

Neurofibromatosis 2: Two Case Reports

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Abstract: Our study presents two cases of neurofibromatosis 2 (NF2) that have been diagnosed at the Ear, Nose, and Throat Department of Hradec Králové (Czech Republic). The first case involved a young man with a history of sudden hearing loss accompanied by tinnitus on the left side. The diagnosis of NF2 was made, and an operation for left acoustic neuroma was performed. Looking toward the future, the acoustic neuroma on the right side should be resolved as well. The second case concerned a woman (the mother of our patient 1) examined at the same Ear, Nose, and Throat Department in 1980, after 4 years of gait instability and progressive loss of hearing and tinnitus on the right side. Computed tomography scan detected a bilateral expansion in the pontocerebellar angles, and a large tumor on the right side was removed. The patient is deaf and has facial palsy without progression of symptomatology during long-term follow-up. These two cases document the rare but serious hereditary disease of NF2. Its most frequent first presentation is acoustic neuroma; further, benign tumors of the nervous system and juvenile cortical cataract also are often detected. The variability of number, location, and biological behavior of tumors associated with NF2 require an individual patient treatment approach, long-term follow-up, and insertion of appropriate hearing aids. Important also is a genetic examination to exclude pathological NF2 genes in the first-degree relatives of the affected individuals.

Key Words: acoustic neuroma; neurofibromatosis; NF2

Our study presents two cases of neurofibromatosis 2 (NF2) diagnosed at the Ear, Nose, and Throat (ENT) Department of Hradec Králové (Czech Republic) in the last 20 years. The typical diagnostic sign of the disease is a bilateral acoustic neuroma [1]; among other benign tumors of the central nervous system, meningiomas initially are present. Another sign of the disease is a juvenile cortical cataract. The criteria for NF2 have been outlined by the National Neurofibromatosis Foundation Clinical Care Advisory Board [2].

The disease is caused by a genetic defect (mutation or one allele depletion) on the long arm of chromosome 22. This gene encodes a tumor suppressor protein called *merlin* (schwannoma), which is believed to participate at the cell connection of the cytoskeleton to the plasma membrane. Thereby, it influences the cell's

shape, motility, and growth regulation [3]. The disease is autosomally hereditary, without gender predilection [4,5]. It has a rate of clinical penetrance of nearly 90% [6]. Fifty percent of NF2 gene mutations occur de novo.

The most common first manifestation of NF2 is an acoustic neuroma [7]. Its clinical behavior is the same as that of the sporadic acoustic neuroma; typical for NF2 is bilateral location and young age at the time of disease presentation. Identification of an acoustic neuroma is usually the first step in the diagnosis. The suspicion of acoustic neuroma is based on the finding of retrocochlear hearing loss with vestibular areflexia. Identification of the neuroma is determined by the patient's history and ENT, audiological, and vestibular examinations. The final examination, leading to the clinical diagnosis, is magnetic resonance imaging rather than computed tomography [7]. This should be performed in a range from brain to the level of the thoracic spine, where further benign tumors of the central nervous system and peripheral nerve bundles can be revealed. In addition, ophthalmological, neurological, and dermatological examinations should be performed.

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Once the diagnosis of NF2 is established, molecular genetic analysis of DNA allows for the eventual determination of the presence of a pathological gene in the relatives of an affected individual.

In the treatment of NF2, the problem of multiple tumors and hearing and sight impairment are a challenge for the therapist. Surgical treatment is combined with a risk of disability after repeated operations. During radiotherapy, the cumulation of adverse effects is to be taken into account. For this reason, an individual treatment approach must be used for each patient, in whom modern hearing aids, such as a cochlear implant or an auditory brainstem implant [8], play an important role.

PATIENT 1

In spring 2001, we examined a young man with a history of sudden hearing loss accompanied by tinnitus on the left side. In his medical history, he mentioned his mother, who had been operated on for a brain tumor 20 years previously. The young man underwent a vasoactive treatment, after which his hearing improved; the tinnitus, however, continued, and an instability in balance also was newly observed. An audiogram at the first examination showed a mild hearing loss on the right side and a deeper hearing impairment on the left side. After another vasoactive treatment, his hearing improved, at least at a higher frequency.

Brainstem auditory evoked potentials were indicated and showed a poor morphology of the right-sided

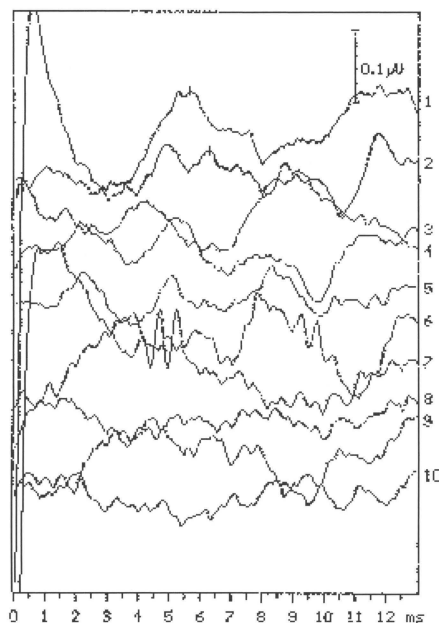


Figure 1. Brainstem auditory evoked potentials in patient 1.

