Neurofibromatosis-I Presenting with Multiple Spinal and Intracranial Neurofibromas

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Abstract
Von Recklinghausen’s neurofibromatosis (NF-1) is a phacomatosis characterised by widespread nervous system tumours with cutaneous manifestations and variably associated anomalies. We report here a case, who, in addition to classical features of NF-1 (café-au-lait spots, cutaneous and subcutaneous neurofibromas) demonstrated radiological evidence of both spinal and intracranial neurofibromas and an incidentally discovered horse-shoe kidney. The unique constellation of spinal and intracranial neurofibromas, with associated horse-shoe kidney.

Introduction
Neurofibromatosis type- 1 is an autosomal dominant phacomatosis with variable expression. It is caused by mutations in NF-1 gene located on chromosome 17q11.2. NF-1 gene encodes a protein neurofibromin that modulates cell signalling through ras pathway. Mutations of the NF-1 gene lead to development of a large number of nervous system tumours including neurofibromas, plexiform neurofibromas, optic nerve gliomas, astrocytomas, and meningiomas. In addition to neurofibromas, other cutaneous manifestations of NF-1 include café-au-lait spots and axillary freckling. Associated anomalies in NF-1 are hamartomas of the iris termed Lisch nodules, pheochromocytomas, pseudoarthrosis of the tibia, scoliosis and mental retardation.

The simultaneous presence of symptomatic spinal and intracranial neurofibromas in NF-1 is a very rare occurrence in neurofibromatosis type 1. The authors believe this case to constitute a medical rarity and thus worthy of being reported.

Case Report
A 15 year old male patient presented to Medicine OPD with complaints of neck pain and gradually progressive weakness of all four limbs. The patient also reported progressive painless loss of vision in both eyes. Detailed history revealed the progression of symptoms to have occurred over a period of one year, starting with neck pain and culminating in sequential loss of power in all four limbs. The associated loss of vision had also resulted over the same period restricting his visual acuity to finger counting at 1 metre at presentation.

The patient gave no history of trauma to the spine. Bowel/bladder involvement in the form of urinary/ faecal incontinence or retention was also remarkably absent.

General examination revealed multiple café-au-lait spots all over the body, of which eight were of size more than 1.5 cm. He also had multiple cutaneous and subcutaneous neurofibromas over the neck, trunk and legs (Figure 1).

Power was reduced to Grade 2/5 in all four limbs across all joints. Corticospinal tract involvement was evident in the form of increased tone and exaggerated deep tendon reflexes with associated patellar and ankle clonus and a positive Babinski’s.

Cranial nerves involvement was notably absent except for partial loss of vision in both eyes.

On fundus examination, optic disc was pale and margins were blurred with arteriolar attenuation around the disk suggestive of optic atrophy on both side.

MRI spine revealed extensive neurofibromas at all spinal levels with evidence of compressive myelopathy in cervical cord and significant dural ectasia with posterior vertebral scalloping (Figure 2). Post-contrast enhancing lesions were seen in the conus and cauda-equina region suggestive of neurogenic tumors. MRI brain was remarkable for presence of enhancing nodular lesions in bilateral hypoglossal canal along 9th, 10th and 11th cranial nerves suggestive of neurofibromas, largest of them in the left hypoglossal canal measuring 16 mm x 11 mm (Figure 3). Possibility of optic nerve glioma was suggested by thick enhancement along the course of the nerve (Figure 4). Mild hydrocephalus, probably as a consequence of obstruction to drainage of CSF flow was also seen.

Contrast-enhanced CT scan of abdomen surprisingly revealed the presence of horse-shoe kidney (Figure 5) with otherwise normal visceral configuration.

Based on clinical and radiological findings, a diagnosis of NF-1 presenting with compressive myelopathy and bilateral optic atrophy was made. In view of multi-level involvement, neurosurgical intervention was deemed too risky and thus ruled out. The patient was managed conservatively with i/v pulse methylprednisolone and showed significant clinical improvement over the next couple of weeks. On follow-up one month the patient was ambulatory with negligible residual weakness. Visual acuity had also recovered substantially.

Discussion
Neurofibromatosis (NF) is a neurocutaneous syndrome. It has two distinct forms- Neurofibromatosis type-1 and Neurofibromatosis type-2.

Neurofibromatosis type I is an autosomal dominant disorder with The worldwide incidence of 1 in 2,500 to 1 in 3,000 individuals. The condition arises

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from a germ-line mutation in the NF-1 gene located on chromosome 17q11.

Based on the 1988 National Institutes of Health Consensus Development Conference on Neurofibromatosis, the diagnosis of NF-1 requires the presence of any 2 of the following clinical features: (1) 6 or more cafe-au-lait spots, (2) axillary or groin freckling, (3) 2 or more Lisch nodules, (4) 2 or more neurofibromas, (5) optic pathway gliomas (OPGs), (6) bone dysplasia, and (7) a first-degree family relative with NF-1.

Variable numbers of hyperpigmented cafe-au-lait spots usually develop in the first years of life, but may be present at birth, and are often the first apparent feature of NF-1. The presence of 6 or more cafe-au-lait macules with diameter 0.5 cm before puberty or 1.5 cm after puberty is a diagnostic feature. Axillary and inguinal freckling (‘Crowe sign’) are usually noted between 3 and 5 years of age. Freckling can also occur above the eyelids, around the neck, and under the breasts.

Neurofibromas are benign Schwann cell tumors that are classified according to their appearance and location: focal or diffuse cutaneous, subcutaneous, nodular or diffuse plexiform, and spinal. Subcutaneous lesions can be noted on palpation of the skin and may present with tenderness or tingling distributed along the affected nerve. Plexiform neurofibromas arise from nerve fascicles, tend to grow along the length of the nerve, may involve multiple nerve branches and plexuses, and can cause significant morbidity.

Clinical diagnosis of NF-1 was confirmed in our patient by the presence of multiple cafe-au-lait spots (eight of size more than 1.5 cm) and multiple cutaneous and subcutaneous neurofibromas.

Cervical cord compression arising due to cervical nerve root neurofibromas has been described as a rare complication of NF-1. The most common presenting symptom among all reported cases was progressive quadriparesis. Paraparesis, incontinence and neck pain were observed less frequently.

The patient in this case, presented with neck pain and progressive quadriparesis demonstrating radiological evidence of extensive neurofibromas at multiple spinal levels and compressive myelopathy of cervical cord as a consequence.

In NF-1, the most common neoplasms (apart from benign neurofibromas) are optic nerve gliomas. Second central nervous system gliomas subsequently occur in at least 20% of individuals with NF-1 who had optic pathway gliomas in childhood.

Multiple case series (Créange et al, Huson et al, Riccardi, Friedman and Birch) variably report the presence of intraspinal neurofibromas in 1-5% and intracranial tumours in 0.7 to 3.1% individuals afflicted with NF-1, making their simultaneous occurrence in the same individual an extremely rare clinical event.
Multitudes of case series study involving large number of NF-1 patients have labelled even the independent occurrence of either spinal or intracranial neurofibromas in NF-1 patients as rare. The case is unique in demonstrating simultaneously, the presence of spinal and intracranial neurofibromas in the same individual and thus, constitutes a medical rarity.

References


Fig. 5: CECT abdomen axial image demonstrating horse-shoe shaped kidney