

Case Report

Comprehensive Care to Improve Quality of Life: A Case of Childhood Adrenoleukodystrophy

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Abstract

Description

The childhood cerebral form of adrenoleukodystrophy (ALD) causes rapid demyelination of cerebral white matter and is clinically characterized by hyperactivity, emotional changes, and poor school performance, as well as progressive cognitive, visual, auditory, speech, and motor decline. While aggressive behavior is a known complication of ALD, treatment of the disease is limited. Moreover, behavioral management is not well described in the available literature, particularly from a psychiatric standpoint. In this case presentation, the patient's parents reported significant agitation and aggression, which may have been secondary to verbal deficits, in addition to the general neuropathological implications of this disease. Although this patient's previously prescribed pharmacotherapy was controlling most of his symptoms, the parents were understandably resistant to a treatment strategy that was so sedating. Therefore, modifications in the patient's original medical therapy were made, including a 50% decrease in his risperidone dosage. He was also referred to a behavioral therapist specializing in autism and speech therapy. He received Applied Behavior Analysis therapy, which was modified to teach a simplified method of communication using shapes identified by tactile sensation. At his 7-month follow-up, the parents reported noticeable improvement in the child's behavior and communication as well as fewer episodes of aggression. Quality of life is of the utmost importance for patients with such a limited life span. Medical care must be individualized for patients with ALD in ways that will enhance their quality of life, focusing on counseling, behavioral management, and interventions designed to address communication difficulties and strengthen social relationships.

Keywords

adrenoleukodystrophy; hereditary central nervous system demyelinating diseases; mental disorders; psychotic disorders; behavioral therapy; tactile communication; child and adolescent psychiatry, aggressive behavior; quality of life

Introduction

Adrenoleukodystrophy (ALD) is a rare disease, affecting approximately 1 in 17000 newborns.¹ Mutations in the ABCD1 gene lead to a defective peroxisomal protein known as the adrenoleukodystrophy protein (ALDP).² ALDP is responsible for transporting very-long-chain fatty acids (VLCFAs) into the peroxisome for beta-oxidation.³ The extracellular accumulation of VLCFAs has direct cytotoxic effects due to oxidative stress, and recent research shows that ABCD1 gene mutations may also lead to alterations in the brain cell junctions and blood-brain barrier permeability.^{4,5} ALD may present

in different forms, including cerebral childhood adrenoleukodystrophy (cALD), cerebral adult form, adrenomyeloneuropathy (AMN), or Addison's disease.⁶ The cerebral childhood form, seen in this case, causes rapid demyelination of cerebral white matter and is clinically characterized by hyperactivity, emotional changes, poor school performance, and progressive cognitive, visual, auditory, speech, and motor decline.⁷ The cALD form has an extremely poor prognosis, with symptoms onset around 4 to 10 years of age. Death usually occurs within 1 to 10 years of diagnosis depending on the severity of the disease.⁸ In this case, the patient was

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diagnosed at age 9. The patient presented with all of the aforementioned symptoms as well as behavioral outbursts, which were the parents' main concern at their psychiatry visit.

The primary treatment is bone marrow stem cell transplantation, which has been found to improve survivability, stabilize the disease process, and prevent further deterioration in neurological function in some cases.⁹ Patients in the early stages of the disease have a 95% 5-year survival rate when treated with stem cell therapy compared to a 54% 5-year survival rate among the untreated group ($P=.006$).⁹ Among those in the later stages of the disease, careful consideration of stem cell transplants is recommended, given the likelihood that the procedure's risks would outweigh the benefits. However, there is a paucity of literature describing the psychiatric implications of cALD and associated treatment strategies. Behavioral issues are not only a concern in patients with ALD but among many children with neurodegenerative disorders. Those who are also visually impaired, as is often the case in ALD, may exhibit challenges with regard to general compliance, routine changes, and emotional outbursts.¹⁰ Neurological diseases are often entwined with psychiatric manifestations, indicating that the biopsychosocial approach to care cannot be exclusive to the field of psychiatry.¹¹ Given that the symptoms experienced by a child depend on their disease process, treatment plans must be developed and adapted to their unique needs. The purpose of this case report is to present the psychosocial needs of a child with ALD and demonstrate an approach to psychiatric care that prioritizes quality of life for both the patient and family.

Case Description

A 9-year-old, 31.6 kilogram male with otherwise normal development initially presented to the pediatrician's office due to hearing loss concerns. Cerumen impaction was found bilaterally. However, upon removal, the patient still failed a hearing test. The pediatrician referred the patient to the hospital for magnetic resonance imaging (MRI) as the hearing loss had progressed over the past 4 to 5 months. The parents had also recently noted horizontal gaze deviation, difficulty understanding words, poor attention and concentration, and behavioral

changes, including irritability, echolalia, and a decline in school grades. The patient was undergoing a workup for attention-deficit/hyperactivity disorder (ADHD) when a brain MRI revealed active demyelinating processes in the posterior deep white matter and corticospinal tracts. The patient was scheduled for an appointment at a genetics and metabolism clinic. He was diagnosed with X-linked ALD within weeks. After the diagnosis, the patient began hematopoietic stem cell transplant therapy within the year, but the disease progressed. He developed adrenal insufficiency and difficulty swallowing, leading to G-tube placement. He also experienced vision loss, seizures, and continued neurological deterioration.

