

Neurofibromatosis Type 2 Associated with Multiple Cerebral Aneurysms- A Rare Case Report

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Abstract:

Intracranial aneurysms have been well described in patients with Neurofibromatosis (NF)-1; however it is very rare in NF-2 patients. There have been only two case reports (to the author's knowledge) of NF-2 associated with intracranial aneurysm 1, 2). We report a case of NF-2 with bilateral vestibular schwannoma and four incidentally found unruptured intracranial aneurysms. This is the first instance where NF-2 has been described with multiple intracranial aneurysms.

Key Words: Neurofibromatosis type 2; intracranial aneurysm; Merlin.

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Case report:

A 14 years old male presented to us with persistent headache for 1 year, blurring of vision in both eyes (right eye more affected than the left) along with subjective hearing loss in both ears for 2-3 months. On examination he has visual acuity of counting finger at 1 feet in the right eye and 3/60 in the left eye, bilateral tractional retinal detachment with macular degeneration due to old hemorrhage on funduscopy exam (as per ophthalmologist review). A TORCH infection was entertained for his ocular disease, but the TORCH titer did not show any sign of infection.

There was no evidence of absent corneal reflex, sensorineural hearing deafness, facial weakness or lower cranial nerve palsies bilaterally on examination. Pure tone audiometry (PTA) revealed normal findings in both ears. Magnetic Resonance Imaging (MRI) with intravenous (IV) Gadolinium contrast demonstrated a 2.2cm left-sided and 1cm right-sided vestibular schwannoma (Figure 1). MRI with contrast also showed a focal dilatation of a vessel in anterior inter-hemispheric fissure apart from enhancing mass in both cerebellopontine angle (CPA). This led to Computed Tomography Angiogram (CTA) with 3-D reconstruction imaging which revealed four intracranial aneurysms. There were two right anterior cerebral artery (ACA) aneurysms (A2 segment aneurysm size is 2.3 mm and A3 segment aneurysm size is 3mm (Figure 2A) , one right middle cerebral artery (MCA) superior division

aneurysm with the size of 3.5 mm (Figure 2B) and one right posterior cerebral artery (PCA) aneurysm whose size is 3.6mm (Figure 2C).

A surgical approach to remove the larger left CPA tumor through retro-mastoid, retro-sigmoid, sub-occipital craniectomy was contemplated to preserve the hearing in the left ear. Patient underwent the abovementioned surgery with near total removal of the tumor. The tumor was firm without a capsule, adherent to the Cranial nerves (CN) VII and VIII complex with a small portion of tumor extending into the internal auditory meatus. The tumor was excised with exception of a small remnant which was firmly adherent to CN VII and VIII complex and was left behind to prevent injury to these nerves. The histopathology report of the tumor sample

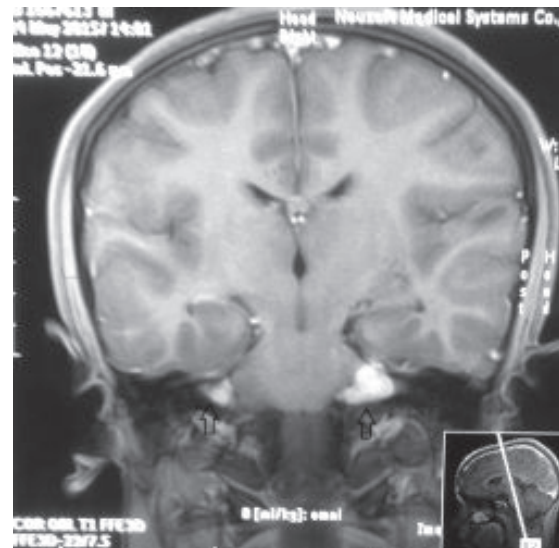


Fig.-1: MRI brain with IV gadolinium contrast administration shows contrast enhancing bilateral CPA region vestibular schwannoma.

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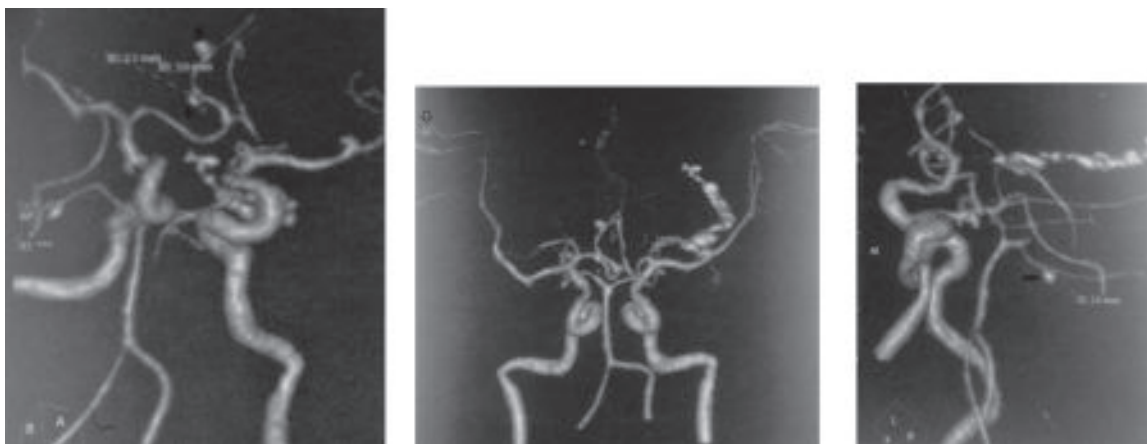


