Review Article

NEUROFIBROMATOSIS WITH SPINAL TUMORS

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Abstract:

Three cases of neurofibromatosis were found which presented with the features of spinal compression. Two of them were NF-2 and one was NF-1. MRI of cervical spine revealed spinal tumors in all the three cases. The NF-1 case had Astrocytoma of the cervical spinal cord which is very rare and also multiple extradural spinal nerve root tumors. Both the NF-2 cases had bilateral acoustic Schwannoma and One had multiple spinal tumors, two brachial plexus tumors and two cutaneous tumors and Lisch nodule in iris which is usually found in NF-1. The other one had one big spinal schwannoma involving intradural, extradural and extraspinal compartments.

Key words: *Neurofibromatosis, Acoustic schwannoma, Spinal tumor.*

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Introduction:

Neurofibromatosis is the most common of the Neurocutaneous disorders. Neurocuteneous disorders, formerly called Phakomatosis, are a group of conditions, each with unique neurologic findings and benign cuteneous lesions (both skin and the CNS derived embryologically from ectoderm), usually with dysplasia of other organ systems (often including the eyes)[1]. Neurofibromatosis (NF) is a multisystem genetic disorder that commonly is associated with cutaneous, neurologic, and orthopedic manifestations. It is the most frequent of the so-called hamartoses[2]. According to involved gene location and phenotypic expression NF is divided into NF-1 and NF-2. NF-1 is the commonest type and representing about 90% of the cases[1] and incidence is 1of every 3000 individuals of the general population. NF-2 is even more rare and occurs in about 1 of every 50.000-100.000 individual[3]. In NF-1 spinal nerve root tumors can occur but incidence is far less than NF-2 and intramedullary spinal cord tumors are very rare.

We have encountered 3 cases of neurofibromatosis with spinal tumors. Among them two were NF-2 and one was NF-1. In 2004, Hong JT et.al. reported one case of NF-1 with astrocytoma and he found only 6 previous cases reported in the world literature[4].

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Case reports:

Case 1:

A young man of 24 years presented with weakness of all four limbs, multiple cutaneous nodules of different sizes all over the body and urinary incontinence. The patient has positive family history of neurofibromatosis, his mother, maternal grandmother and two sisters were also affected (Fig: 1). On examination patient had numerous neurofibromas all over the body, numerous café'-au-lait spots throughout the body mostly marked on trunk and axillary freckling, He was quadriplegic (Muscle power grade- 3/5), spasticity in both lower limbs, reflexes in lower limbs were exaggerated and diminished in upper limbs, no sensory deficit. No Lisch nodule was marked. MRI of cervical spine showed multiple neurofibromas along the exiting cervical spinal nerve roots and intramedullary tumor (astrocytoma) in the cervical spinal cord (Fig: 2,3). MRI brain was normal, no optic nerve sheath tumor seen. Accordingly he was diagnosed as a case of Neurofibromatosis Type- I with multiple spinal schwannomas and astrocytoma of the cervical spinal cord. Decision was made in favor of surgery for cervical spinal cord astrocytoma. After counseling regarding the total situation, fate and result of operation, patient refused operation.

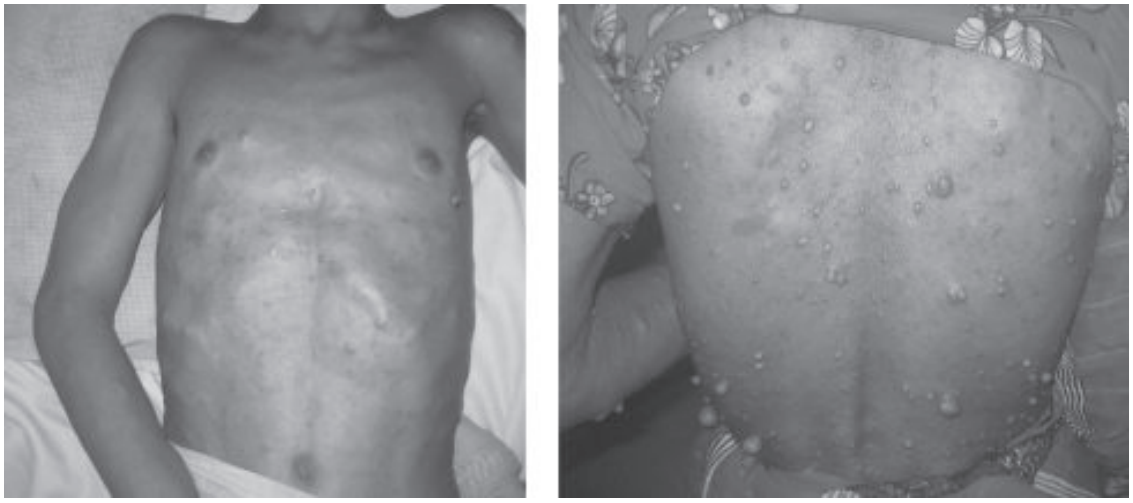

Fig. 1a&b: *Patient and his mother having multiple neurofibromas and café-au-lait spots*