Six years later, at age 15, the patient presented to the children's psychiatry clinic, where the parents reported significant behavioral changes. The father noted that the stem cell therapy had slowed some aspects of the disease, but the patient was becoming easily agitated and increasingly aggressive. Outbursts often occurred in the mornings and in response to loud noises, usually caused by his 2 siblings, both of whom had been diagnosed with ADHD. When frustrated, the patient was known to slam doors, hit, kick, and pinch, as evidenced by several small dark ecchymoses along the father's forearms. His aggressive behavior resulted in his withdrawal from school. Most recently, the patient has begun reaching for and twisting the nipples of his caretakers, a behavior whose origins the parents could not determine.

On admission to the hospital due to a behavioral outburst, the patient was found to be constipated on abdominal radiographs. An X-ray showed moderate stool burden, and the stool caliber was Bristol scale type 1, indicating severe constipation. Upon receiving treatment for constipation, his irritability decreased. At the time of admission, the patient's psychiatric medications included risperidone 2 mg twice daily with 4 mg pro re nata (PRN), diphenhydramine 25 mg daily, sertraline 76 mg daily, and levetiracetam 850 mg daily, for seizure control. Given his deteriorating behavior on the current therapy, his medications were changed during admission, including the discontinuation of diphenhydramine, the addition of clonazepam 0.5 mg twice daily, an increase in sertraline to 100 mg daily, and a decrease in the PRN dose of

risperidone to 2 mg. Additionally, due to known behavioral side effects, levetiracetam was transitioned to oxcarbazepine.

Treatment

At the time of presentation to the psychiatry clinic, the patient was on risperidone 4 mg twice daily, with 2 mg PRN, oxcarbazepine 600 mg every morning and 300 mg every night, sertraline 76 mg daily, and clonazepam 0.5 mg twice daily for behavioral issues. Since his hospitalization for constipation 2 months previously, his medications were changed slightly in a further attempt to manage his behavior, including an increase in risperidone and a decrease in sertraline. Although this medical therapy was controlling most of his symptoms, his parents were understandably resistant to a treatment strategy that was so sedating. His social interactions were limited, and he was becoming less responsive to redirection. Additionally, it was hypothesized that his outbursts may have been due in part to an inability to communicate his distress. For example, his irritability seemed to be attributable to the discomfort of constipation. Quality of life is of the utmost importance for a patient with such a limited life span. Therefore, the patient was continued on pharmaceutical therapy with a decrease in his risperidone dosage to 2 mg twice daily with 2 mg to use PRN. He was also referred to physical therapy, occupational therapy, and a behavioral therapist specializing in autism and speech therapy. The patient received Applied Behavior Analysis (ABA) therapy (45 minutes per session, twice weekly) that was modified to teach him to communicate with shapes, given his other sensory deficits. Objects of different shapes were slowly introduced and used to represent his needs, which he identified by touch and put in a plastic jar. For example, a circle represented food concerns, and a square represented toy concerns. Given his history of aggressive outbursts when frustrated, a triangle was introduced to represent his need for personal space. The parents were also included in the therapy so they could learn management techniques that avoided reinforcing negative behaviors, such as avoiding comforting the patient during instances of aggression.

Outcome and Follow-up

Given the understandable stress that the

family was under, as well as their need for multidisciplinary medical care in multiple cities, psychiatric follow-up was difficult to maintain. However, at the 7-month follow-up, the patient returned to the clinic with significant improvement in symptoms. His parents noted improvements in mood, aggression levels, and sleep. In fact, the patient had not required another hospitalization for behavioral events since his last visit. His communication skills were also developing with the behavioral therapy, which he had received for the past 6 months. At the time of his visit, the therapy was stopped temporarily due to insurance issues. Although his progress was slow, the patient had a recent example of improved communication strategies. In the past, he had become frustrated when his mother assisted him with putting on his socks, resulting in outbursts of hitting or pushing. Now, the patient's mother would place the shapes near him when helping with this task, then watch to see if he placed the triangle in the bucket, thereby communicating his need for space and independence. The only change made to his medications since his last visit was an increase in his oxcarbazepine dose by his neurologist from a total of 900 mg to 1020 mg daily due to a seizure occurring 3 months ago. Given the significant improvement in the patient's symptoms and quality of life, his medical, physical, occupational, and behavioral therapies were continued pending insurance authorization. Family therapy was also recommended to improve intrafamilial relationships and address feelings of anxiety expressed by the patient's parents. Another follow-up appointment was scheduled 6 weeks out.

