

## **ADC 101st Annual Conference**

APRIL 19-21, 2024 | HERSHEY LODGE, HERSHEY, PA



# Central Centrifugal Cicatrical Alopecia: An Update



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#### **DISCLOSURES**

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- Board Member or Executive: Mercer Strategies, Board of Directors
- Receipt of Royalty: McGraw-Hill book royalties
- Contracted Research: Allergan Aesthetics, Concert Pharmaceuticals, Croma-Pharma GmbH, Eli Lilly and Company, Pfizer, Inc.
- Ownership Interest: Armis Scientific, GloGetter, Piction Health

#### **OBJECTIVES**

- 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**.



- 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







- 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%)

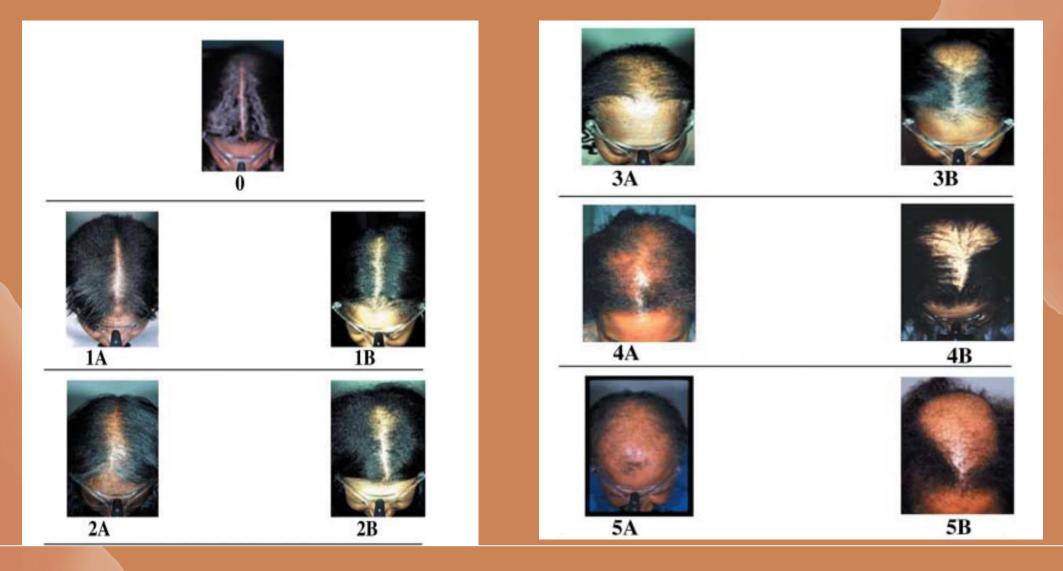






- Likely responsible for more cases of scarring alopecia than all other form in Blacks with prevalence 2.7% to 5.7%
- Mean age 36 years in women with earliest report at age 14
- Infrequently reported in men

## **Central Scalp Photography Scale (Olsen Scale)**



#### Nomenclature

What happens when CCCA does not have a typical presentation?









#### 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



#### Journal of the American Academy of Dermatology



Available online 21 March 2024

#### Lessons from a Scoping Review: Clinical Presentations of CCCA

Yacine N. Sow BA <sup>1</sup>, Tiaranesha K. Jackson MPH <sup>2</sup>, Susan C. Taylor MD <sup>3</sup>, Temitayo A. Ogunleye MD <sup>3</sup> ≥ ⊠

