International Journal of Neurology Sciences

ISSN Print: 2664-6161
ISSN Online: 2664-617X
IJNS 2024; 6(1): 56-58
www.neurologyjournal.in
Received: 29-03-2024
Accepted: 03-05-2024

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Navigating chronic pain in neurofibromatosis type 1: A case report

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DOI: https://doi.org/10.33545/26646161.2024.v6.i1a.27

Abstract
Neurofibromatosis Type 1 (NF1) is a genetic disorder resulting from mutations in the NF1 gene, which encodes the neurofibromin protein. This condition is characterized by the growth of benign tumors within the nervous system, alongside a range of skeletal abnormalities. Patients often present with chronic pain due to neuropathic and orthopedic sources, including neurofibromas, scoliosis, and bone deformities. A multidisciplinary approach is crucial for effective management.

We report a case of a 65-year-old female with NF1 presenting with chronic lumbar radiculopathy. Imaging revealed vertebral scalloping, neuroforaminal stenosis, and bony changes attributed to paraspinal neurofibromas. These findings highlight the dual contribution of nerve compression and skeletal remodeling to the patient's pain. The patient's unresponsiveness to gabapentin underscores the importance of differentiating neuropathic pain from orthopedic pain, necessitating targeted interventions.

Management strategies for NF1-associated pain include pharmacological treatments, such as gabapentin and tricyclic antidepressants, minimally invasive procedures like epidural steroid injections and nerve blocks, and physical therapy. Advanced imaging techniques, including MRI and PET scans, are vital for assessing neurofibromas, skeletal abnormalities, and potential malignant transformations. In refractory cases, surgical interventions, including neurofibroma excision or spinal fusion, may be considered.

This case illustrates the complexity of chronic pain in NF1, emphasizing the need for personalized, multimodal approaches. By integrating diagnostic precision, tailored pain management techniques, and supportive therapies, clinicians can enhance patients' quality of life and functionality. Early and coordinated care is essential to address the multifaceted challenges posed by this disorder.

Keywords: Chhani, consumption, fuel-wood, households, Lanchaan

Introduction
Neurofibromin type 1 (NF1) is a gene located on the long arm of chromosome 17q11.2 that encodes an intracellular protein called neurofibromin (NF) [4]. It is a cytoplasmic protein expressed in a variety of cells including osteoblasts, osteoclasts, chondrocytes, and neurons[4]. Mutations in this protein is responsible for NF1 disorder, an autosomal dominant genetic condition characterized by the growth of non-malignant tumors within the nervous system including the brain, spinal cord and nerves. Typically, patients with this disorder present with cafe-au-lait spots, intertriginous freckling, lisch nodules, neurofibromas, optic pathway gliomas, bony lesions, malignant peripheral nerve sheath tumors, neurocognitive defects, epilepsy and cardiovascular abnormalities [4].

Patients often present with chronic pain caused by the plexiform neurofibromas leading to neuropathic symptoms such as radiculopathy, numbness, burning sensations and paresthesias. As a multisystem disorder, NF1 is also a multisystem disorder, potentially affecting muscles and bones, further contributing to a patient's chronic pain [1]. Individuals with NF1 are at increased risk of developing various bone and skeletal issues, including macrocephaly, short stature, sphenoid wing dysplasia, scoliosis, congenital pseudarthrosis of long bones, a higher risk of fractures, and reduced bone mineral density (BMD) or osteoporosis [4, 5].

Materials and Methods

We report a case of a 65-year-old female with NF1 who presented to an interventional pain clinic with complaints of chronic lumbar radiculopathy. The patient complained of constant, sharp lower back pain radiating bilaterally (L>R) extending beyond the knees to the feet, worsened by flexion of the lumbar spine. MRI findings of the lumbar spine showed scalloping of the L4-L5 vertebrae, neuroforaminal stenosis and other bony changes that may contribute to the patient's lumbar axial and radicular pain. Scalloping is a common finding in NF1 patients due to the presence of paraspinal neurofibromas or skeletal remodeling from chronic stress. Scalloping at the L4-L5 level suggests that neurofibromas may be exerting pressure on the posterior vertebral bodies, which can deform the bones and contribute to neuroforaminal stenosis, leading to nerve root compression. The narrowing of the neuroforamina where nerve roots exit the spinal canal is often a source of radicular pain. In NF1, neuroforaminal stenosis may result from both bony overgrowth and neurofibroma-related expansion. This can lead to nerve compression, causing radiating pain, numbness, and sometimes weakness in the distribution of the affected nerves. Neuroforaminal stenosis at L4-L5 is consistent with this patient's symptoms, as the L4 and L5 nerve roots contribute to lower limb innervation.

