

Clinical neuroimaging

Massive peripheral nerve hypertrophy in a patient with multifocal upper limb demyelinating neuropathy (Lewis-Sumner syndrome)

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Introduction

Some peripheral neuropathies, demyelinating hereditary motor and sensory neuropathies and chronic inflammatory demyelinating polyneuropathy (CIDP) in particular, are associated with hypertrophy of peripheral nerves. We report a patient who developed recurrent cranial and peripheral nerve palsies, spontaneously relapsing and remitting, associated with clinically obvious hypertrophy of the brachial plexus and ulnar nerves. Electrodiagnostic studies were characteristic of multifocal upper limb demyelinating neuropathy (Lewis-Sumner syndrome), a variant of CIDP. Magnetic resonance imaging (MRI) displayed marked, asymmetric enlargement of several peripheral nerves, including the brachial plexuses and the ulnar and median nerves.

Case Report

In February 1997, a 25-year-old female teacher complained of diffuse paresthesias in both hands and arms and of slight weakness in the left hand, which had gradually increased over a ten month period. At that time, there was mild weakness of grip strength in the left hand. Electrodiagnostic studies showed bilateral ulnar neuropathy with motor conduction block in the elbow area, more marked on the right side. Cervical spine MRI was normal. Personal and family histories were non-contributive. On September 28 1997, the patient was subfebrile (37.8°C) and presented with vomiting and diarrhea. Three days later, she described difficulties to move the tongue and to speak and eat. At that time, she was still complaining of paresthesias in both hands. On neurological examination on October 6, deep tendon reflexes were decreased in both arms and the left leg, but they were normal in the right leg. Plantar reflexes were flexor. The motor and sensory examination was normal, but cranial nerve examination revealed a right-sided XIIth cranial nerve palsy. Blood and spinal fluid examination were normal as was con-

trast-enhanced MRI of the brain. The XIIth cranial nerve palsy spontaneously disappeared within a few days.

In February 1998, a few days after a viral pharyngitis episode, the patient became hoarse. Ear, nose, and throat examination showed a left vocal cord paralysis. Neurological examination was unremarkable except for dysphonia. Blood and spinal fluid examination and brain MRI were again normal. The symptoms and signs disappeared within a few days.

In February 2000, the patient presented with recurrence of dysphonia and the clinical examination revealed a right-sided Xth cranial nerve with right vocal cord paralysis. At that time, she was still complaining of numbness and tingling in both hands, especially in the little and ring fingers and in both thumbs. She also had weakness in both hands with difficulties to manipulate small objects. On neurological examination, walking was normal. Cranial nerves were normal except for the right vocal cord palsy. There was distal upper extremity weakness, involving muscles innervated by the ulnar nerves (MRC grade : 3/5) and to a lesser extent the median nerves (MRC grade : 4/5). Muscle strength was normal in the lower limbs. The flexor carpi ulnaris reflexes were absent and the brachioradialis and biceps brachii reflexes were reduced. Triceps brachii and patellar reflexes were normal but somewhat brisker on the left side. Plantar responses were flexor. Touch, temperature, and pain sensation were bilaterally reduced in the ulnar nerve distribution. On palpation, marked hypertrophy of the ulnar nerves was found in the nerve segment between the axilla and the elbow above the ulnar groove. Over a distance of 7-8 cm, the nerves were pencil-thick and wood-hard. In the left supraclavicular region, an induration was noted. Palpation of this induration provoked severe lancinating pain in the ulnar nerve dermatomal distribution. The dysphonia gradually resolved and improvement of hand weakness occurred. Up to the present day, the neurological condition of the patients remains stable.

Table 1

Nerve conduction study results. IM : internal malleolus ; BUG, AUG : below, above ulnar groove ; BFH, AFH : below, above fibular head ; PF : popliteal fossa ; CV : conduction velocity ; APB : abductor pollicis brevis ; ADM : abductor digiti minimi ; EI : extensor indicis ; EDB : extensor digitorum brevis ; AH : abductor hallucis ; NR : no response. Negative peak area []. Segmental conduction velocity { }. Normal values between brackets. Abnormal results are bold printed.

