Case Report

Five Cases of Idiopathic Sciatic Mononeuropathy: Clinical, Electrophysiological, Radiological, and Histological Features

Satish Khadilkar, Saurabh Kamat[1], Narayan Deshmukh[2], Neha Shah[3], Vanaja Shetty[4], Swati Shah[5], Hiral A. Halani, Khushnuma Mansukhani[6]

Department of Neurology, Bombay Hospital and Institute of Medical Sciences, Mumbai, Maharashtra, [1]Department of Neurology, King Edward Memorial Hospital and Seth Gordhandas Sunderdas Medical College, Mumbai, Maharashtra, [2]Fellow in Interventional Neurology, Breach Candy Hospital and Research Centre, Mumbai, Maharashtra, [3]Department of Radiology, Bombay Hospital Institute of Medical Sciences, Mumbai, Maharashtra, [4]Foundation for Medical Research, Worli, Mumbai, Maharashtra, [5]Neurology Clinic and EMG Centre, Ahmedabad, Gujarat, [6]Department of Electrophysiology, Bombay Hospital and Institute of Medical Sciences, Mumbai, Maharashtra, India

Abstract

Background: Common etiologies of sciatic mononeuropathy are compressive, infiltrative, traumatic, or diabetic. However, in a proportion of patients, the etiology remains elusive despite extensive serological, electrophysiological, radiological, and histological investigations. **Methods:** Patients with unexplained sciatic mononeuropathy were studied with regard to their clinical, radiological, pathological, and treatment aspects. **Results:** We could identify five cases of sciatic mononeuropathy wherein the etiology remained unknown even after a comprehensive evaluation. The compressive, metabolic, hematological, and immune causes were ruled out with necessary investigations. The clinical, electrophysiological, radiological, and histological features of these patients are discussed. **Conclusion:** The etiology of sciatic mononeuropathy can remain obscure in certain instances in spite of the comprehensive workup. The role of investigations and the exclusion process of various diagnostic entities are discussed.

Keywords: Idiopathic, mononeuropathy, sciatic

Introduction

Slowly progressive sciatic neuropathies are known to result from compression or entrapment at predictable sites along the course of the nerve. Available studies on sciatic neuropathy are few and consist of case reports and one large study of 73 cases, of which only five patients were idiopathic sciatic neuropathy.[1,2] Some patients develop progressive sciatic neuropathy, but no etiological cause may be found after modern MRI studies and even after surgical exploration.[1-3] Such cases pose a diagnostic and therapeutic challenge; we discuss five such patients.

Objective

To describe cases with progressive sciatic mononeuropathy of unknown etiology and discuss their clinical and therapeutic aspects.

Methods: Patients with electrodiagnostically confirmed sciatic mononeuropathy were studied. The written informed consent was obtained from all the patients. The clinical and investigative details including radiological and pathological findings were documented. The response to treatment was noted on the follow-up clinical assessment in the form of improvement in motor power (in MRC Grades) and mRS scores.

Results

Clinical and demographic details are summarized in Table 1. All five patients were presented clinically with progressive sciatic mononeuropathy. In addition, two patients also had pain in the anterior and posterior compartments and soles, nonradicular in distribution, without any back pain or claudication. There was no history of any preceding illness or event in any of the patients. Patients underwent serological, electrodiagnostic, magnetic resonance neurography (MRN), and fascicular biopsies; findings are summarized in Table 1. Electrophysiology showed evidence of chronic axonal denervation with reservation in the sciatic nerve distribution in lower limbs and normal study in the upper limbs. In addition, patient 2 demonstrated evidence of mild partial conduction block at the fibular head and patient 4 demonstrated chronic axonal denervation with reinnervation in S1 >L5 root distribution. MRN was performed by acquiring multiple sequences and using contrast to characterize the mononeuropathy further. The nerve was considered to have

Address for correspondence: Dr. Satish Khadilkar, Department of Neurology, Bombay Hospital Institute of Medical Sciences, Mumbai 400 020, Maharashtra, India.
E-mail: khadilkarsatish@gmail.com

