Bilateral sequential cochlear implantation in a patient with the CAPOS syndrome—postsynaptic auditory neuropathy related to a missense mutation within the ATP1A3 gene

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ABSTRACT:

Introduction: This paper presents a boy with CAPOS syndrome (Cerebellar ataxia, Areflexia, Pes calvus, Optic atrophy, Sensorineural hearing loss) and postsynaptic auditory neuropathy who underwent bilateral, sequential cochlear implantation.

Aim: The aim of the study is to describe the development of communication skills after bilateral cochlear implantation in a child with multiple disabilities including profound hearing loss and vision impairment.

Material and methods: The patient’s medical history, including the results of diagnostic tests is presented. Sequential, bilateral cochlear implantation was performed at the age of 7 (right ear) and 8 years (left ear).

Results: The results of audiometric tests confirmed postsynaptic auditory neuropathy. Molecular testing revealed a disease-causing heterozygous c.3007C>A variant in the ATP1A3 gene encoding the Na+/K+ ATPase. 14 months after surgery, the ability to speak had not been regained, but the patient was able to distinguish the environmental sounds.

Conclusions: Cochlear implantation is recommended for patients with CAPOS syndrome. The development of communication skills improved the functioning of the child in the family and school environment.

Meaning: The results observed in the presented patient differ from the results achieved by patients with cochlear hearing loss and presynaptic neuropathies, but indicate the validity of bilateral cochlear implantation in patients with postsynaptic neuropathy in the CAPOS syndrome.

KEYWORDS: ATP1A3, auditory evoked potentials, auditory nerve, auditory neuropathy, CAPOS, cochlear implant, hearing loss, Na+/K+ ATPase, postsynaptic neuropathy

STRESZCZENIE:

Wstęp: W niniejszej pracy przedstawiono chłopca z zespołem CAPOS (ang. Cerebellar ataxia, Areflexia, Pes calvus, Optic atrophy, Sensorineural hearing loss) z postsynaptyczną neuropatją słuchową, u którego przeprowadzono obustronną, sekwencyjną implantację ślimakową.

Cel: Celem pracy jest opisanie efektów osiągniętych po obu operacjach przez dziecko ze sprzężoną niepełnosprawnością obejmującą głęboki niedosłuch i niewidzenie obuoczy.

Materiał i metody: Przedstawiono historię choroby pacjenta, uwzględniając wyniki kluczowych badań diagnostycznych: MRI głowy, badania słuchowych potencjałów wywołanych z pnia mózgu, otoemisji akustycznych, audiometrii impedancyjnej, badania molecularne oraz procedurę sekwencyjną, bilateralnej implantacji ślimakowej przeprowadzonej siódmym (ucho prawe) i ósmym (ucho lewe) w roku życia.
**ABBREVIATIONS**

ABR – auditory brainstem response  
ANSD – auditory neuropathy spectrum disorder  
ASSR – auditory steady state response  
CAPOS – cerebellar ataxia, areflexia, pes cavus, optic atrophy, sensorineural hearing loss  
eVEMP – cervical vestibular evoked myogenic potentials  
DNA – deoxyribonucleic acid  
FM – frequency modulation  
LIP – listening progress profile  
MAIS – meaningful auditory integration scale  
MRI – magnetic resonance imaging  
NRT – neural telemetry response  
SNR – speech-to-noise ratio  

**INTRODUCTION**

The auditory neuropathy spectrum disorder (ANSD) is a term encompassing hearing disorders due to desynchronization, reduced quality, or absence of neuronal transmission along the auditory pathway [1]. Auditory neuropathies may result from the malfunctioning of the presynaptic nerve cells (presynaptic neuropathy) or the postsynaptic nerve cells (postsynaptic neuropathy) [2]. The auditory neuropathy spectrum disorder is a heterogeneous group of neuronal conduction disorders characterized by different pathomechanisms, etiologies, natures, and locations. These include the dysfunction of ribbon synapses between the inner auditory cells, asynchronous conduction of impulses along neuronal fibers, and structural damage to the auditory nerve [3]. Primary neuropathies may be caused by molecular defects. Secondary (acquired) neuropathies are associated with the effects of toxic, inflammatory, or idiopathic factors [1–5]. The origin of the polyneuropathic CAPOS (Cerebellar ataxia, Areflexia, Pes cavus, Optic atrophy, Sensorineural hearing loss) syndrome as described by Nicolaides et al. [6] in 1996 and explained 20 years later, consists in the dysfunction of the ATPIA3 gene [7].