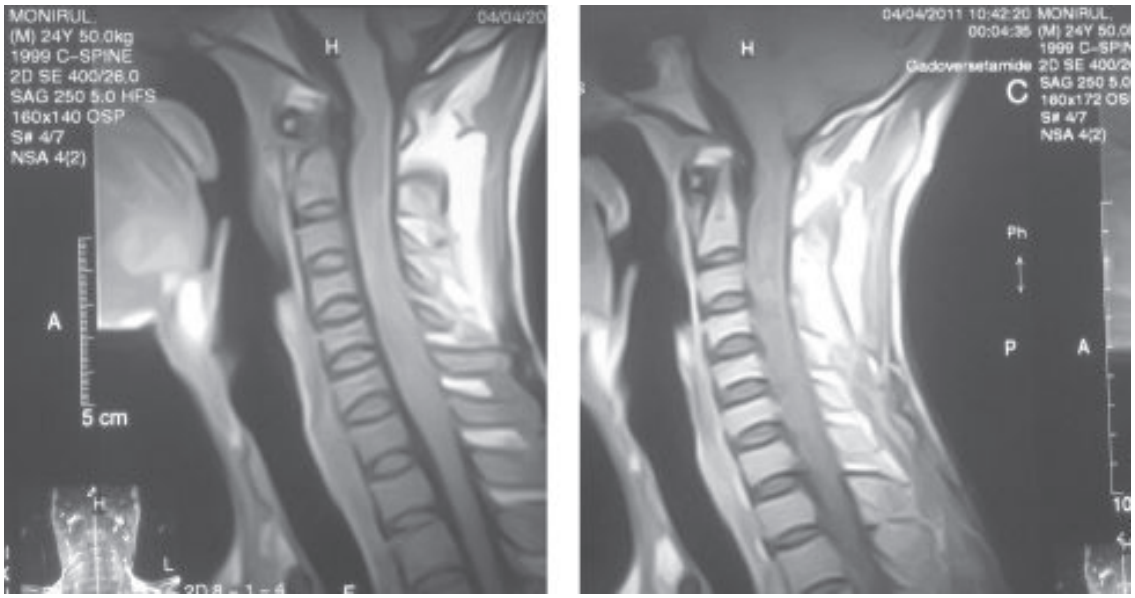

Fig. 2a&b:*Cervical cord astrocytoma (T1WI and Contrast MRI)*

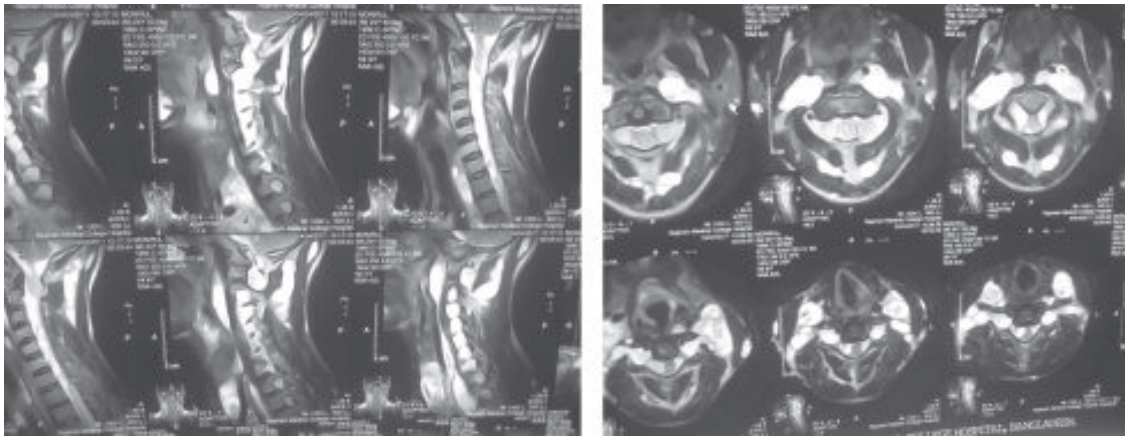

Fig. 3a&b: *Multiple Neurofibromas arising from multiple cervical spinal nerve roots*

Case 2:

A young man of 27 years presented with the complaints of a globular swelling on the right side of neck, which was subcutaneous, free from the skin and measuring of about 7 cm in diameter, and one small swelling on the rt. side of the trunk below the costal margin and another one on the back **(Fig: 4)**, which were fixed with the skin, weakness of all the four limbs, spasticity, tingling and numbness of the body below the upper chest. He was also complaining of pain in the right side of the body. He also gave the history that two years back, tissue was taken from the lesion on the right side of neck by a doctor for histopathology, which was reported as Neurofibroma and following the operation his Rt. arm gradually became wasted specially over the deltoid region. Examination revealed that there were Lisch nodules on iris of Rt. Eye **(Fig: 5)** and café-au-lait spots over the body. MRI showed two Brachial plexus tumors, one was big which was seen on the right side of neck and another one arising from the C7 nerve root and paravertebral in location. There were multiple intra-spinal schwannomas at C_{1-2}, C_{3-4} and T_1 level **(Fig: 6,7,8)**. Cranial MRI showed bilateral acoustic schwannomas. Considering the clinical features and image finding he was diagnosed as a case of NF-2 with multiple spinal nerve root tumor with peripheral nerve (Brachial plexus) tumor. It was then decided to remove the Larger brachial plexus tumor and the bigger intra-spinal tumor at the level of C2-3 which was causing maximum compression on the cord and the one at the adjacent C1-2 level. The patient was then counseled regarding the consequences of the disease, extent of operation and the result of operation, patient refused to undergo operative treatment.

Fig.-4a&b: *Patient having Brachial plexus schwannoma and cutaneous neurofibroma on flank*

