CASE REPORT

Bjornstad syndrome: a case report of progressive hearing loss and motoric deterioration

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SUMMARY

Bjornstad syndrome is a rare autosomal recessive disorder caused by a mutation in the BCS1L gene, crucial for mitochondrial function and complex III assembly in the electron transport chain. It is characterized by twisted hair shafts, bilateral sensorineural hearing loss, alopecia, and mental retardation. The presented case involves a 7-month-old with delayed speech development, feeding difficulties, and distinct hair abnormalities. Audiological testing revealed initial mild to moderate hearing impairment, which progressed to profound sensorineural hearing loss, confirming the diagnosis. Over three years, the patient's condition deteriorated, necessitating cochlear implant surgery due to worsening hearing loss. This case underscores the progressive nature of hearing loss in Björnstad syndrome and highlights the critical need for early diagnosis and ongoing monitoring. Comprehensive auditory evaluations and timely interventions are essential, and a multidisciplinary approach involving otolaryngologists, audiologists, geneticists, and speech therapists is crucial for effective management and improved patient outcomes.

INTRODUCTION

Bjornstad syndrome is an extremely rare inherited autosomal recessive disorder. Its exact prevalence is unknown, but it is considered extremely rare, with fewer than 50 cases reported in medical literature.[1] This condition is associated with the mutation of BCSL1 gene located on chromosome 2q35.[2] The gene encodes a member of the ATPases 'Associated with diverse cellular a Activities' (AAA) family of ATPases, which is essential to assemble complex III in the mitochondria.[2] Mutation in this gene have been previously associated with two other conditions, complex III deficiency and GRACILE (Growth retardation, Aminoaciduria, Cholestasis, Iron overload, Lactic acidosis, and Early death) syndrome.[3]

Bjornstad syndrome is primarily characterized by abnormality twisted hair shaft (pili torti) before the age of two and bilateral sensorineural hearing loss resulting from inner ear abnormalities. The hearing loss is caused by changes in the inner. It typically becomes evident in early childhood and affects both ears.[2,4] The author reports a case report aiming to describe the clinical presentation and progressive hearing deterioration in a patient with Björnstad syndrome, highlighting the importance of early diagnosis, regular follow-up, and comprehensive care to address the multisystemic nature of the syndrome, with particular emphasis on its auditory manifestation.

CASE PRESENTATION

A 7-months-old baby was referred to the ENT department for hearing screening due to delayed speech development. He hasn't begun babbling at 6 months of age and does not respond toward loud sound sources. His parents also reported feeding difficulties characterized by frequent vomiting during mealtimes, which led to low weight. The mother noted that his twisted, dry hair and sparse eyebrows resembled those of his deceased sister, although other family members did not exhibit these features. The prenatal course was uneventful, with no history of infections or complications. The pregnancy concluded with a term delivery of a healthy baby weighing 2850 grams and an APGAR score of 9/10. No complications, such as hyperbilirubinemia, occurred during pregnancy or at birth. There was no history of exposure to chemicals, mechanical trauma, or heat that could damage the hair shaft. Additionally, there was no prior medical history of seizures, altered consciousness, or medication use. The child was born to non-consanguineous parents.

Physical examination revealed underweighted child with stable vital signs, showing disinterest in his surroundings and lacking eye contact. He presented with microcephaly and hair and eyebrows that were twisted, short, thin, brittle, and sparse, with no visible scarring. His skin and nails appeared normal (Figure 1) (Figure 2A). Central hypotonia was noted, and although he could sit without maternal assistance, he achieved this milestone with a delay. Both testicles were normal in size and position. Examination of the outer ears was normal, with intact tympanic membranes.

Microscopic examination of extracted scalp hairs showed a twisting of the hair shaft along its axis, creating alternating light and dark segments known as pili torti (Figure 2B). Audiological testing revealed outer hair cell dysfunction in both cochlea on otoacoustic emissions (OAE). Tympanometry indicated stiffness and limited movement of the tympanic membrane. Auditory Brainstem Response (ABR) testing showed wave V at 30 dB for click stimuli and at 50 dB for tone bursts 1000 Hz in both ears. During the audiology testing, the patient was on a nasogastric tube for feeding support due to ongoing feeding difficulties (Figure 3A). These findings

