Ataxia in a Young Female

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Abstract

Neurofibromatosis type 2 (NF2) is a genetically inherited disorder characterized by the presence of multiple central nervous system tumours, most pathognomonic being bilateral vestibular schwannomas with or without peripheral manifestations in the form of cataract or cutaneous neurofibromas. NF2 is an uncommon disorder compared to NF1. We describe a classical case of neurofibromatosis type 2 with florid clinical manifestations and characteristic neuroimaging features. We also briefly describe the literature pertaining to this rare disorder. The case also emphasizes the fact that NF2 should be considered in the list of differentials for ataxia especially when it is associated with sensory neural hearing loss.

Introduction

Neurofibromatosis type 2 (NF2) is a rare disorder. Bilateral vestibular schwannomas are pathognomonic of type 2 neurofibromatosis. This is an autosomal dominant inherited disease results from mutations involving NF2 gene on chromosome 22. NF2 diagnosis is based on the constellation of clinical and imaging features. Despite advancements in imaging modalities and surgical techniques, prognosis is rather grim and many with NF2 still die young. We report a classical case of NF2 with some unique features and briefly review the literature on this rare disorder.

Case Report

A 25 year female presented with defective hearing, visual impairment and gait unsteadiness. It was progressive hearing loss affecting both ears right more than left and progressive loss of vision more pronounced in the left eye. Eventually she developed unsteadiness while walking. She also had history of difficulty in getting up from squatting position; however there was no history suggestive of distal muscle weakness in lower limb or any motor weakness in the upper limb. Her past, personal and family history were not contributory.

General physical examination revealed two subcutaneous hemispherical swellings one in the paraspinal region 3\(^3\) cm and another one in the pectoral region 6\(^4\) cm. Neurological assessment showed features suggestive of bilateral cerebellar dysfunction, second, fifth and eighth cranial nerve involvement and sensorimotor involvement. Direct ophthalmoscopy revealed pappiledema right and optic atrophy left (Figure 1). FNAC of swelling came as neurofibroma. Pure Tone Audiometry revealed right profound and left mild sensory neural hearing loss. Contrast MRI of brain revealed bilateral large sized cerebello pontine angle tumours with obstructive hydrocephalus and brainstem compression (Figure 2). To substantiate sensorimotor involvement a nerve conduction study was done, which showed axonal type of sensory motor polyneuropathy. According to NIH and Manchester diagnostic criteria a diagnosis of Neurofibromatosis type 2 was made.

She underwent retromastoid suboccipital subtotal excision of the tumour and the lesion was sent for histopathologic examination. It revealed Verocay bodies pathognomonic of schwannoma (Figure 3).

Discussion

The neurofibromatoses consist of at least two distinct autosomal dominantly inherited disorders, neurofibromatosis 1 (NF1) and neurofibromatosis 2 (NF2).

Historically, these conditions were aggregated as generalized neurofibromatosis (von Recklinghausen disease). NF2 was first described by Wishart in 1822. The heritable nature of NF2 was reported in 1920 by Feiling and Ward, who described a three-generation family with vestibular schwannomas (VS). The autosomal dominant transmission (i.e. a 50 percent risk of transmission from an affected parent) was confirmed in a large family reported by Gardner and Frazier in 1930. NF1 was delineated by von Recklinghausen in the late nineteenth century. Harvey Cushing aggregated NF1 and NF2 in 1916, and his scientific stature was such that, despite reports that the conditions were different, many decades were to pass before the distinction between the two diseases was widely recognized.

NF2 is a dominantly inherited genetic disorder resulting from mutations involving NF2 gene in chromosome 22. The disease first described by Wishart in 1822 is indeed arare condition and has prevalence estimated to be about 1 in 60,000. The hallmark phenotypic manifestation...
is vestibular schwannoma which is often bilateral. Vestibular schwannoma occurs in as high as 95% of adult patients with NF2. Ependymomas, meningiomas, and schwannomas involving other cranial nerves are all well-described. Skin manifestations like café au lait spots and neurofibromas may occur in NF2 but are less florid compared with its type 1 counterpart. Axillary or inguinal freckling, Lisch nodules, and malignant transformation of tumors practically never occur in NF2. Instead patients with NF2 may have posterior subcapsular lenticular opacities. Clinical diagnosis used to be based upon the National Institutes of Health (NIH) criteria.

NIH diagnostic criteria for NF2 are as follows:²

1. Bilateral masses of the eighth cranial nerve seen with appropriate imaging techniques.
2. A first-degree relative with and unilateral mass of the eighth cranial nerve.
3. A first-degree relative with and any two of neurofibroma, meningioma, glioma, schwannoma, or juvenile posterior subcapsular lentigolenticular opacity.

However, 50% of patients with NF2 present without the presence of a positive family history and many present with tumors or lenticular opacity prior to development of acoustic neuromas. Hence, the diagnostic criteria were subsequently revised to permit the diagnosis of NF2 in these subgroups of patients. The Manchester clinical diagnostic criteria allow diagnosis of NF2 in the aforementioned subgroups with maximum sensitivity.

Manchester clinical diagnostic criteria

1. Bilateral vestibular schwannomas
2. First-degree family relative with neurofibromatosis type 2 and unilateral vestibular schwannoma or any two of the following: Meningioma, schwannoma, glioma, neurofibroma, posterior subcapsular lenticular opacities
3. Unilateral vestibular schwannoma and any two of the following: Meningioma, schwannoma, glioma, neurofibroma, posterior subcapsular lenticular opacities
4. Multiple meningiomas (two or more) and unilateral vestibular schwannoma or any two of the following: Schwannoma, glioma, neurofibroma, cataract.¹²

Most common clinical presentation includes hearing loss and tinnitus. Other symptoms include disturbances in balance, headache, reduced vision, and facial numbness.³ Neuroimaging [computed tomography or magnetic resonance imaging (MRI)] helps in demonstrating the craniospinal tumors. Genetic studies and mutation analysis confirms the diagnosis. Management of NF2 often confers a major challenge to the treating doctor with respect to the timing of surgery, type of surgery, and surgical approach. Despite these dilemmas, surgical removal remains the treatment of choice.⁴⁻⁵ Surgical management by an expert team is found to confer significant benefit to the patient. However, surgery even in expert hands is associated with a variety of major complications like complete hearing loss and facial nerve damage.¹

Patients who are poor candidates for surgery or those who refuse surgery may be considered for radiation therapy or experimental therapeutic modalities.¹ Being autosomal dominant disorder, children of affected parents should be screened regularly for the phenotypic manifestations of NF2 mutation. Neurological examination, ophthalmologic evaluation, and annual auditory brain stem response are recommended. Imaging modality of choice for screening for neural tumors is MRI. MRI for screening is recommended every 2 years until 20 years of age and after 20 years every 3 yearly.

Our patient fulfilled the diagnostic criteria for NF2. As described classically, the patient has involvement of vestibulocochlear, trigeminal nerves, and evidence of raised intracranial tension. Imaging had also revealed bilateral cerebellopontine angle tumor. The constellation of these clinical features and neuroimaging is consistent with the diagnosis of NF2.

Conclusion

This case is reported for certain unique features such as associated sensory motor polyneuropathy of axonal type and chronic papilledema, secondary to obstructive hydrocephalus as a cause of severe visual loss.

References