



Case Report

Multiple spinal neurofibromas with cervical and lumbar cord compression In neurofibromatosis 1 - A rare presentation

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ABSTRACT

Neurofibromatosis is a multi system genetic condition with a wide range of neurological manifestations. It is clinically characterized by neurofibromas (benign peripheral nerve sheath tumours), skin involvement, visual complaints along with cardiopulmonary and gastrointestinal complaints. On the basis of affected gene and chromosome, neurofibromatosis may be divided into Type I (Chr. 17) and Type II (Chr. 22).

Cervical cord compression due to cervical root neurofibromas represents an important clinical problem in patients with neurofibromatosis type 1 (NF 1), but is rarely reported.^{1,2}

We report here a rare case, who in addition to classical features of NF-1, had multiple spinal neurofibromas in cervical as well as lumbar spine leading to quadriparesis.

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1. Introduction

Neurofibromatosis encompasses two clinically and genetically distinct conditions NF1 and NF2.

Neurofibromatosis type 1 (NF 1) is a common autosomal dominant disorder in which affected individuals develop both benign and malignant tumours.³ 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.^{4,5}

Mutations of the NF-1 gene lead to development of a large number of nervous system tumours including neurofibromas, plexiform neurofibromas, optic gliomas, astrocytomas and meningiomas. Neurofibromas are benign tumours arising from the endoneurium and are characteristic of NF-1. In addition to neurofibromas other manifestations of NF-1 include cafe-au-lait spots, axillary and groin freckling, Lisch nodules, glaucoma, congenital ptosis, pheochromocytomas, pseudoarthrosis of the tibia, scoliosis, pulmonary stenosis, duodenal carcinoid tumours, cognitive impairment and mental retardation.

NF2 is caused by mutations in NF2 gene located on chromosome 22. It is characterised by Schwannomas, cafe-au-lait spots and meningiomas.

NF1 is commoner than NF2.

In the present case the presence of multiple spinal neurofibromas in cervical as well as lumbar spine leading to quadriparesis is very rare in neurofibromatosis type 1 and thus worthy of being reported.

2. Case Report

A 40 years old female came to our out patient department with complaints of multiple swellings all over the body since 20 years, radicular pain and tingling numbness in all four limbs since 1 year and weakness in the upper and lower limbs since 3 months. The patient did not have any bladder or bowel complaints.

General examination revealed multiple cutaneous and subcutaneous neurofibromas of varying sizes present all over the body. She had multiple cafe'-au -lait spots all over the body of which eight were of size more than 1.5 cm.

The range of movement (ROM) in the cervical region was limited flexion extension with the lateral flexion and

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rotations painful. In the upper extremities motor power was 3/5 in both limbs at all joints. The touch and pain sensation was decreased, and proprioception maintained. The deep tendon reflexes of the upper extremities were brisk (4+). Hoffman sign was bilaterally positive. Finger grip was weak (3/5).

The range of motion at the lumbar spine was painless and full range. The straight leg raise test was negative bilaterally. Motor power was 3/5 at hip joint, 4/5 at the knee, and 2/5 at the ankle and toes bilaterally. The pain and touch sensations were decreased on both sides. Her deep tendon reflexes in both lower limbs were brisk (4+), ankle and patellar clonus was well sustained bilaterally. Plantars were extensor bilaterally (Babinski was positive bilaterally).

Cranial nerves involvement was notably absent also the fundus examination was normal in both the eyes.

The laboratory investigations revealed normal values for whole blood count, alkaline phosphatase, renal and hepatic function test, erythrocyte sedimentation rate, C- reactive proteins, calcium and parathormone and urinary tests.

Plain radiograph showed degenerative spondylotic changes.

3. Magnetic Resonance Imaging (MRI)

MRI revealed well defined altered signal intensity extra-medullary, intradural mass lesions in the spinal canal with extradural extensions along the exiting nerve roots through widened neural foramina at multiple cervical level at C1, C7 - D1 vertebral level, causing cord compression predominantly at C1 and C7 level. There was nodular thickening of bilateral exiting nerve roots from C3 TO D1 level, appearing hypo intense on T1W1 and hyper intense on T2W1 and STIR with widening of neural foramina.