Results

Although compression of nerves by neurofibromas causes chronic pain seen in NF1 patients, studies have shown that spinal deformities are one of the most common orthopedic manifestations affecting 10-33% of children with NF1 [2]. Changes may be dystrophic or nondystrophic. Generalized skeletal abnormalities include osteoporosis, osteopenia, osteomalacia and macrocephaly. Dystrophic changes include scalloping of vertebral body margins, as seen in this patient [3]. Around 10-20% of patients with NF1 have some disorder of the spine, resulting in chronic pain [3]. This case underscores the necessity of considering both neuropathic and orthopedic sources of pain in NF1. This patient failed therapy with gabapentin, indicating that the pain may not be purely neuropathic secondary to neurofibroma impingement. It is important to obtain imaging such as an MRI without contrast in order to appropriately and effectively treat the patient. In patients with NF1, one may consider minimally invasive procedures such as medial branch blocks or epidural steroid injections to alleviate both facetogenic and radicular pain sources. In patients who do not respond favorably to minimally invasive procedures, spinal surgery may be considered.

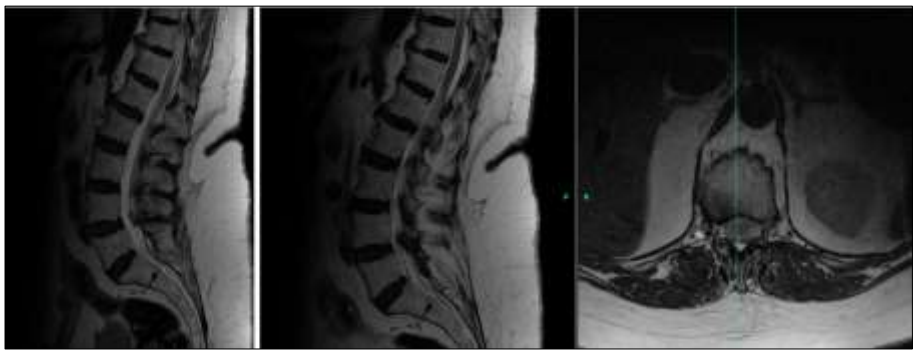

Fig 1: Lumbar spine MRI in both sagittal and axial planes of patient with NF1.

Conclusion

Chronic pain management in patients with Neurofibromatosis Type 1 (NF1) is complex and requires a multidisciplinary approach due to the multifaceted sources of pain associated with the condition. NF1 is characterized by the development of benign nerve sheath tumors (Neurofibromas) and skeletal abnormalities, both of which can contribute significantly to pain. For effective management, it's essential to differentiate between neuropathic pain from neurofibromas and pain originating from skeletal issues, as each type of pain requires distinct treatment strategies. Understanding the nature, location, and triggers of pain is crucial. Pain diaries and patient-reported outcomes can also help in tracking the pain's impact on daily life and any patterns or exacerbating factors. A thorough neurological exam can help localize neuropathic pain and evaluate for any sensory deficits, muscle weakness, or reflex changes that may indicate nerve involvement from neurofibromas. MRI is particularly useful for identifying neurofibromas along peripheral nerves and the spinal cord. Contrast-enhanced MRI can help distinguish between benign and potentially malignant peripheral nerve sheath tumors (MPNSTs) that may arise in NF1 patients. CT scans are also useful for evaluating bone abnormalities. PET scans can sometimes be used to assess the metabolic activity of lesions and may be helpful if there's concern for malignant transformation of neurofibromas. Neuropathic pain may respond to medications such as gabapentin, pregabalin, or duloxetine. Tricyclic antidepressants can also be considered for pain modulation, although they are often limited by side effects. For focal neuropathic pain due to neurofibromas, nerve blocks can provide targeted relief. These may involve local anesthetics and corticosteroids to reduce inflammation and interrupt pain signaling. RFA can be considered for specific nerves impacted by neurofibromas, especially if pain is localized and other treatments have been ineffective. This technique uses heat generated by radiofrequency energy to reduce pain signaling in the affected nerve. In some cases, surgical removal of painful neurofibromas may be warranted. This is typically considered if neurofibromas are accessible, causing significant neuropathic pain, and unlikely to regrow rapidly. However, surgery must be approached with caution due to potential nerve damage and the risk of recurrence. For pain originating from scoliosis, long bone dysplasia, or pseudarthrosis, bracing, physical therapy, and pain management are crucial.

Targeted physical therapy can help improve muscle strength, joint mobility, and posture, which can reduce pain

associated with skeletal deformities. In severe cases, corrective orthopedic surgery may be necessary to address bone deformities or instability contributing to chronic pain. Surgical fusion, for instance, may be considered in cases of severe scoliosis or pseudarthrosis. Early intervention is often beneficial for skeletal abnormalities to prevent further complications. In conclusion, chronic pain management in NF1 requires a multifaceted approach involving diagnostic clarity, targeted pain interventions, and a focus on the individual's overall quality of life. With coordinated care, many patients with NF1 can experience meaningful relief and improved functionality despite the complex challenges posed by the condition.

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