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Table 1: Demographic, clinical, electrophysiological, and histopathological features of five patients

Patient	1	2	3	4	5
Age of onset	61 years	51 years	21 years	37 years	33 years
Sex	Male	Male	Female	Male	Male
Duration	3 years	3 months	1 month	2 years	1 year
History	Painful progressive left sided foot drop with paresthesias	Painless progressive left-sided foot drop with paresthesias	Painful progressive right sided foot drop with paresthesias	Painless progressive left sided foot drop	Painless progressive thinning of left calf with inability to walk on toes
Examination	TA-2/5, Gastroc-3/5, Hamstrings-3/5	TA 0/5, Gastroc-3/5, Hamstrings-2/5	TA-2/5, Gastroc-4/5, Hamstrings-3/5	TA-1/5, Gastroc-3/5, Hamstrings-3/5	TA-4/5, Gastroc 4+/5, Hamstring-4/5
Clinical localization	Left sciatic nerve	Left sciatic nerve	Right sciatic nerve	Left sciatic nerve	Left sciatic nerve
Serological tests *	Normal	Normal	Normal	Normal	Normal
NCV EMG STUDY (Type and Localization of Neuropathy)	Axonal left sciatic sensory motor neuropathy (fibular + tibial) distal to biceps femoris short head	Axonal left sciatic neuropathy in the thigh proximal to biceps femoris short head with mild partial conduction block at fibular head	Axonal right sciatic sensory motor neuropathy in the thigh proximal to biceps femoris short head	Left S1>L5 root involvement	Axonal left sciatic sensory motor neuropathy proximal to biceps femoris
MRN	Left sciatic nerve Isointense on T1 Hyperintense on T2/ STIR Enhancement on contrast study with fascicular hypertrophy of left sciatic nerve till bifurcation	Left sciatic nerve Isointense on T1 Hyperintense on T2/STIR Enhancement on contrast study with fascicular hypertrophy left sciatic nerve, proximal common peroneal, proximal tibial nerve	Right sciatic nerve Isointense on T1 Hyperintense on T2/ STIR Enhancement on contrast study with fascicular hypertrophy Right sciatic nerve till bifurcation	Left sciatic nerve Isointense on T1 Hyperintense on T2/ STIR Enhancement on contrast study with fascicular hypertrophy left sciatic, proximal tibial, and peroneal nerves	Left sciatic nerve Hyperintense on T2/STIR Thickened, moderate enhancement on contrast study; left sciatic and proximal tibial nerves
Biopsy	Left sciatic nerve/cross section: uniform loss of fibers (>90%) and the presence of regenerating units are seen. No infiltrating cells, and no other abnormalities seen in the endo and epi-neural area	Left sciatic—total loss of myelinated fibers (100%). No regenerating fibers seen. Sparse lymphocytic infiltrate is seen around endo and epi-neural blood vessels.	Right sciatic—uniform loss of fibers (>80%) and presence of regenerating units seen. Increased vascularity seen. No infiltrating cells seen	Left sciatic—loss of fibers seen in patchy areas. (overall>50%) No regenerating fibers seen. No infiltrating cells seen.	Left sciatic—mild asymmetric, loss of large and small myelinated fibers. Occasional regenerating clusters. No infiltrating cells seen.
Treatment	Tab prednisolone 1 mg/kg for 2 months followed by taper	No steroids	Tab prednisolone 1 mg/kg for 2 months followed by taper	Tab prednisolone 1 mg/kg for 6 weeks followed by taper	None