Intra medullary altered signal intensity noted at C1 and C7-D1 level appearing hyper intense on T2W1 and STIR suggestive of cord edema.

There were well defined altered signal intensity extra medullary, intradural mass lesions in the spinal canal with extradural extensions along the exiting nerve roots through widened neural foramina at all lumbar levels and causing spinal cord compression predominantly at L2 and L3 vertebral levels. There was nodular thickening of bilateral exiting nerve roots from L1 to L5 level, appearing hypo intense on T1W1 and hyper intense on T2W1 and STIR with widening of neural foramina. Disc desiccation was noted at L1-L2, L3-L4, L4-L5 and L5-S1. Modic II end plate changes in the inferior end plate of L4 and superior and inferior end plates of L5.

Post contrast enhancing lesions were seen in the cervical and lumbar region suggestive of the neurogenic tumours. Multiple extensive sub-cutaneous nodules were noted on MRI study.

Based on the above findings the MRI for whole spine revealed Multiple Neurofibromas at multiple cervical and

lumbar levels along the cervical and lumbar nerve roots causing spinal canal and neural foraminal widening and spinal cord- thecal sac compression at multiple levels, these features were consistent with Neurofibromatosis.

Based on the clinical and radiological findings, a diagnosis of NF-1 with compressive myelopathy in cervical and lumbar region was made.

Patient presented with spastic quadriparesis without bladder bowel involvement. Patient was unable to walk even with support.

Patient was subjected to posterior decompressive surgery at C1 C2 level with excision of the tumour at this level. The posterior arch of C1 excised. The lesion was arising from C2 roof, C2 roof cut, first left sided and the right sided lesion excised.

Postoperatively the spasticity decreased over a period of 15 days after which the patient was discharged. On follow up at one month the patient was ambulatory, was able to walk with support.

At 2 years of follow up patient has recovered upper limb and lower limb weakness and can walk with a stick. Also the spasticity has reduced significantly.

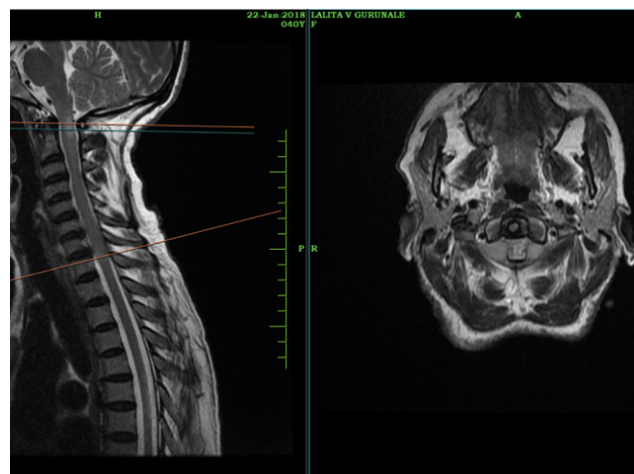


Fig. 1: Coronal and axial section at C1 level (T2 image)

3.1. Histopathological examination

Suggestive of Ganglioneurofibroma.

4. Discussion

Freidrich Von Recklinghausen in 1882 first described Neurofibromatosis.⁶

Neurofibromatosis (NF1, NF2, Schwannomatosis) affects more than 2 million people worldwide.^{7,8}

NF1 gene is found on 17th chromosome and a tumour-suppressor gene which codes the protein neurofibromin.^{9,10}

Neurofibroma is one of the major characteristic feature. Single or multiple cutaneous neurofibromas were observed



Fig. 2: Axial section at C1 level (T2 image)

