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ORIGINAL COMMUNICATION

Neuroimaging in diagnosis of atypical polyradiculoneuropathies: report of three cases and review of the literature

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Abstract Neuroimaging is increasingly used in the study of peripheral nerve diseases, and sometimes may have a pivotal role in the diagnostic process. We report on three patients with atypical chronic inflammatory polyradiculoneuropathy (CIDP) in whom magnetic resonance imaging (MRI) and nerve Ultrasound (US) were crucial for a correct diagnostic work-out. A literature review on MRI and US in acquired demyelinating polyneuropathies is also provided. Awareness of the imaging features of CIDP will assist in confirmation of the diagnosis, institution of the appropriate therapy, and prevention of inadequate or delayed treatment in atypical CIDP.

Keywords MRI · Ultrasound · Neuropathy · Neurophysiology · CIDP

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Introduction

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an immune-mediated neuropathy with a broad spectrum of clinical phenotypes, including atypical forms with pure motor or sensory impairment and distal, multifocal, or focal distribution [1].

The diagnosis of CIDP is based on a set of clinical and neurophysiological criteria; however, in clinical practice CIDP may be difficult to diagnose, especially in atypical cases. Identification of patients with atypical CIDP is crucial because they respond to immunomodulatory therapy as well as patients with the classic phenotype.

Electrodiagnostic studies do not provide information on morphological changes of affected nerves in neuropathies, and imaging techniques, especially Magnetic Resonance Imaging (MRI) and nerve ultrasound (US), are gaining an increasing role in the evaluation of polyneuropathies [2].

According to several recent reports hypertrophy of spinal nerve roots is frequently observed with MRI or US in patients with CIDP, and detection of these findings may be helpful for the diagnosis.

A recent revision of the European Federation of Neurological Societies/Peripheral Nerve Society on Multifocal Motor Neuropathies (MMN) included MRI as a supportive criterion for the differential diagnosis with other neuropathies such as CIDP or multifocal acquired demyelinating sensory and motor (MADSAM) neuropathy (Lewis-Sumner syndrome) and motor neuron disease (MND) [3]. Consistently, also the guidelines of the European Federation of Neurological Societies/Peripheral Nerve Society on CIDP consider MRI among the supportive criteria [4].

With technological advancement in MRI, such as parallel imaging, new coil design and introduction of MR neurography (MRN) techniques, the Magnetic Resonance

evaluation of peripheral nerves has significantly improved, allowing a precise visualization of the anatomical complexity of brachial and lumbar plexuses and peripheral nerves trunks [5].

High-resolution US of peripheral nerves, besides widespread assessment of accessible nerves trunks at four limbs, is capable of evaluating cervical nerve roots at their emergence from the intervertebral foramina. Both MRN and US have been applied to the evaluation of mononeuropathies [6, 7] and recently also to diffuse neuropathies [8, 9].

The aim of this paper is to describe three patients with atypical polyradiculoneuropathy whose neuroimaging findings were critical for the diagnostic work-out, and to review the literature concerning MRI and US in acquired polyneuropathies.

Case reports

Patient no. 1 was a 40-year-old man, who came to our attention 4 years after the onset of paraesthesias and impaired sense of touch at left hand, that had subsequently extended to the whole forearm and the right sole. He did not report loss of strength. His past clinical history was unremarkable except for heavy smoking. He had previously undergone several inconclusive diagnostic investigations. Neurological examination showed tactile hypoesthesia from left elbow down and at right foot, abolished vibratory sensation and stereognosis with pseudoathetosis at left arm, areflexia at four limbs; no strength deficits. Neurophysiological study showed absence or significant reduction of sensory nerve action potentials (SNAPs) amplitude at four limbs with normal sensory nerve conduction velocity (CV), motor nerve CV, and compound muscle action potentials (CMAPs) amplitude (Table 1). A possible involvement of proximal motor fibers was indicated by the presence of a widespread increase of F-waves latency and by the difficulties in registering left ulnar and median nerves motor action potential after stimulation at the Erb position. Nevertheless, according to the clinical picture and neurophysiological findings, a sensory neuronopathy was finally diagnosed. Routine haematological, biochemical, and immunological tests, including ANA, ENA, anti-neuronal antibodies, anti-gangliosides and anti-sulfatides antibodies, serum protein electrophoresis, Lyme serology, and cerebrospinal fluid analysis all resulted normal. Spinal MRI was negative. No posterior columns T2-weighted hyperintensity was detected, a common finding in sensory neuronopathy [10]. MRN unexpectedly revealed diffuse enlargement and marked hyperintensity of the left brachial plexus from the ventral rami to the axilla (C5–C8 nerve roots mean diameter 6.5 mm, normal values up to 5 mm [11]), mild enlargement of the right C6 nerve root (5.5 mm) and primary trunk, bilateral asymmetric enlargement and hyperintensity of L5-S1 nerve roots (mean diameter 11 mm), with no contrast enhancement after gadolinium administration (Fig. 1a–c).

