Spinal root and plexus hypertrophy in chronic inflammatory demyelinating polyneuropathy


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Summary

MRI was performed on the spinal roots, brachial and lumbar plexuses of 14 patients with chronic inflammatory demyelinating polyneuropathy (CIDP). Hypertrophy of cervical roots and brachial plexus was demonstrated in eight cases, six of whom also had hypertrophy of the lumbar plexus. Of 11 patients who received gadolinium, five of six cases with hypertrophy and one of five without hypertrophy demonstrated enhancement. All patients with hypertrophy had a relapsing–remitting course and a significantly longer disease duration. Gross onion-bulb formations were seen in a biopsy of nerve from the brachial plexus in one case with clinically evident nodular hypertrophy. We conclude that spinal root and plexus hypertrophy may be seen on MRI, particularly in cases of CIDP of long duration, and gadolinium enhancement may be present in active disease.

Keywords: chronic inflammatory demyelinating polyneuropathy; magnetic resonance imaging; spinal root hypertrophy; brachial and lumbar plexus hypertrophy; demyelination

Abbreviations: CIDP = chronic inflammatory demyelinating polyneuropathy; EAN = experimental allergic neuritis; Gd = gadolinium

Introduction

Abnormal enhancement of the cauda equina and spinal roots has been demonstrated on MRI after administration of gadolinium (Gd) in Guillain–Barré syndrome (Crino et al., 1994; Gorson et al., 1996) and chronic inflammatory demyelinating polyneuropathy (CIDP) (Crino et al., 1993; Morgan et al., 1993; Midroni and Dyck, 1996; Mizuno et al., 1998). Hypertrophic lumbar spinal roots and cauda equina have been demonstrated in some patients (De Silva et al., 1994; Ginsberg et al., 1995; Midroni and Dyck, 1996; Schady et al., 1996; Mizuno et al., 1998), in some of whom the symptoms mimicked spinal stenosis (Ginsberg et al., 1995; Schady et al., 1996). Hypertrophy of cervical roots (Midroni and Dyck, 1996; Schady et al., 1996) and the brachial plexus (Van Es et al., 1997) has been less commonly described.

The present study was prompted by the observation of a patient with an 18-year history of relapsing–remitting CIDP, developing nodular swellings in the neck and supraclavicular fossae, with MRI features of massive nodular hypertrophy of the brachial plexus, cervical roots and cauda equina. Since previous studies have been on small numbers of patients, we performed MRI on brachial and lumbar plexuses of 13 other patients with CIDP to ascertain the frequency of these abnormalities, whether they were correlated with any clinical features, and the value of MRI in diagnosis.

Patients and methods

Patients

Fourteen consecutive patients (10 males and four females, aged between 20 and 79 years) attending the Neuromuscular Clinic at the Royal Prince Alfred Hospital agreed to have MRI performed. All patients conformed to the clinical and neurophysiological criteria for CIDP (Ad Hoc Subcommittee, 1991). Ten patients had previously undergone sural nerve biopsy. Disease duration at the time of MRI ranged from 3 months to 34 years (mean 11.6, SD ± 12). Eleven patients had a relapsing–remitting form of the disease and three patients had progressive disease that was steroid-dependent. All patients could walk without assistance at the time of their scan.

MRI

Coronal and axial fast spin echo T2-weighted images and coronal T1-weighted images were acquired through the cervical and lumbar plexuses of all patients. Gd was administered in all but three cases (cases 3, 7 and 10). A 1.5 Tesla (General Electric Signa) MRI system was used for 10 patients and a 0.5 Tesla system (General Electric Vectra) for four cases (cases 5, 7, 8 and 10). Two neuroradiologists,
Results

Clinical features and MRI findings

The relevant clinical data and results of investigations of all patients are summarized in Table 1.

All patients satisfied the clinical and neurophysiological criteria for the diagnosis of CIDP (Ad Hoc Subcommittee, 1991). Onion bulb formations were noted on sural nerve biopsy in cases 1, 2 and 4 and were also seen in the biopsy from the brachial plexus in case 1. Two cases (cases 3 and 5) with hypertrophy had evidence of demyelination in the nerve biopsy but in case 8 the changes were predominantly those of axonal degeneration and were not diagnostic of CIDP.