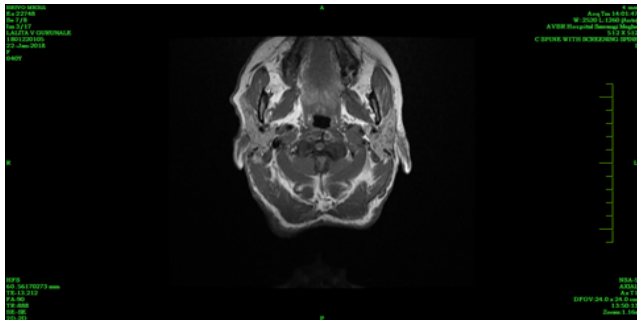


Fig. 3: Axial section at C1 level (T1 image)

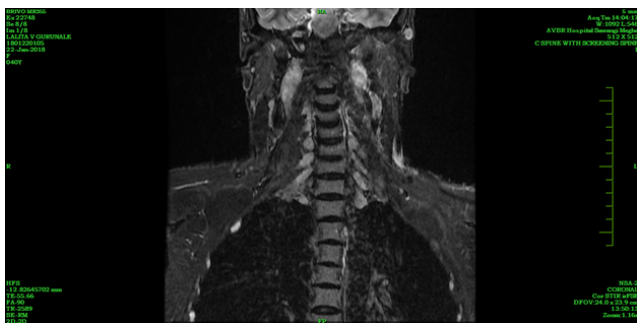


Fig. 4: Coronal (STIR image) section of cervical spine

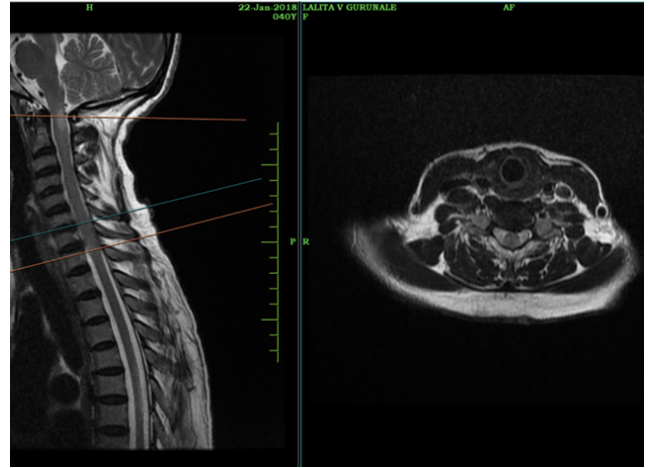


Fig. 5: Coronal and axial section at C7 level

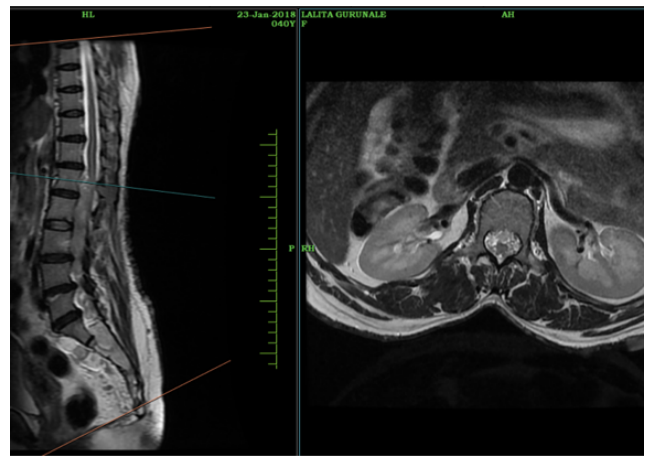


Fig. 6: Coronal and axial image at L1 level

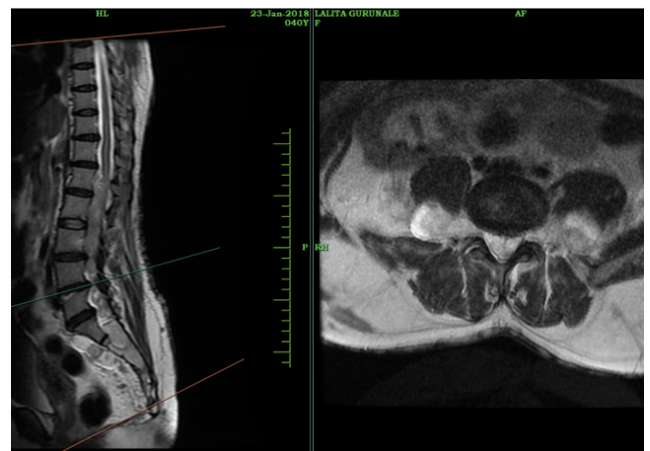


Fig. 7: Coronal and axial section at L5 level (T2 image)

