Complicated Decisionmaking in Indications for Auditory Brainstem Implant (ABI) in a Patient with Neurofibromatosis 2

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Abstract: A case of an accidental finding of neurofibromatosis 2 in a practically asymptomatic patient is described. Various therapeutic modalities, including restoration of hearing after vestibular schwannoma surgery with an auditory brainstem implant (ABI), are considered.

Introduction

Neurofibromatosis 2 (NF2) is an autosomal dominant syndrome characterized by bilateral vestibular schwannomas, multiple meningiomas and ependymomas. Although it bears the same name as neurofibromatosis 1 (von Recklinghausen disease), these two pathological conditions are completely different entities, both from clinical and genetical point of view. Neurofibromatosis 1 is caused by a mutation of a gene on the long arm of chromosome 17 which encodes a protein known as neurofibromin, which plays a role in intracellular signalling. The neurofibromin is a negative regulator of the Ras oncogene. The mutant gene is transmitted with an autosomal dominant pattern of inheritance, but up to 50% of NF1 cases arise due to spontaneous mutation.

Neurofibromatosis 2 is caused by a defect in the gene that normally gives rise to a product called “Merlin” or “Schwannomin”, located on chromosome 22, band q11-13.1. This peptide is thought to have a tumour-suppressive function. In a normal cell, the concentrations of active (dephosphorylated) merlin are controlled by things such as cell adhesion (which would indicate the need to restrain cell division). It is known that Merlin’s deficiency can result in unmediated progression through the cell cycle due to the lack of contact-mediated tumour suppression, sufficient to result in the tumors characteristic of neurofibromatosis 2. The NF2 gene is presumed to result in either a failure to synthesize Merlin, or the production of a defective peptide that lacks the normal tumor suppressive effect. The Schwannomin-peptide consists of 595 amino acids. Comparison of Schwannomin with other proteins shows similarities to proteins that connect the cytoskeleton to the cell membrane. Mutations in the Schwannomin-gene are thought to alter the movement and shape of affected cells with loss of contact inhibition. Neurofibromatosis 2 has been described for the first time in 1822 by the Scottish surgeon Wishart [1].

Diagnostic criteria for NF2 are defined by bilateral vestibular schwannomas or unilateral vestibular schwannoma with at least two other brain tumours (meningiomas, gliomas, neurofibromas) [2, 3].

Most of the patients with NF2 are initially examined for an unilateral sensorineural hearing loss accompanied or preceded by tinnitus. Also dizziness can be the very first symptom.

Complex approach towards patients with NF2 includes restoration of hearing with an auditory brainstem implant (ABI). During a vestibular schwannoma removal, the hearing nerve is usually severed, so the sensation of hearing is irreversibly damaged. Auditory brainstem implant can elicit hearing sensations by a
direct electrical stimulation of the hearing nuclei in the brainstem. Due to a limited number of channels, the neuroprosthesis does not restore hearing completely in its full natural spectrum. Nevertheless, it helps handicapped patients in speech communication and basic orientation in a world of sounds [4].

Material and Methods
A young twenty six years old woman has been referred to the Department of Otorhino-laryngology, Head and Neck Surgery, First Faculty of Medicine, Charles University in Prague. The aim of the referral was to establish a therapeutic plan and suggestion of further treatment. In her history, during last two years she has observed multiple occurrences of small subcutaneous tumours, first in lower extremities, then around lips, on hands and around joints and tendons. According to a biopsy from one of these tumours in the neck (neurofibroma) and to a typical history of multiple progressive subcutaneous tumours, a diagnosis of neurofibromatosis 1 had been suspected. For a complete diagnostic picture, four café-au-lait spots have been found on a skin of thigh and neck. Nevertheless, additional symptoms for a diagnosis of NF1 (hamartomas of the iris) were missing. Family history of neurofibromatosis was negative; therefore the disease was probably caused by a new gene mutation.

The patient did not complain of any hearing problem. She had no tinnitus, pure-tone audiogram and word audiometry was normal (Figure 1). According to the results of auditory brainstem responses (ABR), a well expressed supracocholear lesion with a dominant neural component was present.

![Figure 1 – Normal hearing in both ears, as tested by pure tone audiometry.](image-url)
From a vestibular point of view, central vestibular lesion with a vertical nystagmus, decreased irritability of both labyrinths without signs of decompensation has been present.

Neurologically, there was a light paresis of n. VII in the left platysma muscle, light vestibular harmonic syndrome, decaying in the right side, subclinical central paresis in the left lower extremity.