**Wyniki:** Wyniki badań audiometrycznych i genetycznych potwierdziły neuropatię słuchową o postsynaptycznym charakterze, co potwierdzono identyfikacją heterozygotycznego wariantu c.3007C>A w genie ATP1A3 kodującym ATP-azę Na+/K+. Słyszenie i różnicowanie dźwięków z otoczenia stwierdzono 14 miesięcy po przeprowadzeniu drugiej operacji.  

**Wnioski:** Leczenie metodą implantów ślimakowych jest rekomendowana metodą w zespole CAPOS. Stymulacja akustyczna po implantacji ślimakowej umożliwia rozwój zdolności komunikacyjnych i poprawę funkcjonowania dziecka w rodzinie i środowisku szkolnym.  

**Znaczenie:** Efekty słuchowe obserwowane u przedstawianego pacjenta odbiegają od wyników osiąganych przez pacjentów ze ślimakowymi ubytkami słuchu oraz z neuropatiami o charakterze presynaptycznym, ale wskazują na zasadność bilateralnej implantacji ślimakowej u chorych z neuropatią postsynaptyczną w zespole CAPOS.

**SŁOWA KLUCZOWE:** ATPIA3, ATPaza Na+/K+, CAPOS, implant ślimakowy, nerw słuchowy, neuropatia postsynaptyczna, neuropatia słuchowa, niedosłuch, słuchowe potencjały wywołane

**ATPIA3** encodes the α3 catalytic subunit of Na+/K+ ATPase – a transmembrane sodium-potassium pump responsible for the maintenance of concentration gradients of sodium and potassium ions on both sides of the neuronal cell membranes, which is crucial for osmoregulation, sodium-related molecular transport, and electrical nerve excitability [8]. The dysfunction of Na+/K+ ATPase disturbs the regulation of neuronal transmembrane electrochemical gradients, resulting in the inability to restore resting membrane potentials following the stimulus [8]. This results in the impaired excitability of auditory pathway neurons. ATPase is a heterotrimeric protein complex consisting of α, β, and γ subunits. In humans, four isoforms of the α subunit (α1–4) as encoded by ATPIA3 genes, have been identified. The ATPIA3 gene is located on chromosome 19q13.2 and consists of 23 exons and 22 introns. Within the central nervous system, it is expressed mainly within the dendritic cells of the spiral ganglion forming ribbon synapses with inner auditory cells, the ends of cochlear efferent innervation reaching the outer auditory cells, as well as the basal ganglia of the brain, hippocampus and cerebellum [9].

Pathogenic variants of the ATPIA3 may cause isolated or syndromic neurological disorders: alternating hemiplegia of childhood, developmental and epileptic encephalopathy, childhood schizophrenia or rapid onset dystonia-parkinsonism [8–10]; asymptomatic carriers (parents or relatives of patients) have also been reported on. Rapid onset of the disease, understood as the onset of neurological symptoms, is often caused by fever or infectious agents, although idiopathic development is also possible [7, 10]. Some authors emphasize the role of abnormal ATPIA3 gene products in the prenatal period as leading to anatomical defects within the central nervous system [11].

One of the constituents of the CAPOS syndrome is postsynaptic auditory neuropathy characterized by a very complex pathomechanism. The disorder results from asynchronous activation of neuronal fibers within the spiral ganglion, abnormal release of glutamate within the ribbon synapse, and asynchronous propagation of the nerve impulse along the auditory pathway [9].