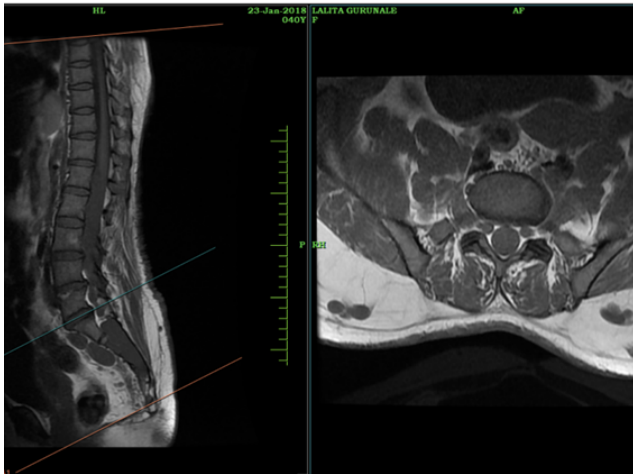


Fig. 8: Coronal and axial sections at L5 level

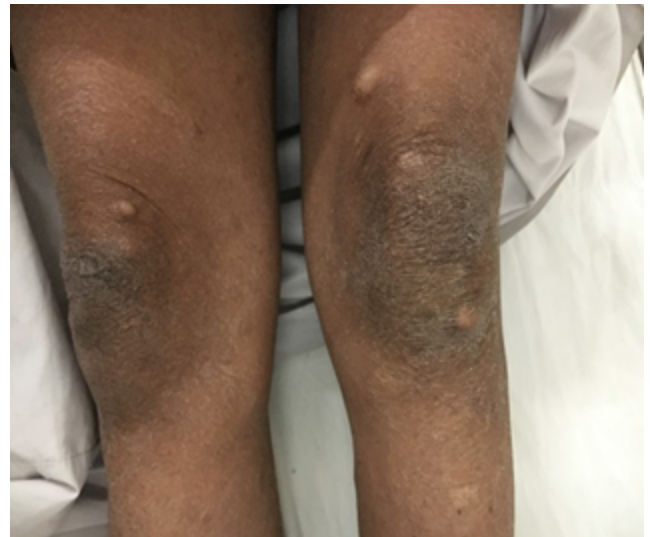


Fig. 10: Knee and legs showing the nodules



Fig. 9: Face and neck showing the presence of nodules and café-au-lait spots

in 95% cases.¹¹ The plexiform neurofibroma (PN) is found in 30% cases.¹²

Spinal neurofibromas are found in up to 38% of NF1 patients.^{13–16} However they cause clinical implications only in about 5% of the patients.^{17–19} In contrast, multiple symptomatic spinal neurofibromas are the main clinical finding in patients with familial spinal neurofibromatosis.^{20–22}

Neurofibromatosis type 1 (NF1) is one of the most common autosomal dominant disorders, affecting approximately 1 in 3500 individuals.^{23,24} The hallmark of NF1 is the extreme heterogeneity in clinical expression, even among related individuals carrying the same mutation.^{23,24}

In Patients with NF1, the cervical cord compression occur due to compression of neurofibromas to the cervical nerve root. However, they have not been frequently reported.^{25–32}

Physical therapy is useful in mild cases. The duration of the physical therapy programme which is effective may be changed for patients. Severe cases may require surgery.²