EMG=electromyography, MRN=magnetic resonance neurography, e/o=evidence of, TA=tibialis anterior, Gastroc=gastrocnemius. *Serological tests: complete blood counts, erythrocyte sedimentation rate, fasting and post prandial blood sugars, HbA1c, liver and kidney function tests, HIV-ELISA, hepatitis C serology, HbsAg. Special investigations ANA, anti-ds DNA, ANA blot, anti-neutrophil cytoplasmic antibody (ANCA), venereal disease research laboratory (VDRL), angiotensin converting enzyme (ACE) levels, cerebrospinal fluid (CSF) study, immunofixation electrophoresis, serum light chain assay

been enlarged when it was larger than the accompanying artery.[3] MRN demonstrated abnormal hyperintense signal over long and focal segments of the sciatic nerve [Figure 1b and c]. The involved portion of nerves was enlarged and enhanced on post-gadolinium images [Figure 1a]. Fascicular biopsy was performed in all patients. On surgical exploration, no intrinsic masses or compressive lesions were detected. Histopathological examination was done using light microscopy with hematoxylin and eosin, Ziehl–Neelson, Fite Faraco, myelin stains, and others as indicated. Biopsies detected extensive nerve fiber loss with preserved perineurial structure and endoneurial cross-sectional area in all patients. There was no evidence of inflammation, granuloma, vasculitis, malignancy, or any infiltrating lesion. Regenerating units were detected in the biopsy of patient 1 [Figure 2a]. In the biopsy of patient 2, there was sparse perivascular lymphocytic infiltrate around small endoneurial and epineurial vessels [Figure 2b] and mild to moderate axon loss [Figure 2c]. All patients underwent hematological, biochemical, and immunological tests [Table 1] to look for any evidence explaining the cause for axonal sciatic mononeuropathy, which were normal. Thus, having ruled out known infectious and neoplastic conditions, patients were offered corticosteroid therapy in view of progressive deficits. Three of five patients agreed. Follow-ups ranged from 6 months to 6 years. All had objective improvement in their clinical deficit, as documented by improvement in Modified Rankin Scale [Table 2].

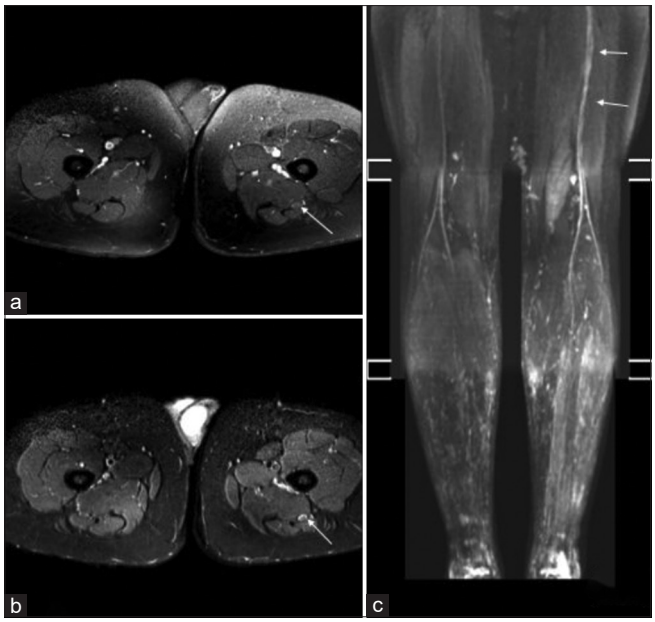

Figure 1: MR neurography of patient 1 post-contrast T1-weighted fat saturated axial (a) and STIR axial image (b) showing abnormal post-contrast enhancement within the left sciatic nerve at the level of mid-thing. (c) DWIBS image showing diffuse thickening and abnormal hyperintensity within the left sciatic nerve from origin up to its bifurcation.* STIR = short T1 inversion recovery, DWIBS = diffusion-weighted whole-body imaging with background signal suppression.