Nerve US evaluation at four limbs confirmed the enlargement of cervical roots (C5–C6–C7 nerve roots cross-sectional area (CSA) 18–35 mm^2, normal values 6–12 mm^2 [12]) and also showed significant swelling of upper limbs nerves, confined to their proximal segments (ulnar nerve CSA at forearm: 5 mm^2, normal values up to 8 mm^2; right ulnar nerve CSA at arm: 13 mm^2, normal values up to 11 mm^2) (Fig. 1d–f).

Neuroimaging findings were suggestive of polyradiculoneuropathy. Neurophysiological data were then re-examined and the results, namely prolonged F waves latencies and failure in registering left ulnar and median nerves motor action potential stimulating at the Erb position, were re-interpreted and asymmetric sensory CIDP was eventually diagnosed.

A nerve biopsy of the sural nerve, showing histological findings of asymmetric fascicular involvement and inflammatory signs with epineural pericapillar infiltrates, confirmed the diagnosis (Fig. 2).

Patient underwent steroid therapy with no benefit.

At 6 months follow-up, mild weakness was present at left triceps and left hand clumsiness and sensory deficits had worsened; a new neurophysiological examination revealed a more severe picture with the presence of proximal conduction blocks at left median and ulnar nerves and at tibial nerves at popliteal cavus, and markedly prolonged F waves latencies. IV Ig therapy was started with benefit: paresthesias decreased and the patient, who needed bilateral support for walking, returned to walk independently outdoors.

Patient no. 2 was a 52-year-old woman, affected by Hashimoto thyroiditis, who started complaining of burning pain and dysaesthesia in lumbar and perineal region that progressively extended to lower limbs, neck, and upper limbs. She did not report loss of tactile sensibility or limbs hypostenia. Her neurological examination was unremarkable; she had normal gait; strength was normal at four limbs; sense of touch and vibration sense were preserved; deep tendon reflexes were symmetric. Extensive biochemical, immunological and microbiological tests, anti-gangliosides, anti-sulfatides and anti-neuronal antibodies and cerebrospinal fluid analysis were negative. A neurophysiological study at four limbs revealed normal motor and sensory nerve conduction velocities and amplitudes of the CMAPs and SNAPs, but mild increase of F waves chronodispersion at upper limbs (Table 1).

Spinal MRI was unremarkable. MRN revealed bilateral symmetric enlargement of L2-S1 nerve roots (mean

Table 1 nerve conduction studies

Nerve	Stimulation site	DL (ms)			CV (m/s)			Amplitude (cMAP = mV SAP = μV)			F latency (ms)		
Patient		#1	#2	#3	#1	#2	#3	#1	#2	#3	#1	#2 (min–max)	#3
L median (m)	Wrist	3.5	3.3	2.9				13	9	6	34	25–36	29
	Elbow				50	64	53	12	9	6			
	Axilla				54		67	12		6			
	Erb				NR			NR					
R median (m)	Wrist	2.9	3.7					13	6		33	25–37	
	Elbow				50	64		10	6				
	Axilla				67			10					
	Erb				54			10					
L ulnar (m)	Wrist	2.6	2.9	2.1				4	6	7	35	25–27	30
	BE				55	55		4	5				
	AE				50	63	57	4	5	7			
	Axilla				54		55	4		7			
	Erb				NR			NR					
R ulnar (m)	Wrist	2.4	3.1					4	8		33	27–29	
	BE				56	57		4	7				
	AE				52	56		4	7				
	Axilla				65			4					
	Erb				61			4					
L tibial (m)	Ankle			3.9						4		52–56	
	PF						44			3			
R tibial (m)	Ankle			4.1						3		34–57	61
	PF						46			2			
L peroneal (m)	Ankle	4.2	3.6	4.1				4	3	0.3	59		NR
	BFH				42	46	43	3	3	0.3			
	AFH				52	45	50	3	3	0.3			
R peroneal (m)	Ankle	4.8	4.3	5.1				3	3	0.5	60		
	BFH					51	43		3	0.5			
	AFH				43	47	46	3	3	0.5			
L median (s)	1th finger				NR	52	50	NR	45	15			
	3rd finger				NR	51	59	NR	26	20			
R median (s)	1th finger				54	54		9	37				
	3rd finger				57	47		11	16				
L ulnar (s)	5th finger				NR	52	63	NR	13	6			
R ulnar (s)	5th finger				NR	54		NR	42				
L radial (s)	1th finger				NR		48	NR		19			
R radial (s)	1th finger				55			8					
L sural (s)	Mild calf				NR	48	46	NR	8	11			
R sural (s)	Mild calf				NR	49	48	NR	9	8			

