

Cranial and Spinal involvement in Neurofibromatosis type 2

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Citation

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Abstract

Neurofibromatosis type 2(NF-2) is an often devastating autosomal dominant disorder which, until relatively recently, was confused with its more common namesake neurofibromatosis type 1. NF2 is a distinct disease which must be separated clinically & radiologically from neurofibromatosis1. Subjects who inherit a mutated allele of the NF2 gene inevitably develop schwannomas, affecting particularly the superior vestibular branch of the 8th cranial nerve, usually bilaterally. Meningiomas and other benign central nervous system tumours such as ependymomas are other common features. Much of the morbidity from these tumours results from their treatment. As a classical tumour suppressor, inactivation of the NF2 gene product, merlin/schwannomin, leads to the development of both NF2 associated and sporadic tumours. Merlin/schwannomin associates with proteins at the cell cytoskeleton near the plasma membrane and it inhibits cell proliferation, adhesion, and migration.

INTRODUCTION

Neurofibromatosis type 2, formerly called central neurofibromatosis or Schwannomatosis, presents with Multiple inherited Schwannomas, Meningiomas, Ependymomas (MISME syndrome).

In 1998, National institute of health (NIH) devised criteria for the diagnosis of NF-2.

Definite diagnostic criteria are:

Bilateral CN VIII schwannomas on MRI or CT scan (no biopsy necessary).

First degree relative with NF-2 & either unilateral early onset CN VIII schwannomas (age<30yrs) or any 2 of the following:

Meningiomas, Gliomas, Schwannomas, Neurofibromas, Juvenile posterior subcapsular lenticular opacity.

Our case is unique as it depicts the wide spectrum of findings that are generally not seen in one patient.

NF 2 in an autosomal dominant disorder. The genetic defect responsible for NF2 is a deletion of a portion of chromosome 22₁₂. The reported incidence is 1:30,000 – 40,000⁸⁹. Male & female patients are approximately equally affected²³. A racial predilection exists for NF2, although the disease is autosomal dominant with a high penetrance, many patients have a strong family history⁸²¹²².

CASE HISTORY

A 32 yr old female complained of progressive hearing loss from left ear for last 7 yrs and right ear for last 2yrs. Her problem became more apparent during her pregnancy. She underwent audiometry tests & was diagnosed to have sensorineural hearing loss in both ears. She also developed unilateral left sided facial palsy 6yrs back, from which she recovered gradually but it was incomplete.

She also complaint of off and on headache associated with vomiting for last 2 months. There was no history of fever, ear-ache or ear discharge, visual disturbance or trauma.

On examination, vitals were stable. General and systemic examination was normal. GCS was 15/15. She was oriented to time, place and person. Visual acuity and visual fields were normal. There was bilateral papilloedema but pupils were equal and reacting to light. Left facial palsy was present. There was complete hearing loss in left ear with some sensorineural type of loss in right ear. Bilateral gag reflex were diminished. Truncal ataxia was present. Power was grade 5/5 in all four limbs with normal tone.

NCCT Brain was done and dilatation of bilateral internal auditory meatuses along with multiple meningiomas in foramen magnum region and left frontal region were noted [Figure -1]. Benign non-specific intra-cranial calcifications were seen along

Figure 1

Figure 1 showing dilatation of bilateral internal acoustic meatuses and meningioma in foramen magnum region

