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BRIEF REPORT

Neuropathy in the Hemodialysis Population: A Review of Neurophysiology Referrals in a Tertiary Center

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Abstract

This was a retrospective observational study of neurophysiology referrals over 8 years from a tertiary referral center in Ireland. A total of 68 of the 73 referrals yielded one or more abnormalities. Thirty-nine (53%) patients had one or more mononeuropathies; iatrogenic mononeuropathies believed to be associated with arterio-venous fistula creation occurred in 15 patients. Polyneuropathy was identified in 43 patients (59%). Access to an experienced neurophysiology department offers valuable insight into dialysis-associated neuropathies, especially when associated with arterio-venous fistulae.

Keywords: arterio-venous fistula, hemodialysis, mononeuropathy, neuropathy, ischemic monomelic mononeuropathy

INTRODUCTION

Metabolic complications of end-stage renal failure, its management, and the presence of comorbid conditions frequently give rise to neuropathic complications in the hemodialysis population.[1–4] The characteristic polyneuropathy observed in dialysis patients is presumed to be uremic in etiology. The principal neurophysiological and histopathological abnormality is an axonal polyneuropathy with secondary segmental demyelination.[5] Inhibition of neurotrophic enzymes by circulating toxins,[6] alterations in endoneural barrier function, and dysfunction of axonal membrane Na^+/K^+ ATPase have all been described.[7] Our aim was to retrospectively document the pattern of electrodiagnostic studies identified in symptomatic patients on maintenance hemodialysis.

METHODS

We reviewed all electrodiagnostic studies from two dialysis units catering for a population of approximately 663,000 people for 8 years between 1 January 2003 and 31 December 2010, during which time approximately 600 patients received maintenance hemodialysis for end-stage renal failure. All studies were performed by a single neurophysiologist (BMcN). All patients had nerve conduction studies with more extensive testing including electromyography (EMG) being performed where necessary. Ethical approval was obtained from the local Medical Ethics Committee.

RESULTS

Seventy-eight patients were referred during the study period. We excluded five patients who had a successful working transplant at the time of referral and were no longer representative of the hemodialysis population. A total of 98 studies were performed on the 73 remaining patients; only 5 had a normal study.

Mononeuropathies

A total of 39 of the 73 patients (53%) referred were diagnosed with one or more mononeuropathies; 14 were unifocal and 25 were multifocal (Table 1). These consisted of 34 median nerve compression neuropathies at

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Table 1. Mononeuropathies identified by nerve conduction studies.

Diagnosis	N^a (%)
Carpal tunnel syndrome	20 (51.2)
Unilateral	6 (15.3)
Bilateral	14 (35.8)
Median cutaneous nerve of forearm	6 (15.3)
Median nerve mononeuropathy	7 (17.9)
Ulnar entrapment neuropathy	7 (17.9)
Unilateral	5 (12.8)
Bilateral	2 (5.1)
Ischemic monomelic mononeuropathy	3 (7.6)
Miscellaneous	3 (7.6)
Total number of patients	39 (100)

Note: [a]Some subjects had multiple mononeuropathies.

the wrist or carpal tunnel syndrome (CTS), 14 of which were bilateral.

Five patients had unilateral mononeuropathies of the median cutaneous nerve of the forearm, all of whom had recent fistula formation. Two of these patients had a brachial–basilic transposition, and it was noted that the surgical scar ran close to the course of the median cutaneous nerve. The remaining three had brachiocephalic fistulas in the antecubital fossa.

Six patients had median nerve lesions localized to the elbow, four of whom had recent fistula formation at the elbow. The other two had later complications of established fistulas: one neurapraxia following resection of a brachial artery aneurysm and the other following cannulation of the fistula during dialysis.

Eight ulnar entrapment neuropathies at the elbow were diagnosed in six patients, two being bilateral.

In addition to the above neuropathies, one patient had a compressive neurapraxia of the median nerve, median and lateral cutaneous nerves of forearm, and ulnar nerve following hemorrhagic complications of arterio-venous fistula surgery (this patient's mononeuropathies are shown in Table 1).

Three patients from the study who were found to have multiple mononeuropathies affecting a single limb (the fistula limb) were diagnosed with an ischemic monomelic mononeuropathy, one of which has been previously reported in the literature.[8] Two of these were female.

Regarding the remaining mononeuropathies, one with a diagnosis of polyarteritis nodosa had a pattern of neuropathy that was felt to be consistent with a mononeuritis multiplex and another patient had a common peroneal neuropathy.

Furthermore, two of the five patients in the study with normal nerve conduction studies presented with a short history of symptoms that suggested a secondary median neuropathy due to a steal effect from a newly fashioned brachiocephalic fistula although nerve conduction studies were normal. The fistula was ligated with rapid resolution of symptoms in both cases.