Normal values: median nerve DL $\leq$ 3.5 ms; SCV $\geq$ 48 m/s; SAP $\geq$ 15 μV; MCV $\geq$ 50 m/s; cMAP $\geq$ 6 mV; ulnar nerve DL $\leq$ 3.1 ms; SCV $\geq$ 48 m/s; SAP $\geq$ 10 μV; MCV $\geq$ 50 m/s; cMAP $\geq$ 4 mV; radial nerve SCV $\geq$ 40 m/s; SAP $\geq$ 10 μV; peroneal nerve DL $\leq$ 5,5 ms; MCV $\geq$ 40 m/s; cMAP $\geq$ 3 mV; tibial nerve DL $\leq$ 6.0 ms; MCV $\geq$ 40 m/s; cMAP $\geq$ 3 mV; sural nerve SCV $\geq$ 40 m/s; SAP $\geq$ 5 μV; F-wave median/ulnar <32 ms; peroneal/tibial <56 ms

DL distal latency, *CV* conduction velocity, *cMAP* compound motor action potential, *SAP* sensory action potential, *BE* below elbow, *AE* above elbow, *PF* popliteal fossa, *BFH* below fibular head, *AFH* above fibular head, *NR* no response, *R* right, *L* left, *m* motor, *s* sensory

diameter 7.8 mm), of femoral nerves and proximal tracts of sciatic nerves, with mild signal hyperintensity and no enhancement after gadolinium administration. A similar pattern of bilateral diffuse nerve enlargement was identified in the brachial plexus (C6–C8 nerve roots mean diameter 5.7 mm), also involving the nerve trunks at the