Discussion

While aggressive behavior is a known complication of ALD,¹² options for treatment of the disease are limited and behavioral management is not well described in the available literature, particularly from a psychiatric standpoint.¹³ In other case reports, risperidone has been used to treat disruptive behavior,¹⁴ while valproate has been used to control manic-like behavioral changes.¹⁵ However, the use of these anticholinergics and antipsychotics in some cases may do more harm than good, resulting in a variety of side effects with minimal improvement in the psychiatric symptoms.¹⁵ Dose-related neurological side effects of these medications, such

as impairments in concentration, memory, and attention, are particularly undesirable, especially for a patient with limited cognitive function.¹⁶

Aggressive behavior is not a clinical presentation unique to ALD, especially since psychiatric and neurological diseases often overlap. Among the psychiatric and behavioral comorbidities associated with childhood neurological diseases, autism spectrum disorder (ASD) is especially frequent.¹⁷ ASD and its subtypes have been implicated in children with cerebral palsy, epilepsy, learning disabilities, speech impairments, and a broad range of genetic and metabolic diseases.^{17,18} In many cases, ASD is secondary to the underlying disease process, rather than coincidental.¹⁹ One study showed that almost 50% of all admissions to psychiatric inpatient units among children and adolescents were due to aggression.²⁰ The study found that a standardized behavioral management plan significantly decreased aggressive incidents, injuries, and the necessity of physical restraint. In addition, the extent of expressive language deficits was found to be positively correlated with levels of aggression in children who have experienced physical abuse.²¹ Verbal deficits can cause children to express themselves through physical actions.²² For that reason, developing strategies to improve communication and behavior is vital to help children express themselves in healthier ways. ABA-based interventions have been found to improve communication and expression in patients with autism.²³ However, there is no available literature regarding the use of ABA for patients with adrenoleukodystrophy to the authors' knowledge. In this case, ABA was adapted to include the use of shapes, identified by feel, to indicate various needs. This simplified communication strategy is also minimally studied in the literature, with the majority of research surrounding more complex tactile communication methods such as Braille and American Sign Language. However, these communication methods were not appropriate in this case given the patient's neurological and sensory deficits.

Care must also be taken to address the underlying issues that may be contributing to a child's behavior. A revised consensus statement regarding the care of individuals with leukodystrophies emphasizes the importance of identifying mood disorders, pain, irritability,

and sleep disturbances among these patients.²⁴ Targeting the underlying causes of these symptoms is critical to improving the quality of life for the patient as well as their caregivers. In this case, recognizing and treating the patient's constipation had a significant impact on his comfort and, therefore, his behavior.

Suggested strategies for managing behavior among visually impaired children with neurodegenerative disorders include: involving the child in decisions regarding their activities, developing schedules and routines, using physical prompts as reminders and guides, and acknowledging their fears and frustrations.¹⁰ Integrating these strategies can become even more complicated with a patient who also has auditory and verbal impairments. A Cochrane review looking at communication interventions for minimally verbal children with ASD found that verbal- and picture-based interventions demonstrated no significant improvement in communication outcomes over time.²⁵ However, the review was quite limited by strict inclusion criteria and only assessed the results of 2 studies. Although they identified other, smaller studies that may have shown communication improvements, those studies were excluded due to a lack of control groups. In patients with Down syndrome, the use of both Natural Language Paradigm and Milieu Communication therapy strategies have shown efficacy in improving communication skills.²⁶ Both methods prioritize altering the environment to encourage communication and interaction. For example, a child's progression through an enjoyable activity is determined by the child's initiative to communicate.

Finally, in cases of chronic illness, care must also be offered to the patient's caretakers. A 2019 systematic review found that psychotherapeutic interventions, specifically cognitive-behavioral therapy (CBT) and problem-solving therapy (PST) have been found to improve mental health and behaviors in parents caring for children with chronic illnesses.²⁷ In fact, CBT may also improve children's behaviors and symptoms. Although the authors found minimal literature regarding family therapy,²⁷ there is some evidence that it is effective for families of children suffering from chronic diseases, including asthma and diabetes mellitus, by decreasing parental stress and improv-

ing intrafamilial relationships.^{28,29} Involving the family in the treatment plan has been shown to improve treatment compliance and outcomes by allowing parents to become more engaged in their child's care and creating a better home environment.³⁰ In this case, teaching the parents to avoid reinforcing negative behaviors was instrumental to maintaining consistency in behavioral adaptations.

Conclusion

The psychiatric and social impacts of ALD cannot be overlooked. Behavioral changes significantly impact the quality of life of the patient, their family members, and their relationships with others. The lack of a standardized treatment algorithm makes medical management challenging, especially in cases where the patient faces a poor prognosis. Efforts need to be made to refine pharmacotherapy for patients in ways that address their symptoms while minimizing dose-related side effects, such as those associated with antipsychotics. It is also imperative that patients with neurocognitive disorders and their families are provided with multidisciplinary, holistic care, including counseling and related resources designed to maximize their quality of life, improve communication strategies, and strengthen social relationships. In cases where patients face comprehensive neurological and sensory deficits but maintain haptic competence, simplified communication strategies using shapes are a possible solution.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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