Jewett's waves, with a prolonged latency of the V wave (Fig. 1). There was no identifiable wave on the left side. Ophthalmological and neurological examinations did not show any pathology. On the basis of this investigation, magnetic resonance imaging was indicated. This imaging showed a large acoustic neuroma at the left pontocerebellar angle (PCA), compressing the pont but without blockage of liquid flow (Fig. 2). Another small neuroma with both an intra- and extrameatal portion was detected at the PCA on the right side. Further, a large neuroma was noted at the level of the C1–C2 cervical vertebral foramen, and magnetic resonance imaging further detected several meningiomas above and below the tentorium cerebelli and one oblongata tumor, most probably astrocytoma.

The patient was examined at the Department of Stereotaxisurgery in Prague and at the neurosurgical department of Hradec Králové, and tumor removal was found to be the optimal treatment. This was performed at the neurosurgical department of Hradec Králové on February 21, 2002, via a suboccipital craniotomy. The patient emerged deaf from the operation with a peripheral facial nerve palsy, for which an anastomotic suture of the twelfth to the seventh cranial nerve was planned. In the subsequent treatment phase, removal of the spinal neuroma is planned because it jeopardizes the spine with compression. In the more distant future, the acoustic neuroma on the right side should be resolved as well. We are considering gamma-knife irradiation as the treatment of first choice.

PATIENT 2

After the diagnosis in patient 1 was made, we revised the diagnosis in his mother, patient 2. The evaluation of

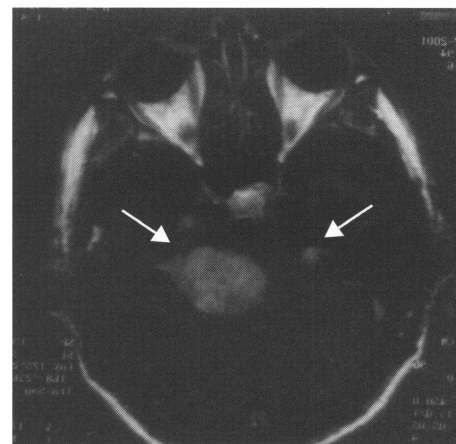


Figure 2. Magnetic resonance imaging of bilateral acoustic neuroma in patient 1 (arrows).

her uncertain neurological problems as brain inflammation led to repeated inpatient neurological treatment. In 1980, she was examined at the ENT Department of Hradec Králové after 4 years of gait instability and progressive loss of hearing and tinnitus on the right side. At the same time, she experienced hoarseness and sporadic food aspirations. Clinical examinations revealed bilateral sensorineural hyperacusis with bilateral vestibular areflexia and partial paresis of cranial nerves IX, X, XI, and XII on the right side. The computed tomography scans then detected a bilateral expansion in the PCA. A large tumor on the right side was removed via suboccipital craniotomy at the neurosurgical department of Hradec Králové and was histologically confirmed as a fibrillary variant of meningioma. The patient emerged completely deaf after the operation, with peripheral facial paresis on the right side. Her condition has been stable without further audiovestibular or neurological progression of symptomatology, and she has not required any further operations.

At present, the sister of patient 1 has been examined for NF2 and is scheduled for a genetic analysis. She is older than 30 years and has neither subjective problems nor audiovestibular pathological findings. Her risk of having the pathological gene is low.

REFERENCES

1. Bailey BJ. *Head Neck Surg Otolaryngol* 2(148):2173–2176.
2. Gutmann DH, Aylsworth A, Carey JC, et al. The diagnostic evaluation and multidisciplinary management of neurofibromatosis 1 and neurofibromatosis 2. *JAMA* 2:51–57, 1997.
3. Chen AF, Samy RN, Gantz BJ. Cerebellopontine angle tumor composed of Schwann and meningeal proliferations. *Arch Otolaryngol Head Neck Surg* 127:1385, 2001.
4. Hirsch NP. Neurofibromatosis: Clinical presentations and anaesthetic implications. *Br J Anaesth* 86(4):555, 2001.
5. Evans DGR, Lye R, Neary W, et al. Probability of bilateral disease in people presenting with a unilateral vestibular schwannoma. *J Neurol Neurosurg Psychiatry* 66(6):764, 1999.
6. Palacios E. Neurofibromatosis 2 (bilateral acoustic neuromas). *Ear Nose Throat J* 78(12):894, 1999.
7. Sobol SE, Rappaport JM, Al-Abdulhadi K, et al. Diagnosis of neurofibromatosis type 2 in a patient with long-standing bilateral sensorineural hearing loss. *J Otolaryngol* 30(6):368, 2001.
8. Skřivan J, Zvěřina E, Betka J, et al. Sluchová kmenová neuroprotéza z pohledu otolaryngologa (První vlastní zkušenosti a výsledky). *Otorhinolaryngology* 48(4):203–206, 1999.