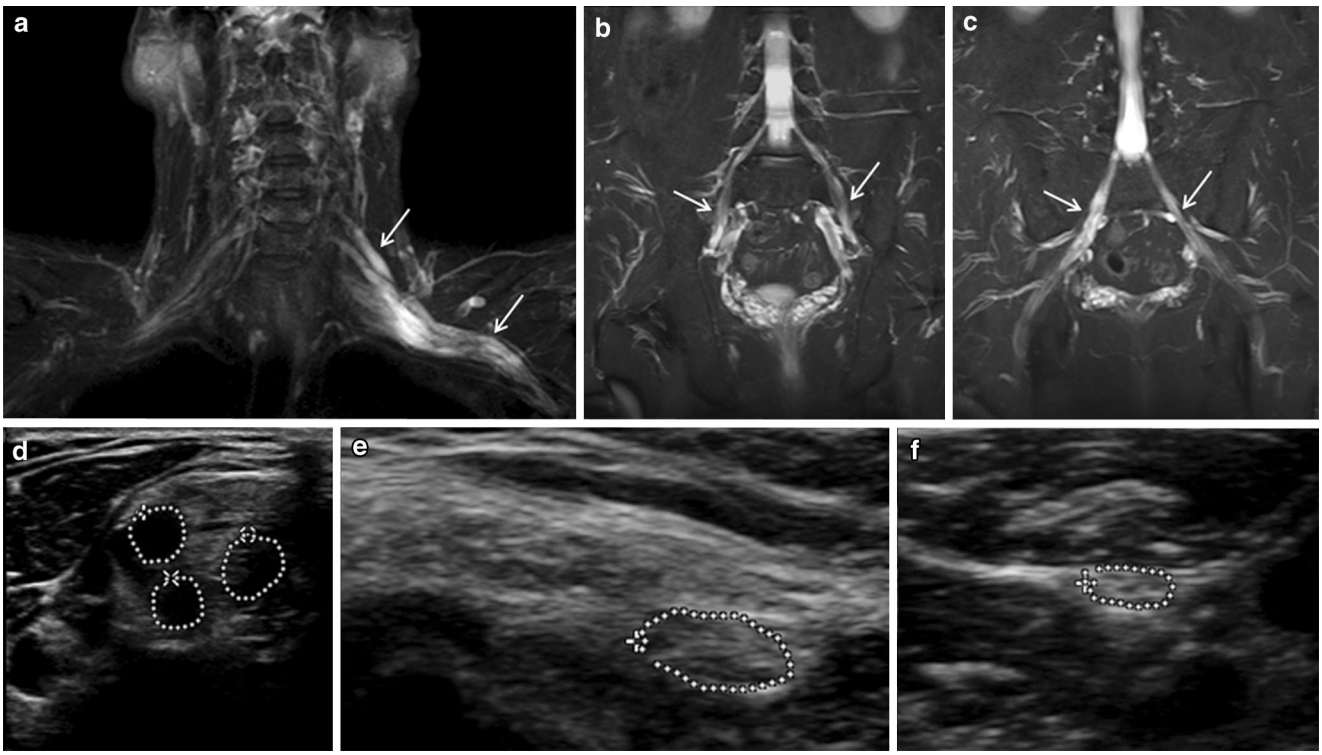

Fig. 1 Patient 1. 3D MR Neurography of brachial (**a**) and lumbosacral (**b**, **c**) plexus, MIP coronal views. Prominent, diffuse enlargement, and hyperintensity of the left brachial plexus from cervical nerve roots to the axilla (*arrows* in **a**). Asymmetric enlargement and hyperintensity of L5 (*arrows* in **b**) and S1 nerve roots (*arrows* in **c**). US of left C5–C7 nerve roots (CSA = 18–35 mm^2) (**d**), ulnar nerve at the arm (CSA = 13 mm^2) (**e**) and forearm (CSA = 5 mm^2) (**f**)

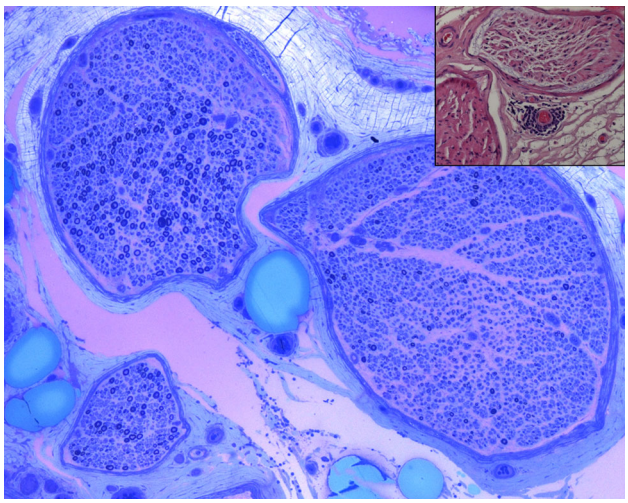

Fig. 2 Patient 1. Sural nerve biopsy, semithin transverse section, showing focal distribution of the pathologic lesions. Immunohistochemical characterization of the inflammatory response, with epineural perivascular inflammatory infiltrate, predominantly containing activated T lymphocytes. Macrophages are identifiable in the endoneural perivascular infiltrate and scattered in the endoneurium. The inset shows an epineurial perivascular inflammatory cell infiltrate (paraffin-embedded section, H&E staining)

level of the axilla (Fig. 3). These findings were suggestive of CIDP.

Nerve US evaluation confirmed the significant enlargement of the cervical nerve roots (C5–C6–C7 nerve roots, CSA 14–18 mm^2 at their emergence). Sensory CIDP was diagnosed, and steroid therapy started with benefit (burning pain and dysaesthesias significantly decreased). A subsequent neurophysiological study showed normal motor and sensory nerve conduction velocities and amplitudes of the CMAPs and SNAPs. F waves latencies were normal at four limbs.

Patient no. 3 was a 54-year-old man with a 2-year history of progressive gait impairment and pain at lower limbs. Neurological examination revealed stepping gait, more severe on the left side, distal weakness and mild hypotrophy at lower limbs (tibial anterior and exstensor hallucis longus MRC 3/5 in the left side and 4/5 on the right side), no hyposthenia at upper limbs, no sensory loss, and symmetric deep tendon reflexes. Neurophysiological examination showed a motor polyradiculoneuropathy with axonal involvement associated with chronic and active denervation signs, both proximally and distally at lower

