# Seizure, spinal schwannoma, peripheral neuropathy and pulmonary stenosis – A rare combination in a patient of Neurofibromatosis 1

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**Abstract**

Neurofibromatosis 1 (NF1) is the most common neurocutaneous syndrome. It is estimated to occur in approximately 1 out of every 3300 infants. The manifestations of this condition are diverse and can arise from almost any system in the body. The neurofibroma is the hallmark lesion of NF1 that develops from peripheral nerves. Here, we are reporting an 18-year-old girl with NF1. Clinical diagnosis was made according to the diagnostic criteria established by the National Institutes of Health Consensus Development Conference in 1987. She presented with quadriparesis due to dumbbell-shaped spinal schwannoma in the cervical region. She had history of recurrent seizures in the past, with poor scholastic performance. There were clinical and electrophysiological features of peripheral neuropathy and clinical and echocardiographical features of pulmonary stenosis. These are uncommon features of NF 1. The presence of all these features in a single patient makes it a unique case.

**Key Words**

Epilepsy, neurofibromatosis 1, neuropathy, pulmonary stenosis, spinal tumor

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## Introduction

Neurofibromatosis 1 (NF1), the most common neurocutaneous syndrome, is estimated to occur in approximately 1 out of every 3300 infants.[1] Clinical diagnosis is made according to the diagnostic criteria established by the National Institutes of Health Consensus Development Conference in 1987.[2] Manifestations are diverse and can arise from almost any system in the body. Neurofibroma is the hallmark lesion of NF1 and develops from peripheral nerves. Here, we are reporting a patient of NF1 with multiple systemic involvements which are reported as rare in the literature.

## Case Report

An 18-year-old girl admitted with history of weakness of all four limbs for 6 weeks. The weakness started in right upper limb, followed by involvement of right lower limb, left lower limb and finally the left upper limb within 3 weeks. She subsequently developed burning sensation of limbs and trunk. There was no history of sphincter involvement. She had past history of few episodes of generalized tonic–clonic seizures in 1 year preceding her admission. There was no history of headache, vomiting or visual impairment. She was born at home at full term, and according to her father, she had delayed milestones. She relinquished her study at Class I because of poor performance as well as financial constraints. She had her menarche at the age of 14 years. On enquiry, she disclosed that she had multiple nodular swellings all over her body since her childhood, which increased in number with increasing age. Similar swellings were also noticed by her father and one of her younger sisters.

Her general examination revealed normal vital functions, multiple rubbery nodular swellings all over her body and multiple areas of skin pigmentation of varying sizes all over the body, more than six of which were measuring 1.5 cm or more. Both pupils were eccentric, with features of hypertelorism (distance between inner canthus of both eyes is more than half of inter-pupillary distance). She also had pes cavus deformities in both feet.

The neurological examination revealed grossly normal

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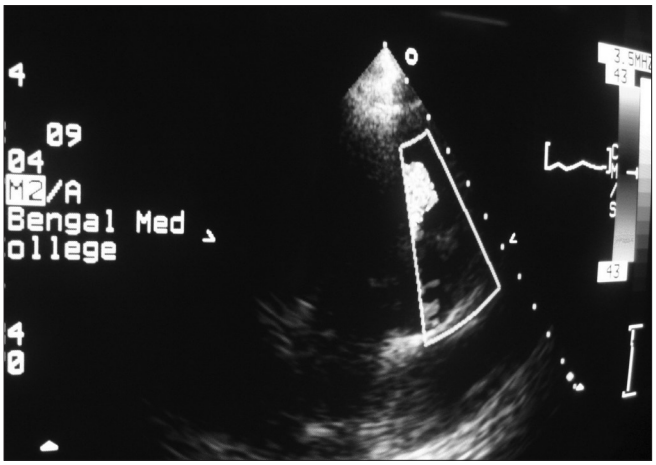


**Figure 1: Parasternal short axis view of echocardiography showing pulmonary valve stenosis**

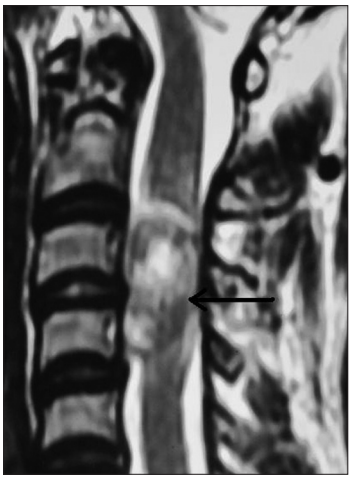

**Figure 3: T2W saggital image of cervical spine showing schwannoma (black arrow)**

higher mental function and cranial nerves. She had wasting of both legs with normal tone in lower limbs and spasticity in upper limbs. The upper limbs had MRC grade 3 power and lower limbs had MRC grade 4 power. All deep tendon reflexes were exaggerated except ankle jerks which were depressed on the left side and absent on the right. The Babinski sign was positive on both sides. There was no abnormal movement and co-ordination was normal. The sensory examination revealed absent joint and position senses in toes with impaired vibration senses up to C5 spinous process with normal pain and temperature senses. The examination of cranium and spine did not reveal any abnormality.