Hypertrophy of both spinal roots and plexuses was demonstrated on MRI in eight cases (cases 1–8). In most cases there was hypertrophy of the brachial plexus, cauda equina, spinal roots and lumbosacral plexus. In two cases the plexus hypertrophy was extreme. In cases 3 and 7 hypertrophy was noted only in the brachial plexus. Of the six patients with spinal root and plexus hypertrophy to whom Gd was administered (cases 1, 2, 4–6), five demonstrated enhancement, although in some cases this was mild. In case 9, in whom there was no spinal root or plexus hypertrophy, Gd enhancement of the cauda equina was noted. There was interobserver agreement on the findings.

Cases with hypertrophy had a significantly longer duration of disease (mean 15.9 years, SD = 14.0 years) than those without (mean 3.3 years, SD = 1.7 years) (P = 0.05, Wilcoxon rank sum test), but there was no clear relationship between hypertrophy and patient age, sex, time from last relapse, current therapy or disability. All patients with hypertrophy had a relapsing–remitting course, whereas three patients without hypertrophy had a progressive course. However, because the number of progressive cases studied was small this relationship cannot be considered as established.

There was no clear relationship between known activity of disease and Gd enhancement. All patients were being treated at the time that MRI was performed.

Illustrative case histories

Case 1

Female, aged 51 years, first presented at the age of 31 years, when, in the late stages of her third pregnancy, she developed pain in both legs that lasted for about a week; following prolonged labour she developed generalized weakness of the legs with inability to run or to go up stairs. Improvement followed but during her fourth pregnancy she had a recurrence of symptoms. Electrophysiological studies and nerve biopsy (Fig. 1) confirmed the diagnosis of CIDP. She subsequently had many relapses which responded to plasma exchange, but she had no benefit from prednisone, azathioprine, cyclophosphamide or intravenous immunoglobulin. Over a period of 19 years she has been maintained on weekly plasma exchange and cyclosporin and, more recently, methotrexate. At the age of 48 years she developed swellings in the neck due to nodular enlargements of nerves in the posterior triangle and supraclavicular fossa (Fig. 2). On examination she walked without assistance. There was mild distal and proximal weakness. Tendon reflexes were absent. There was impairment of light touch and painful sensation distally. A chest X-ray revealed bilateral, well demarcated apical extrapleural masses (Fig. 3). MRI demonstrated enlargement of components of the brachial plexus, cauda equina and spinal roots (Fig. 4). The brachial plexus and cauda equina enhanced with Gd. Biopsy of a nodular mass in the neck showed large onion-bulb formations and 60% of teased fibres showed segmental demyelination (Fig. 5). There has been no improvement in the neck swelling following treatment for 2 years with methotrexate and weekly plasma exchange.

Case 2

Female, aged 42 years, presented at the age of 19 years with an acute onset of demyelinating polynuropathy requiring treatment with tracheostomy and ventilation for three weeks. She remained in hospital for 2.5 months and then returned to work after 18 months with residual numbness in the hands and feet. A relapse followed smallpox vaccination 3 years later and she was readmitted to hospital, where neurophysiological studies and nerve biopsy confirmed the diagnosis of CIDP. She was treated with prednisone and improved. She represented at age 42 years, having developed a hand tremor ~5 years previously; in the past 6 months she had poor balance, increasing tremor and a tendency to fall. On examination there was a slow action tremor of the hands, distal wasting and weakness of the lower limbs, absent reflexes and impaired light touch and painful sensation distally in the lower limbs. Vibration sense was impaired at the toes; position sense was intact. Nerve conduction studies showed marked slowing of conduction and conduction block. She responded well to treatment with plasma exchange and prednisone. Plasma exchange was initially weekly for 4 weeks; the intervals then increased to 3 weeks and 6 weeks and finally stopped after a period of 5 months. She continued on prednisone in reducing doses for 1 year. MRI at the second presentation demonstrated hypertrophy of the brachial plexus and cauda equina; there was slight enhancement with Gd.