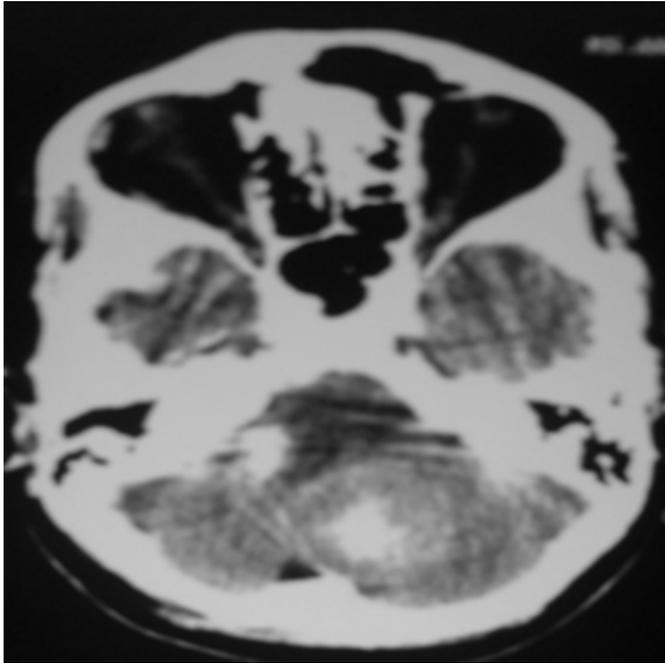
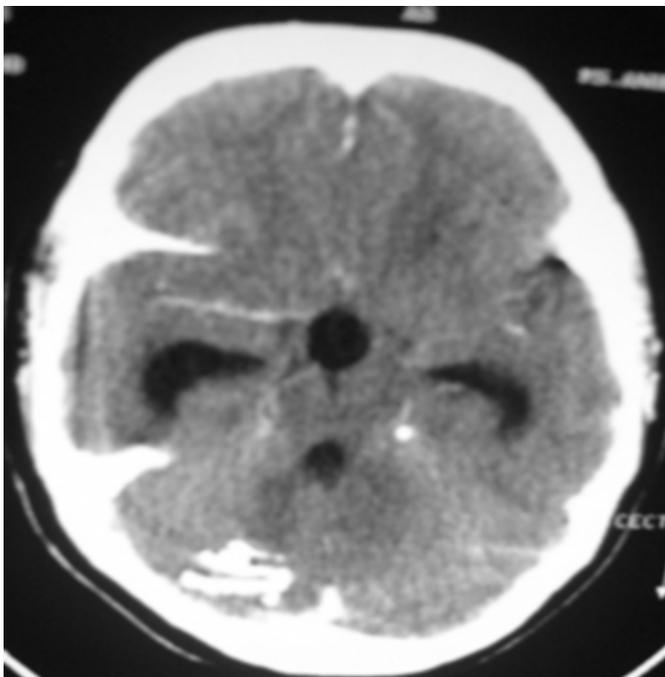


Figure 2

Figure 2 showing intracranial calcification at right CP angle and tentorium



right CP angle and bilateral tentorial region [Figure – 2]. Multiple small rounded hyperdense lesions are seen in anterior falx, left frontal lobe, mid part of falx, below splenium of corpus callosum and in parietal region. [Figure –

3, 4]

Figure 3

Figure 3 showing hyperdense lesion in anterior falx

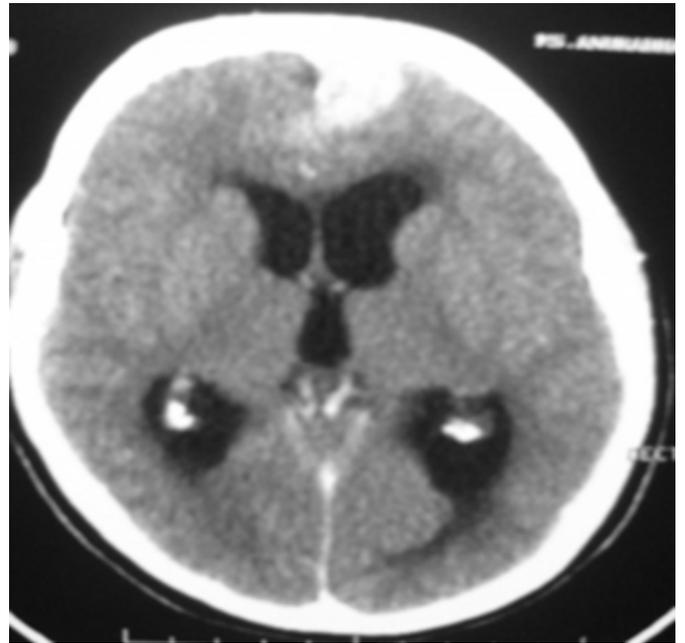
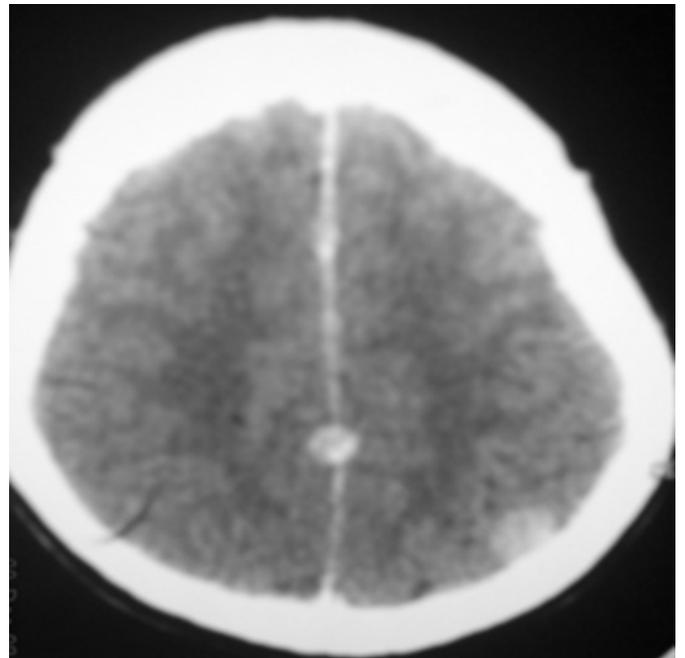