Fig.-2: (A) CTA showed two right ACA aneurysms in A2 and A3 segment of maximal dome size 2.3 and 3 mm respectively, (B) one MCA aneurysm post-bifurcation superior division aneurysm of size 3.5 mm and (C) one PCA aneurysm of size 3.6 mm.

revealed schwannoma. Since the tumor arose from the vestibular nerve as evident during operation; a diagnosis of “vestibular schwannoma” was confirmed. Patient’s post-operative recovery was uneventful and had improved hearing in the left ear, normal facial function and no lower cranial nerve palsies at the time of discharge. We aim to follow the right untreated and small residual left CPA tumor and all the incidentally found small intracranial aneurysms with repeat MRI with MRA on a yearly basis, at least for the first few years after surgery.

Discussion:

NF-2 occurs in 1 in 30,000-50,000 individuals who harbor a mutation in the NF-2 tumor suppressor gene^{1,2}. This autosomal dominant gene is located on chromosome 22q12, which accounts for tumorigenic development of schwannomas and meningiomas^{3,4}. Clinical diagnosis of NF-2 is determined by the presence of either bilateral vestibular schwannoma(3) or a first-degree relative with NF-2 plus a vestibular schwannoma, at age <30 years⁵, or two of the following: juvenile posterior subcapsular lenticular opacity or juvenile cortical cataract, meningioma, glioma, or schwannoma(6). Approximately half of all NF-2 cases are familial⁴. The mean age at diagnosis is 22 years, whereas the mean age of death is 36 years⁷. We have a case that has bilateral vestibular schwannoma which meets the criteria to be classified as NF-2 patient.

Although there is a well-established association between NF-1 and visceral aneurysms including intracranial aneurysms, a similar association with NF-

2 has not been reported⁸. To the author’s knowledge, only 2 case reports exist mentioning the presence of intracranial aneurysm with NF-2. A case report elucidated an incidental finding of an unruptured middle meningeal artery aneurysm in a case of NF-2 with meningiomatosis, which underwent N-Butylcyanoacrylate embolization prior to surgical resection of parafalcine meningioma(1). The second NF-2 case had MRI brain with IV Gadolinium contrast which showed bilateral vestibular schwannoma(2). She underwent surgical removal of the larger, more symptomatic right sided tumor. However while recuperating in the post-operative phase in the hospital, patient developed seizure and deterioration of the consciousness level. A computerized tomography (CT) revealed SAH with CTA demonstrating an aneurysm in the P1 segment of the left PCA. The aneurysm was managed conservatively due to poor neurological status and the patient ultimately expired.

Pathogenesis of arterial aneurysms in NF-1 remains ill defined but it has been attributed to loss NF-1 gene product, that is, neurofibromin(8). Neurofibromin expression has been demonstrated in vascular endothelium and smooth muscle cells (8). The product of NF-2 gene is Merlin and has been clearly shown to be associated with formation of meningiomas and other neoplastic lesions seen in NF-2 patients but is not known to have a role in vascular lesions⁹. Whether there is a mechanism perhaps similar to NF-1, or whether this association is incidental remains unknown.

However the 3 case reports (including ours) which showed the presence of intracranial aneurysms with NF-2, especially in the setting of our case of NF-2 associated with multiple incidentally found cerebral aneurysms builds a strong hypothesis that this association is not likely to be incidental. The genetic aberration in NF-2 which is mutation in chromosome 22q12.2 with loss of tumor suppression peptide Merlin may also have role in the development of intracranial aneurysm.

Non-invasive radiographic screening for intracranial aneurysm [CTA or Magnetic resonance angiogram (MRA)] for patients which presents with NF-2 considering the paucity of data to clearly establish association of NF-2 with intracranial aneurysms is hard to propose. However, the neurosurgeon in charge of the patient with NF-2 should be aware of the building literature elucidating association of NF-2 with cerebral aneurysm. He or she should use his or her individual judgment whether or not to radiographically screen NF-2 patient for the presence of cerebral aneurysm.

Conclusion:

Currently accumulating literature on the association of NF-2 and intracranial aneurysm, especially in the setting of our case of a teenager with NF-2 presenting with multiple incidentally discovered cerebral aneurysms makes us think that NF-2 may be a risk factor for the development of intracranial aneurysm. We recommend that the neurosurgeon should thoroughly evaluate the existing MRI with contrast sequence(s) to look for any vascular out pouching in the intracranial circulation which may suggest an aneurysm in patients with established NF-2 (albeit the fact this sequence may not pick a cerebral aneurysm). If this is seen, non-invasive radiographic screening (CTA or MRA) should be considered seriously to rule out cerebral aneurysm.

Abbreviations:

Neurofibromatosis (NF)

Toxoplasmosis Rubella Cytomegalovirus Herpes (TORCH)

Pure Tone Audiometry (PTA)

Magnetic Resonance Imaging (MRI)

Intravenous (IV)

Cerebellopontine Angle (CPA)

Computed Tomography Angiogram (CTA)

Anterior Cerebral Circulation (ACA)

Middle Cerebral Circulation (MCA)

Posterior Cerebral Circulation (PCA)

Cranial Nerve (CN)

Magnetic resonance angiogram (MRA)

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