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Multiple central nervous system tumors, neurofibromatosis type 2

Çoklu santral sinir sistemi tümörlü bir olgu sunumu, nörofibromatozis tip 2

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Abstract

Neurofibromatosis type 2 is an inherited autosomal dominant syndrome. This sendrom is associated with ocular abnormalities and is characterized by multiple tumors of the central and peripheral nervous system. The most common tumor associated with the disease is the vestibulocochlear schwannoma. The aim of this report is to present a 35-year-old female patient who was seen for generalized seizures, diplopia, lack of vision and hearing loss in the right ear. Magnetic resonance imaging showed low grade glial tumor in the left temporal lobe, a pinealoma and bilateral optic nerve tumors. The diagnosis of Neurofibromatosis type 2 was made on the basis of clinical and imaging findings. Since early detection of the tumors and proper treatment decrease both morbidity and mortality of NF-2, it is important that a multisystemic approach to patients in whom concomitant spinal and/or brain tumors exist is taken.

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Key words: Central nervous system, Tumor, Neurofibromatosis type 2.

Özet

Nörofibromatozis tip 2, santral ve periferik sinir sisteminin çoklu tümörleri ile karakterize otozomal dominant kalıtılan bir sendromdur. Hastalıkla ilişkili en sık tümör vestibülokohlear schwannomdur. Bu yazıda, jeneralize nöbetler, diplopi, görme ve işitme kaybı ile değerlendirilen 35 yaşında bir kadın hasta sunulmuştur. Hastada, magnetik rezonans görüntülemede, pinealoma, iki taraflı optik sinir tümörü ve sol temporal lobda düşük dereceli glial tümör saptandı. Klinik ve görüntüleme bulguları ile nörofibromatozis tip 2 tanısı ile takibe alındı. Nörofibromatozis tip 2 hastalarında erken tanı ve uygun tedavi hastalıkla ilişkili morbidite ve mortaliteyi düşürebileceğinden, spinal ve/veya beyin tümörü bulunan hastaların multisistemik bir yaklaşımla değerlendirilmeleri önemlidir.

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Anahtar sözcükler: Santral sinir sistemi, Tümör, Nörofibromatozis tip 2.

Introduction

Neurofibromatosis type 2 (NF-2) is a rare autosomal dominant disorder caused by mutations in the NF-2 gene located on chromosome 22. The average age of onset is 18 to 24 years [1]. The age of onset ranges from birth to 70 years [2]. NF-2 is associated with significant morbidity and early mortality secondary to the development of multiple tumors including tumors of the central nervous system (CNS) [3].

NF-2 is associated with bilateral vestibular schwannomas and other CNS tumors. Brain tumors are predominantly meningiomas. However, low-grade gliomas and ependymomas have also been observed. NF-2 patients represent 2.5% of all patients with intramedullary spinal tumors and intramedullary tumors of the spinal cord, such as ependymoma, occur in 5 to 33% of individuals with NF-2 [4]. Patients with spinal cord involvement can have multiple tumors. Spinal cord tumors typically remain quiescent for lengthy periods with a potential lag time of 3 to 4 years between onset of symptoms and the diagnosis. Imaging of the brain and spine at yearly intervals is usually recommended in patients who have been known to have

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brain and spinal tumors or sooner if symptoms develop [4,5].

In this paper we report a NF-2 patient with multiple CNS neoplasms who became symptomatic in a very short time.

Case Report

A 35-year-old woman, with a known history of surgery due to cervical ependymoma and thoracic schwannoma (Figure 1) presented with generalized seizures, diplopia, lack of vision and deafness in the right ear. No cutaneous signs were observed in the dermatological examination. In her neurologic examination, she had lack of abduction in both eyes. Her right and left eye vision acuity was 0.2. Her hearing examination including brainstem auditory evoked response (BAER) showed a deaf ear on the right. We evaluated cranial, inner ear and orbital magnetic resonance imaging (MRI) and MR-venography. Cranial MRI revealed a vestibular schwannoma on the right, a low grade glial tumor on the left temporal lobe, a pinealoma and bilateral optik nerve tumors (meningioma/ glial tumor?) (Figure 2). Intracranial lesions were found inappropriate for surgery by the neurosurgeons.

