Unusual Presentation of Neurofibromatosis Type 2 with Hemiparesis and Ataxia

Hemiparezi ve Ataksi ile Bulgu Veren Nörofibromatozis Tip 2 Olgusu

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Summary

Neurofibromatosis 2 (NF2) is an autosomal-dominant disease, which is characterized by vestibular Schwannomas (acoustic neurinoma) as well as tumors of the peripheral and central nerve system, demonstrating a variety of expression. In this study, an 18 year-old girl referred to our unit with left hemiparesis and gait imbalance is presented. During her stay in hospital; by examining detailed history of complains physical examination, magnetic resonance imaging and genetic analysis, she had the diagnosis of Neurofibromatosis 2. The hemiparesis and ataxia resolved completely after treatment with a rehabilitation program and she left our unit walking without any support. Since early diagnosis of NF2 remains the single most important factor for the best outcome, altough it is a rare condition, NF2 must be examined in differential diagnosis in such cases. *Turk J Phys Med Rehab 2007;53:38-40*
Key Words: Neurofibromatosis 2, hemiparesis, ataxia

Özet

Nörofibromatozis tip 2 (NF2), vestibüler Schwannomalar (akustik nörinom) ile karakterize, santral ve periferik sinir sistemi tümörlerinin de eşlik edebildiği, farklı bulgularla kendini gösterebilen otozomal dominant geçişli bir hastalıktır. Bu vaka takdiminde, sol tarafta kuvvetsizlik ve yürüme güçlüğü nedeniyle rehabilitasyon kliniğimize yönlendirilen 18 yaşında bayan hasta sunulmuştur. Hastanın yattığı süre içerisinde, detaylı hastalık öyküsü, fizik muayene, manyetik rezonans görüntüleme ve genetik analizler sonucunda NF2 tanısı konulmuştur. Hemiparezi ve ataksi düzenlenen rehabilitasyon programı ile tamamen düzelmiştir ve desteksiz yürüyerek taburcu edilmiştir. Erken tanı NF2'de son durumu etkileyen önemli bir faktör olduğu için, nadir görülen bir hastalık olmasına rağmen, benzer vakalarda, ayırıcı tanıda mutlaka araştırılması gerektiği sonucuna varılmıştır. *Türk Fiz Tıp Rehab Derg 2007;53:38-40*
Anahtar Kelimeler: Nörofibromatozis 2, ataksi, hemiparezi

Introduction

Neurofibromatosis type 2 (NF2) is an autosomal dominant disease characterized by vestibular Schwannomas and the development of multiple nervous system tumors, ocular abnormalities, and skin tumors as well as tumors of the peripheral and central nerve system, demonstrating a variety of expression. Although classically considered a disease of adults, initial signs and/or symptoms may be evident in childhood and are often unrecognized (1-3).

An early diagnosis of NF 2 may prevent deafness by early surgical intervention. Due to primary and secondary reasons like age-related processes, different sensations like hearing or vision may be compromised. Neuropathy may lead to vestibular disturbances and loss of muscle control. Therapeutic options include cataract surgery, implantation of cochlear or brainstem implants as well as conservative therapy of the ocular surface in paresis of the VIIth cranial nerve or learning to read from the lips.

The human NF2 gene was cloned from chromosome 22 in 1993. The major part of the genetic alterations described so far are point mutations as well as deletions or insertions in or around the exons. Geno-phenotype correlations allow some predictions of the course of the disease to be made (2). NF2 has the highest spontaneous mutation rate of any human genetic disorder. The incidence of NF2 is thought to be approximately 1:40,000 to 1:50,000 (4). Central nervous system tumors

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associated with NF2 are multiple and occur in an unpredictable fashion. Clinical manifestations depend upon the localization of these tumors. The disease tends to manifest itself in the second and third decade, often with insidious symptoms (3,4).

Case Report

An 18 year-old girl was referred to our unit from neurosurgery department after operation for spinal tumors with left hemiparesis and gait imbalance. Her primary symptoms had started four months ago as gradually developing weakness of the left side and difficulty in walking and did not resolve after surgery. Preoperative cervical magnetic resonance imaging (MRI) revealed epandymoma at C2-Th4 vertebral levels, spinal syringomyelia cavity at C2-Th1 vertebral level and meningiomas at several levels.

Her physical examination revealed bilateral deafness, asymmetric face, proptosis of the right eye, hemiparesis and hemihypoestesia at the left side and ataxia. Her global left side muscle strength score was 4/5. Romberg test was positive. Her standing balance was good but she was unable to walk independently and safely, lead to left or right side while walking. She had no spasticity.

Especially multiple spinal tumors and deafness was taken into consideration and to investigate the possibility of NF2, cranial MRI scan was performed which revealed bilateral neurofibromas on fifth, seventh and eighth cranial nerves. The genetic analysis showed a de novo mutation in the NF2 gene. The diagnosis for NF2 was based on National Institutes of Health Consensus (5). The criteria were as follows: Bilateral vestibular Schwannomas or family history of NF2 plus 1. unilateral vestibular Schwannoma, 2. any two of: menengioma, glioma, neurofibroma, Schwannoma, posterior subcapsular lensicular opacities.

