CASE REPORT

Neurofibromatosis II

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ABSTRACT

Neurofibromatosis type II is an inherited autosomal dominant syndrome, characterized by multiple neoplasms of the central and peripheral nervous system associated with ocular abnormalities. The most common tumor associated with the disease is the vestibulocochlear schwannoma, and as many as 10% of patients with this tumor have neurofibromatosis type 2. In this report, we aim to present a 36-year-old female who presented with chief complaints of unilateral tinnitus, and, during her workup, which included cranial and whole spine magnetic resonance imaging, we found bilateral acoustic neuroma with multiple meningiomas. Based on clinical and imaging findings, the diagnosis of neurofibromatosis type 2 was made.

Keywords: Neurofibromatosis II, Acoustic neuroma, Multiple meningioma.

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Conflict of interest: None declared

INTRODUCTION

Neurofibromatosis 2 (NF2) is a slow-growing and non-malignant, autosomally dominant inherited cancer syndrome with an estimated incidence of 1:40 000.[1] It has a penetrance of nearly 100% by the age of 60 years[2] and there is no gender predilection.[1] It results from a germline mutation of the NF2 tumor suppressor gene located on the long arm of chromosome 22, which encodes a tumor suppressor protein called Merlin (schwannoma).[3] While the clinical manifestations of NF2 include central and peripheral nervous system tumors (nerve sheath tumors, meningiomas and ependymomas), cutaneous lesions, ocular pathology and peripheral neuropathy,[4] the hallmark of NF2 is the development of bilateral acoustic neuroma.[5] Bilateral vestibulocochlear schwannomas are present in 90 to 95% of NF2 patients.[5]

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CASE REPORT

A 36-year-old female patient presented with a 1 year history of unilateral tinnitus (right side) which was continuous, unmaskable and high pitched. It was not associated with sleep deprivation, hearing loss, vertigo and other ENT complaints. There were no similar complaints in the past, and the family history too was insignificant.

Physical examination revealed an alert and oriented patient with normal cognitive function. On otoscopic examination, tympanic membrane was normal on both the sides, tuning fork tests showed Rinne to be positive in both the ears with a centralized Weber. An audiogram was done which showed mild high frequency sensorineural hearing loss on the right side, and normal hearing on the left side. Speech discrimination score, SISI (short increment sensitivity index), TD (tone decay) and brain-stem evoked response audiometry (BERA) were within normal limits.

Magnetic resonance imaging (MRI) of the brain showed two small meningiomas arising from left parietal region, measuring about 12 × 11 mm and 7 × 5 mm (Figs 1A to D). It also showed bilateral small vestibular schwannoma with the right measuring about 8 × 3 mm and left measuring about 4 × 3 mm (Fig. 2). Following this, MRI of spine was done but nothing significant was found.

Neurological, ophthalmological and dermatological consultations were done but nothing significant was found.

Therefore, on the basis of clinical presentation and radiological imaging, a diagnosis of neurofibromatosis II was made.