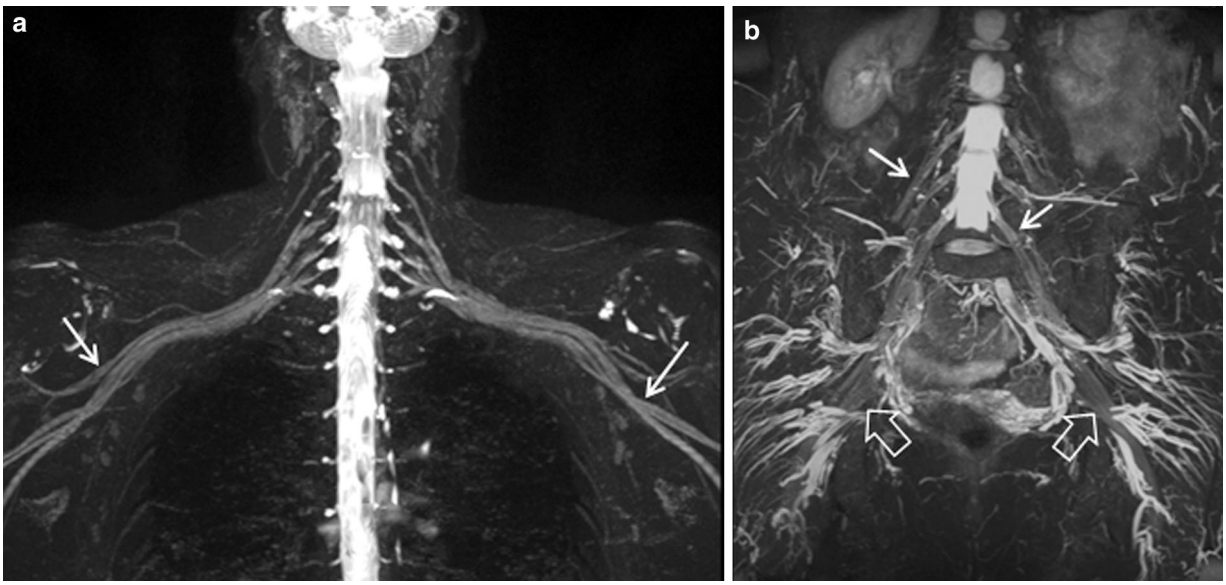

Fig. 3 Patient 2. 3D MR Neurography of the brachial (**a**) and lumbosacral (**b**) plexus. Diffuse and symmetric enlargement and increased signal intensity of the brachial plexus extending to nerve trunks at the level of the axilla (*arrows* in **a**). Symmetric enlargement of lumbar and sacral roots (*arrows* in **b**) and sciatic nerves at the level of the greater ischiatic foramen (empty *arrows* in **b**)

limbs (Table 2). Routine haematological, biochemical, and immunological tests, including ANA, ENA, anti-neuronal antibodies, anti-gangliosides and anti-sulfatides antibodies, serum protein electrophoresis, Lyme serology, all resulted normal. Cerebrospinal fluid analysis was unremarkable.

MRI revealed lumbar spinal stenosis at multiple levels (T12–L1, L1–L2 and L3–L4) with redundant and enlarged nerve roots of cauda equina (Fig. 4a–c) and no signal intensity abnormalities of the lumbosacral spinal roots at MRN. The MRI findings were inconsistent with the clinical presentation.

Nerve US revealed significant and diffuse enlargement of nerve trunks at four limbs (left median nerve CSA at forearm: 16 mm^2, normal values up to 8 mm^2; right ulnar nerve CSA at arm: 46 mm^2, normal values up to 11 mm^2, right peroneal nerve at fibular head 17 mm^2, normal values up to 14 mm^2, right tibial nerve at popliteal fossa 41 mm^2, normal values up to 35 mm^2) (Fig. 4d, e).

A diagnosis of motor CIDP was made, and IV Ig therapy was started with improvement in strength and patient's autonomy in walking. After 21 months of IVIg therapy US nerve evaluation dramatically improved, with nerve CSA returning to normal limits.

Magnetic resonance imaging and ultrasound in CIDP

The first reports on MRI findings in patients affected by CIDP described nerve root enlargement mostly within the cauda equina and spinal roots [13, 14], with different degrees of gadolinium enhancement, which is not considered sufficient for a differential diagnosis with Guillan-Barrè syndrome (GBS) [15, 16].

In a consecutive series of 16 patients with CIDP, enhancement of the cauda equina was found in 69 % of cases, with no correlation with disease activity/severity and laboratory tests [17].

Cervical root and brachial plexus abnormalities have also been identified in association with CIDP [13, 18].

Investigating 14 patients affected by CIDP with MRI, Duggins et al. [19] discovered hypertrophy and increased signal intensity of the cervical roots and brachial plexus on T2-weighted images in eight cases (57 %), six of whom also had also hypertrophy of the lumbar plexus. All patients with nerve root hypertrophy had a relapsing-remitting course and a significantly longer disease duration, which may be related, according the authors, with the process of demyelination and remyelination, as demonstrated by a biopsy of the brachial plexus showing gross onion-bulb formations.

Similar findings of enlargement and increased MR signal intensity have been observed in the median and ulnar nerves of patients with CIDP, correlating with the site of conduction block and contrast-enhancement during relapses or active progression [20].