The ophthalmological examination revealed eccentric pupils with slightly thin limbal area and elevated limbal curvature, the presence of two Lisch nodules and changed corneal curvature in the left eye, and normal cornea and five to seven Lisch nodules in the right eye. The cardiovascular examination revealed normal 1st heart sound with single 2nd heart sound and a systolic click followed by a crescendo–decresendo murmur over the pulmonary area. The respiratory

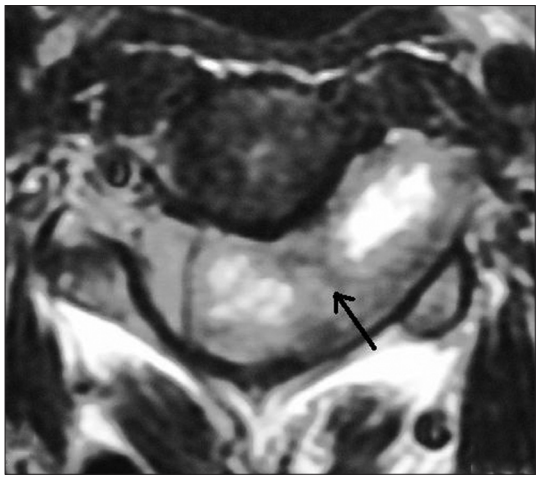

**Figure 2: Axial section of MRI of cervical spine showing "dumbbell"-shaped schwannoma (black arrow)**

**Table 1: Parameters of nerve conduction study of lower limbs**

| Nerve | Distal latency (msec) | Conduction velocity (m/sec) | CMAP amplitude (mV) |
|---|---|---|---|
| Right peroneal nerve | 7.5 | 35 | 5.3 |
| Left peroneal nerve | 6.9 | 36 | 4.9 |
| Right tibial nerve | 7.1 | 38 | 5.2 |
| Right tibial nerve | 7.2 | 38 | 5.0 |

CMAP = Compound muscle action potential

and gastrointestinal (GI) systemic examinations were unremarkable.

Her investigations revealed Hb of 10 g/dl with normal total and differential counts, erythrocyte sedimentation rate (ESR) of 26 mm/hour, normal liver and renal functions and serum electrolytes. ECG showed features of right ventricular hypertrophy with strain pattern. Echocardiography showed situs solitus, congenital pulmonary stenosis (both infundibular and valvular) with right ventricular outflow tract gradient of 37 mmHg [Figure 1]. Ultrasonography of the whole abdomen was normal. Cranial computed tomography (CT) scan was also unremarkable. Magnetic resonance imaging (MRI) of the cervical spine showed a rounded enhancing intradural extramedullary mass on the left side at C1 –C2 level, compressing the cord from outside with extension through the intervertebral foramen on the left side suggesting "dumbbell"-shaped schwannoma [Figures 2 and 3]. Nerve conduction study revealed prolonged distal latencies, slow conduction velocities with preserved Compound Muscle Action Potential amplitude of lower limbs, suggesting demyelinating type of neuropathy with absent sural Sensory nerve Action Potential on both the sides [Table 1].

## Discussion

The girl had the cutaneous features of NF1, namely, multiple subcutaneous nodules and *café au lait* spots. She also had ocular changes with hypertelorism, eccentric pupils, keratoconus,

and Lisch nodules. The family history signified an autosomal dominant pattern of inheritance in our patient. The presence of these features qualifies the diagnosis of NF1. However, other clinical features observed in our patient are reported as rare manifestations in the literature.

Our patient presented with history of recurrent generalized tonic–clonic seizures. The prevalence of seizures in NF1 has been reported to range from 3.8 to 6%, which is much higher than that in the general population.[3] Although NF1 is a neurodevelopmental disorder with a high potential to cause subcortical focal brain lesions, in majority of patients with seizure, no significant cortical dysplasias or subcortical focal brain lesions have been identified radiographically in the NF1 population.[4] We also did not find any abnormalities in cranial CT scan in our patient.

Cognitive deficits and academic learning difficulties are the most common neurologic "complications" of NF1 in childhood.[5] Academic difficulties are common, as are specific deficits in visuospatial ability, executive function, expressive and receptive language, and attentional skills.[5] Our patient also could not continue her studies probably because of poor cognitive function.

The patient also had extradural compression of cervical spinal cord by schwannoma, manifested as quadriparesis. In NF1, spinal tumors cause neurological symptoms in 2% of cases. Kakkar *et al*. reported symptomatic spinal tumors in 23 (1.6%) patients out of over 1400 patients with NF1.[6] However, among 54 patients of NF1, aged 5–56 years, who were studied with MR imaging of spine, they reported incidences of 96% and 40% for symptomatic and asymptomatic patients, respectively.[6] In a study, Kong *et al*. reported 13.2% asymptomatic children with a mean age of 12.6 years (age range 5–18 years) to have spinal neurofibromas.[7]

Our patient also had features of peripheral neuropathy characterized by bilateral pes cavus, peroneal atrophy, abnormal tone in lower limbs and loss of ankle reflexes. This was documented by abnormal nerve conduction study. Although neurofibroma is the hallmark lesion of NF1 and develops from peripheral nerves, the clinically significant peripheral neuropathy is not common. Neurofibromatous neuropathy has been regarded as a common feature of NF2, but is an unusual and unexplained complication of NF1. In a study, Drouet *et al*. could demonstrate peripheral neuropathy by electrophysiological studies in only 2.3% of cases.[8] In another study, Ferner *et al*. reported neurofibromatous neuropathy in 1.3% of 600 patients with NF1.[9]

Our patient also had pulmonary stenosis. Cardiovascular malformations (CVMs) are known in patients of NF1. In a recently published large series, CVMs were reported in 54/2322 (2.3%) NF1 patients.[10] In this study, pulmonic stenosis was present in 25 NF1 patients (1.65%) and aortic coarctation in 5 (0.2%) patients. Together, these two malformations constituted the bulk of all CVMs observed in the series.[10]

Thus, our patient had many uncommon features suggesting multisystem involvement. Presence of any one of them is considered as a rare manifestation in a single patient. Our case had a combination of multiple uncommon features. Presence of constellation of multiple rare systemic features makes this a unique case of NF1.

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