Polyneuropathies

A total of 43 of the 73 patients were found to have a polyneuropathy. Forty-one were axonal sensorimotor polyneuropathies and the remaining two patients were diagnosed with demyelinating polyneuropathies based on typical neurophysiological abnormalities; one patient was diagnosed with hereditary motor-sensory neuropathy and the other with chronic inflammatory demyelinating polyneuropathy. None of these patients had a nerve biopsy.

Of the 41 patients, 35 (85%) had vitamin B_{12} and folate levels checked, 19 (46%) had serum protein electrophoresis performed, and 28 (68%) had thyroid function tests checked. All values were within normal limits apart from the serum protein electrophoresis and paraprotein titer in four patients with multiple myeloma and one patient who was followed up for a monoclonal gammopathy of undetermined significance.

Eighteen patients had no other cause for neuropathy established and were therefore presumed to be related to the retention of neurotoxic molecules, that is, considered uremic in etiology.

One patient's polyneuropathy was in the setting of a prolonged intensive care stay and together with EMG findings was consistent with a critical illness polyneuropathy.

Four patients had received chemotherapy (bortezomib and/or thalidomide) for treatment of multiple myeloma although biopsies were not performed to rule out a primary amyloid neuropathy. Another patient was diagnosed with primary amyloidosis.

A total of 17 of 18 patients in the study with a diagnosis of diabetes mellitus had a distal sensorimotor axonal polyneuropathy.

Plexopathies, Polyradiculopathy, and Others

One patient had a lumbosacral plexopathy. Three patients had a lumbosacral polyradiculopathy based on EMG findings, one being bilateral. One of these had nerve conduction studies suggestive of a background axonal sensorimotor polyneuropathy; another had bilateral reduction in common peroneal motor amplitudes on nerve conduction studies with a bilateral lumbosacral polyradiculopathy. The third had normal nerve conduction studies.

One patient was found to have bilateral Martin Gruber anastomoses identified on nerve conduction studies.

DISCUSSION

This study describes the wide spectrum of neuropathies that may complicate maintenance hemodialysis. We considered over 70 referrals and we found only 5 with a normal study. The most frequent nerve conduction abnormality observed was the symmetrical, length-dependent axonal sensorimotor polyneuropathy. This can often occur subclinically, as has been previously described.[9] The two most frequent attributed

causes identified were uremic polyneuropathy and diabetes mellitus. Despite these patients having existing risk factors, screening blood tests for secondary causes of neuropathy should always be performed where abnormalities are identified.

The increased liability of patients receiving maintenance hemodialysis who develop mononeuropathies has been described in the literature.[10] CTS is found commonly in the dialysis population, and some investigations suggest that it increases in incidence with duration of renal replacement therapy.[11–13] It has been hypothesized that the deposition of B_2-microglobulin within the carpal tunnel may account for this.[1] A postoperative study of tissue samples from patients undergoing decompression has revealed cases both with and without evidence of amyloid deposition.[14] It has been suggested that the median nerve at the wrist is vulnerable to pressure from aneurysmal vessels or venous congestion and is susceptible to ischemia in the carpal tunnel.[15] In addition to the above-described iatrogenic mononeuropathies (see Results section), our analysis revealed three patients, each with a newly formed radio-cephalic fistula, who presented with symptoms and who were each found to have an ipsilateral median nerve mononeuropathy at the wrist (CTS), which suggested a relationship. However, recent studies offer conflicting evidence and suggest that no difference in the frequency of CTS occurs with either the duration of dialysis or the side of the arterio-venous fistula.[16] Some authors have investigated nerve conduction study methods that demonstrate reliability in distinguishing CTS from background polyneuropathy.[17]

We identified a greater than anticipated number of iatrogenic neuropathies. Of the 39 patients with a mononeuropathy, 15 patients (38.4%) had their mononeuropathy attributable to the complications of vascular access surgery. An ischemic steal effect has been proposed as a result of fistula formation.[18] Diabetes mellitus is recognized as the predominant risk factor for the development of upper limb neuropathy and ischemia post vascular access due presumably to preexisting neuropathy or calcific atherosclerosis but we found it in only 4 of the 15 (26.6%) patients with mononeuropathies following arterio-venous fistula formation in our study. Ischemic monomelic mononeuropathy, identified in three patients, is a rare complication affecting a fistula limb requiring urgent closure of the fistula for recovery.[19,20] It most commonly occurs in patients with diabetes mellitus[21]; in our study two patients with ischemic monomelic mononeuropathy had diabetes.

The nephrology community increasingly highlights the need to improve fistula rates and to utilize the predialysis period as a time to provide patients, where possible, with a working arterio-venous fistula by their expected commencement of maintenance hemodialysis. Cases such as ischemic monomelic neuropathy and the high frequency of other abnormal studies emphasize the importance of immediate access to an experienced neurophysiology department for renal patients who have a fashioned fistula. Physicians treating these patients should have a low threshold for referral for investigation of symptoms associated with vascular access surgery that may be treatable if recognized early.

***Declaration of interest*:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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