The therapeutic management of hearing disorders developing against the background of postsynaptic neuropathy is established on a case-by-case basis. In some patients experiencing mild and moderate hearing loss, beneficial effects may be brought about by hearing aids with FM systems used to improve the effective signal reception, i.e. the speech-to-noise ratio (SNR). In patients with significant and deep hearing loss, cochlear implantation can be recommended [3]. The signal generated by the cochlear implant system is believed to improve neural synchronization of the impulses traveling along the auditory pathway as the result of...
systematization of the sequence for stimulation of specific groups of nerve fibers within the spiral ganglion. The auditory effects reported on in the literature are positive yet not always satisfactory, as most authors emphasize that they may be weaker than those observed in cochlear implant users without post-synaptic neuropathy [3, 12]. The best outcomes following cochlear implantation are obtained in patients with presynaptic neuropathy, as implant electrodes directly stimulating the spiral ganglion cells bypass the ribbon synapse damaged by the disturbed mechanism of glutamate release from the inner auditory cells [1, 3]. Both very good and poor auditory benefits from cochlear implantation were reported on in the literature with regard to the CAPOS patients [13–15]. It should be emphasized that this is a special group of patients who develop simultaneous impairment of vision, hearing, speech, balance, and gait [16].

The potential benefits of cochlear implantation in auditory neuropathies are determined on the basis of the etiology, pathomechanism, and location of the disorder. Significantly better results of implantation were observed in the carriers of pathogenic variants within the OTOF, SLC17A8, CACNA1D, and CABP2 genes as compared to patients with the dysfunction of the spiral ganglion and defects within the OPA1, DFNB59, AIFM1, and DIAPH3 genes [1, 3]. The authors of the reports emphasize the assessment of the condition of the spiral ganglion is important when predicting potential benefits of using a cochlear prosthesis. Better outcomes of cochlear implantation as observed in presynaptic neuropathies caused by the disruption of neurotransmitter release within the ribbon synapse are attributed to the proper function of the spiral ganglion. The outcomes of cochlear implantation are relatively worse in postsynaptic neuropathies. This is due to the impaired function of spiral ganglion cells, their axons, dendrites, as well as central nerve pathways within the brain stem [2, 5].

Examination of electrically evoked auditory brainstem responses in patients with postsynaptic auditory neuropathy reveal initial absence of neuronal responses. In some patients, responses may develop some time after implantation, potentially due to the maturation of the electrically stimulated segment of the auditory pathway [17, 18].

An important issue in the auditory and verbal rehabilitation training of patients with auditory neuropathies is related to the neuropsychology of the central nervous system. Cochlear implant can be treated as a “neuroprosthesis” which induces neuronal changes within the cortical and subcortical centers, facilitating sound recognition: either primary (patients with congenital deafness), or secondary (patients with peri- and postlingual deafness). Changes taking place within the cortical centers are both passive and active in nature. An important passive change consists in deprivation of hearing centers due to the lack of incoming stimuli whereas acquisition of new functions by the “deprived” neurons is considered an active process [19]. Changes resulting from the lack of stimulation result in exclusion of non-stimulated areas of the auditory cortex from performing their dedicated function in the process of communication as based on sound recognition. In individuals with congenital hearing loss, these areas are taken over by the remaining, properly functioning senses. Non-stimulated areas of the auditory cortex become prone to excitation by visual and/or vibrotactile stimuli in a process referred to as cross-modal neuroplasticity [20]. In the hearing impaired people, changes within the auditory cortex are induced by an optimally fitted prosthesis as the result of receptor activation and propagation of nerve impulses along the auditory pathway. As the result of auditory stimulation, establishment of nerve connections and activation of target cortical areas, the area becomes useful in cognitive processes. Stimulation facilitates the establishment of connections that are functionally relevant, e.g. for speech recognition [21].

The quality of the delivered stimuli plays a key role in the proper development of auditory functions. Asynchronous stimuli significantly disturb the neuroplastic processes as they prevent the establishment of new synaptic connections within the auditory centers [17, 22]. Cochlear implantation is believed of being capable of significantly impacting the quality of the cortical function-modeling impulses in patients with auditory neuropathy [17, 23].

The aim of this study is to present auditory benefits as achieved following bilateral cochlear implantation in a patient with the CAPOS syndrome with post-synaptic auditory neuropathy.