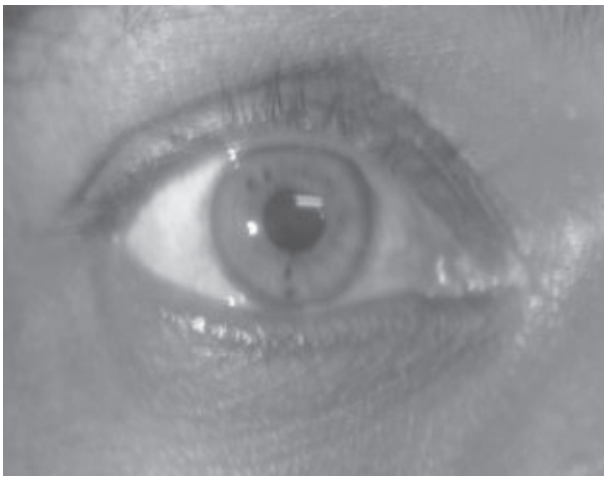

Fig.-5: *Lisch nodule in iris*

Fig.-6: *Multiple intra-dural extra-medullary tumors*

Fig.-7: *Multiple intradural extramedullary tumors from multiple nerve roots*

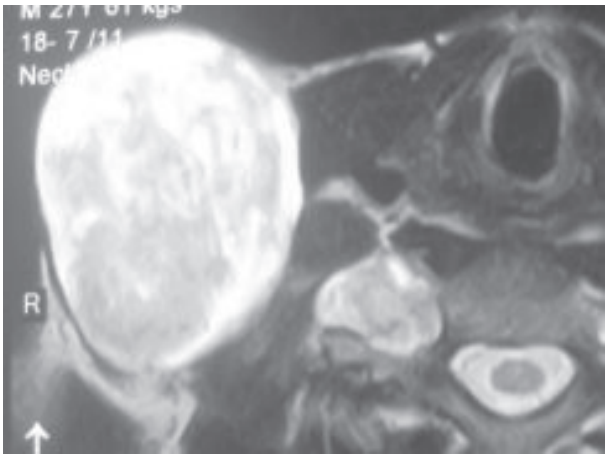

Fig.-8: *Schwannoma from Brachial plexus and from roots*

Case-3

A young lady of 20 years presented with spastic quadriplegia for 3 months and urinary retention for the last 15 days. She gave the history of operation in the neck for quadriparesis 8 months back by a fellow neurosurgeon. Immediately after operation she was improved of symptoms. But after 3 to 4 months of operation she again started to develop the preoperative symptoms. From 3 months back she developed heaviness of both the lower limbs, spasticity of lower limbs and became unable to walk independently and she was feeling difficulty in voiding. 15 days back she developed retention of urine. On examination it was found that her lower limbs' muscle power were 1/5 in Lt. and 3/5 in Rt. side and both were spastic, all the reflexes were exaggerated and she also had ankle and patellar clonus. Upper limbs' muscle power were 3/5 in Lt. and 4/5 in Rt. side. She showed impaired both lateral and dorsal column sensation. X-ray cervical spine showed the evidence of laminectomy from C3-C6. MRI of cervical spine revealed intra-dural extra-medullary SOL enhanced with contrast also extending extradurally towards the extraspinal space through the intervertebral foramen at the level of C4-5 vertebra (Fig:10,12). But upper part of the saggital scan showed one contrast enhancing lesion in the posterior cranial fossa. Then cranial MRI was done and it revealed bilateral acoustic schwannomas (Fig:9). Accordingly she was diagnosed as a case of Nf-2 with recurrent spinal schwannoma involving extraspinal, intra-spinal extra-dural and intra-dural compartment. She then underwent re-operation and complete and intact removal of the schwannoma was done (Fig:11), which was histologically confirmed. After operation she was improved of symptoms markedly and she could walk with minor assistance on the 10th POD.

Fig.-9: *Bilateral acoustic Schwannoma*

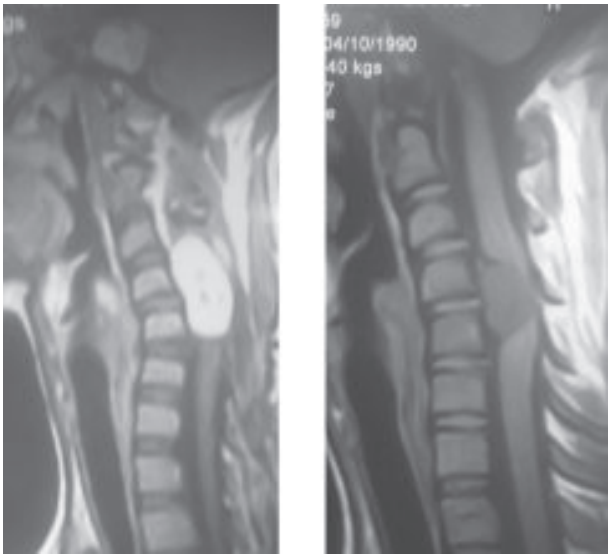

Fig.-10: *Recurrent intra-dural extra-medullary tumor*

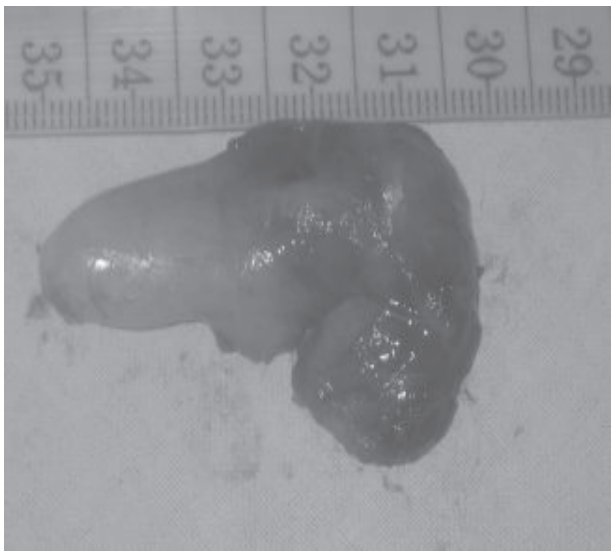

Fig.-11: *Resected recurrent tumor*

Fig.-12: *Tumor before first operation*

Discussion:

Commonest neurocutaneous disorder is neurofibromatosis, an autosomal dominant inherited disorder which has two subtypes Neurofibromatosis type-1 and Neurofibromatosis type-2. Both have defects in genetic constitution in different location. NF-1 gene by located on chromosome 17q11.2 and codes for neurofibromin and NF-2 gene on chromosome 22q12.2 and codes for merlin[1]. NF-1 has variable expressibility and almost 100% penetrance by the age of 5 years[1,5,8]. The spontaneous mutation rate is high[1,8]. In NF-2 there by nearly 100% penetrance by 60 years of age[15].

NF type 1 (NF-1), so called peripheral NF, is the more common type, and is characterized by cafe-au-lait spots, neurofibromas, optic gliomas, iris hamartomas, and musculoskeletal abnormalities. NF type 2 (NF-2), so called central NF, is characterized by bilateral schwannomas of the vestibular portion of cranial nerve VIII, while dermal lesions are unusual[4,9].NF type 1 (NF1) is differentiated from central NF or NF type 2 in which patients demonstrate a relative paucity of cutaneous findings but have a high incidence of meningiomas and acoustic neuromas (which are frequently bilateral). NF1 has a better prognosis with a lower incidence of CNS tumors than NF2. However, morbidity and mortality rates in NF1 are not negligible. Some of the more severe complications are visual loss secondary to optic nerve gliomas, spinal cord tumors, scoliosis, vascular lesions, and long-bone abnormalities, which sometimes necessitate amputation[2]. Iris hamartoma or Lisch nodule usually found in NF-1 but Author found one case of NF-2 with Lisch nodule.

