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Treatment of Trichotillomania in a Female Pediatric Patient with a Combination of Aripiprazole and N-Acetylcysteine

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Abstract: *Trichotillomania is still a clinically difficult condition to treat with no available FDA-approved medications. Multiple drugs have been reported to improve outcome and reduce the hair pulling behavior, including acetylcysteine, fluvoxamine, and fluoxetine in combination and with or without CBT. This case describes a 14 year old Caucasian female with a 12 month history of hair pulling behavior and one previous failure of SSRI treatment. The patient was referred by her therapist, so CBT was initiated simultaneously with pharmacotherapy. The patient was fully aware of her habit. Her hair pulling behavior was resistant to an initial trial of lamotrigine which was discontinued after 1 month. Treatment with acetylcysteine 1200 mg twice a day was initiated and CBT continued for 2 months. After two months of the above treatment her hair pulling persisted. However, it improved rapidly after the addition of aripiprazole 5 mg daily, as evident by the Massachusetts General Hospital Hair Pulling Scale score, which decreased from 24 to 9, while she was receiving combined pharmacotherapy for 2 months.*

Keywords: *Trichotillomania, N-acetylcysteine, aripiprazole*

1. INTRODUCTION

Trichotillomania (TTM) is currently viewed as a part of obsessive-compulsive and related disorders group in DSM-5. More commonly known as a hair-pulling disorder; it involves an individual recurrently pulling hair from any part of the body. TTM is also sub-classified under body-focused repetitive behavior (BFRB), along with skin picking, nail biting, lip chewing, and cheek biting [1].

Per DSM-5, recurrent pulling of the hair is required along with repetitive attempts to decrease the habit. The 12-month prevalence in the general population is 1-2 % with female predominance of 10:1 [2]. The first description of trichotillomania dates back to 1889 [3].

TTM is a serious social burden and remains a challenging clinical target. Different interventions have been studied, including habit-reversal therapy and pharmacotherapy with either SSRI (selective serotonin reuptake inhibitors) or tricyclic antidepressant (TCA) clomipramine [4]. However there are no FDA drugs approved for treatment of this condition. Multiple medications have been tested; historically, SSRIs and TCAs were considered the first choice medications. Along with clomipramine and fluoxetine, there were data for the use of naltrexone [5], lamotrigine [5], and N-acetylcysteine [6]. Aripiprazole was reported to have a beneficial effect in SSRI resistant cases. Up to date, there have been multiple case reports, including one case from Australia [7], a pediatric female patient and adult male patient in Japan [8,9], and a pediatric male patient from Turkey [10]. There was also an 8-week open-label trial in 12 patients in the USA, where seven patients developed 50% reduction of Massachusetts General Hospital Hair Pulling Scale (MGHHPS) [11].

There have been studies describing the use of bupropion in nine patients in Israel [12], as well as case reports of an adult female patient in India [13] and an adult male patient in New York [14]. Another recent review summarized studies of other medications for the purpose of TTM treatment, including, but not limited to, antiepileptic drugs, lithium, opioid antagonists and stimulants [15].

Considering the serious social stigma of hair pulling, other body repetitive behaviors associated with hair pulling and unresolved treatment issues, the interest and perceived need for treating trichotillomania is still awaiting further research and data collection. The case report below provides information about seven months of treatment of this condition with acetylcysteine and aripiprazole.

2. CASE REPORT

The patient is 14 year old Caucasian female, who presented to the office with her parents with complaints of pulling her hair at home, in school and other public places. She was referred by her psychotherapist after the initial visit.

2.1. History of Present Illness

Pulling behavior started developing about a year ago and is observed in both home and school settings. This behavior is observed on daily basis. It causes severe discomfort and recently became obvious due to bold spots, which prompted the patient to cover her head. The patient had been seen a psychiatrist before and fluoxetine was prescribed in the dose of 20 mg, later 40 mg daily for 3 months without improvement. The treatment course was complicated by diarrhea and the parents stopped giving her medication. The behavior became severe enough to cause impairment of social interaction and self-esteem.

