Dramatic Improvement of Trichotillomania with 6 Months of Treatment With N-Acetylcysteine

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Abstract
We present a case of a 17-year-old male with recurrent hair twirling resulting in patchy alopecia, who improved dramatically on N-acetylcysteine (NAC). Trichotillomania is characterized by repetitive hair pulling, twisting, or twirling and can vary from a mild habit to an impulse-control disorder. Standard treatment for pediatric trichotillomania includes cognitive behavioral therapy or medical therapy with selective serotonin reuptake inhibitors. NAC is a more recently utilized, safe, and well-tolerated over-the-counter supplement with some evidence of benefit for habitual skin and hair disorders. For this patient, we recommended 600 mg twice daily, increasing to 1200 mg twice daily as tolerated. After 6 months, our patient reported decreased desire to twirl his hair and his hair had almost completely regrown. Pediatricians who see patients with trichotillomania or other habitual disorders can consider treating these patients with NAC given its potential benefits and favorable side effect profile.

Keywords
Trichotillomania, Hair Pulling, Hair Loss, Habit Disorder

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Article Summary
N-acetylcysteine is a safe and well-tolerated over-the-counter supplement that can be very effective for some pediatric patients with trichotillomania.

Introduction
Pediatric trichotillomania, or hair pulling disorder, is a habit disorder that can result in alopecia and cause patients significant emotional distress. Although a few treatment options exist, including cognitive behavioral therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs), they are not effective for all patients. N-acetylcysteine (NAC), an acetylated formulation of the amino acid L-cysteine, is an over-the-counter supplement shown to be effective for obsessive compulsive disorder (OCD) and other habit disorders. Even though it is most widely used at higher doses for acetaminophen toxicity and as a mucolytic, it is also available over-the-counter in a low-dose oral formulation because of its safety, tolerability, and minimal toxicity risk at low doses.

NAC is used more commonly for trichotillomania in adults than kids. Multiple case reports and one randomized controlled trial (RCT) in adults with trichotillomania showed that NAC was effective at reducing hair pulling. Despite this evidence, one small RCT for pediatric trichotillomania did not find a difference between NAC and placebo, contradicting multiple case reports. But this RCT may not be generalizable to all pediatric patients, particularly teenagers. Age correlates with the frequency and severity of hair pulling in pediatric patients and NAC is hypothesized to work by reducing these urges. The pediatric RCT of NAC for trichotillomania highlighted the need for age-stratification of pediatric patients in future trials to determine whether teenagers respond differently than younger children. We present a

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case of a teenage patient with trichotillomania who failed management with behavioral modifications and CBT but dramatically improved on NAC. His case shows that NAC may be effective for some patients with pediatric trichotillomania. In teenagers in particular, NAC’s main downside, inefficacy, is small compared to its potential benefits.

Case

A 17-year-old male presented to clinic with a history of recurrent hair twirling and persistent hair loss. His hair was recently shaved in an effort to stop twisting his hair and he had a large area of alopecia with irregular borders (Figure 1a). When he presented, he was about to finish 3 months of CBT (Table 1, Timeline). He initially received CBT for adjustment disorder related to his chronic granulomatous disease (CGD), but in these sessions, they also discussed his hair twirling. Nonetheless, his habit of rubbing at his head and touching his hair persisted, even after shaving his hair short twice. He told us that now, after shaving his hair this second time, he was more aware that he was frequently running his hands over his hair and rubbing the top of his head even when there wasn’t hair to pull. Although CBT made him more aware, he and his parents reported, they did not feel it was helping his strong urge to rub his head. They were concerned as he had already relapsed once after shaving his head, and his CBT sessions were ending because he had made enough progress on other fronts. On exam, he had patchy alopecia with irregular borders and hairs of various lengths. There was no involvement of his eyelashes or eyebrows. Dermoscopic examination revealed broken hairs and proximally split ends.

![Figure 1](image1.png)

Figure 1. Before (a) and after (b) treatment with 1200 mg NAC twice a day for 6 months.

| Table 1. Timeline. |
|--------------------|
| **2019–2020** | Initial occurrence of alopecia due to hair pulling. Tried wearing hats and gloves and shaving hair short. Relapsed once hair was long enough to pull. |
| **Nov 2020** | CBT started for adjustment disorder related to his diagnosis of chronic granulomatous disease. Hair fidgeting and pulling was noted by his therapist; additional goal of addressing this was added. |
| **Early January 2021** | Anxiety and depression were markedly improved, and so a plan was made to stop CBT. Hair pulling had not improved. Patient shaved his head again. |
| **End of January 2021** | Presented to Pediatric Dermatology with severe patchy alopecia and history consistent with trichotillomania. Treatment options discussed; NAC initiated. |
| **Early February 2021** | Patient completed CBT. Reported persistent desire to rub top of head at his last CBT session. Continued taking NAC. |
| **July 2021** | Returned for follow-up visit after 6 months of therapy on NAC. His hair had almost completely regrown and he reported decreased desire to twirl his hair and rub at his head. |
Diagnosis