Sensory nerve	Amplitude (µV)		CV (m/sec)		Peak latency (msec)	
	R	L	R	L	R	L
Median	NR	13.0 (>20)	–	–	–	3.7 (< 3.5)
Ulnar	NR	9.9 (>17)	–	–	–	4.1 (< 3.1)
Radial	63.7	31.0 (>20)	67	53 (> 58)	2.6	2.4 (< 2.7)
Sural	17.5 (> 6)				3.5 (< 4.4)	
Motor nerve	Amplitude (mV)		CV (m/sec)		Latency (msec)	
	R	L	R	L	R	L
Median (APB)						
wrist	1.1 [5.8]	5.5 [17] (> 4.0)			5.4	4.6 (< 4.4)
elbow	0.4 [2.1]	2.6 [16]	7	35 (> 49)	31.0	9.7
F					NR	51.3 (< 32)
Ulnar (ADM)						
wrist	5.0 [25.7]	6.0 [24] (> 6.6)			4.1	4.2 (< 3.3)
BUG	1.6 [7.8]	4.2 [19]	28	58 (> 49)	10.6	7.1
AUG	1.6 [7.8]	2.4 [19]	30 {38}	48 {31}	12.7	9.5
Axilla	1.2 [5.1]	1.3 [17]	7 {3}	9 {3}	58.8	45.2
Erb	1.0 [5.1]	1.3 [11]	10 {43}	12 {29}	63.7	53.2
F					NR	NR
Radial (EI)						
Elbow	10.5 (> 4.0)				1.9 (< 3.9)	
spiral groove	10.3		70 (> 52)		3.9	
Peroneal (EDB)						
ankle	10.1 (> 2.0)				3.9 (< 6.5)	
BFH	10.0		51 (> 44)		9.0	
AFH	9.7		53		10.5	
F					40.0 (< 56)	
Tibial (AH)						
IM	13.7 (> 4.0)				4.8 (< 5.8)	
PF	13.5		51 (> 42)		10.7	
F					41.0-44.0 (< 56)	

Routine hemogram, blood chemistry, serum protein electrophoresis, and auto-immune serology were normal. There were no anti GM1 antibodies. No deletion was found in the *PMP22* gene. Spinal fluid examination was normal with a protein level at 34 mg/dl (normal values < 55).

Electrodiagnostic studies (Table 1)

On nerve conduction study, the sensory nerve action potential (SNAP) of the median and ulnar nerves was absent on the right and reduced in amplitude on the left ; the sensory distal latency of both nerves were prolonged on the left side. Radial and sural nerve SNAPs and distal latencies were normal. The amplitude of the compound muscle action potential (CMAP) of the right median nerve was significantly reduced and a partial motor conduction block was observed in the elbow to wrist segment, where the motor conduction velocity was extremely slow (7 m/sec). Partial motor conduction block was also noted in the elbow to wrist segment of the right ulnar nerve. Motor conduction velocity

was slowed in both ulnar nerves, especially in the axilla to elbow segment (3 m/sec), corresponding to the hypertrophic nerve segments. Motor conduction was normal in the radial, peroneal, and posterior tibial nerves. Electromyography showed evidence of chronic denervation only in muscles innervated by the ulnar nerves. These findings were indicative of chronic, multifocal, upper limb demyelinating neuropathy, affecting the median and ulnar nerves, right more than left.

Neuroimaging (Figure 1-3)

MRI showed considerable hypertrophy of the brachial nerves from the brachial plexus level down to the peripheral nerves at the wrist. Massive enlargement was multifocal and irregular and clearly asymmetric. The left brachial plexus was much more involved as was the right median nerve. Only very slight enhancement of enlarged nerves was obtained after intravenous perfusion with gadolinium. MRI of the lumbosacral plexuses, the cranial nerves, and the brain was normal.

