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Case Report

Reduction of Ritualistic Behavior in a Patient with Autism Spectrum Disorder-treated with Antibiotics: A Case Report

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Abstract

Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder with wide-ranging symptoms, including deficits in social communication and social interaction, and restricted, repetitive patterns of behavior, interests or activities. Recent research suggests that antibiotics may have therapeutic effects on patients presenting with ritualistic and/or repetitive behaviors. In this study, we present a case report of a 34-months-old boy with ASD with repetitive and ritualistic behaviors. The child's repetitive and ritualistic behaviors were significantly reduced after

taking the antibiotics amoxicillin, cefazolin, and bactrim for several infections across a six-month period. Short-term improvements were observed during multiple concurrent and short term post-therapy evaluations. Shortly after antibiotic discontinuation, behavioral deterioration was reported. We conclude that in this case study, a child with ASD experienced improvements in ritualistic behaviors during antibiotic therapy. Evidence of improvements in symptomatic behavior warrants further research.

Keywords: Antibiotic; Autism; Ritualistic behavior; Single case experimental study

Abbreviations: ASD-Autism Spectrum Disorder; OCD-Obsessive Compulsive disorder

1. Introduction

Antibiotic medications have received limited attention as a possible therapeutic option for Autism Spectrum Disorder (ASD). In one of the few case studies published, a patient experienced substantial improvements in ASD symptoms after being prescribed a 10-day course of amoxicillin [1]. Improvements were temporary and the patient's behavior deteriorated after the antibiotic treatment was completed. Similar behavioral changes were reported for 8 out of 10 children with ASD who were participating in a clinical trial of another antibiotic, vancomycin [2]. The authors speculated that the observed behavioral effects were associated with changes to the subjects' microbiome composition, induced by the antibiotic treatment. This line of research has recently captured the interest of the scientific community, with a number of mouse models being developed. In fact several papers have recently demonstrated that administration of beneficial bacteria can ameliorate a subset of behavioral abnormalities in a mouse model of autism [3-5]. Consequently, understanding the effects of antibiotics on ASD behaviors warrants further research.

2. Case Presentation

We present the case of a 34-month old boy with ASD. At 11 months old, the patient's behavior was characterized by frequent tantrums, fixation on toys, staring episodes, and disinterest in his surroundings. Additionally, the parents reported that his stools were unformed, malodorous, and voluminous. No other health concerns were reported. Speech therapy was initiated at 15 months of age, and by 18 months, the patient had expanded his vocabulary from two to five words, although he continued to avoid social interactions and displayed increased irritability and inattention. At 18 months, a comprehensive diagnostic evaluation indicated that he met criteria for ASD.

At a 24 month appointment with our clinical team, the parents reported ongoing significant difficulty with transitions, self-soothing, and social interactions. A month prior to this appointment, the parents reported the child was diagnosed with an upper respiratory tract infection by his pediatrician and treated with a cephalosporin antibiotic for 10 days. The parents noted that the patient was calmer, easier to redirect and “more cuddly” while taking cephalosporin. Further, they noted that his bowel movements firmed to the point of solid stool and the acrid, “rotting” smell associated with his bowel movements disappeared. After completing antibiotic treatment, looser, malodorous stools were almost immediately observed.

At 26 months, the patient was diagnosed with a strep infection. His pediatrician prescribed amoxicillin 250 mg/5 ml, 7 ml po bid, for 10 days. Within 48 hours of treatment, parents reported that he seemed calmer and less agitated, and he was no longer fixating on opening and closing cabinets and doors. The maladaptive behaviors returned within a week following the completion of treatment. Based on the child’s response during treatment, the same amoxicillin prescription was initiated the following month with positive behavioral response. Parents reported that the patient developed a rash on the 9th day of a 10-day treatment, and immediately stopped the amoxicillin. Within 48 hours, parents reported returned onset of tantrums, meltdowns, and severe and significant perseveration.

Over the course of the next month, the patient’s behaviors deteriorated significantly per parent, therapist, and teacher report. Gastrointestinal symptoms declined once again. A stool culture revealed significant growth of *Proteus mirabilis*. Upon consultation with the parents regarding the risks of on-going antibiotic treatment, Cefazolin oral solution, 375 mg po bid for 7 days was prescribed. Concerning behaviors such as prolonged tantrums, inability to self-soothe, inability to transition, and perseveration all improved within days of treatment intervention per parental and therapist report.