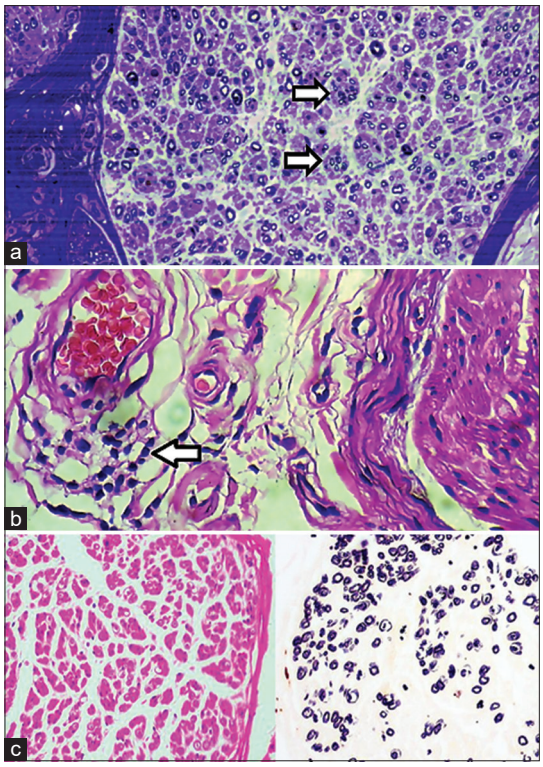

Figure 2: (a) Left sciatic nerve biopsy of patient 1 fixed in glutaraldehyde + osmium tetroxide and embedded in araldite. One micron thick semithin transverse section stained with toluidine blue showing uniform loss of over 90% of nerve fibers and presence of axonal sprouts indicating regeneration (arrows) following axonal degeneration. Perineurium appear normal (Mag X 450). (b) Left sciatic nerve biopsy of patient 2 fixed and processed glutaraldehyde + osmium tetroxide and embedded in araldite. Semithin transverse section stained with toluidine blue-showing total loss of nerve fibers. No regenerating fibers seen. Sparse lymphocytic infiltration is seen around some of the blood vessels both in the endoneurial and epineurial area (arrow). Perineurium appear normal (Mag x 120). (c) Kpal stain showing mild to moderate axon loss.

Discussion

We report observations on a short series of five patients with progressive sciatic mononeuropathy. Electrophysiology helped in localization to the sciatic nerve, and MRN characterized the extent of involvement. Fascicular root biopsy excluded infectious and infiltrative causes. Hematological and serological tests did not show any systemic conditions or any lead to vasculitis. Thus, despite extensive investigations, these patients could not be assigned to a particular disease category. The lack of a demonstrable cause in our patients raises several questions.

Could there be some occult tumor or localized inflammatory or immune pathology that was not discovered by our investigations?

Yuen and colleagues[2] reviewed 73 patients having clinical and electrophysiological features of sciatic mononeuropathy. Out of these, 12 patients had unexplained neuropathies similar to the patients in our study. The larger group of etiologies included hip fracture, dislocation or surgery, external compression or compartment syndrome, nerve infarction, post-radiation, and hip tuberculosis. In our patients, there was neither history of trauma or any surgery nor there were any compression or entrapment on MRI. The lack of evidence of vasculitis makes ischemia or infarction unlikely.

Could these cases represent unusual neuralgic amyotrophy?

Jolly *et al.*[4] in 1960, described 20 cases of a rare entity, lower limb neuralgic amyotrophy. Clinically, majority of the patients presented with painless weakness in the sciatic nerve distribution. But electrophysiological and imaging data were not described and 6 out of 12 patients who underwent nerve biopsy showed findings of demyelinating neuropathy. In a case of neuralgic amyotrophy reported by Kim DH[5], electrophysiology showed active denervation in L5-S1 roots with imaging showing gadolinium enhancement with increased intensity in L5-S1 roots. In the present study, four of five cases, clinical, electrophysiological, and imaging findings localized the pathology at the sciatic nerve. In case 1, while the hamstrings were clinically affected, electrophysiology did not pick up the changes as the changes could be mild. In case 4, however, there is discordance in electrophysiological and clinical/imaging findings. Clinical presentation was over a period of 2 years in the sciatic nerve distribution. But the electrophysiology localized it to S1 > L5 roots, and imaging showed hyperintensity and gadolinium enhancement in the sciatic nerve. There was no hyperintensity, thickening or gadolinium enhancement in L5/S1 roots, or other nerves except the sciatic nerve. Thus, while a single nerve involvement