**CASE REPORT**

**Patient description**

A 6-year-old male patient with CAPOS syndrome, a son of healthy, unrelated parents, was qualified for bilateral cochlear implantation. The patient was born of the first pregnancy, completed at 36 weeks by cesarean section due to maternal preeclampsia to receive the Apgar score of 10. The hearing screening performed in the neonatal period yielded an unremarkable result. In infancy, the patient was developing well, with good sucking, weight gain, babbling, and timely completion of successive developmental milestones, such as sitting up, crawling, and walking. By the age of 2.5, speech had been developing normally.

In the 6th week of life, the patient was subjected to ophthalmological examination due to prematurity. Fundal examination revealed pallor of the optic disc. Alternating convergent squint developed at the age of about 8 months, followed by nystagmoidal eye movements at the age of 2 and subsequent moderate amblyopia. In this period, first observations of balance disorders were made by the patents. An MRI scan of the brain as acquired at the age of 2.5 years revealed isolated hypoplasia of the optic nerves accompanied by compression of the optic chiasm (Fig. 1.). Starting from the age of 2.5 years, the speech continued to develop at an insignificant pace. Despite his vision problems, the patient exhibited no signs of auditory perception disorders.

Prior to the completion of 4th year of age, deterioration in the boy’s auditory responses and the resulting reduction in communication capabilities was observed by parents and preschool educators. For this reason, a comprehensive audiological examination was performed. Cochlear microphonics was observed in the auditory brainstem response (ABR) exam; no response was recorded for tonal stimuli at the frequencies of 500, 1000 and 2000–4000 Hz and intensities of 90, 90, and 100 dB NH, respectively. No responses to
the tonal stimuli at the frequencies of 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz were recorded in the auditory steady state response (ASSR) test. In impedance audiometry, tympanometric curves of type A (right ear) and C (left ear) were observed, with no stapedial reflexes following ipsi- and contralateral stimulation being recorded. Distortion product otoacoustic emissions were observed within the range of 1500–6000 Hz for the right ear and in the range of 2000–6000 Hz for the left ear. No P1–N1 waves were observed in the cervical vestibular evoked myogenic potentials (cVEMP) in response to stimulation with an air-conducted 500 Hz 100 dB tone stimulus administered separately to the right ear and left ear via an insert handset.

As the result of the exams, the patient was diagnosed with auditory neuropathy and vestibular neuropathy. The patient received air-conduction hearing aids with an FM system and started on with an intensive speech and language therapy. Initially, he willingly used the hearing aids, signaling low battery levels and responding to loud, low-frequency ambient sounds, such as a dog barking. After a few months of use, the boy’s reactions to the sounds became unstable. In the fifth year of his life, the patient stopped responding even to loud low-frequency sounds (either with or without the hearing aids). Neither behavioral assessment of hearing thresholds nor the assessment of the auditory benefits of hearing aids within a free acoustic field could be made during the audiology follow-up exams. Speech development was halted, and a regression in communication skills was observed. Sensory-motor aphasia was diagnosed. The patient no longer communicated using sound-based speech. He was capable of uttering several distorted words, such as “come” or “let’s go”. Visual communication with the child with the use of gestures or pictures was limited due to the vision impairment.

Medical documentation was complete with an opinion issued by the educational advisory and psychological team of the educational advisory and psychological counseling center and an opinion from kindergarten staff. In the opinion of a psychologist, the boy was capable of uttering several distorted words, such as “come” or “let’s go”. Visual communication with the child with the use of gestures or pictures was limited due to the vision impairment.

In order to determine the cause of the disorder, a molecular study was performed using the next generation sequencing technique. A novel, heterozygous variant of the missense type, c.3007C>A, p.(Pro1003Thr) was detected. The variant was located within the 22nd exon of the ATP1A3 gene and was most probably pathogenic (according to ten predictive algorithms used). The variant was detected in 14 out of 49 possible readings (29%) which suggests the possibility of genetic mosaicism. The analysis of parental DNA revealed the presence of DNA alteration in the healthy mother, which suggests a variable penetrance of the variant and an autosomal dominant inheritance pattern.

As the result of audiological and molecular studies, the 6-year-old patient was diagnosed with deep hearing loss due to postsynaptic auditory neuropathy. Due to the lack of benefits from the use of hearing aids, a procedure of qualification for cochlear implantation was initiated.

