is limited information to support the use of PRP or fibrin matrix as treatment for CCCA.</td>
<td>14/16</td>
<td>3</td>
</tr>
</tbody>
</table>

*Statement met strong consensus agreement.*

†New statement added and voted on.

‡Experts voted to replace “inadequately studied” with “not enough evidence to recommend.”

- **Intralesional steroids 5-10 mg/cc for active disease (q4-12 wks) or as maintenance therapy**
- **Max 20 mg of intralesional steroids in one session**
- **No evidence of active scalp disease for at least 1 yr before hair transplant**
- **Not enough evidence to recommend PRP or fibrin matrix**
Central Centrifugal Cicatricial Alopecia Treatment
Delphi Consensus Recommendations

- **Supplements**
  - Screen for vitamin D and iron/ferritin and correct deficits with oral supplements

- **Behavioral**
  - Recommend discontinuing or limiting traction inducing hairstyles
  - Assess how much a patient is bothered by their hair loss and refer for counseling or support groups if needed
  - Shampoo scalp at least once every 2 weeks

- **Did Not Reach Consensus**
  - Recommendation for zinc and other antioxidant, anti-inflammatory, and anti-androgenic supplements
  - Screening for T2DM
  - Recommendation to limit thermal heat practices or permanent dye
Oral hydroxychloroquine is appropriate treatment (alone or in combination) for active CCCA in patients with inadequate response to other therapies.

It is important to discuss discontinuing or limiting the use of chemical hair relaxers and straighteners in patients with CCCA.

Central Centrifugal Cicatricial Alopecia Treatment Delphi Consensus Recommendations

CONCLUSION

- The framework for treatment recommendations was established using 5 categories
- Dermatologists formed 20 consensus statements for treating CCCA in adults
- Strongly recommended topical and intralesional corticosteroids, oral antibiotics, topical and/or low-dose oral minoxidil, and hair transplantation, while recommendation for oral hydroxychloroquine only reached moderate consensus agreement
- Lacked consensus for other therapies including topical calcineurin inhibitors or metformin and oral supplements

Central Centrifugal Cicatricial Alopecia Treatment
Oral doxycycline, IL triamcinolone, topical minoxidil
Central Centrifugal Cicatricial Alopecia Treatment
Intralesional triamcinolone and oral minoxidil

Courtesy Temitayo Ogunleye, MD
Central Centrifugal Cicatricial Alopecia

Summary

Central Centrifugal Cicatricial Alopecia

- Update of Clinical Subtypes
- CCCA in Male Patients
- Comorbidities in Patients with CCCA
- Delphi Consensus Therapeutic Recommendations
Central Centrifugal Cicatricial Alopecia

Summary

- Dermatologists must consider CCCA in the differential diagnosis for adult Black males with alopecia
- More research is needed to explore advanced CCCA in males, factors limiting timely diagnosis, and the impact on quality of life
- Patients with CCCA may not only present with typical central hair loss with centrifugal evolution
- Patients with CCCA experience significant diagnostic delay and present to dermatologists with advanced scarring
- Awareness of comorbidities and impact on quality of life is needed
- Consensus was reached for several statements to help clinicians manage CCCA
References

5. Sow, Yacine (2024), "Supplementary materials of “Lessons from a Scoping Review: Clinical Presentations of CCCA”", Mendeley Data, V1, doi: 10.17632/6ppwxfvpr4.1
THANK YOU
Susan C. Taylor, MD, FAAD