Further evaluations showed sensory polyneuropathy in the electroneuromyography (EMG) and, right temporoparietal epileptogenic activity in the electroencephalography (EEG). She was put on antiepileptic therapy (Levetiracetam 3000 mg per day and carbamazepin 800 mg per day) and became seizure free in the follow up examinations.

Genetic consultation confirmed the diagnosis of neurofibromatosis type 2 for the patient.

After investigating the patient's first degree relatives, the patient was discharged with symptomatic treatment and was advised to have regular MRI and oncological controls.

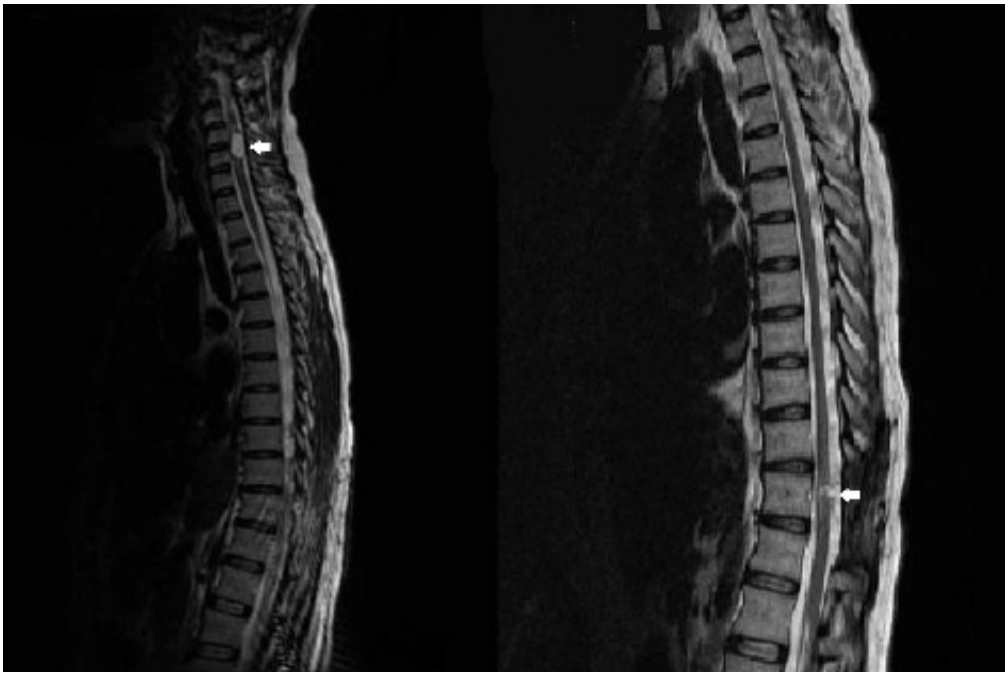

Figure 1. Spinal MRI, sagittal FLAIR sequence showing cervical ependymoma and thoracic schwannoma (*arrows*).

Discussion

Spinal ependymomas, meningiomas and schwannomas are the most frequently neoplasms found in the course of NF-2. However NF-2 associated syndromic lesions tend to be multiple and present in the earlier stages [6]. In this case, presentation of NF-2 was relatively late. This would be one of the main causes of the delayed diagnosis for this patient. In addition, lack of family history would be another main reason, but it is well known that 50 % of patients represent new mutations and as many as one third are mosaic for the underlying disease causing mutation. Mosaicism has been suspected in individuals with unilateral vestibular schwannoma in accordance with our case and recent evidence suggests that 20–30 % of NF-2 patients without a family history of the disease are mosaic [6].