Case 5

Male, aged 46 years, initially presented in 1978 at age 27 years with progressive paraesthesiae in hands and feet, and distal limb weakness. Nerve conduction studies and sural nerve biopsy confirmed a diagnosis of CIDP. He was treated with oral corticosteroids and went into remission until January
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<th>Clinical type</th>
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A = axonal degeneration; Az = azathioprine; BP = brachial plexus; CE = cauda equina; CsA = cyclosporin A; D = demyelination; Gd = gadolinium; IVIg = intravenous immunoglobulin; LSP = lumbosacral plexus; MTX = methotrexate; OB = onion-bulb formations; P = progressive; PE = plasma exchange; Pred = prednisone; R = relapsing–remitting. Disability score (Prineas and McLeod, 1976): 0 = normal; 1 = signs but no symptoms or vice versa; 2 = mild motor and sensory symptoms with signs; 3 = moderately disabled by motor or sensory symptoms including ataxia; 4 = requiring assistance eating, dressing or using a walking aid; 5 = not ambulant. *+ = is indicative of demyelination.
1995, when he had recurrence of numbness of face, hands and feet followed by weakness of all four limbs and bilateral foot-drop. On examination there was distal muscle wasting, mild proximal and more pronounced distal muscle weakness, absent tendon reflexes and impairment of light touch and pain sensation distally in upper and lower limbs; vibration sense was impaired at the toes. MRI demonstrated massive enlargement of the brachial plexus, cauda equina and lumbosacral plexus (Fig. 6). He failed to respond to treatment with oral corticosteroids, azathioprine, plasma exchange or intravenous immunoglobulin, and was treated with cyclosporin for 1 year. There was little improvement, but his condition has remained stable.

Fig. 1 Case 1. Sural nerve biopsy in 1983. There is a reduction in nerve fibre density, several thinly myelinated fibres in early onion-bulb formations (long arrows) and occasional naked axons (short arrows). Toluidine blue. Scale bar = 10 µm.

Fig. 2 Case 1. Nodular swellings in the neck (arrows) in 1996.

Fig. 3 Case 1. Chest X-ray shows bilateral symmetrical apical extrapleural masses (arrows).
Fig. 4 Case 1. Coronal fast spin echo T2-weighted MRI of the neck reveals extensive hyperintense nodular masses along the cervical ventral rami and brachial plexus bilaterally (black arrows). Nodules protrude into the lung apices resulting in the appearance of apical pleural masses on the chest X-ray (white arrows).

Fig. 5 Case 1. Biopsy of nerve from brachial plexus in 1996. The specimen consists largely of massive onion bulbs (long arrows). Increased numbers of mononuclear cells (short arrows) are evident throughout the section. Toluidine blue. Scale bar = 10 μm.
Abnormal Gd enhancement of the cauda equina and spinal roots has been reported in Guillain–Barré syndrome (Crino et al., 1994; Gorson et al., 1996) and some but not all cases of CIDP (Crino et al., 1993; Ginsberg et al., 1995; Midroni and Dyck, 1996; Schady et al., 1996; Mizuno et al., 1998). Hypertrophy of the lumbar spinal roots has been demonstrated on myelography and MRI in patients with CIDP, and in some cases has been associated with symptoms of spinal canal stenosis (De Silva et al., 1994; Ginsberg et al., 1995; Midroni and Dyck, 1996; Schady et al., 1996; Mizuno et al., 1998). There have been fewer reports of hypertrophy of the cervical roots (Midroni and Dyck, 1996; Schady et al., 1996). Increased signal intensity on T2-weighted images consistent with inflammation or hypertrophy of the brachial plexus has been observed in three of five cases of CIDP and two patients with multifocal motor neuropathy (Van Es et al., 1997). Brachial plexus hypertrophy has also been described on CT scan in a case of CIDP (Midroni and Dyck, 1996).

In only one of our cases (case 1) and in four other reported cases (Schady et al., 1996; Mizuno et al., 1998) was nerve hypertrophy clinically apparent. Case 1 was considered to have radiological appearances of neurofibromatosis, and this was also the radiological diagnosis in another reported case (De Silva et al., 1994).

All our patients with spinal root and plexus hypertrophy had a relapsing–remitting course and a significantly longer duration of disease than those without hypertrophy. Some other reported cases (De Silva et al., 1994; Ginsberg et al., 1995; Schady et al., 1996), but not all of them (Mizuno et al., 1998), had a long duration of disease. There was no clear relationship between spinal root and plexus hypertrophy on MRI and the patients’ age, sex, time from last relapse, type of therapy or disability status. The level of CSF protein was raised, as is almost always the case in CIDP, but there was no significant difference in level between those with and those without hypertrophy.