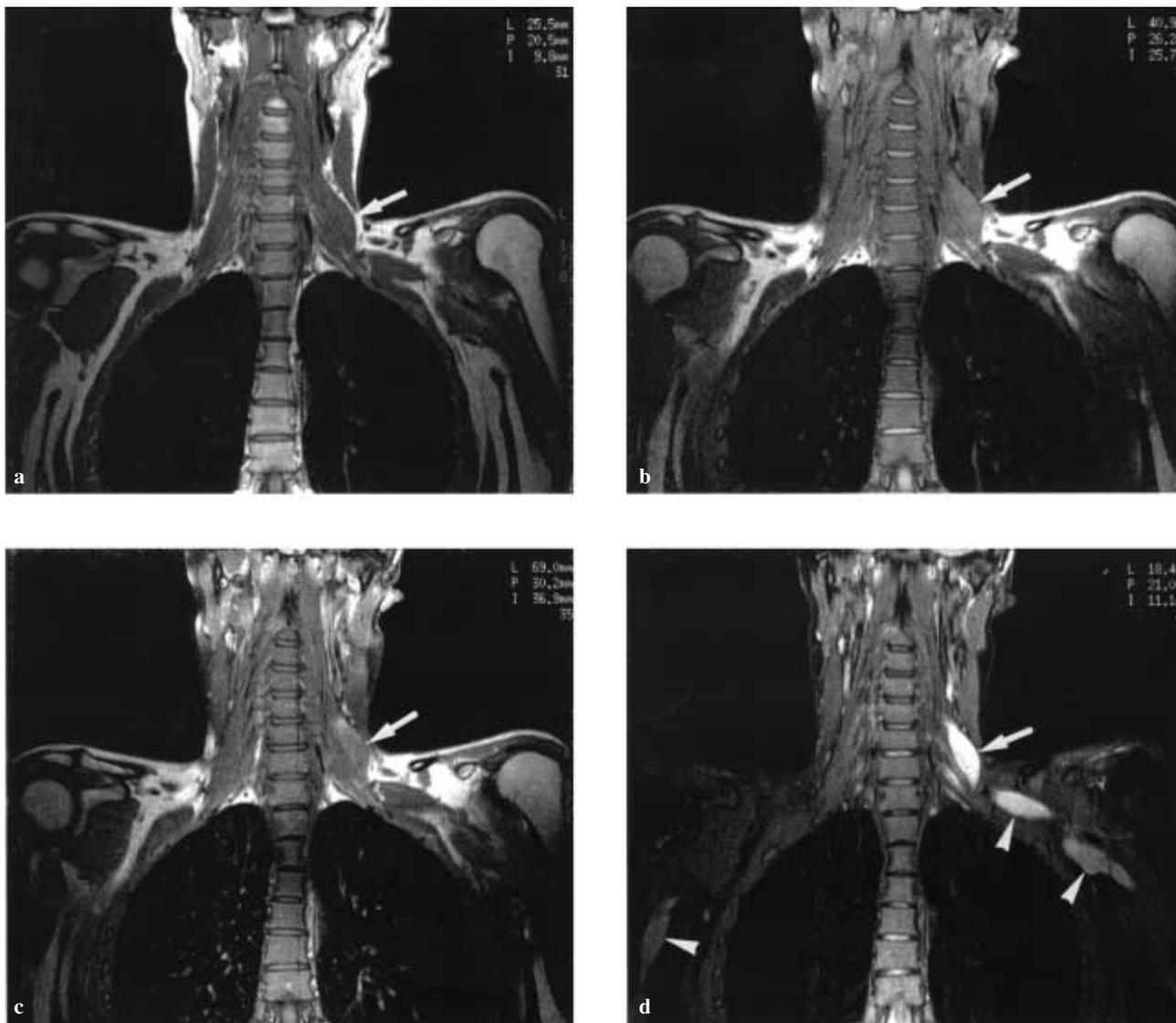


FIG. 1. — MR coronal view of the brachial plexuses (similar slice location of all images)

1A : pre-contrast T1-weighted spin echo (SE) image showing discrete enlargement of left brachial plexus trunks (arrow), which is underestimated because of isointensity of nerves and muscles.

1B : pre-contrast T1-weighted SE image with fat suppression option showing similar features

1C : post-contrast T1-weighted SE image showing slight contrast-enhancement of the enlarged trunks (arrow)

1D : short tau inversion recovery (STIR) image depicting exquisitely hyperintense, enlarged trunks, well contrasting with hypointense environment. Additional abnormal nerve segments are well depicted in the axilla and arms (arrowheads).