2.2. Past Psychiatric History

An important landmark was speech delay until 3 years of age, and she was diagnosed with autism at that time. Her parents report one episode of reactive behavior when the patient observed her classmate throwing up in school, which caused her to refuse food and to lose 10 pounds. In 6thgrade, she was bullied and parents reported her behavior changed. She was irritable, sometimes agitated and even aggressive at times.

2.3. Interview

During the interview, she patient seemed to be withdrawn, admitted pulling behavior, but seemed to be downplaying the importance of the problem. She endorsed pulling hair “every now and then” but could not explain whether it makes her calm or releases tension. Both of her parents seem to be more concerned. The patient was cooperative, calm, with incongruent affect at times. No psychotic manifestation was found during the interview. Appetite and sleep were not changed. No weight gain or loss recently. No self-mutilating behavior. Patient denies using any illicit substances now or in the past. PHQ-2 was negative on the day of initial evaluation. MGHHPS score 23.

2.4. Social History (7th grade student)

No conduct/discipline problems in school. Academic grades A and B.

2.5. Family History

She has two sisters with no reported psychiatric problems. Parents are separated and share 50/50 joint custody. The patient was born by full term vaginal delivery.

2.6. Assessment and Plan

The diagnosis of trichotillomania was established and documented in the patient’s record. Different options were discussed with the patient and her parents. Parents disagreed about the course of action, but they both declined the suggested use of Clomipramine and Fluoxetine because of fear of side effects. Considering the compulsive nature of her behavior, and the use of lamotrigine for treatment of skin picking disorder [16, 17], lamotrigine in the dose of 25 mg was initiated. That concluded the initial ***visit # 1.***

Follow-up visit # 2**:** The patient returned in 4 weeks with no improvement. MGH scale score 23. Parents and patient reported good compliance. School reported patient being irritable and acting out. Recommended continuation of lamotrigine in the increased dose of 50 mg

Follow-up visit # 3: The patient returned in 4 weeks [total duration of patient observation 8 weeks]. As no change in behavior reported after 8 weeks of treatment with lamotrigine, the situation was discussed with parents. They were presented with the evidence of N-acetylcysteine benefits and acetylcysteine was initiated at the dose of 600 mg BID. Lamotrigine was tapered down and eventually discontinued as parents did not want to increase the dose or continue medication. The patient continued to see her therapist weekly.

Follow-up visit # 4**:** Follow up visit in 4 weeks. The total duration of patient encounter 12 weeks. The patient continues pulling hair, MGHHPS score 21. Acetylcysteine dose treatment duration 4 weeks, dose increased to 1200 mg BID. Lamotrigine stopped.

Follow-up visit # 5: Total duration 16 weeks. Treatment with acetylcysteine 8 weeks. Parents report no improvement in hair pulling behavior. MGHHPS score 21. Acetylcysteine continues 1200 mg BID. Parents are very dissatisfied. Discussed different options. Started aripiprazole 2 mg with an increase to 5 mg aft6er 2 weeks. Initial weight 113 lb (51 kg), Height (5’1”) 154 cm.

Follow-up visit # 6: Total duration 20 weeks. Acetylcysteine duration 12 weeks. Aripiprazole treatment duration 4 weeks. Mother reports dramatic improvement in behavior. MGHHPS score 13 of 28. Continue acetylcysteine 1200 twice daily. Continue aripiprazole 5 mg.

***Follow-up visit # 7*:** The total duration of the case 24 weeks. Acetylcysteine treatment duration 16 weeks. Aripiprazole treatment duration 8 weeks. MGHHPS score 13. Less pulling hair from the head, but father endorsed picking eyelashes. The patient is observed picking her hair during the interview. Continue acetylcysteine 1200 BID. Increase Aripiprazole to 7.5 mg

Follow-up visit # 8: Total duration 28 weeks (7 months). Acetylcysteine treatment 20 weeks. Aripiprazole treatment 12 weeks. MGHHPS 11 of 28.Weight increase to 134 lb [60.8 kg]. Height 5' 21/2" or 159 cm. Appetite stable. No akathisia. Next scheduled visit in 4 weeks.