Qualification for cochlear implantation

As part of the qualification for cochlear implantation, the patient was examined by a speech and language therapist using modified versions of the Listening Progress Profile (LIP) [24] and Meaningful Auditory Integration Scale (MAIS) [25] questionnaires; observations taken into account in the analyses included patient’s behavior, reactions to the presented sounds, instructions, and verbal communications. During examination by the speech and language therapist, the patient responded to none of the presented sounds or verbal communications, either with or without the hearing aids. He was unable to call or recognize designata presented in either spatial (objects) or pictorial forms. As revealed by the assessment of the MAIS questionnaire, parents were also unable to notice any repeatable reactions to sounds when the boy was wearing hearing aids. According to the parents, the boy had withdrawn from verbal communication a few months prior to presentation without effectively entering any of the alternative communication systems. Attempts at introduction of gestures, pictograms, or other symbols were unsuccessful. The patient had communicated with his parents through sporadic vocalizations, vestigial words and simple natural gestures. During observation of free behavior at the speech and language therapist’s study, it was noted that the patient’s vision was very limited, and the boy was probably unable to see the pictures or toys presented to him during the examination. The patient looked at objects from a distance of 1–2 centimeters and examined them by touch. He verified the presence of his parents in the same way. The patient used a system of natural gestures to communicate with his parents. He was able to read messages addressed to him by placing his hands on his father’s hands. Ataxic gait disorder was observed in the course of the examination. The boy moved around the room in a clumsy fashion, with slow, wobbly movements on a wide base of support, tripping over toys scattered on the study floor. He verbally called for examination to be terminated by using distorted forms of the words “come, let’s go”.

As the result of audiological and molecular studies, the 6-year-old patient was diagnosed with deep hearing loss due to postsynaptic auditory neuropathy. Due to the lack of benefits from the use of hearing aids, a procedure of qualification for cochlear implantation was initiated.
Implantation of the first cochlear implant
An intraoperative measurement of the response from the auditory nerve was performed during the Cochlear CI612 (Cochlear Ltd, Sydney, Australia) implant placement surgery using the neural telemetry response (NRT) software provided by the implant manufacturer (intraoperative mode); the result was analyzed using the CustomSound EP 5.2 (Cochlear Ltd, Sydney, Australia) software. Similar measurements at modified stimulation levels (suitable for post-operative examination in a conscious patient) were performed during while setting up the sound processor (Nucleus CP1000) parameters. Impedance within the cochlear electrodes was measured during each of the processor setup sessions. For the purposes of the setup of the operating parameters of the sound processor, stimulation thresholds were set at the level of comfortable hearing based on stimulation of individual electrodes and collective stimulation in the so-called Life Mode, i.e. with the processor switched on with the proposed settings for observation of the patient’s behavior. Auditory responses were also verified using a control service speech processor to ensure that the auditory responses were not different.

No significant change in the patient’s behavior was observed after the sound processor had been connected to the cochlear implant within the right ear. Each measurement of impedance in the cochlear electrodes showed no deviations from the normal level. No electrophysiological responses could be obtained from the auditory nerve both intraoperatively and during the subsequent setup sessions. No behavioral reactions were also observed in the child as potential indicators of the effectiveness of electric stimulation. No auditory responses could also be observed when assessing the effective stimulation thresholds (Comfort Level, C) with either selective electrode stimulation or Life Mode operation. For this reason, the stimulation thresholds were set at tentative values with no symptoms of patient discomfort being observed in response to electric stimulation. The subsequent sessions held to verify the settings of the right ear device were held at intervals of 1–2–3–5–9 months. After 9 months, the boy was found to begin to repeatedly react to loud low-frequency sounds, such as a dog barking, or a motorcycle motor running. He demanded wearing the processor and signaled when the battery was running low.