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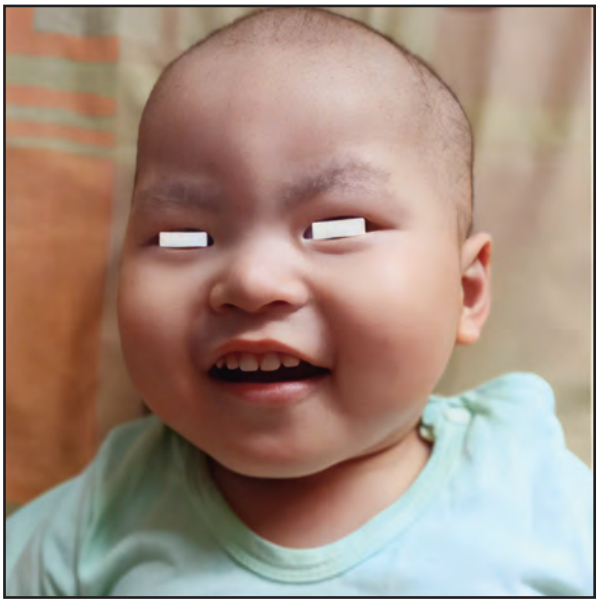

Fig. 1: Patient with pilli torti (hair and eyebrow)

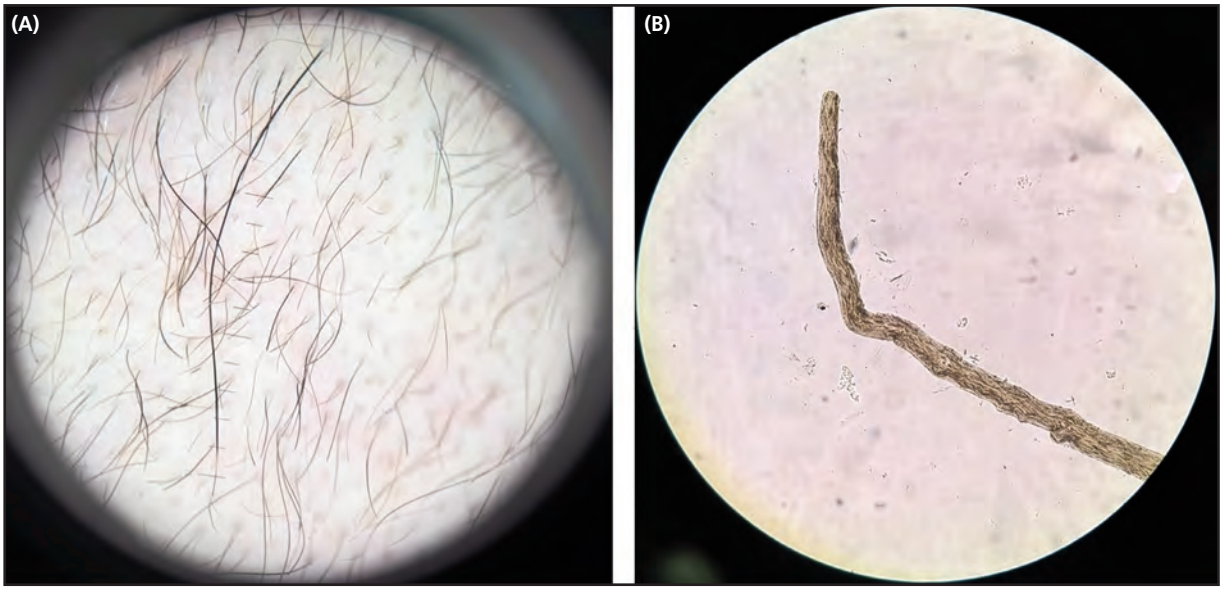

Fig. 2: (A) Hair sample under magnification; (B) Hair sample under 40x microscope

suggest that the patient exhibits mild to moderate hearing impairment at 1000 Hz, associated with conductive hearing loss. Genomic testing using CentoXome® Solo, including NGS-based CNV analysis, identified a positive variant in the BCSL1 gene, consistent with autosomal recessive mitochondrial complex III deficiency nuclear type 1. A diagnosis of Björnstad syndrome was confirmed. The patient's parents were advised to undergo regular hearing monitoring and to use hearing aids, but the parents defaulted from the treatment plans.

Two years later, the patient returned for follow-up hearing monitoring after the initial assessment, with no significant improvement in their condition. Additionally, there was no prior history of seizures, altered consciousness, or medication use. Anthropometric measurements indicated a weight of 11.35 kg and a height of 86 cm. Re-evaluation audiological assessment using ABR click revealed wave V responses at 70 dB in both ears, indicating moderate sensorineural hearing loss (Figure 3B).