Discussion

We herein report a patient with relapsing-remitting cranial nerve palsies, involving the XIIth and Xth cranial nerves, and upper limb demyelinating neuropathy, involving the median and ulnar nerves bilaterally. MRI revealed marked hypertrophy of the left brachial plexus, both ulnar nerves, and the right median nerve. Such MRI findings have been reported in CIDP, multifocal motor neuropathy, hereditary neuropathy with liability to pressure palsies, hereditary demyelinating motor and sensory neuropathy, and neoplastic peripheral nerve infiltration (van Es, 2001). In our patient, there was no evidence of a hereditary neuropathy because of lack of a family history and absence of a deletion or

duplication in the *PMP22* gene, the former being the genetic hallmark of hereditary neuropathy with liability to pressure palsies. The relapsing-remitting evolution and lack of pain were evidence against a neoplastic origin. The clinical pattern together with the electrodiagnostic findings were in favour of a diagnosis of chronic, relapsing, acquired demyelinating neuropathy. CIDP typically is a generalized peripheral neuropathy. Although most CIDP patients present with generalised motor and sensory deficit, regional variants have been described (Rotta *et al.*, 2000) with selective involvement of the lumbar plexus (Ginsberg *et al.*, 1995), brachial plexus and upper limbs (Thomas *et al.*, 1996 ; Gorson *et al.* 1999 ; Van den Bergh *et al.*, 2000), or cranial nerves (Niino *et al.*, 1999 ;

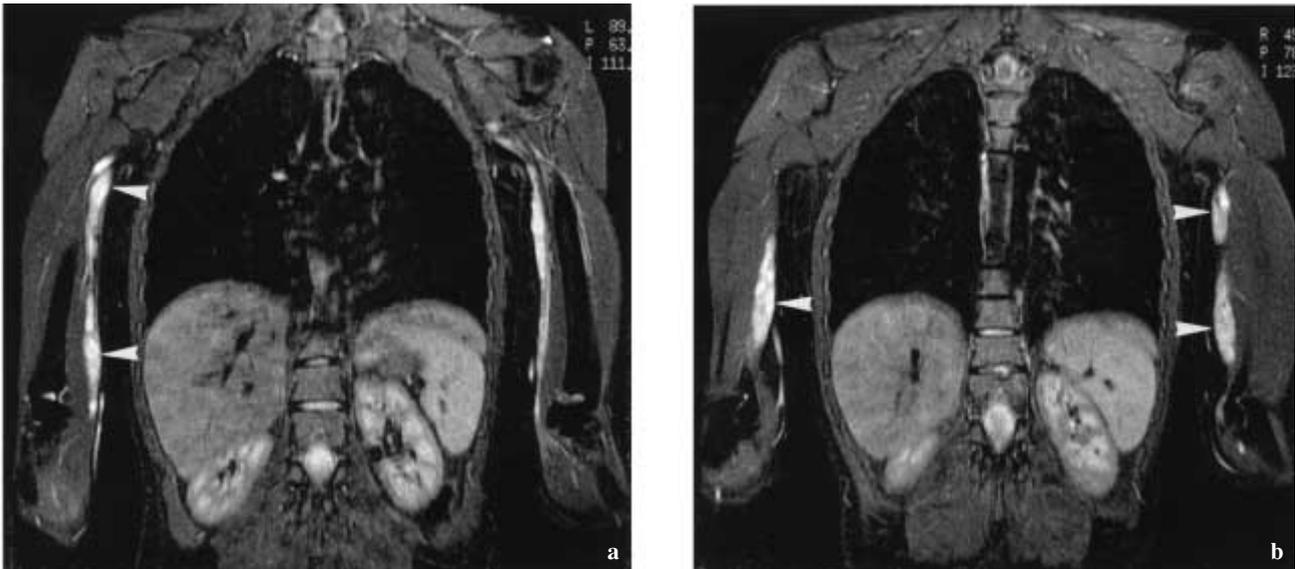


FIG. 2A-B. — Coronal STIR images of the thorax and the arms. Irregular and multifocal enlargement of the ulnar nerves is well seen (arrowheads).

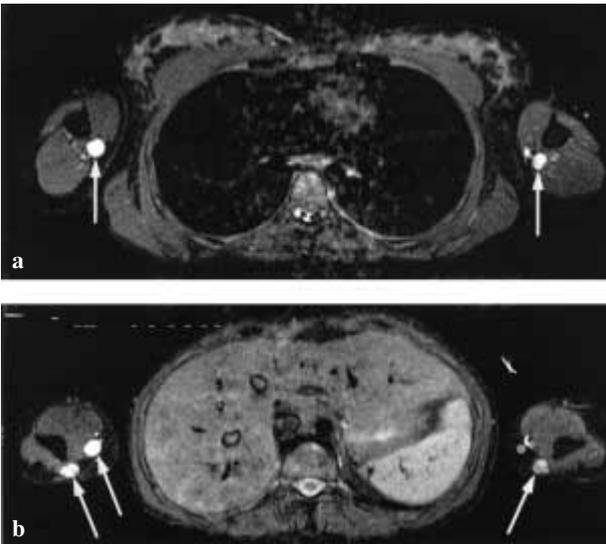


FIG. 3A-B. — Axial transverse STIR images through the thorax (a) and the upper abdomen (b)

3A : Enlargement and hypersignal intensity of the ulnar nerve is seen bilaterally at the mid-level of the upper arm (arrows)

3B : Similar feature with major symmetric involvement of both ulnar nerves, and with unilateral involvement of the right medial nerve at the distal pre-elbow level of the upper arm (arrows).