Figure 4

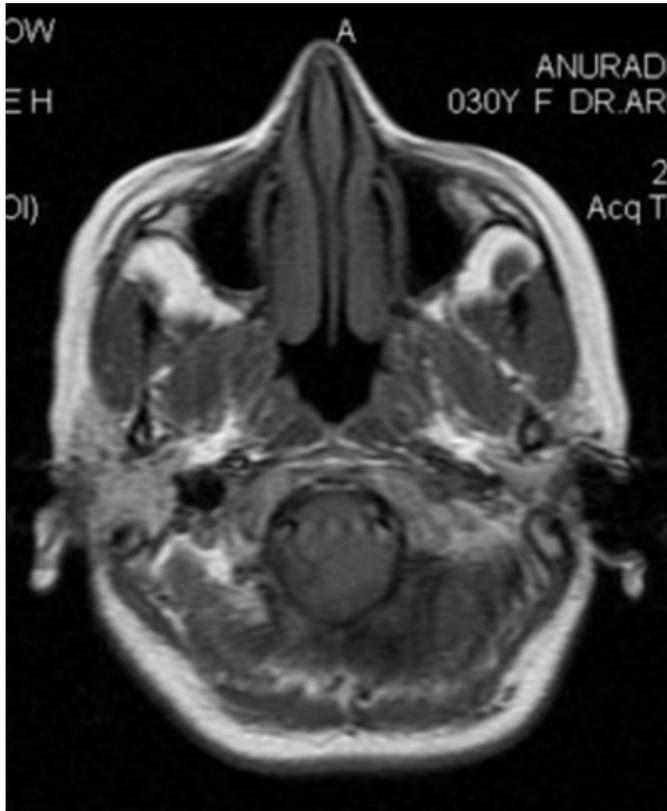
Figure 4 Multiple meningiomas are well visualised in mid



A plain and contrast enhanced MRI brain was performed on 1.5 T superconducting magnet revealed multiple, small irregular, ill-defined intensely enhancing altered signal lesions in bilateral CP angles cistern (R>L) with extension into internal auditory meatuses suggesting acoustic schwannomas [Figure – 5]. Multiple small to large

Figure 5

Figure 5 MRI showing intensely enhancing altered signals in bilateral internal auditory meatuses



well-defined extra-axial hyperintense and intensely enhancing space occupying lesions in supratentorial & infratentorial compartment & mid-line posterior fossa region with obstructive hydrocephalus suggesting multiple meningiomas [Figure 6 & 7].