There was a tendency for spinal root hypertrophy to be present in patients with marked slowing of motor conduction velocity in peripheral nerves (e.g. cases 1 and 5). This correlation has also been noted by others (Schady et al., 1996) and may suggest that hypertrophic changes, when present, are widespread in the peripheral nervous system. Tremor was also present in several of our cases, a clinical feature sometimes associated with marked slowing of motor conduction.

Biopsy of the clinically enlarged nodular brachial plexus in case 1 showed frequent large onion-bulb formations. Similar findings have been noted in lumbar spinal roots (Matsuda et al., 1996; Midroni and Dyck, 1996; Schady et al., 1996). It is likely that the hypertrophy visible on MRI is caused by demyelination and remyelination, with Schwann cell proliferation and onion-bulb formation leading to increased nerve volume. Gd enhancement may occasionally provide additional information about the presence of active disease in these cases when hypertrophy is not detected. The increased signal intensity on T2-weighted sequences and the

**Fig. 6** Case 5. Coronal fast spin echo T2-weighted MRI of the lumbosacral region demonstrates enlargement of spinal roots in the lower spinal canal. The lumbar and sacral ventral rami are massively enlarged (arrows).

**Case 6**

Female, aged 22 years, presented at the age of 19 years with weakness of the hands 7 days after an attack of chickenpox. Weakness of upper and lower limbs progressed over a period of 3 weeks. On examination she had difficulty walking, and there was moderate proximal and distal weakness, absent reflexes, decreased light touch and painful sensation in a glove-and-stocking distribution. CSF protein was 0.8 g/l. Nerve conduction studies supported a diagnosis of Guillain–Barré syndrome; she was treated with plasma exchange and made a good recovery. However, 3 months later she had a relapse and again responded to plasma exchange. Two months later she had another relapse, and went into remission following intravenous immunoglobulin therapy. MRI revealed enlarged enhancing cervical ventral rami (Fig. 7). She was maintained on prednisone and azathioprine for 2 years, and after this treatment was stopped she had a further relapse which remitted following another course of intravenous immunoglobulin.

**Discussion**

In 14 cases of CIDP (10 males, four females) eight cases (57%) had MRI evidence of hypertrophy of the cervical roots and brachial plexus, and of these, six cases also had hypertrophy of the cauda equina. There was Gd enhancement in five of six cases with hypertrophy but there was no enhancement in the four of five cases without hypertrophy to whom Gd was administered.
variable contrast enhancement of roots and nerve trunks reflect increased water content within the nerve fascicles and breakdown of the blood–nerve barrier (Crino et al., 1994; De Silva et al., 1994; Kuwabara et al., 1997). Kuwabara and colleagues (Kuwabara et al., 1997) performed MRI on peripheral nerve trunks in 10 patients with CIDP and found a correlation between the site of conduction block and nerve hypertrophy seen on T2- and proton-weighted images on MRI; in four patients there was Gd enhancement of the enlarged segment during relapses or active progression.

From this study it is evident that hypertrophic changes in the spinal roots are a common finding in CIDP and may relate to breakdown of the blood–nerve barrier in this region, similar to that seen in nerve trunks (Kuwabara et al., 1997). The continuing demyelination and remyelination that follows results in nerve hypertrophy. The frequency of hypertrophy in the region of the spinal roots (57% in this series) is striking. It is consistent with the hypothesis that antibody or some other circulating factor is involved in the process of demyelination, since the blood–nerve barrier is known to be deficient in this region (Thomas et al., 1993). A similar finding has been demonstrated in the animal model of CIDP, chronic experimental allergic neuritis (EAN) in the rabbit, in which high levels of circulating antimyelin (antigalactocerebroside) antibody are present, and there are marked hypertrophic changes in the spinal roots, but not within peripheral nerves (Harvey et al., 1987). Adam and co-workers (Adam et al., 1989) also found prominent onion-bulb formation in the dorsal roots of rats with chronic EAN.

References


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