Frohman *et al.*, 1996) have been reported. Multifocal upper limb demyelinating neuropathy was initially described by Lewis *et al.* (1982) and is referred to as Lewis-Sumner syndrome or multifocal acquired demyelinating sensory and motor neuropathy (MADSAM) (Saperstein *et al.*, 1999).

Before the advent of MRI, hypertrophy of peripheral nerves in CIDP had been reported, based on clinical and pathological observations (Adams *et al.*, 1956 ; Bradley *et al.*, 1988 ; Cusimano *et al.*, 1988). MRI is now the best suited imaging modality to assess the anatomy of the brachial plexus (van

Es, 2001) and easily demonstrates peripheral nerve enlargement. In CIDP patients, radiological demonstration of hypertrophic nerves has been reported since 1996. Thomas *et al.* (1996) reported brachial plexus enlargement on MRI in one of 9 patients with focal upper limb demyelinating neuropathy. Suarez *et al.* (1996) reported one patient with recurrent demyelinating neuropathy of the brachial plexus, enlarged on MRI. Schady *et al.* (1996) reported 3 patients with CIDP, one with hypertrophy of cervical nerve roots and two with hypertrophic lumbar nerve roots. Duggins *et al.* (1999) reported that 8 of 14 patients with CIDP had hypertrophy of cervical spinal roots and brachial plexus and 6 of 14 had lumbar plexus enlargement. Similar observations were reported by several authors (Midroni and Dyck, 1996 ; Kuwabara *et al.*, 1997 ; Mizuno *et al.*, 1998 ; Niino *et al.*, 1999 ; Duarte *et al.*, 1999 ; Van den Bergh *et al.*, 2000). Nerve hypertrophy has also been found in multifocal motor neuropathy, another CIDP variant (van Es *et al.*, 1997) Whereas signal hyperintensity on T2-weighted MR images or with gadolinium is relatively frequent in nerve roots of CIDP patients, this phenomenon only occurs in a minority of patients with hypertrophic CIDP. Cranial nerve involvement has been reported in up to 60% of CIDP patients (Ormerod *et al.*, 1990), but cranial nerve hypertrophy has rarely been found (Duarte *et al.*, 1999 ; Niino *et al.*, 1999 ; Frohman *et al.*, 1996). Despite several episodes of cranial nerve palsy, no MRI abnormalities of cranial nerves were found in our patient.

There is a correlation between electrophysiological findings and radiological findings. Kuwabara *et al.* (1997) reported 10 patients with CIDP. In 8 of these, motor conduction blocks were located at the enlarged nerve segments. In the other 2 patients, in whom conduction slowing but no demyelinating

focus was found, neither nerve enlargement or gadolinium enhancement was observed. Our patient had motor conduction block and/or dramatic slowing of motor conduction velocity almost only in hypertrophic median and ulnar nerve segments.

There is also a correlation between MRI findings and clinical evolution. In the series of Kurabawa *et al.* (1997), the enlarged nerve segments showed gadolinium enhancement in four patients with progressive or relapsing disease, while in patients in remission no gadolinium enhancement was found. Duggins *et al.* (1999) reported a series of 14 patients with CIDP. All patients with nerve hypertrophy had a relapsing-remitting course and a significantly longer disease duration. Gadolinium enhancement was only present during relapses. Our patient had very slight gadolinium enhancement, corresponding to only mild symptoms and rapid remission. This suggests that gadolinium enhancement of hypertrophic nerves might be a marker of disease activity and useful for monitoring response to therapy.

In conclusion, this case report is an illustration of multifocal upper limb demyelinating neuropathy (Lewis-Sumner syndrome) with massive enlargement of the brachial plexus and upper limb peripheral nerves on MRI, representing a variant of CIDP.

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