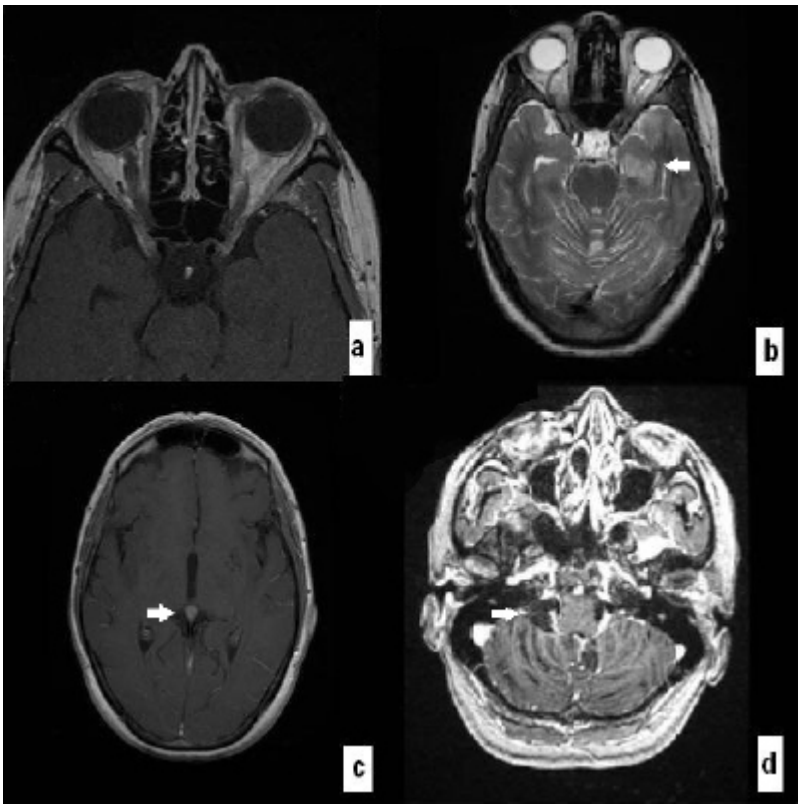

Figure 1. Cranial MRI. (a) bilateral optik nerve tumors (b) a low grade glial tumor on the left temporal lobe (c) a pinealoma (d) a vestibular schwannoma on the right (*arrows*).

Evans [7] showed that at least 18 % of NF-2 sufferers presented in childhood with isolated features of the disease had no family history. These pediatric patients presented with a more severe course of the disease with multiple tumors. Although the age at the onset of the disease is very late in our case the clinical presentation and the serious course of the disease are similar.

Our patient had an atypical onset of this autosomal-dominant disorder. After a few months, she presented with hearing loss, most often related to the development of vestibular schwannomas. Hearing loss, often accompanied by tinnitus, occurs in around 60 % of adults and up to 30 % of children [8,9]. Bilateral vestibular schwannomas are found in 90–95 % of patients with NF-2. It is reported that more than 99 % of vestibular schwannomas in NF-2 are benign but they remain an important cause of mortality due to their location [10]. In this case unilateral vestibular schwannoma with total hearing loss was an important cause of morbidity. Early surgical management is recommended for tumors which are less than 3 cm in diameter to preserve normal hearing [11]. This result would be different if our patient's detailed examination had been performed during the time of the first surgery because the patient was totally deaf when she was admitted to our clinic.

It is proven that meningiomas associated with NF-2 frequently have a higher proliferative activity and a tendency to form more atypical and anaplastic grades than sporadic meningiomas [12]. This would be the cause of radiological suspense of MRI findings of our case.

In conclusion, being aware of this rare syndrome, in which potentially malignity processes would be seen, is very important in the follow-up period of patients with NF-2. As early detection of tumors and proper treatments may decrease both morbidity and mortality of NF-2, we strongly suggest a multisystemic approach to patients in whom concomitant spinal and/or brain tumors exist.

Conflict of interest: The authors declared no conflict of interest.

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