- 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

Methods

**Textbooks** 

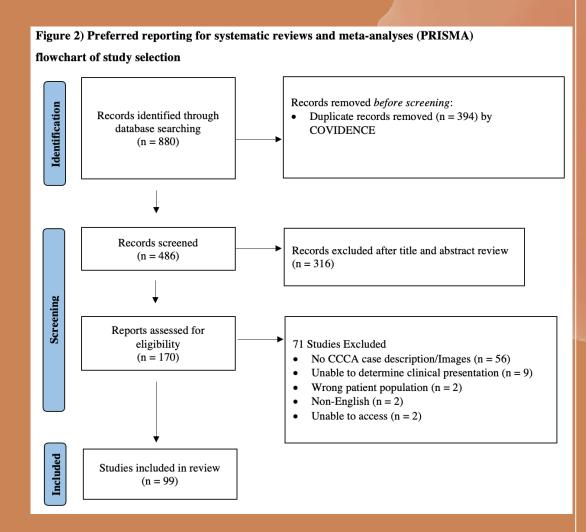
**Case Reports** 

**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





**Publications: 99** 

CCCA Cases: 281

**Classic:** 203 (72%)

**Atypical:** 78 (28%)

**Atypical** 

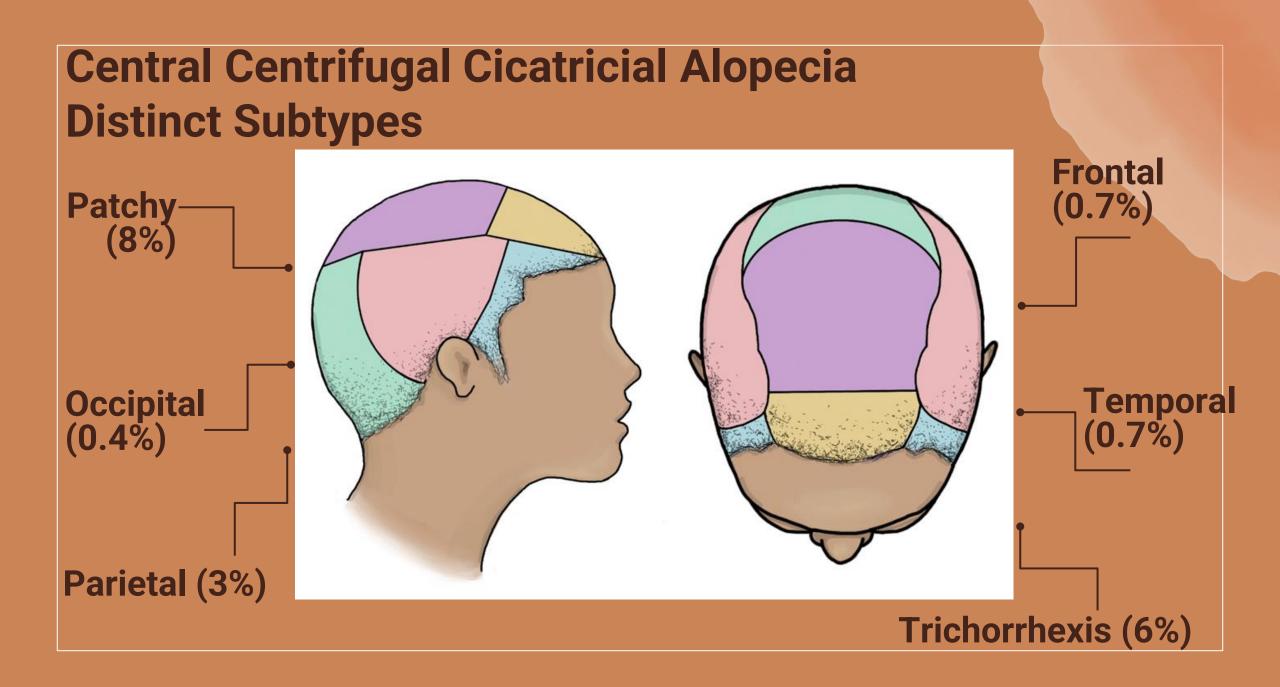
Hair loss distribution other than only symmetric, vertex involvement

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





Classic



**Occipital / Posterior Vertex** 



Frontal - Parietal



**Patchy** 



**Temporal** 



**Decreased Hair Density** 

## Central Centrifugal Cicatricial Alopecia Frontal, Parietal, Temporal Subtypes



53 yr old AA F Biopsy Proven



79 yr old AA F Biopsy Proven



48 yr old AA F Clinical Diagnosis



43 yr old AA M Biopsy Proven

## Central Centrifugal Cicatricial Alopecia Frontal and Bitemporal Subtypes



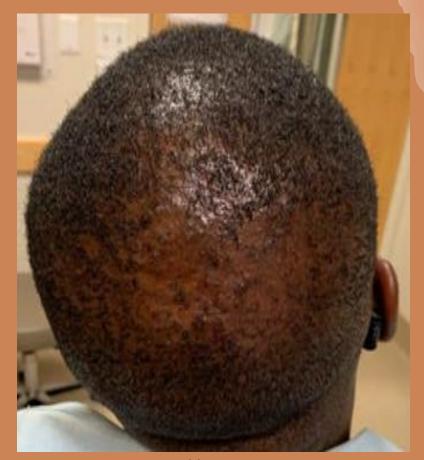


75 yr old AA F Biopsy Proven

## 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

Subtype	Differential	Differential	Differential
Patchy	Alopecia Areata	Tinea Capitis	Syphilitic Alopecia
Temporal	Traction Alopecia	Female Pattern Hair Loss	Discoid Lupus Erythematosus
Frontal/ Parietal	Frontal Fibrosing Alopecia	Lichen Planopilaris	Traction Alopecia