3. DISCUSSION

The above case is an important example of successful use of a combination of partial dopamine agonist antipsychotic medication and glutamate modulator for the treatment of trichotillomania in the pediatric patient. It also presents the non-successful use of lamotrigine in outpatient psychiatric practice.

The clinical repertoire of medications to address TTM is rather wide at the present time, but clinicians frequently start with an SSRI [fluoxetine or fluvoxamine], as happened with our patient. Continuation of fluoxetine and suggestion of clomipramine were out of the picture due to the family's bad previous experience and a prejudice against this type of medication.

Cognitive behavioral therapy has great efficacy, especially in combination with pharmacotherapy. Our patient had been visiting psychotherapist twice a month during the whole course of the psychiatric encounters. No special habit reversal technique was employed to our knowledge. Patient demonstrated less than perfect compliance with above therapy and therapeutic alliance was broken after five months of treatment, when mother discontinued therapy due to perceived conflict between the therapist and herself.

Use of different pharmacological agents has been reported, though there are still no FDA approved medications for treatment of TTM. There is no approved algorithm for choosing medications, although Grant [5] suggested starting with N-acetylcysteine (NAC). If there is no response after 3 months, other options can be considered, including augmentation with naltrexone if the patient has first degree relatives with addiction, clomipramine if there is significant anxiety, SSRI in case of associated depression, and antipsychotics for people who have failed everything else. At the same time, with the desire for faster response and to engage conscious patient participation, a psychiatrist can be tempted to employ antipsychotics, and specifically, aripiprazole earlier in the course of the disorder.

In our patient with documented failure of SSRI, we initiated lamotrigine, because of the implied etiological association between TTM and other BRRB, and the existence of double-blind placebo controlled trials for lamotrigine used for treatment of skin-picking disorder [16, 17]. Unfortunately, the short period of exposure of our patient to lamotrigine and presumably insufficient dose (50 mg) does not allow us to make any conclusion about the efficacy of this medication for TTM symptoms in our patient.

Then we employed NAC. It alone did not cause significant clinical improvement after 8 weeks of treatment in adequate dose, determined in a double-blind, placebo-controlled study of 50 patients. Once again, we cannot conclude that this medication does not work because the clinical trial reported a dose of 2400 mg and significant improvement beginning after 9 weeks. Our patient [mainly, her parents] had lost faith in the medication after 8 weeks of no improvement. We also unfortunately could not guarantee 100% compliance of our patient with this medication. One of the "psychological" reasons could have been the fact that NAC is an over-the-counter medication, and family did not believe it would work.

Facing the failure to obtain clinical improvement we started aripiprazole. As of now, there are no placebo controlled studies of aripiprazole, but a lot of case reports from all over the world [7-11]. Interestingly, along with the bulk of data describing the beneficial effect of aripiprazole, there was a report of the paradoxical development of TTM as a result of aripiprazole use in male teenager patient with ADHD and conduct disorder [18]. Aripiprazole was used in different doses: 1.5 mg [9], 3 mg [10] to 10 mg [10]. Mean dose of aripiprazole in the open-label study was 7.5+3.4 mg [11].

We started our patient at 2 mg with an increase to 5 mg after 2 weeks, and have detected significant improvement after 4 weeks of combined treatment (aripiprazole and NAC) of this previously resistant case. The mechanism of action of aripiprazole in TTM is still speculating and attributed to partial agonism to D2 receptors, as well as its serotoninergic activity. NAC was reported to allegedly decrease urges in patients with TTM, though reports from two studies are inconsistent [5]. It is difficult to speculate which one is responsible for clinical success or failure in non-research settings when the physician combines agents in the attempt to get maximal clinical benefits within the shortest period of time and while preserving patient safety. In this context the reported case presents is interesting as an example of considerable clinical and social improvement while combining two agents previously reported as effective in the treatment of TTM. We will continue to follow our case, encourage patient and parents to further participate in the CBT while maintaining compliance with pharmacotherapy regimen.

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