The exact pathogenesis of the increased signal intensity of roots and nerve trunks on MR T2-weighted sequences in CIDP patients is not known, although it may reflect increased water content within the endoneurial spaces of nerve fascicles and disruption of the blood-nerve barrier due to the inflammatory process [20].

Table 2 Patient #3, needle EMG

Muscle	SA	Rec	Amp	Dur	Poly
L deltoid	0	N	N	N	N
L biceps brachii	0	N	N	N	N
L triceps brachii	0	N	N	N	N
L brachioradialis	0	N	N	N	N
L 1st dorsal interosseous	0	N	N	N	N
L gluteus medius	0	↓↓	↑	↑	N
L gluteus medius	0	↓↓	↑	↑	N
L gluteus maximus	0	↓	↑	↑	N
R gluteus maximus	0	↓	↑	↑	N
L biceps femoralis	0	↓	↑	↑	N
R biceps femoralis	0	↓	↑	↑	N
L vastus lateralis	0	↓	N	↑	↑
R vastus lateralis	0	↓	N	↑	↑
L vastus medialis	0	↓	N	↑	↑
R vastus medialis	0	↓	N	↑	↑
L tibialis anterior	0	↓↓↓	↓↓	↑	↑
R tibialis anterior	0	↓↓	↑	↑	N
L extensor digitorum comunis	++	↓↓↓	↓↓	↑	↑
R extensor digitorum comunis	++	↓↓	↑	↑	N
L gastrocnemius	0	↓	↑	↑	N
R gastrocnemius	0	↓	↑	↑	N
L extensor digitorum brevis	0	↓↓↓	↓↓	↑	↑
R extensor digitorum brevis	0	↓↓	↓↓	↑	↑

SA, spontaneous activity; Rec, recruitment; Amp, amplitude; Dur, duration; Poly, polyphasia; N, normal; 0, absent; ++, moderate; ↑, increased; ↓, slight reduction; ↓↓, moderate reduction; ↓↓↓, marked reduction

Nerve hyperintensity can be observed also in other conditions such as hereditary and toxic neuropathies, compressive nerve lesions, and cannot be considered specific for CIDP, especially when considering that no reliable quantitative methods for evaluating the signal intensity of normal versus abnormal nerves have been so far developed.

MRI may be of value in defining subtypes and atypical variants of CIDP [21] and in the differential diagnosis with MMN, classified as a variant of CIDP in the past and now considered a separate nosological entity [22].

About 40–50 % of the patients with MMN show asymmetric hypertrophy and signal intensity abnormalities or contrast-enhancement on MR of the brachial plexus and the pattern of signal alterations closely correlates with the distribution of muscle weakness [23].

Brachial and lumbosacral plexus hypertrophy on MRI is also well documented in patients with demyelinating Charcot–Marie–Tooth disease (CMT) [24] and the differential diagnosis with CIDP, besides genetic abnormalities, can also rely on the measurement of the sciatic nerve CSA at mid-thigh by means of MRN [25].

In the last decade, conventional MRI has been progressively replaced by MRN in the evaluation of peripheral neuropathies due to of its superior soft tissue contrast and sensitivity to pathology [26].

The size and the signal intensity changes of cervical and lumbar nerve roots can be reliably assessed with MRN in CIDP patients [11], although the correlation between the diameters of spinal nerve roots and findings of nerve conduction studies is not clear.

Three-dimensional (3D) MRN represents a further refinement of conventional MRN, providing enhanced contrast between nerves and muscles and oblique and curved-planar reformations of nerve roots, peripheral nerves and plexuses. Using 3D MRN techniques Shibuya et al. [27] showed longitudinal morphological changes from the cervical roots to the nerve trunks in the proximal arm in 88 % of patients affected by CIDP.

Although there are no studies comparing the diagnostic accuracy of MR to clinical and neurophysiological criteria, the combination of nerve enlargement and increased signal intensity has been consistently reported as a reliable imaging marker of CIDP, in which different patterns of nerve hypertrophy may reflect the diverse distribution of demyelinating lesions in each subtype.

New MR techniques such as diffusion weighted (DWI) and diffusion tensor (DTI) imaging have proven to be particularly useful for the investigation of peripheral nerve disorders.

High signal intensity in DWI sequences and increased values of the apparent diffusion coefficient (ADC) were detected in 55.6 % of cases in a small cohort of 13 CIDP patients, which might be strictly correlated with proliferating layers of Schwann cells and increased endoneurial collagen surrounding the axons [28].

DTI is a relatively new MR technique which allows the calculation of quantitative measures such as Fractional Anisotropy (FA) and Mean Diffusivity (MD), representing an index of structural integrity and directional coherence of the nerve fibers.