#### **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

#### **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



#### Journal of the American Academy of Dermatology



Volume 89, Issue 6, December 2023, Pages 1136-1140

Original article

## Central centrifugal cicatricial alopecia in males

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





8 Classic



**3 Occipital** 



1 Diffuse



2 Patchy



Only 8/17
cases
presented
with the
classical
subtype

**2 Posterior Vertex** 

1 Undetermined

### **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)



Original article

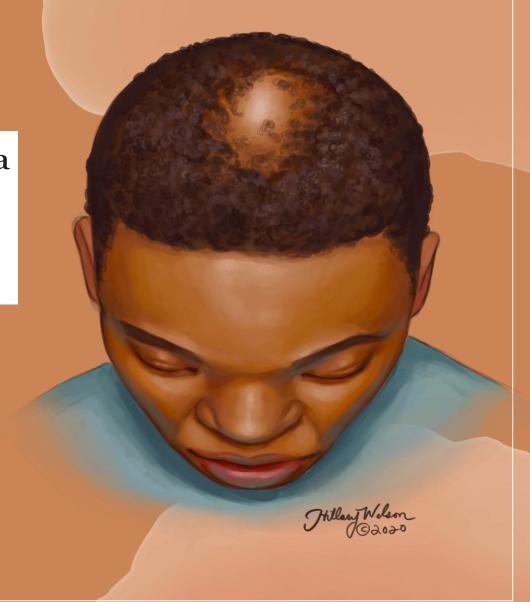
## Central centrifugal cicatricial alopecia in males severity and time to

Tiaranesha K. Jackson MPH a, Yacine Sow BAO, S i S

Katherine Omueti Ayoade MD, PhD c, John T. Seykora MD, PhD c d,

Susan C. Taylor MD c, Temitayo Ogunleye MD c S

Accepted for publication





- Early 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

#### **CCCA** in Males – Severity and Time to Diagnosis

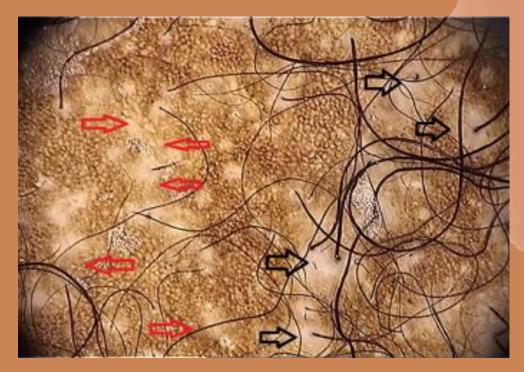
Patient	Time Between	CCCA Severity	CCCA Severity
N = 12	CCCA Onset and	Score (reviewer 1)	Score (reviewer 2)
	Diagnosis		
1	1 year, 10 months	4B	4B
2	5 years	2A	2A
3	9 months	3A	3A
4	unknown	4B	4B
5	3 years	4B	4A
6	9 years	3A	3B
7	12 years	5B	5B
8	6 years	3B	3B
9	8 months	3B	3B
10	1 year	4B	4A
11	15 years, 2 months	5A/B	5A/B
12	16 years, 6 months	4B	3B

- 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

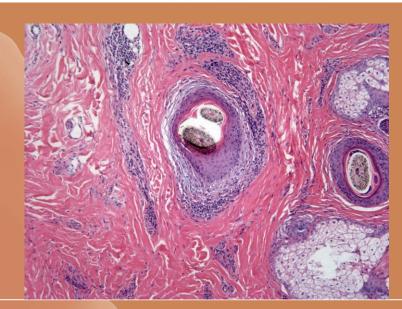


ORIGINAL ARTICLE

Characterization of the inflammatory features of central centrifugal cicatricial alopecia

Alexandra Flamm, Ata S. Moshiri, Fritzlaine Roche, Ginikanwa Onyekaba, Jennifer Nguyen, Alaina J. James, Susan Taylor, John T. Seykora ⋈

First published: 18 February 2020 | https://doi.org/10.1111/cup.13666



- 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

# **Central Centrifugal Cicatricial Alopecia Quality of Life**



Research letter 🙃 Full Access

Quality of life in patients with central centrifugal cicatricial alopecia: a preliminary study

Abena Maranga, Fritzlaine C. Roche, Maryam Alausa, Tara McWilliams, David J. Margolis, Gabriella Fabbrocini, Carlo Natale Lauro, Rosanna Cataldo, Susan C. Taylor 

▼

First published: 15 June 2022 | https://doi.org/10.1111/bjd.21710

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 impared 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 JOURNAL OF DERMATOLOGY

Comorbid anxiety and depression among black women with central centrifugal cicatricial alopecia: A retrospective study

