 Updates in Our Understanding of Central Centrifugal Cicatricial Alopecia

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It has been more than 50 years since central centrifugal cicatricial alopecia (CCCA) was first defined by LoPresti and colleagues as hot comb alopecia. Fifty years later, we are only just starting to understand the pathogenesis of CCCA and its systemic implications.

Then and Now
The use of hot combs, a metal device used to straighten naturally curly hair, was ubiquitous in the households of black women in the 1960s. It is no surprise then that this styling process was labeled as the culprit of this disease that affects black women almost exclusively. As the use of hot combs waned but the prevalence of CCCA persisted, its name evolved to chemically induced alopecia—an ode to the popular styling product of the 1990s, the chemical relaxer—and eventually CCCA, a name that reflects its clinical progression and histologic findings.

Since then, research has explored the association with systemic diseases, some noting increased rates of type 2 diabetes mellitus and thyroid disease, and more recently, an increased rate of fibroids in affected patients.

Clues to Pathogenesis
Compared to other primary cicatricial alopecias, CCCA is unique in that active progression is difficult to detect. Symptoms, such as pruritus, often are minimal or absent, rendering clinical assessment quite difficult. Unlike other forms of scarring hair loss, fibrosis, not inflammation, is the predominant clinical feature. The clinical presentation is not unlike a group of disorders termed fibroproliferative disorders, which includes systemic sclerosis, uterine fibroids, atherosclerosis, and keloids, among others. It has been postulated that diseases of aberrant scarring are more common in black individuals due to the protective effect profibrotic alleles have against endemic helminthic infections of sub-Saharan infections, including oncocerciasis.

A recent study showed an increased expression of fibroproliferative genes, particularly those implicated in other fibroproliferative disorders, in affected scalp of patients with CCCA. Most notably, an expression in gene overlap was noted between fibroids and CCCA in this study, though the relationship between these two diseases needs to be further explored.

Gene Variants Identified in CCCA
More recently, a new study has identified a gene variant of peptidyl arginine deiminase 3, PADI3, that is present in approximately one-quarter of studied patients with CCCA. PADI3 plays a role in hair shaft formation and has been implicated in another hair disorder, uncombable hair syndrome, though the latter presents in children, improves with age, and is not associated with a scarring phenotype. However, this study has provided greater insight into our understanding of CCCA by establishing a possible genetic predisposition in patients affected with this disease.

What’s Next for CCCA?
For years, many patients with CCCA have been turned away with few answers and left thinking that it is their own styling habits that have led to their hair loss, when in fact the data we have now suggest a possible link with other systemic diseases and a genetic predisposition for disease. Armed with this knowledge, we can start working to identify treatment options and discuss strategies for early detection of CCCA. Future research should address 1 of 4 large domains: (1) understanding the influence of PADI3 on the scarring pattern seen in CCCA and identifying additional genetic variants implicated in CCCA; (2) identifying what, if any, inheritance pattern is associated with CCCA; (3) identifying other systemic disease associations; and (4) optimizing treatment options for patients with CCCA.

The future is bright for CCCA. Although our understanding of CCCA is still in its infancy, it is my hope that with greater understanding of this disease will come greater empathy for our patients.
REFERENCES