One month post-treatment, the parents reported a decline in gastrointestinal status and an increase in behavioral concerns. As a result, cefazolin oral solution was again prescribed, pulsed for 6-weeks, with 7-days of treatment, 7-days off for a total of 3 rounds. A clinical appointment with a stool test was scheduled 8-weeks from initiation of this treatment plan. The parents reported that the child’s behaviors and levels of frustration improved and he had a happier demeanor throughout this time-frame.

At the follow up appointment at 32 months, the parents reported a significant decline in target behaviors over the previous month, and requested another course of antibiotics to address the patient's behavior. A stool test indicated negative fecal lactoferrin, negative occult blood, low fecal calprotectin, and negative *C.difficile* cultures but significant growth of both *Hafnia alvei* and *Enterobacter cloacae*. Bactrim pediatric elixir 200 mg/40 mg per 5 ml was prescribed, 5 ml po bid for 10 days. Parents reported that the patient's behavior and stool status improved quickly.

When the child was 34 months of age, the parents reported a general pattern of behavioral improvements while their son was on antibiotic therapy followed by an increase in his ritualistic and other negative behaviors when discontinuing treatment. After again discussing the concerns with long-term antibiotic usage with the parents, Cefazolin oral solution was recommended, dosed at 375 mg po bid every other day, for 4-weeks. The child was referred for comprehensive neurological evaluation and gastroenterology services to provide additional information and insight on the best plan of care moving forward.

3. Discussion

This case report describes a patient who exhibited substantial reductions in repetitive and ritualistic behaviors after taking the antibiotics amoxicillin, cefazolin and bactrim. The improvements were temporary and behavioral deterioration was typically seen within 3-days of completion of each antibiotic. There are a handful of case studies available that report similar findings. In one study, a patient experienced substantial improvements in ASD symptoms after a 10-day course of amoxicillin [1]. However, the patient's behavior deteriorated after antibiotic treatment was completed. Cefdinir has also been found to be effective in reducing OCD-like behaviors and tic symptoms [6].

In another study, vancomycin was found to be an effective antibiotic treatment for children with regressive-onset autism [2]. Behavioral observations reported an increase in on-task performance, compliance with parental requests, and persistence when engaging in positive activities. Improvements were temporary and persisted only while the subjects were undergoing the antibiotic treatment [2]. The short-term, behavioral improvements during antibiotic treatment in these studies suggest a gut-brain etiologic connection and provide supporting evidence for further research of the efficacy of antibiotics in reducing repetitive and ritualistic behaviors

There is existing literature regarding effects of antibiotics on a subgroup of children with OCD and/or a tic disorder that experience symptom exacerbations following streptococcal infections (pediatric autoimmune neuropsychiatric syndrome or PANS) [7]. Preliminary studies involving patients with PANS have reported symptom improvements following antibiotic intervention [6, 8]. Due to the known effectiveness of penicillin prophylaxis for rheumatic fever [9], Snider and colleagues hypothesized that children with episodes of OCD and tics would have improved outcomes while maintained on antibiotic prophylaxis [7]. Observations showed significant decreases neuropsychiatric exacerbations during the study year when compared to the baseline year. Although research has shown antibiotics to reduce gut inflammatory responses as well as temporarily modulate behavioral problems associated with ASD and OCD, outcomes remain inconclusive and merit further investigation.

There is also an emerging consensus that gut microbiota plays a major role in regulating the human brain, modulating mood and behavior [10]. The case study being reported further supplements recent literature suggesting an association, in at least a subset of children, between ASD and the gut microbiome [1, 2, 11, 12]. There are several limitations of this study. First, given the clinical nature of this work, there is limited quantitative data to show the decrease in ritualistic behaviors observed in the patient. Further, the study is also limited in that most of the data collected was from observations documented by the patient's parents, therapists, and treating pediatrician. While the benefits of antibiotics at this time appear to be short-term and cannot be a consistent source of reliable long-term treatment, more research is required to fully understand the clinical effects of antibiotics on ASD/OCD behaviors.

4. Conflicts of Interest

The authors declare that they have no competing interests.

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