In a magnetic resonance imaging, multiple extraaxial meningiomas and brain schwannomas, intramedullar ependymomas of the cervical and thoracic spine segments have been described. Frontally, there was a small parasagittal meningioma with a largest diameter of 13 mm, in the posterior fossa, there was 19 mm meningioma under the skull bone, in the left side, posterior to the temporal bone, there was another 17 mm meningioma (Figure 2). In the left pontocerebellar angle, there was a vestibular schwannoma with an intracanalicular growth (size of 26 mm in an anterioposterior plane and 20 mm in a laterolateral plane). In the right pontocerebellar angle, there was a smaller vestibular schwannoma (size of 10 mm in an anterioposterior plane and 6 mm in a laterolateral plane) (Figure 3). In a cervical spine segment, there were multiple tumours present – large 15 mm schwannoma in the C3 level with a marked dilatation of the right neuroforamen, in the C4-5 level semicircular tumorous mass originating from the dorsal capsule measuring 30 mm – probably a meningioma-compressing the spinal cord against vertebral bodies; in a laterolateral plane this expansion was 22 mm big and it was filling up the whole width of the spinal canal (Figure 4). Another tumour was situated in the dorsal aspect of the spinal cord in the C7-Th1 level, measuring 6 mm in a craniocaudal plane. Another tumour could be seen in the Th4 level and was situated dorsally from the spinal cord. Its diameter was 10 mm. Last lesion was
represented by an intramedullar expansion located in the Th6 level, with a dimension of 13 mm in a craniocaudal plane and 5 mm in an anterioposterior plane and subsequent fusiform spinal cord thickening.

Questioning further approach, patient’s data had been presented during the 6th European Congress of OtoRhinoLaryngology, Head and Neck Surgery, taking place June 30th – July 4th 2007 in Vienna. In the panel discussion participated by Offeciers E., Colletti V., Laszig R., Lenarz T., Betka J., and Ramos Macias A., the following recommendation regarding therapeutic possibilities had been made.

The tumour in the spinal canal in the C4-5 level compressing the spinal cord should be considered as a life and health threatening emergency and should be removed surgically as soon as possible. Due to a completely normal hearing, no vestibular schwannoma surgery is indicated so far, under the condition the tumour status is monitored by a serial MR imaging. In case of the vestibular schwannoma growth and/or progressive hearing loss, the tumour would be indicated for resection with an auditory brainstem implantation. Since the contralateral hearing would be expected to be normal, the ABI can remain inactive, as a sleeper, and would be programmed later in case of a contralateral surgery with a hearing loss on this side. Or, as a variety of this approach, ABI can be implanted during the second vestibular schwannoma surgery, in the right side, where the tumour is smaller.

Figure 3 – Magnetic resonance imaging of the head, coronal plane, T1-weighted images. Bilateral vestibular-schwannomas, larger in the left pontocerebellar angle, smaller in the right pontocerebellar angle. Intracanalicular growth was present in both tumours, but cannot be seen in this section.

Figure 4 – Magnetic resonance imaging of the spine, sagittal plane, T2-weighted images. Schwannoma in the C3 level, probably a meningioma in the C4-5 level, originating from the dorsal capsule, compressing the spinal cord against vertebral bodies.
Discussion
The primary indication for an auditory brainstem implant is neurofibromatosis 2 with bilateral vestibular schwannomas. More rare indications for ABI include bilateral cochlear ossification, skull base fracture with hearing nerves transsection and congenital aplasia of hearing nerves [5]. Negative prognostic factors for the ABI outcome in patients with NF2 are (1) long time of deafness (over 10 years), (2) difficult positioning of stimulating electrodes, (3) postoperative complications and (4) number of active electrodes lower than 10 [6]. Recently, there have been published studies showing an excellent benefit of ABI in nontumour patients (children with bilateral congenital aplasia of hearing nerves) compared with tumour patients (classical NF2 patients). Results in a speech comprehension in the non-tumour group are significantly higher than in the tumour group. One possible reason for this fact is a damaged and disfigured hearing pathway due to a tumour growth and maybe a defect in the hearing nuclei cells, which are responsible for a perception of speech modulation [7, 8].

Auditory brainstem implantation is usually performed as onestage surgery after vestibular schwannoma removal. In classical NF2 indications, the ABI does not represent an ideal regarding the possibility of speech understanding without lip reading. Compared with a lipreading only, the improvement in communicative functions in patients using ABI is just about 30% [9]. In spite of the proven fact that the ABI benefit is much higher in the nontumour patients, due to a complex character of symptoms in the neurofibromatosis 2, even a small contribution to communication skills represents a success. The benefit of neuroprosthesis is the highest in NF2 patients with small vestibular schwannomas and a short duration of deafness.

In the above discussed patient, it was crucial to preserve her health and life – so the surgery removing the tumour compressing the spinal cord was indicated first. After that, neuroprosthesis implantation can be considered; nevertheless, due to a normal hearing in both sides, wait-and-rescan policy seems reasonable. If surgery in the large tumour is performed first, then the ABI as a sleeper can be realized. Or – due to the fact that in smaller tumours there is a better ABI outcome – ABI can be introduced in the left right side, where the tumour is smaller. Even a cochlear implantation is an option, if the hearing nerve is anatomically and functionally preserved during a vestibular schwannoma removal (which is logically much easier in smaller tumours) [10–14].

Generally said, decision making in such a complex diagnosis as NF2 is always difficult and not straightforward. Therefore, we considered decision made by a team of specialized experts in the field of auditory neuroprostheses as the best solution.

Conclusion
Neurofibromatosis 2 in its clinically well expressed form brings a plenty of problems to its bearer. Considering the timing of surgery and ABI indications it is
necessary to take into account various factors, which can influence – in a positive or negative way – resulting quality of life. It is necessary to solve first life or health threatening conditions of the patient. Benefit of an auditory brainstem implant in patients with NF2 is not as high as in patients with cochlear implants or non-tumour patients with ABI, nevertheless it improves communication and aids in lip-reading. This is especially important for people, whose quality of life is lowered by the basic diagnosis.

References