Implantation of the second cochlear implant
Due to the insufficient communication skills and the literature reports suggesting the benefits of cochlear implantation in patients with CAPOS, a decision to perform cochlear implantation within the second (left) ear was made one year after the first surgery. Audiological diagnostic tests were repeated prior to the left ear surgery. A panel of objective and subjective audiometric tests was performed, similar to that before the surgical placement of the implant within the right ear. Auditory brainstem responses were measured within the left ear alone while the protocol for the examination of cVEMP was extended to include the right ear with the sound processor on. No responses were obtained to stimulation of the right and left vestibular organs. The results of the exams did not differ from those obtained prior to the right ear surgery. Auditory and vestibular neuropathy was confirmed.

No neuronal response was obtained in NRT exams, similarly as in the case of the first surgery. Waves potentially suggestive of NRT responses were isolated in manual analysis. However, the waves were flattened upon subsequent measurements at higher pulse intensities. No evident auditory responses were observed either during NRT measurement or upon determination of effective stimulation thresholds. The sessions for the second processor setup were held at 1–2–4–14 months after the second implantation. The settings of the first cochlear implant system were also verified during these visits.

The outcomes of sequential bilateral cochlear implantation
Fourteen months after the second implantation, a significant improvement in patient’s functioning was observed. He had developed reactions to being called, being referred to by name, or to the sounds within the environment. The boy demanded both processors to be put on and activated, being able to notice the batteries running out. He was able to deliberately change the predefined processor program, striving to achieve optimum stimulation adequate to his current communication needs. The patient responded to stimulation from both the right and left implants during an attempt at behavioral evaluation of effective stimulation and determination of C (Comfort Level) thresholds, as well as in the course of the NRT study. However, these reactions were non-specific, preventing precise assessment of comfort/discomfort levels and stimulation thresholds.

When examined by a speech and language therapist, the boy responded to silent knocks and sounds of a drum, rattle and bell. A significant change was observed in the boy’s behavior as he willingly expressed emotions and non-verbally communicated his needs, e.g. the desire to grab the car keys, play with a selected toy or end the examination, using simple gestures and facial expressions. The patient calmed down at verbal messages such as “wait”, “we’re almost done”, “sit still” or “we’re leaving soon”. Although he did not use verbal messages himself, he began to regularly react to simple verbal messages spoken in both raised and normal voice, including in the presence of disturbing sounds. Situational understanding and the functioning at home and peer group at school have improved.

DISCUSSION
The present paper presents a case of a Polish patient with postsynaptic auditory neuropathy and the CAPOS syndrome, in whom a c.3007C>A molecular defect was confirmed within the ATPIA3 gene. This is the first patient with the CAPOS syndrome to receive bilateral cochlear implantation. The boy was subjected to sequential bilateral cochlear implantation at the age of 6 and 7 years, respectively, with the second surgery carried out 12 months after the first one. The paper presents the developmental progress and the auditory outcomes achieved by electrical stimulation using sound processors 14 months after the second surgery.

The literature contains isolated reports on the management of patients with CAPOS syndrome. These include mainly adults with mild clinical course, i.e. isolated auditory neuropathy, managed by unilateral cochlear implantation. The auditory outcomes observed in these patients vary, with very good results also being observed [8].
Han presented a case series consisting of three Korean patients with molecular-confirmed CAPOS syndrome [9], including two female patients (aged 24 and 61) subjected to unilateral (right ear) cochlear implantation. Both patients had presented with isolated, postlingual, progressive, low-pitched hearing loss due to auditory neuropathy with significant impairment of speech recognition in noisy conditions. Speech recognition was slightly above 0% in the 24-year-old patient and 49% in the 61-year-old patient. The follow-up tests carried out 3 and 6 months revealed speech understanding at the level of 94 and 100%, respectively, in the younger patient, and 90% and 88%, respectively, in the older patient. Atilgan et al. [13] reported on the outcomes of unilateral cochlear implantation (right ear) in a 11-year-old female patient with auditory neuropathy and a confirmed ATP1A3 gene defect who had developed clinical signs of CAPOS syndrome in the eighth year of life immediately following chicken pox infection. A rapid, moderate bilateral low- and mid-range hearing loss was accompanied by significant speech impairment, lack of improvement when using hearing aids, visual impairment, and dizziness. Speech recognition test as performed before the surgery revealed a verbal understanding level of 0% which further increased to 50% 3 months after the implantation and nearly 80% six months after the procedure. Wang et al. [14] reported on a 22-year-old male Chinese patient with auditory neuropathy in the course of CAPOS syndrome subjected to unilateral cochlear implantation in the left ear. The hearing loss in the presented patient had developed in the seventh year of life, showing a progressive character and being accompanied by severe tinnitus and chronic fatigue. The authors reported that speech recognition did not improve significantly one year after implantation, with no results of the test being provided in the publication. Tranaebyaerg et al. [26] reported on a series of 18 patients with molecular-confirmed CAPOS syndrome. In four cases, unilateral cochlear implantation was performed due to auditory neuropathy. Significant improvement in speech recognition as assessed using sound processors was observed in only two patients. The authors attributed the observed auditory benefits of cochlear implants to the younger age of these patients.