Shanice A. McKenzie, Fritzlaine C. Roche, Ginikanwa Onyekaba, Devin M. Williams, Temitayo A. Ogunleye, Susan C. Taylor

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

#### Central Centrifugal Cicatricial Alopecia - Associations



RESEARCH LETTER | VOLUME 86, ISSUE 3, P661-662, MARCH 01, 2022

Association of type 2 diabetes with central centrifugal cicatricial alopecia: A follow-up study

Fritzlaine C. Roche, MS • Jasmine Harris, MS • Temitayo Ogunleye, MD • Susan C. Taylor, MD 😕 🖂

- 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



#### Journal of the American Academy of Dermatology



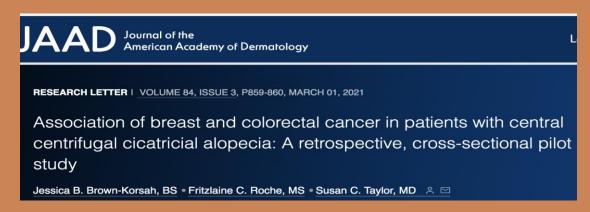
Available online 23 August 2022 In Press, Journal Pre-proof ?

Type 2 diabetes mellitus and central centrifugal cicatricial alopecia severity

Shaheir Ali BA <sup>1</sup>, Maya Collins BS <sup>1</sup>, Susan C. Taylor MD <sup>3</sup>, Kristen Kelley BA <sup>1</sup>, Emma Stratton BSN <sup>1</sup>, Maryanne Senna MD <sup>1</sup>, <sup>2</sup>  $\stackrel{\boxtimes}{\sim}$ 

 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

#### **Research Letter**

FREE

February 2018

#### Association of Uterine Leiomyomas With Central Centrifugal Cicatricial Alopecia

Yemisi Dina, BS<sup>1</sup>; Ginette A. Okoye, MD<sup>2</sup>; Crystal Aguh, MD<sup>2</sup>

> Author Affiliations | Article Information

JAMA Dermatol. 2018;154(2):213-214. doi:10.1001/jamadermatol.2017.5163

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

#### **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

Risk Factor	Odds Ratio
Hyperlipidemia	5.20
Hypertension	8.62
Type 2 diabetes	5.66
Allergic rhinitis	6.03
Asthma	3.55
Atopic dermatitis	4.94
Autoimmune condition	4.92
Depression	3.23
Anxiety	5.37

### 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

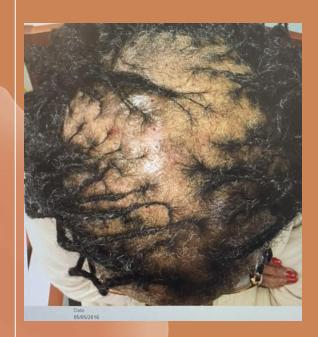
### **Central Centrifugal Cicatricial Alopecia Treatment**

- 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

### Central Centrifugal Cicatricial Alopecia Treatment

#### Dermatologists must avoid a "nothing can be done mentality"



05/05/2016



05/19/2022

- 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, 5aRI for scalp FFA, intralesional triamcinolone for eyebrow FFA

### Central Centrifugal Cicatricial Alopecia Treatment

> J Am Acad Dermatol. 2024 Feb 9:S0190-9622(24)00308-6. doi: 10.1016/j.jaad.2023.12.073. Online ahead of print.

#### Treatment for central centrifugal cicatricial alopecia-Delphi consensus recommendations

Tiaranesha Jackson <sup>1</sup>, Yacine Sow <sup>2</sup>, Jewell Dinkins <sup>3</sup>, Crystal Aguh <sup>4</sup>, Katherine Omueti Ayoade <sup>5</sup>, Victoria Barbosa <sup>6</sup>, Cheryl Burgess <sup>7</sup>, Valerie Callender <sup>8</sup>, George Cotsarelis <sup>5</sup>, Pearl Grimes <sup>9</sup>, Valerie Harvey <sup>10</sup>, Chesahna Kindred <sup>11</sup>, Jenna Lester <sup>12</sup>, Kristen Lo Sicco <sup>13</sup>, Tiffany Mayo <sup>14</sup>, Amy McMichael <sup>15</sup>, Michelle Oboite <sup>16</sup>, Temitayo Ogunleye <sup>5</sup>, Elise Olsen <sup>17</sup>, Achiamah Osei-Tutu <sup>18</sup>, Melissa Piliang <sup>19</sup>, Maryanne Senna <sup>20</sup>, Jerry Shapiro <sup>13</sup>, Antonella Tosti <sup>21</sup>, Cheri Frey <sup>22</sup>, Prince Adotama <sup>13</sup>, Susan C Taylor <sup>23</sup>

Affiliations + expand

PMID: 38341148 DOI: 10.1016/j.jaad.2023.12.073

#### Gap

No established guidelines exist for the treatment of CCCA

#### **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



20 total statements met strong consensus (≥75%)

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

70 statements did not meet consensus (<55%)

Table I. Delphi consensus rec

#### Statements meeting strong consensus

High-potency topical corticostero treatment (alone or in combination)

A high-potency topical corticoste scalp (alone or in combination)

maintenance dose.