Malignant peripheral nerve sheath tumors (MPNSTs) and neurosarcomas are not uncommon in adolescents and adults with NF1, with an approximate lifetime risk of 10%. These malignancies frequently arise from large plexiform neurofibromas or extensive peripheral nerve lesions. MPNSTs in patients with NF1 carry a poorer prognosis than in patients without this condition; tumor volume is an independent prognostic indicator.[6]

Diagnostic criteria[1,5,7] for NF-1: Two or more of the following:

1) 6 or more Café-au-lait spots, each 5mm or more in greatest diameter in prepubertal individual or 15 mm or more postpubertal individual.
2) 2 or more neurofibromas of any type or one plexiform neurofibroma
3) Axillary freckling
4) Optic nerve glioma
5) 2 or more Lisch nodule
6) Distinctive osseous abnormality
7) One first degree relative with NF-1.

There are some associated conditions: Schwann cell tumors of any nerve, spinal or peripheral nerve neurofibroma, multiple cutaneous neurofibromas, aqueductal stenosis, macrocephaly, kyphoscoliosis, syringomyelia, neurologic or cognitive impairment etc[7].

Diagnostic criteria[1] for NF-2:

1. Bilateral eighth nerve masses on imaging OR
2. A first degree relative with NF-2 and either

a) unilateral eighth nerve mass OR
b) Two of the following: Neurofibroma, meningioma, glioma, Schwannoma and juvenile posterior subcapsular lenticular cataract.

Other clinical features include seizure or focal deficit, skin nodule, dermal neurofibromas, café-au-lait spots, multiple intra-dural spinal tumors(less common in NF-1), including intra-medullary and extra-medullary lesions.

Bilateral vestibular schwannomas are pathognomonic for NF2 and occur in 90% of adult patients with NF. Patients with NF2 virtually frequently have spinal nerve tumors, which are usually schwanomas, and also have an increased incidence of intracranial meningiomas and intramedullary spinal cord tumors (ependymoma, astrocytoma, schwannoma)[3,15]. Sporadic vestibular schwannomas more frequently originate within the inferior vestibular portion of cranial nerve VIII (vestibulocochlear nerve), but in this disorder this predilection is not present[15,16,17].

NF is associated with multiple types of CNS tumors. However, because of the relative rarity of intramedullary spinal cord astrocytomas, which represent only 6% to 8% of spinal cord tumors, the association between NF and intramedullary spinal cord tumors has not been firmly established[4,10]. Since the National Institute of Health Consensus Development Conference set the diagnostic criteria in 1988,[7,9,11], reports on NF associated intramedullary spinal cord astrocytoma have been extremely rare, with only three reports concerning intramedullary spinal cord astrocytoma associated with NF-1 being documented in the literature. Egelhoff et al. reported 1 case of cervical astrocytoma associated with NF-1[13] and Lee et al. reported astrocytoma in 3 cases of NF-1[11]. Yagi et al. also identified 2 cases with NF-1 among their series of 44 cases of intramedullary spinal cord tumors[10]. Spinal cord involvement in NF-1 is typically from extramedullary growth of spinal nerve root tumors. Meanwhile intramedullary spinal cord tumors in NF-1 have been reported as scattered, single cases in the literature[10,11]. Hong et.al. reported one case in 2004 and he found 6 previously reported cases of intramedullary spinal cord tumor with an evident pathological diagnosis of NF-1, the tumors were astrocytoma[4]. Authors found one case of NF-1 with astrocytoma of the cervical spinal cord.

In the literature, there is a trend for spinal cord ependymomas to occur in the patients with NF-2 and for spinal cord astrocytomas to occur in the patients with NF-1[10,11,14].

There is no cure for NF. The main goal of treatment is to monitor its development and intervene when necessary. Healthy children with NF should be followed-up and examined every 6-12 months by a paediatrician. Genetic counselling and education about NF is important[18]. For patients with multiple medical problems associated with NF2, management by a team of specialists through a multidisciplinary clinic may provide the most comprehensive and cost-effective care over time. This is especially important with rapid advances in surgical management, including the use of such tools as stereotactic radiosurgery and auditory brainstem implants (ABIs)[2]. Spinal tumors, acoustic schwannomas and peripheral nerve tumors should be treated according to their merits and patient's clinical

condition. Every patient should be considered individually.

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