At the three-year-follow-up after the initial assessment, the patient returned after being referred by the pediatric team for hearing assessment. He still could not speak, and his condition had deteriorated. Previously able to sit independently, he was now unable to sit and spent most of his time lying down. There was no history of seizures, altered consciousness, or drug intake. On physical examination, he was underweight (12.94 kg, 93 cm) with stable vital signs, showing no interest in his surroundings and lacking eye

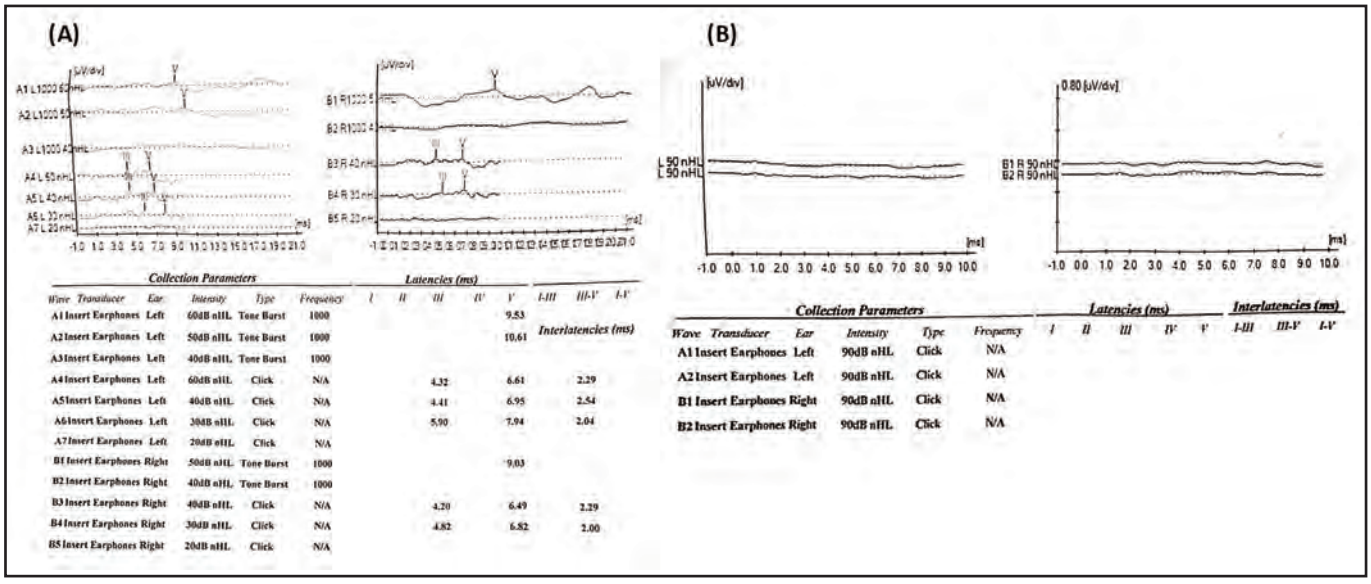

Fig. 3: (A) ABR test result at the age of 7 months, wave V detected at 30 Db (ABR click) and 50 Db (ABR tone burst) in both ears; (B) Recent ABR test, wave V detected at 90 dB in both ears

contact. The physical findings remained consistent with microcephaly, hair and eyebrow was twisted, thin, and sparse. Skin and nails were normal, but central hypotonia was noted. Examination of the outer ears revealed no abnormalities, with intact tympanic membranes. However, ABR hearing examination indicated a worsening to profound sensorineural hearing loss, with wave V was not detected at 90 dB in both ears (Figure 3C). Due to the severity of hearing loss, cochlear implant surgery was recommended for the patient. However, the parents opted for hearing aids instead, citing socio-economic challenges that made the recommended treatment infeasible.

DISCUSSION

In our case, the patient exhibited significant hearing impairment. He had not begun babbling by six months and had not spoken any word by the age of four. Ancillary examinations revealed a shift in hearing loss from conductive to sensorineural, with a further decline in auditory function. ABR testing confirmed this deterioration; wave V previously detected at 30 dB (click) 50 dB (tone burst) in both ears, to 70 dB in both ears ear (click) and was now not detected at 90 dB (tone burst) in both ears.