Table 2: Follow-up clinical assessment of the patients

Patient	MRC before treatment	mRS score	MRC after treatment	mRS score
1	TA-2/5, G-3/5, H-3/5	3	TA-3+/5, G-3/5, H-4/5	2
2	TA-0/5, G-3/5, H-2/5	4	TA-3/5, G-4/5, H-4/5	2
3	TA-2/5, G-4/5, H-3/5	3	TA-5/5, G-5/5, H-5/5	0
4	TA-1/5, G-3/5, H-3/5	4	TA-4/5, G-4+/5, H-4/5	0
5	TA-4/5, G-4+/5, H-4/5	1	N/A	1
	Average mRS score	3		1

MRC=Medical Research Council's scale, mRS score=Modified Rankin Scale, TA=tibialis anterior, G=gastrocnemius, H=hamstrings

and progression over 2 years would be unusual in neuralgic amyotrophy, however, the possibility cannot be completely ruled out.

Thomas *et al*.[6] and Gross and Schwartz.[7] reported that all patients with sciatic nerve tumors had painful neuropathy. In our series, two patients had painful neuropathy, but preserved architecture on histopathology with no evidence of tumor in sciatic nerves.

Lack of conduction blocks in other nerves, normal conduction velocities and F-wave response, and no onion bulb formation on histology are features against a demyelinating process such as chronic inflammatory demyelinating polyradiculoneuropathy and multifocal motor neuropathy. Involvement of single nerve territory also makes demyelinating or vasculitis process unlikely.

Could this be an odd presentation of Hereditary Neuropathy with Liability to Pressure Palsy (HNPP)?

In HNPP, a mild demyelinating polyneuropathy is seen in clinically normal nerve segments with recurrent focal mononeuropathies and conduction blocks at entrapment sites in clinically affected nerves. None of the above findings matched our data. Also, no such previous episodes in the same or different nerve distribution, no family history, and biopsy findings not favoring HNPP make it unlikely.

Localized hypertrophic neuropathy (LHN) of the sciatic nerve is a rare condition characterized by progressive mononeuropathy. Zachary Simmons *et al*.[8] described four patients with mononeuropathies. The MRI findings similar to the present series were described, but the lack of concentric whorls of perineurial cells is an evidence against LHN.

We could find a near complete correlation between clinical, electrophysiological, and radiological findings in four out of five patients, whereas in one patient (case 4), electrophysiological localization did not match. All patients had hyperintensity with gadolinium enhancement along the sciatic nerve. Thus, MRN helped in localizing the pathology to the sciatic nerve in all cases. As the workup had excluded infections, infiltrations, and neoplasia, we discussed and offered corticosteroid therapy to patients, and three patients opted for therapy. Follow-ups showed improvement in mRS raising the possibility of an inflammatory or immune process, which is not identified. Two patients did not opt for corticosteroid therapy, and one of them still showed improvement. This would argue for a naturally limiting disease process and is open to further observations.

Thus, progressive sciatic mononeuropathies can be puzzling in some patients. Modern methods of investigation like MRN help the evaluation. The advantages of MRN include a detailed anatomic depiction of the deeply seated sciatic nerve, assessment of pathological segment of the nerve, localization of any injury or entrapment, demonstration of any extrinsic or intrinsic masses, and regional denervation changes supporting the diagnosis of sciatic neuropathy. In such cases, a tissue diagnosis becomes important to look for infective, inflammatory or infiltrative diseases, but none may be discovered. If in spite of such extensive evaluation, when a specific disease category cannot be identified, a trial of corticosteroids may be carefully considered.

Conclusion

The etiology of progressive sciatic mononeuropathy remains elusive in a small number of patients. MRN helps in the localization and exclusion of common etiological diagnoses of sciatic mononeuropathy. Long-term follow-up of a larger cohort of such patients may shed more light on the diagnostic and therapeutic possibilities.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients 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.

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Conflicts of interest

There are no conflicts of interest.

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