Broadly, hair loss in children can be divided into congenital and acquired causes, and can further be classified by whether it is scarring or non-scarring, and whether it is diffuse, focal, or patchy. Most commonly, pediatric hair loss is acquired, non-scarring, and patchy, such as in tinea capitis, alopecia areata, and trichotillomania. Our patient had acquired, non-scarring, and patchy alopecia, with a history of hair twirling, all consistent with trichotillomania. Commonly known as hair pulling disorder, trichotillomania can also be caused by other repetitive actions such as hair twisting or twirling. It is a clinical diagnosis that can be aided by dermoscopy. Like our patient, physical exam in trichotillomania shows irregularly shaped patches of alopecia with broken hairs of different lengths. Most commonly it affects the scalp, but eyebrow and eyelash involvement is also possible. Diagnosis is more difficult in patients who are younger or who deny hair pulling. Additionally, more mild and focal cases can be difficult to distinguish from alopecia areata. When in doubt, dermoscopy can aid diagnosis and referral to dermatology may be appropriate.

Treatment

There are multiple accepted treatment options for trichotillomania depending on the severity of hair loss and patient and family preferences. For moderate to severe cases, treatment typically includes CBT and/or SSRIs, based on evidence from multiple RCTs and meta-analyses. Mild cases can either be observed or behavioral modifications such as wearing gloves or hats can be recommended. Our patient was nearing the end of his CBT and he and his family did not feel that therapy was helping with his hair pulling. He was also still on a number of medications for his CGD and his parents wanted to avoid additional prescription medications. After discussing the options, we decided to trial N-Acetylcysteine (NAC) at 600 mg twice per day, increasing to 1200 mg twice a day. The adult RCT titrated up from 600 mg once a day. This dosing is standardized across NAC trials for different habit disorders.1,2,14 To further support NAC’s use for habitual disorders, there is evidence for a biologically plausible mechanism. NAC’s multiple uses (in acetaminophen toxicity, as a mucolytic, and for habitual disorders) stem from its mechanisms of action as an antioxidant, a modulator of the inflammatory nitric oxide pathways, and a precursor to glutathione. Its mechanism in habit disorders relates to its role in modulating glutamate levels during glutathione synthesis. In animal models of habitual disorders, glutamate is markedly decreased in the nucleus accumbens, the main input center to the basal ganglia, and restoring extracellular glutamate levels with glutamate-modulating agents improved symptoms. Since the underlying pathophysiology of other habit disorders is very similar, NAC’s efficacy for trichotillomania is thought to derive from the same mechanism.

Outcome

Our patient returned for follow up after 6 months on NAC. He denied having any side effects at the 1200 mg twice a day dose. He and his mother reported good medication adherence. There were no changes in social stressors or medications and no additional CBT. He reported less desire to twirl his hair and rub at his head. On physical exam, he had almost complete regrowth of his hair (Figure 1b). The patient and his family felt that NAC was very helpful given their prior intervention attempts that failed. We recommended that he continue taking NAC 1200 mg BID until his next follow up visit.

Discussion

Our patient improved dramatically after 6 months of treatment with NAC. Several factors make it likely that his response was due to treatment with NAC. First, starting NAC was the only change during the time that his hair regrew and that his desire to rub at his head and pull his hair decreased. Second, he previously relapsed after shaving his hair once it was long enough to pull. Third, he was still having strong urges to rub his head after finishing CBT, but no longer having them after treatment with NAC. Additionally, in past RCTs some patients’ responses were attributed to education about trichotillomania, but this patient and his family were already taught about the behavioral aspects of trichotillomania when he started CBT, so this is not likely. Finally, placebo effect is possible, but theoretically the patient would have responded to the medication sooner, in the first few days to weeks of initiation. However, documentation from his last CBT appointment, 2 weeks after initiating NAC, shows that he was still having a persistent desire to rub at his head at that time. This case is representative of several pediatric patients with habitual dermatologic disorders that we have effectively treated with NAC. We have found that NAC at this dose, 1200 mg twice a day, is well-tolerated with few side effects and can yield favorable responses. This dose was based on adult and pediatric trials which used 1200 mg twice a day. The adult RCT titrated up from 1200 mg once a day and the pediatric RCT titrated up from 600 mg once a day. This dosing is standardized across NAC trials for different habit disorders.1,2,14
Conclusions

NAC is a safe and well-tolerated over-the-counter supplement that has previously been shown to be effective for pediatric OCD and pediatric habitual skin disorders. Some patients with trichotillomania who are treated with NAC at 1200 mg twice a day experience improvement. NAC may be a particularly good option for patients with trichotillomania who are hesitant to starting other therapies or who have failed trials of behavioral modifications or CBT. Beyond trichotillomania, there is evidence that NAC can benefit other patients with habitual disorders including nail biting, lip licking dermatitis, and chronic skin picking/excoriation. Pediatricians who see patients with other habitual skin disorders can consider treating these patients with NAC.