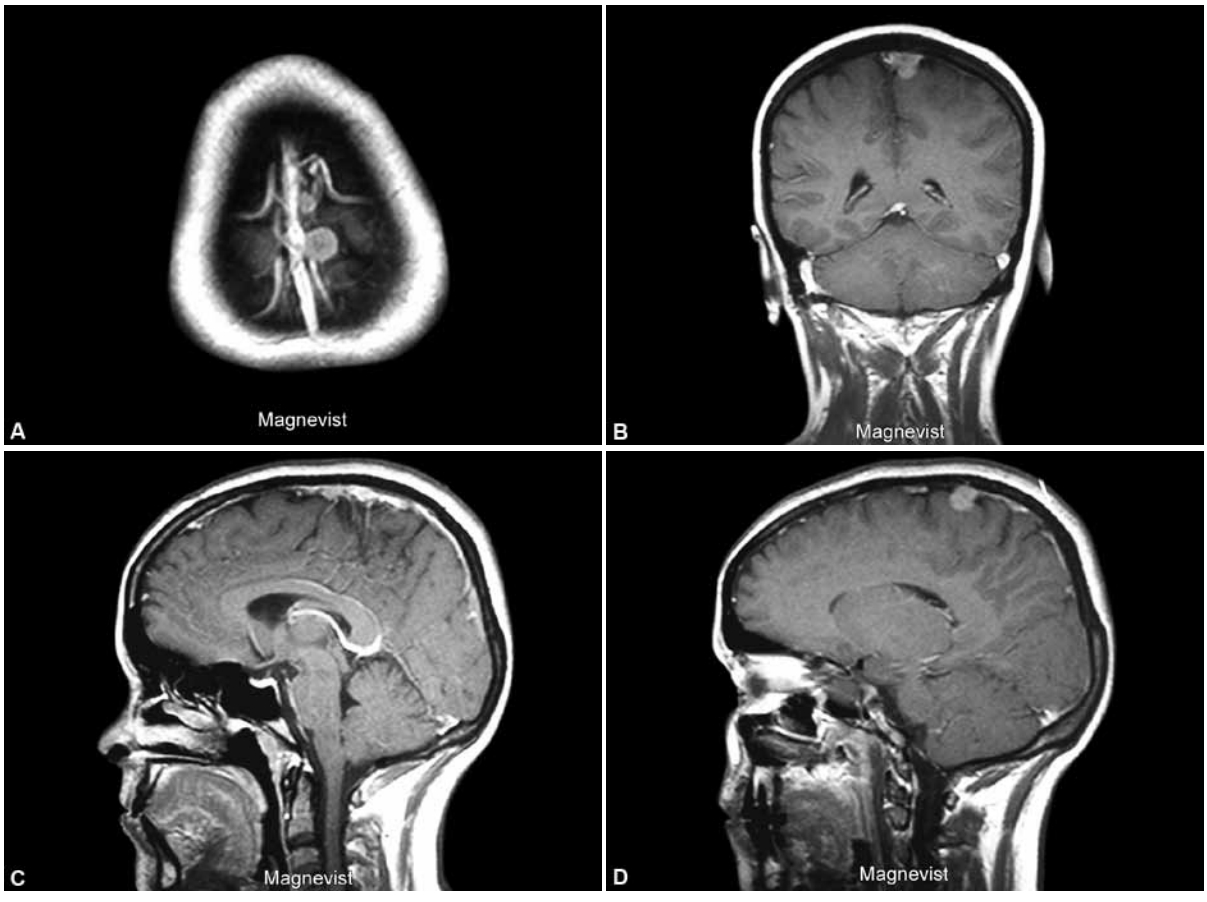
DISCUSSION

Neurofibromatosis II is a rare syndrome characterized by bilateral vestibular schwannomas, multiple meningiomas, cranial nerve tumors, spinal tumors and eye abnormalities.[1] The NF2 case reported in 1882 by Wishart was probably the first that had ever been reported on the very subject.[6]

In 1997, Gutmann et al proposed revised criteria for diagnosis of the syndrome.[7]

Confirmed or Definite Diagnosis of NF2

Bilateral vestibular schwannoma or family history of NF2 (first degree family relative) plus



Figs 1A to D: (A) Axial T1W postcontrast image showing two small enhancing meningiomas in the left high parietal parasagittal location. (B) coronal T1W postcontrast image showing enhancing meningioma. (C) and (D) T1W postcontrast left parasagittal images showing two small meningiomas

- Unilateral vestibular schwannoma before 30 years of age (Figs 1A to D).
- Any two of the following: meningioma, glioma, schwannoma, or juvenile posterior subcapsular lenticular opacities/juvenile cortical cataract.