Figure 6

Figure 6

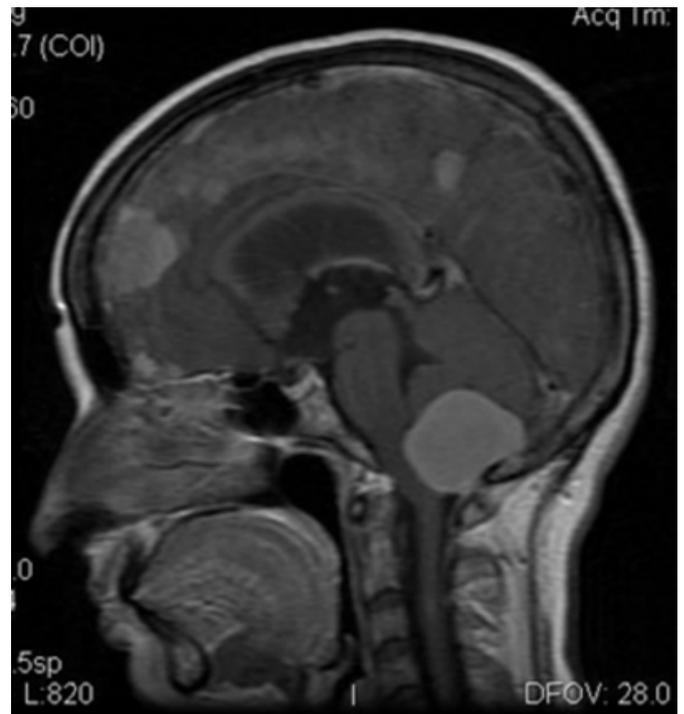
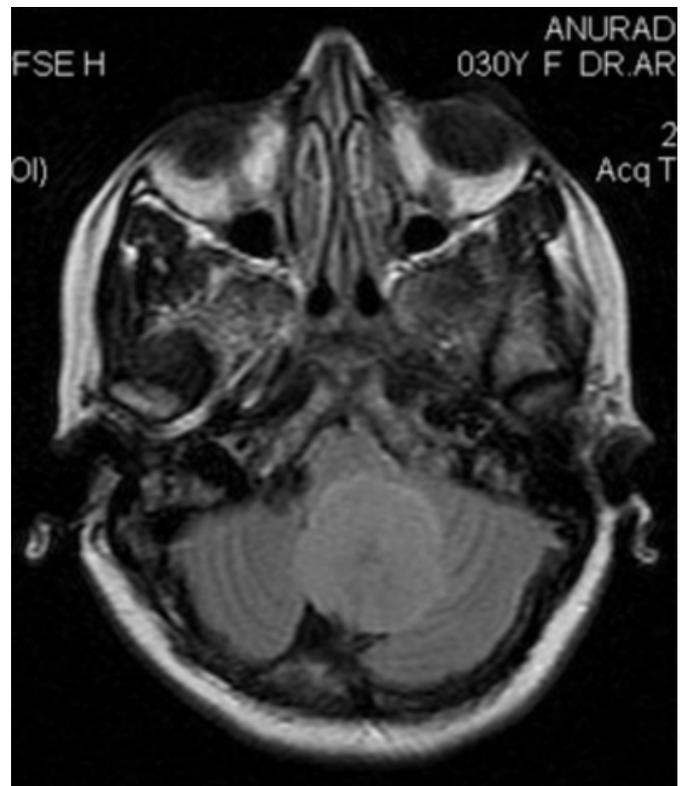


Figure 7

Figure 7



Also post contrast T1 sagittal screening of spine demonstrated multiple, small irregular ill-defined enhancing

altered signal lesions in spinal canal involving intra-dural & intramedullary & extramedullary compartment suggesting ependymomas & schwannomas [Figure – 8].

Figure 8

Figure 8



For her complaints of off & on headache with vomiting and truncal ataxia, it was decided to operate her for posterior fossa meningioma. She underwent surgery (suboccipital craniectomy and excision of foramen magnum meningioma). Her gag reflex & truncal ataxia improved after surgery but is still having left facial nerve palsy & bilateral sensorineural hearing loss(R>L).

Patient underwent plain CT head next day of surgery & demonstrated to have: Craniectomy defect with fluid collection & air pockets with high attenuation with ?foci embolization material with pneumocephalus in basal cisterns, ventricular system & sylvian fissures. Rest findings were same [Figure – 9 & 10].

Figure 9

Figure 9

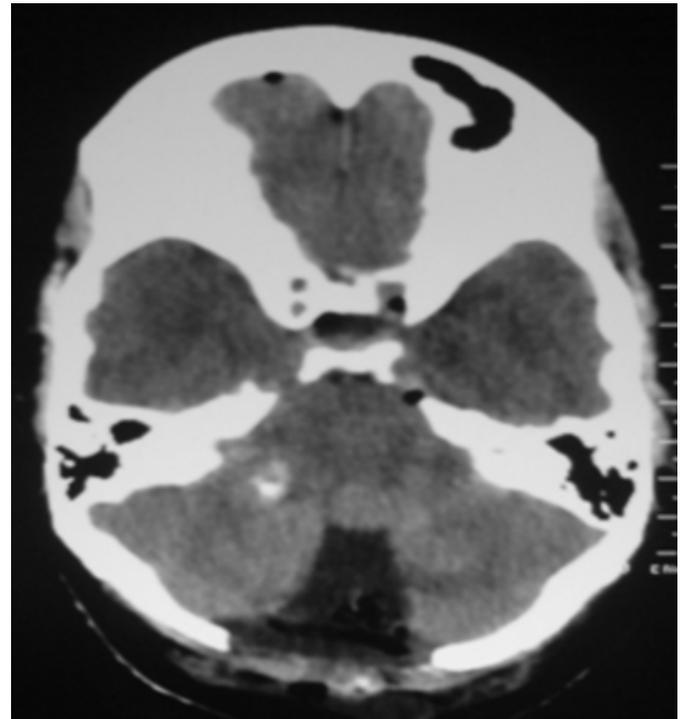
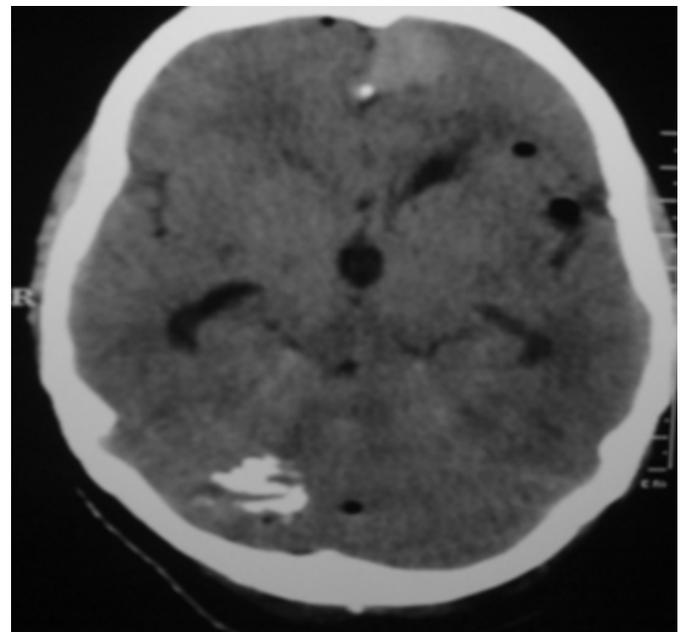