During her stay in hospital, she participated in a conventional rehabilitation program, 5 days a week, 2-3 hours a day, for 6 weeks. The conventional program consists of muscle strengthening exercises, coordination training, balance training (with balance board and different environmental conditions, gaze stabilization exercises), gait training (gait on uneven surfaces etc.). The hemiparesis and ataxia resolved completely at discharge and she left our unit walking without any support.

Discussion

Bilateral vestibular Schwannomas are pathognomonic for NF2 but may not be noticed at the initial assesment. People with a negative history of NF2 at initial assessment present the greatest diagnostic difficulties (6). Approximately half of the patients seen are the first case in their families. There is increasing evidence that a small but significant proportion of these cases arise through somatic mutation of NF2 genes (7). Patients with NF2 also develop other cranial, spinal, and peripheral tumors (meningiomas, gliomas, neuromas) (3,6).

Causes of referral prior to a definitive diagnosis of NF2 were: 1) Ophthalmologic problems: early onset lens opacities, strabismus, ambylopia (due to underlying cranial nerves and/or brain tumors); 2) Otolaryngology problems: hearing loss and tinnitus in early teens disregarded or treated as ear infections; hoarse or bitonal voice; 3) Neurological dysfunction: seizures secondary to intracranial meningioma or vestibular Schwannomas, neurological dysfunction related to brainstem and/or spinal cord tumours, isolated and multiple cranial nerve deficits, and peripheral neuropathy secondary to Schwannomas; 4) Skin manifestations: Schwannomas misdiagnosed as neurofibromas because of associated cafe-au-lait spots; cafe-au-lait spots and skin tumors (1).

Recent reports of series of patients with NF2 screened with MRI of the neuraxis have focused attention on the occurrence of spinal tumors. The histologic findings of excised intramedullary tumors were epandymomas, altough astrocytomas and Schwannomas are also reported (3). Not only the acoustic neuromas but also the spinal tumors manifest the disease by spinal cord compression. Patronas et al. (3), find that genotype-phenotype correlations may extend to specific categories of spinal tumors. According to their results; patients with nonsense and frame shift mutations have more severe disease than the others and may be more likely to have intramedullary tumors and at a younger age than the others. According to spinal tumor location, number and suspected histological type, frequency of the follow-up examinations and MRI should be considered in order to establish the time for surgery.

According to Halliday et al. (8), Schwannomas are the most associated nerve sheath tumors with NF2. They suggest that the primary inherited mutation of NF2 is recessive to the normal allele at the cellular level and that a tumor occurs only when a secondary mutation eliminates the normal allele. Mutation of a tumor-supressor gene on human chromosome 22 has been found to be associated with vestibular Schwannoma formation. Specific mutations in the NF2 gene may produce specific clinical characteristics or phenotypic expressions (9).

Most patients with neurofibromatosis type 2 (NF2) lose hearing either spontaneously or after removal of their neurofibromas.

The patient may benefit from conventional hearing aids if, due to modern microsurgery and intraoperative monitoring the integrity of the cochlea and the 8th nerve is preserved. With lost auditory function but preserved electrical stimulibility of the 8th nerve a cochlear implant may be appropriate. But if the patients have no remaining 8th nerve to stimulate, there is no benefit from cochlear implants. Until some years ago, vibrotactile aids, lip-reading, and sign language have been the only communication modes available to these patients. With auditory brain stem implants it is now possible to bypass both the cochlea and the 8th nerve and to stimulate the cochlear nucleus directly (10,11). Stimulation of the devices produces useful auditory sensations in almost all patients. Testing of perceptual performance indicated significant benefit from the device for communication purposes, including sound-only sentence recognition scores and the ability to converse on the telephone. Also lip-reading is significantly improved with brain stem implants. The successful work of an auditory brainstem program center depends very much on the close interdisciplinary collaboration between the Departments of Neurosurgery and ENT-surgery. In the future new developments like speech processing strategies and new designed electrodes accessing the complex tonotopic organization of the cochlear nucleus may further improve rehabilitation in these patients who would have been deaf some years ago (10).

As the condition has an insidious course and vestibular Schwannomas may reach large dimensions before the onset of audiological, vestibular and facial symptoms, early detection of NF2 is very important for the preservation of hearing and prevention of other neurological sequelae (4). The patients

should be offered the benefit of multidisciplinary approach including rehabilitation for a better quality of life. Early diagnosis of NF2 remains the single most important factor for the best outcome in this condition (4).

Despite the rarity of this disorder, our case suggests that hemiparesis and ataxia in a child requires rapid and extensive investigation that must include NF2 in the differential diagnosis.

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