All patients have been found to have some mutation of the same gene located on chromosome 22. Statistically, one-half of cases are inherited and one-half is the result of *de novo* mutations. Inactivation of the NF2 gene and loss of expression of its products, merlin or schwannomin, has been reported for all NF2-associated tumors.[8] A truncating mutation (nonsense and frame shift) may be linked to a more severe form of NF2 that is the Wishart form, in which there is an early onset of the disease with multiple intracranial schwannomas and meningiomas that result in blindness, deafness, paralysis and possible death by 40 years of age. The milder form of the disease that is the Gardner form, is less debilitating, few meningiomas develop, and patient may not develop symptoms until later in life and often have fewer associated abnormalities.[1]

The average age of diagnosis of NF2 is 25 years and there is an average delay in the diagnosis of approximately

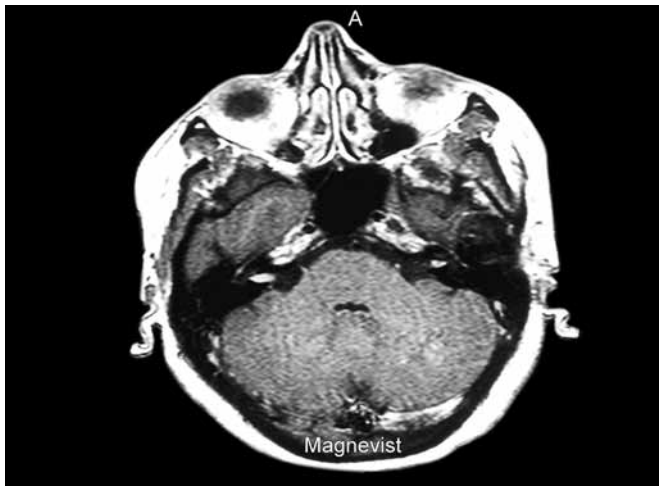


Fig. 2: Axial T1W postcontrast image showing bilateral enhancing small acoustic neuromas

7 years. There is no gender preponderance and no prevalence has been described based on ethnicity.[1] Epidemiological studies place the incidence of NF2 between one in 33,000 live births[9] and one in 87,410 live births.[8]

The clinical presentation of NF2 varies, but approximately 30 to 45% of patients are diagnosed because

of symptoms resulting from cranial nerve (CN) VIII schwannomas, such as hearing loss, tinnitus, balance impairment, and weakness in CN VII distribution. The reason for this is that CN VIII schwannomas are symptomatic at a relatively small size. The tumor causes symptoms by compressing or stretching the cochlear nerve, compressing the blood supply to the nerve or to the cochlea, or causing hemorrhage into the nerve or cochlea.[10]

Radiological investigations are the mainstay of diagnosis, with gadolinium-enhanced MRI forming the current gold standard. Acoustic neuromas appear as iso- to hypointense on T1-weighted (T1W) images and hyperintense on T2-weighted (T2W) images with intense enhancement on gadolinium contrast administration.[11] Computed tomography is not ordered routinely because it is inferior to MRI in its resolution of soft tissue and can miss tumor till 1 cm into the cerebollo-pontine angle (CPA). Audiological tests, such as auditory brainstem response (ABR), were useful before the advent of MRI with the amplitude, latency and interval difference between wave I and V being the most reliable indicators.[12]

NF2 presents many difficult management dilemmas. The mainstay of management of NF2 is surgical removal of symptomatic cranial and spinal tumors. Small vestibular tumors that are localized completely intracanalicularly can often be totally resected with preservation of both hearing and facial nerve function. If the cochlear nerve is preserved, a CI can be inserted. In cases with cochlear nerve sacrifice, a brain stem implant (ABI) would be indicated.[13] The timing of removal of vestibular schwannomas is a more difficult area. It is important to balance the use of microsurgery and radiation treatment, which can have a role in patients who have particularly aggressive tumors, or who have surgical risks, or who refuse surgery. In view of the multiplicity of problems affecting many patients, it is strongly recommended that NF2 patients are managed by a multidisciplinary team in specialist centers.[14]

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