Author Contributions

Lilia Popova contributed to the design, analysis, and interpretation, and drafted and critically revised the document. Jennifer Mancuso, MD, contributed to the conception and design, acquisition, analysis, and interpretation, and critically revised the manuscript.

Declaration of Conflicting Interests

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Ethical Approval and Informed Consent

The patient’s mother consented to publication of this case and the associated pictures. The patient, a minor, assented to publication.

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References

1. Janeczek M, Moy L, Riopelle A, et al. The Potential Uses of N-acetylcysteine in Dermatology: a Review. J Clin Aesthet Dermatol. 2019;12(5):20-26.
2. Oliver G, Dean O, Camfield D, et al. N-acetyl Cysteine in the Treatment of Obsessive Compulsive and Related Disorders: a Systematic Review. Clin Psychopharmacol Neurosci. 2015;13(1):12-24. doi:10.9758/cpn.2015.13.1.12
3. Millea PJ. N-acetylcysteine: Multiple Clinical Applications. Am Fam Physician. 2009;80(3):265-269.
4. Grant JE, Odlaug BL, Kim SW. N-acetylcysteine, a glutamate modulator, in the treatment of trichotillomania: a double-blind, placebo-controlled study. Arch Gen Psychiatry. 2009;66(7):756-763. doi:10.1001/archgenpsychiatry.2009.60
5. Rodrigues-Barata AR, Tosti A, Rodríguez-Pichardo A, Camacho-Martínez F. N-acetylcysteine in the Treatment of Trichotillomania. Int J Trichology. 2012;4(3):176-178. doi:10.4103/0974-7753.100090
6. Kılıç F, Keleş S. Repetitive behaviors Treated with N-acetylcysteine: Case Series. Clin Neuropharmacol. 2019;42(4):139-141. doi:10.1097/WNF.0000000000000352
7. Bloch MH, Panza KE, Pittenger C, Leckman JF. N-acetylcysteine in the treatment of pediatric trichotillomania: a randomized, double-blind, placebo-controlled add-on trial. J Am Acad Child Adolesc Psychiatry. 2013;52(3):231-240. doi:10.1016/j.jaac.2012.12.020
8. Barroso LAL, Sternberg F, Souza MNIFE, Nunes GB. Trichotillomania: a good response to treatment with N-acetylcysteine. An Bras Dermatol. 2017;92(4):537-539. doi:10.1590/abd1806-4841.20175435
9. Özcan D, Seçkin D. N-acetylcysteine in the treatment of trichotillomania: remarkable results in two patients. J Eur Acad Dermatol Venereol. 2016;30(9):1606-1608. doi:10.1111/jdv.13690
10. Panza KE, Pittenger C, Bloch MH. Age and gender correlates of pulling in pediatric trichotillomania. J Am Acad Child Adolesc Psychiatry. 2013;52(3):241-249. doi:10.1016/j.jaac.2012.12.019
11. Xu L, Liu KX, Senna MM. A Practical Approach to the Diagnosis and Management of Hair Loss in Children and Adolescents. Front Med. 2017;4:112. https://www.frontiersin.org/articles/10.3389/fmed.2017.00112/full; https://pubmed.ncbi.nlm.nih.gov/28791288/
12. Shim WH, Jwa SW, Song M, et al. Dermoscopic approach to a small round to oval hairless patch on the scalp. Ann Dermatol. 2014;26(2):214-220. doi:10.5021/ad.2014.26.2.214
13. McGuire JF, Ung D, Selles RR, et al. Treating trichotillomania: a meta-analysis of treatment effects and moderators for behavior therapy and serotonin reuptake inhibitors. J Psychiatr Res. 2014;58:76-83. doi:10.1016/j.jpsychires.2014.07.015
14. Grant JE, Chamberlain SR, Redden SA, Leppink EW, Odlaug BL, Kim SW. N-acetylcysteine in the Treatment of Excoriation Disorder: a Randomized Clinical Trial. JAMA Psychiatr. 2016;73(5):490-496. doi:10.1001/jamapsychiatry.2016.0060
15. Grados MA, Atkins EB, Kovacikova GI, McVicar E. A selective review of glutamate pharmacological therapy in obsessive-compulsive and related disorders. Psychol Res Behav Manag. 2015;8:115-131. doi:10.2147/PRBM.S58601.