Although postsynaptic neuropathies are considered to be associated with poorer prognosis, most of the reported patients experienced auditory benefits from cochlear implantation [3, 13, 14, 26]. The results of the tests carried out in patients receiving implants and presenting with ATP1A3 gene defects are suggestive of the following factors being beneficial in terms of hearing outcomes following the implantation procedure: isolated nature of auditory neuropathy, short interval between the onset of symptoms and implantation, and younger age of the patients.

In Polish literature, the topic of postsynaptic auditory neuropathies and outcomes of cochlear implantation in patients with postsynaptic auditory neuropathy has been rarely discussed [27]. Piecuch et al. [28] reported on a female pediatric patient with postsynaptic auditory neuropathy and Brown-Vialetto-Van Leare syndrome subjected to bilateral sequential cochlear implantation in the 4th year of life. In a manner similar to the case presented herein, the girl had presented with neurological symptoms accompanying the auditory neuropathy, namely bulbopontine paralysis (dysphagia, dysarthria), ataxia, visual impairment, and muscle weakness. The patient failed to develop active speech following the surgery. In the enclosed result of behavioral visual reinforcement audiometry, repetitive auditory reactions to the presented sounds were observed, with a published comment stating that auditory stimulation had a positive effect on the child’s cognitive development.

Malfunctioning of the Na+/K+ ATPase pump may lead to impaired pulse propagation not only within the auditory pathway, but also in visual pathways, speech centers, or the equilibrium system [9, 10, 26]. Complex deficits in the functioning of the sensory organs significantly hinder auditory rehabilitation as the patient is not capable of helping themselves by reading the speaker’s lips in order to improve the understanding of the message [29].

The results of audiological examinations as carried out in the patient described herein are typical for patients with post-synaptic auditory neuropathy and include absence of auditory brainstem responses in the ABR exam, presence of evoked otoacoustic emissions and absence of stapedial reflexes, as well as absence of auditory benefits from the signal being enhanced by hearing aids [1, 3]. The gradual deterioration of hearing down to the level of deafness (lack of response to sounds in behavioral assessments) was the basic criterion for the qualification to cochlear implantation in the presented case.

Electrophysiological studies of patients with postsynaptic auditory neuropathy as caused by an ATP1A3 gene defect reveal no electrically evoked auditory brainstem potentials from the spiral ganglion. This is due to dysfunction of the Na+/K+ ATPase, which is responsible for restoration of the resting membrane potential within the spiral ganglion neurons following the preceding stimulus. In some patients subjected to cochlear implantation, systematic electrical excitation facilitate a gradual improvement in the records of electrically evoked potentials within the spiral ganglion, which is clinically linked to improved hearing [30, 31]. To date, no clear responses could be observed in the presented case; this is due to the nature of the disorder and coincides with observations by other authors [30, 31].

The ability to obtain correct impedance measurements from both implant electrodes confirms the proper basic functioning of the internal cochlear implant systems [32]. No changes in patient’s responses were observed upon the use of backup processors. This approach makes it possible to determine whether the lack of response is due to a processor failure without the need to perform a technical inspection of the device. As the result, potential malfunctioning of both systems potentially affecting the patient’s auditory responses could be ruled out.