Créange et al in 1999 reviewed a series of 158 patients with NF1, 92 females (58%) and 66males (42%); 138 patients were adults and 20 were children. In their series they found intraspinal neurofibromas in 3 patients, of which 2 patients with cervical cord compression developed quadriplegia despite surgery and one of them died. Intraspinal neurofibromatosis did not show any progression in 1 patient for 7 year follow up.³²

Leonard J R, Gutmann D H et. al in 2007 reviewed 1500 patients with NF1 at two major centres. Approximately 1500 clinical records were assessed from the patients with NF1 between 1996 and 2006. Their study of 13 patients with NF1 (aged between 9 and 61 years) and cervical cord compression is the largest series to date and raises several important points regarding age at presentation, presenting

symptoms, role of neuro imaging and long term follow up. Neurofibromas can involve any of the cervical nerve roots, in this series cord compression occurred most commonly in the upper cervical spine at C2 and C3. Majority of patients presented with progressive quadriparesis and paraparesis, and incontinence and neck pain were observed less frequently.³³

Sarica et. al (2008) have presented a 32 year old case diagnosed NF1 with quadriparesis who had neurofibromas along the entire length of the spinal cord and cord compression at the level of C4 - C5 and who had undergone a partial resection at the level of C3 and a total resection at the levels of C4, C5, C6. Postoperatively, clinical course of the patient significantly improved.³⁴

Duong et. al 2011 made a retrospective study between 1980 - 2006 and examined 1895 patients with NF1. Spinal cord compression was found in 3% patients as a part of the complications.³⁵

Helmets and Irwin (2009) reported a 17 year old case with NF1 with cervical pain and headache who had 4/5 extremity muscle power and was treated with 20 sessions of cervical stabilisation, posture exercises, stretching, interferential current during 13 weeks. The motor power of the patient increased up to 4+/5 and his complaints significantly decreased.³⁶

In 2013 Mustafa GÜLER et al., presented a case with cervical cord compression with hemiparesis, the patient discontinued the physical medicine after 8 sessions because of social reasons, nevertheless, the frequency of falling and fatigue of lower extremity decreased at the end of this process.³⁷

Multiple case series have described the surgical management of isolated cervical cord neurofibromas and associated spine deformities.^{38,39} Adequate documentation of clinical presentation, management and follow-up is reported in only 12 cases.⁴⁰

However, in contrast with other manifestations of NF1 (eg., optic glioma), the risk of becoming symptomatic from a cervical cord neurofibroma does not decrease with age, and patients at any age are prone to developing signs or symptoms of cervical cord compression.⁸

In the present case patient had spastic quadriparesis with significant weakness in both lower limbs and both upper limbs since 3 months. On MRI it was suggestive of cervical cord compression and also evidence of lumbar cord compression. Since the presenting symptoms were more of cervical cord compression we decided excision of neurofibromas at the C1C2 level. Postoperatively patient had decreased spasticity which over a period of 15 days disappeared significantly. Her weakness improved over a month period and at the first follow up at 1 month she was able to walk with support. At two years of follow up the patient walks with a stick comfortably. Also the spasticity has reduced significantly.

Katharina Wilmmmer et al. in their short report on a patient severely affected by spinal neurofibromas in 2002 categorically mentioned that the severe spinal involvement in their patient was striking and may indicate that the patient belongs to the distinct clinical entity of spinal neurofibromatosis.⁴¹

Similarly we also present this case of severely affected multiple neurofibromas with quadriparesis due to cervical cord compression along with lumbar cord compression which is infrequent and very few cases have been reported which makes this case a rare presentation of NF1.

5. Abbreviations

NF1 = Neurofibromatosis type 1, NF2 = Neurofibromatosis type 2, PF = Plexiform neurofibroma.

6. Declaration of Patient Consent

The authors certify that they have obtained all appropriate consents from the patient and her first degree relatives. The patient and her relatives have given their consent for their images and other clinical information to be reported in the journal. The patient and her relatives understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

7. Financial Support and Sponsorship

Nil

8. Conflicts of Interest

The authors report no conflict of interest concerning the findings specified in this paper.

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