Hearing impairment is one of the two major primary clinical manifestations of Bjornstad syndrome, resulting from changes in the inner ear that lead to varying degrees of sensorineural hearing loss. This loss typically bilateral, ranging from mild, where individuals may not be able to hear sound at certain frequencies to severe, where complete deafness occurs.[4] Although the progressivity nature of hearing loss is not frequently highlighted in the literature, it usually becomes evident in early childhood and progress differently overtime, indicating that the condition may progressive overtime.[5,6] The progression usually stabilizes around puberty, likely due to cellular adaptation and developmental milestones when further degeneration of the auditory system becomes less pronounced.[7] In addition to hearing impairment and pili torti, additional symptoms that may raise suspicion to Bjornstad syndrome include abnormal skin and hair findings (alopecia, anhidrosis, brittle hair), mental retardation and developmental delays, and hypogonadism.[6] In most cases, Björnstad syndrome is suspected due to similar clinical presentations in relatives and families.[6]

The patient's progressive sensorineural hearing loss, attributed to a mutation in the BCS1L gene, which is crucial for mitochondrial function, particularly in forming complex III in the electron transport chain. This mutation disrupts oxidative phosphorylation, reducing ATP production and leading to the accumulation of unreacted electrons that combine with oxygen to produce reactive oxygen species (ROS). These ROS degrade cellular components such as DNA, lipids, and proteins, ultimately resulting in cellular damage and progressive degeneration of the inner ear structure responsible for hearing.[2]

In this case, the patient's worsening condition over three years, including the inability to sit and deteriorated hearing, highlights the importance of early diagnosis and regular monitoring of disease progression, including hearing loss and other clinical manifestation. Infants suspected Björnstad syndrome should undergo a comprehensive series of auditory tests to assess potential hearing issues, establish a baseline for comparison, and facilitate early intervention. This evaluation includes behavioral audiometry, OAE, and ABR testing.[8,9]

The patient's deteriorated hearing, with wave V was not detected at 90 dB, underscores the necessity of timely intervention. A study by Gulsen et al. reported two cases of Björnstad syndrome with profound hearing loss, where cochlear implantation resulted in significant improvement, reducing hearing loss to a mild-to-moderate level. In this

context, the recommendation for cochlear implant surgery is consistent with the need for advanced hearing restoration methods given the patient's severe hearing impairment.[10] Additionally, other interventions option such as hearing aids and speech therapy are essential for optimizing sound perception and addressing communication delays, reinforcing the need for a tailored approach to manage and improve outcomes in similar case. These suggest that, while Björnstad syndrome may cause debilitating hearing loss, its impact on the patient's daily functioning and quality of life can be mitigated with early diagnosis and timely intervention.[10] Furthermore, to this date, no literature has reported a lethal variant of Björnstad syndrome, indicating its low mortality rate yet potentially significant morbidity.[1]

A multidisciplinary approach is crucial in managing Bjornstad syndrome due to its complex, multisystemic nature. Otolaryngologists play a key role in diagnosing and treating hearing loss, while audiologists monitor hearing function and provide interventions such as hearing aids or cochlear implants. Geneticists contribute by identifying the BCS1L gene mutation, offering genetic counseling to families. Speech therapists address communication delays caused by hearing impairment, helping patients achieve better language outcomes. Pediatricians coordinate care, ensuring that all specialists work together effectively, while neurologists assess any potential neurological issues related to mitochondrial dysfunction. Psychologists provide emotional support to patients and families, and physical or occupational therapists help manage motor function challenges. This coordinated, team-based approach ensures that all aspects of the patient's health are addressed, improving both medical outcomes and quality of life.

This case reports present with some limitations. follow-up evaluations after cochlear implantation could not be conducted, as the patient declined the procedure due to socio-economic challenges. This restricts the ability to assess the potential outcomes and benefits of cochlear implantation, focusing instead on the progression of hearing loss and the effectiveness of alternative interventions like hearing aids.[10] Further reports are required to confirm whether this anomaly is an incidental finding or a feature associated with Björnstad syndrome.

CONCLUSION

The patient's case highlights the progressive nature of hearing impairment in Bjornstad syndrome, with a shift from conductive to sensorineural hearing loss and a decline in auditory function confirmed by ABR testing. The hearing loss, attributed to a BCS1L gene mutation affecting mitochondrial function, leads to progressive degeneration, which may stabilize around puberty due to a combination of genetic, cellular, and developmental factors. As the body adapts and compensates for underlying cellular damage, the progression of sensorineural hearing loss slows. This underscores the importance of early diagnosis and regular monitoring to manage disease progression effectively. A multidisciplinary approach, involving otolaryngologists, audiologists, geneticists, speech therapists, and other specialists, is crucial in addressing the complex, multisystemic nature of the condition and improving the patient's overall quality of life.

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None

DECLARATIONS

The patient's parents had given consent for this case publication. No external funding was received for this study.

ABBREVIATIONS

dB: Decibel (sound intensity)
Hz: Hertz (frequency)
cm: Centimeter (length)
kg: Kilogram (weight)

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