Kakuda et al. [29], investigating 10 CIDP patients with 3T DTI, found significantly reduced FA values in the tibial nerves of patients compared to controls and an association between FA and the amplitude of action potentials in electrodiagnostic tests, suggesting a correlation with axonal damage more than with the degree of demyelination.

In the last decade, US has become a useful tool for evaluating peripheral nerves [30, 31].

Some studies have reported the usefulness of US in the evaluation of CIDP, mostly case reports and small case–control series, varying in imaging protocols regarding numbers, sites, and aspects of the investigated nerves.

Hypertrophy of the cervical nerve roots has been identified with US in 9 of 13 (69 %) CIDP patients as compared

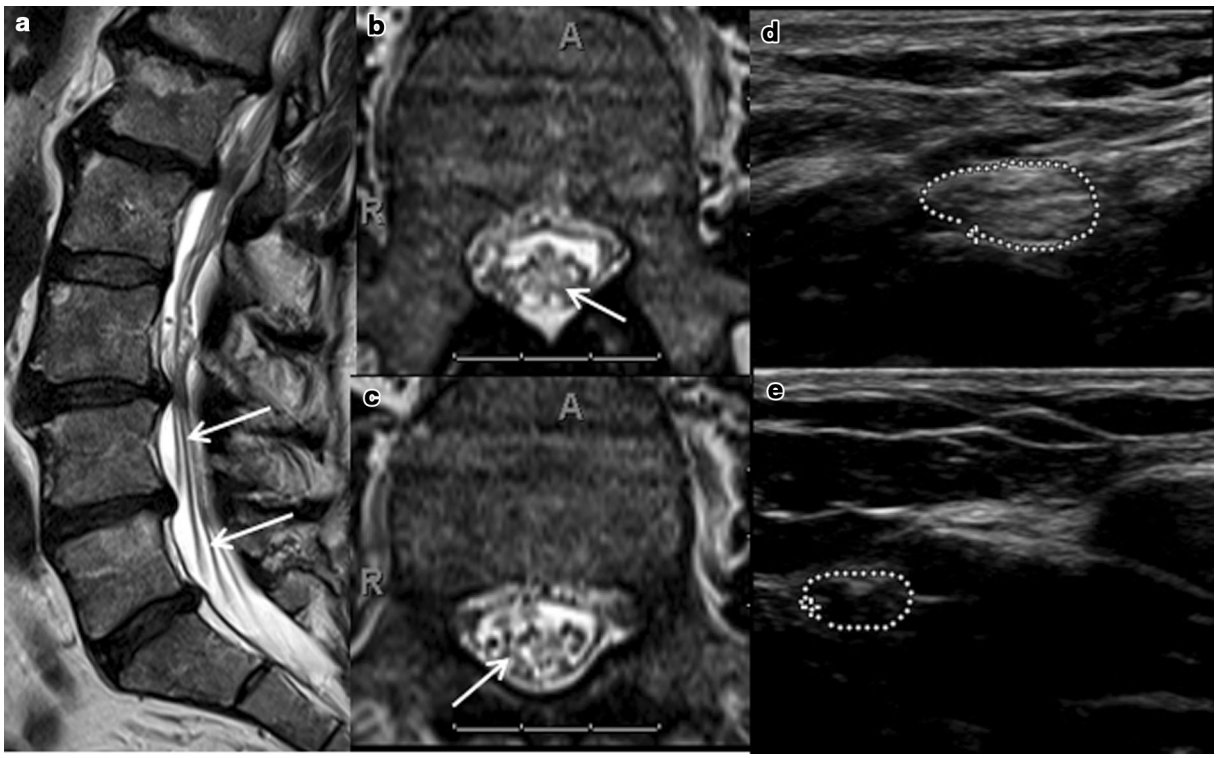

Fig. 4 Patient 3. MRI of the lumbar spine, sagittal (**a**) and axial T2 W sections at L3 (**b**) and L4 (**c**) showing lumbar stenosis and cauda equina redundant and enlarged nerve roots (*arrows*). US, right tibial nerve at the popliteal fossa (CSA = 41 mm^2) (**d**), left median nerve at forearm (CSA = 16 mm^2) (**e**)

with control subjects [32], and the degree of hypertrophy was significantly associated with CSF protein content, but not with other clinical features.

In a consecutive series of 36 CIDP patients, median or ulnar nerve enlargement was demonstrated in 86 % of cases, without correlation with average motor conduction velocity [9].

With the development of a reproducible method for measuring the nerve size at multiple sites with US, such as the CSA [33], nerve enlargement has been consistently reported at sites of conduction block [9, 34, 35], although details on nerve echogenicity were not reported.