Figure 10

Figure 10



Tumor tissue was sent for histopathology. On gross examination, it was gelatinous and soft. On cut section, whorled and trabeculated appearance like that of leiomyomas was seen.

On microscopic examination, tumor tissue was composed of

fascicles, bundles & whorls of spindle cells with oval nuclei. Psammoma bodies are present with no evidence of necrosis or increased mitotic activity suggesting transitional meningioma grade 1.

DISCUSSION

Neurofibromatosis type 2 is also known as central neurofibromatosis or bilateral acoustic schwannomas or MISME syndrome. It is an autosomal dominant disorder, related to deletion of portion of chromosome 22¹².

NIH consensus committee has devised criteria for NF2¹⁵.

Bilateral CN VIII schwannomas on MRI or CT scan (no biopsy necessary).

First degree relative with NF-2 & either unilateral early onset CN VIII schwannomas (age<30yrs) or any 2 of the following:

Meningiomas, Gliomas, Schwannomas, Neurofibromas, Juvenile posterior subcapsular lenticular opacity¹²³⁴.

This case is being reported to highlight the above mentioned definite criteria. Typically, the diagnosis of NF2 is made in 2nd and 3rd decade of life with peak in 20s. Hearing loss resulting from CN VIII schwannomas constitute the most common morbidity associated with NF2²⁴. Mortality varies with age at diagnosis, presence of intracranial meningiomas, previous treatment.

Cutaneous markers are rarer in NF2 as compared to NF-1. CNS lesions are seen in virtually all cases and include neoplasms, non neoplastic intra-cranial calcifications and spinal cord nerve root tumors³. CN VIII schwannomas are hallmark of diseases most frequently affecting 8th nerve complex. Unilateral tumors arise from vestibular nerve but schwannomas can be found involving any cranial nerve from CN III to CN XIII, with CN V as the next most frequently involved

Intracranial Meningiomas found in NF2 are usually multiple and appear as well circumscribed intensely enhancing extraxial masses with dural attachment²⁴. Ependymomas are most common intraparenchymal tumor in NF2. Spinal tumors seen in NF2 include schwannomas, meningiomas & ependymomas. Schwannomas may present as intradural extramedullary masses⁵. Benign intracranial calcifications, particularly of choroids plexus, cerebellar hemispheres & cerebral cortex in association with NF2 are seen³. Ocular abnormalities including juvenile posterior subcapsular

lenticular opacity, hamartomas of retina and choroids are common^{7 16171819}.

Although patients with NF2 may have cutaneous schwannomas that resemble skin tag, they rarely have café-au-lait spots and do not demonstrate cutaneous neurofibromas that typically result in early diagnosis of NF1²⁵. Because symptoms from CN VIII schwannomas usually begin in 3rd decade, patients with NF2 are typically diagnosed later in life than NF1. Unilateral bell's like palsy is also seen⁹²⁶.

Osseus abnormalities in NF2 are secondary to spinal tumors and unlike NF1 dural dysplasia is not a feature.

Our patient fulfils the definite criteria for the diagnosis of NF2 and typically presents the wide spectrum of findings that are generally not seen in one patient.

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