A high-potency topical corticoste or in combination) as a mainte Topical minoxidil 5% or greater cadjunct treatment in adults with

CCCA, Central centrifugal cicatricial al \*Statement combines 2 therapeutic c

- High potency topical corticosteroids (alone or in combination) for at least 4 weeks then tapered to maintenance dose of 2-5x weekly
- Topical minoxidil 5% or greater or oral minoxidil as adjunct therapy (oral dose unspecified)

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Delphi round for consensus
1
2
1
3

Table II. Delphi consensu:

#### Statements meeting strong conser

Oral doxycycline (or other tet or in combination) up to 3 DISAGREEMENT)\*,†

Oral doxycycline (or other tet or in combination) up to 6 Oral antibiotics are appropria CCCA.

Systemic corticosteroids are a DISAGREEMENT)<sup>†</sup>

\*Statement met strong consensudiscussion in round 3.

<sup>†</sup>CONSENSUS DISAGREEMENT = 5

Oral doxycycline 200mg daily for up to 6 months in patients with active disease

Systemic corticosteroids are NOT appropriate

s—systemic

	n	Delphi round for consensus
ne US	14/16	3
ne	15/20	2
ive	16/20	2
SUS	14/16	3

ement after clarification and group

Table III. Delphi consensus

#### Statements meeting strong consensu

Intralesional triamcinolone acetor prescribed (alone or in comb Intralesional triamcinolone acetor as maintenance therapy for a It is appropriate to limit the material administered in 1 session to The maximum dose of intralesion to an adult with CCCA is upon Hair transplantation should be active scalp inflammation.

Hair transplantation may improactive scalp inflammation for There is limited information to as treatment for CCCA.<sup>‡</sup>

 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

-procedural

n	Delphi round for consensus
18/21	1
16/20	2
17/20	2
15/16	3
20/21	1
14/16	3
14/16	3

to 10 mg/cc.

CCCA, Central centrifugal cicatricial \*Statement met strong consensus a

<sup>‡</sup>Experts voted to replace "inadequal

New statement added and voted



#### **Supplements**

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



#### **Behavioral**

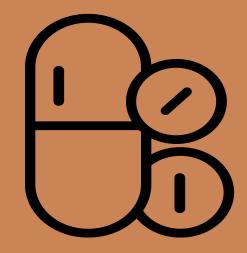
Recommend discontinuing or limiting traction inducing hairstyles
Assess how much a patient is bothered by their hair loss and refer for counseling or support groups if needed
Shampoo scalp at least once every 2 weeks



#### **Did Not Reach Consensus**

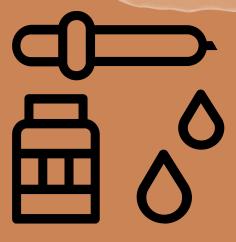
Recommendation for zinc and other antioxidant, anti-inflammatory, and anti-androgenic supplements
Screening for T2DM
Recommendation to limit thermal heat practices or permanent dye

# Central Centrifugal Cicatricial Alopecia Treatment Delphi Consensus Recommendations Moderate Consensus



### **Systemic**

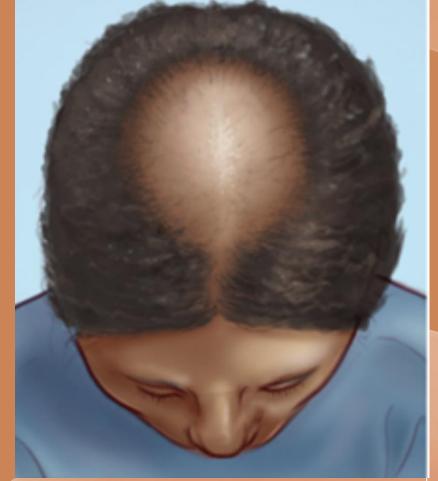
Oral hydroxychloroquine is appropriate treatment (alone or in combination) for active CCCA in patients with inadequate response to other therapies.



#### **Behavioral**

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

- 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





# **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

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