In the light of the currently available therapeutic options, cochlear implants are the only solution with a potential for improving the patient’s functioning. The absence of satisfactory outcomes of electric stimulation only confirms the observations of other authors who had reported on the auditory outcomes achieved by patients with postsynaptic neuropathies [31, 33]. Cochlear implantation were not able to restore the speech abilities as acquired before the development of symptoms while allowing to improve the overall auditory perception-related functioning of the patient.
The appearance of responses to sounds improved the quality of social interactions. It is interesting that despite the lack of possibility for unambiguous assessment of the thresholds of comfortable stimulation, the patient independently discovered the possibility of manipulating and changing pre-programmed settings of sound processors, adapting the intensity of stimulation to his needs own needs, possibly indicating the presence of auditory awareness.

It is not possible to clearly evaluate the extent to which the Na⁺/K⁺ ATPase dysfunction affects the propagation of the impulses along the auditory pathway as well as within other areas of the central nervous system in this patient. For this reason, it is difficult to estimate the extent to which the classical mechanisms of neuroplasticity and the resulting processes of function restoration and learning as observed following implantations in patients with cochlear defects, can occur in the reported case [17, 22]. It is assumed that one of the mechanisms responsible for neuroplasticity consists in the growth of axons and formation of synapses in the maturing nervous system in the course of regular neuronal activity, while a constant and repetitive activity in the forming neurons results in fixation of synaptic connections [22]. During the development of the central nervous system, a kind of “competition” takes place between functional and non-functional synaptic connections, leading to the fixation of the former and the elimination of the latter, useless ones [22, 34]. The lack of synchronous stimulation has the potential to significantly model and impair the establishment and fixation of these connections as well as affect the maturation of neurons [22]. Achieving synchronization of neuronal stimulation opens up the opportunity for the establishment of synaptic connections within the auditory pathway and the cortical centers of the patient. Even imperfect hearing facilitates the establishment of conditions for acquiring the understanding of verbal messages [29]. This is because cross-modal neuroplastic processes allow to increase the effectiveness of another available stimulus to compensate for the absence of a particular modality [20].

Significant impairment of the visual perception as observed in the study patient prevents the use of visual cues for speech rehabilitation purposes. Acquisition of the knowledge of spoken language on the basis of lip-reading, gestures, sign language, facial expressions, language- and non-language-based non-verbal messages, including written text or pictorial communication, was impossible in the presented case. In the case of disorders of neuronal conduction for both visual and acoustic stimuli, as in the presented patient, not only the possibility of providing a continuous, unchanging and effective stimulation pathway within dedicated areas, but also the development of compensation strategies based on cross-modal neuroplasticity are significantly limited. Bilateral cochlear implantation aimed at the establishment of systematic stimulation of the auditory pathway and dedicated areas of the brain cortex is currently the only method with the potential of being beneficial for patient rehabilitation within the area of sound-based communication [1, 3, 13, 14, 26]. Although the desired therapeutic effects have not been achieved to date, positive changes in the behavior and functioning of the patient, systematic use of both processors, and independent selection of the most appropriate stimulation programs, are suggestive of the positive outcomes of binaural implantation. According to the parents who are capable of observing the boy on a daily basis, the contact with the child has significantly improved, allowing for previous relationships to be rebuilt.

CONCLUSIONS

The developmental progress and the improvement in the behavioral test results as observed in the patient facilitate the conclusion that even small auditory benefits from cochlear implants are of great help for the functioning of patients experiencing deafness in the course of postsynaptic neuropathy in the CAPOS syndrome. The deep vision impairment accompanying the hearing loss significantly hinders auditory rehabilitation, preventing lip reading, the use of phonogestures, sign language, pictorial systems or written texts. The bilateral placement of cochlear implants significantly improved the overall functioning of the child, including communication based on situational understanding, gesture systems (touch-based) and understanding of simple verbal messages as spoken by parents. The development of symptoms of the underlying disease, as well as their rate and scope, is indicative of the need for implementation of the most effective communication methods available in order to provide the child with the opportunity to establish contact with their environment. Due to the small number of CAPOS patients subjected to cochlear implantation being described in the literature, their genetic and phenotypic diversity, as well as to the short observation periods, no data are available for the formulation of any prognosis. Further research is indicated on the improvement of neural conduction and neuroplastic processes in patients with postsynaptic neuropathies subjected to cochlear implantation.

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