Zaidman et al. [36] have recently measured the CSA of ulnar and median nerves at the arm in normal controls and patients with neuropathies including CMT and CIDP, demonstrating nerve enlargement in 100 % of CMT1A and 86 % of CIDP patients.

In all these studies, the US imaging protocols included only a few nerves, such as the cervical roots, median, or ulnar nerves, and only one or a few sections of the nerve.

US evaluation of multiple points for each nerve in a bilateral manner may be time consuming; however, its sensitivity in detecting mononeuropathies and plexopathies may be superior to MRI, according to a recent report [37].

A multiparametric US evaluation at multiple sites, including minimal and maximal CSA enlargement and pattern evaluation of fascicles, has been recently proposed by Padua et al. [38] with the aim to demonstrate the heterogeneous involvement of peripheral nerves in CIDP.

The high variability of the fascicular pattern in CIDP patients has been observed also by Jang et al., who demonstrated increased CSA at proximal and no at entrapment sites, correlating with nerve conduction velocity of the corresponding region, using a US imaging protocol including CSA measurement of several nerves (vagus, brachial plexus, musculocutaneous median, ulnar, radial, sciatic, tibial, common peroneal, and sural nerves) [39].

Discussion

The diagnosis of CIDP is based on a combination of clinical, electrodiagnostic, and laboratory features, primarily directed at detecting signs of demyelination. However, despite the good overall sensitivity and specificity of the current electrophysiological criteria, almost 20 % of patients in CIDP cohorts do not match these criteria [40].

In patients with atypical clinical presentations, such as pure motor or sensory impairment or distal, multifocal, or

focal distributions, the differential diagnosis is wider and different laboratory data, including nerve biopsy and cerebrospinal fluid examination have been suggested as supportive criteria. However, the percentage of normal cerebrospinal fluid analysis in CIDP may be as high as 14 % [41] and it increases to up to 44 % in sensory CIDP [42].

In addition, MRI showing gadolinium enhancement or hypertrophy of the cauda equina, nerve roots, or plexuses has been recommended as an additional supportive exam in a recent revision of the European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of CIDP [4].

In all our patients, the diagnosis was challenging due to the atypical clinical picture and the scarce or unconvincing neurophysiological data.

3D MRN, aimed at investigating both brachial and lumbosacral plexus in a single study, played a crucial role in the work-out process, disclosing different patterns of nerve enlargement and signal intensity abnormalities.

In the first case, it prompted us to reconsider the subtle neurophysiological signs of myelin damage; in the second case it revealed signs of radicular involvement that were not recognizable from neurophysiological examination. In the third case, MRI identified lumbar spinal stenosis which was not consistent with clinical findings and US showed diffuse enlargement of nerve trunks at the four limbs despite neurophysiological findings of asymmetry and absence of conduction blocks. The clinical and US improvement after IVIg supported the diagnosis.

We have recently developed a standardized neuroimaging approach to patients with clinical and/or neurophysiological atypical polyradiculoneuropathy comprehensive of widespread nerve US evaluation at upper and lower limbs, and brachial and lumbar plexus with advanced 3D MRN.

Compared to conventional MRI, which provides a visualization of short segments of peripheral nerves, 3D MRN has the advantage of 3-dimensional reconstructions of the complex anatomy of the brachial and lumbar plexus over long trajectories, which favors a more precise evaluation of the extent of signal intensity abnormalities and patterns of nerve hypertrophy.

MRN, compared to conventional MRI, is a tissue-selective diagnostic tool directed at identifying characteristics of nerve morphology, such as fascicular pattern and longitudinal variations in signal intensity and size [43]. Phenotypic features can be noninvasively characterized in patients with atypical variants of CIDP using 3D MRN for a detailed evaluation of brachial and lumbosacral plexus hypertrophy and signal intensity abnormalities, which typically involve long segments with a different distribution, symmetric or asymmetric, diffuse or multifocal [27].

On the other hand, MRN is a time consuming and expensive diagnostic tool, mostly unavailable in clinical routine, although a whole-body diffusion weighted evaluation of peripheral nerves has been recently proposed for investigation of diffuse polyneuropathies such as CIDP [44].

Also when MRN does not show the typical pattern of symmetric or asymmetric diffuse enlargement of the brachial and or lumbar plexus, US can provide additional information on peripheral nerve trunks, which is crucial for the final diagnosis, like in our third case.

In such cases, US may not only contribute to the diagnosis, confirming the neurophysiological pictures as in classical neuropathies, but it may also identify pitfalls in the neurophysiological examination and re-direct the diagnostic process [8].

Considering the respective potentials and limitations of US and MRI, the combination of the two diagnostic modalities seems a useful approach for investigating atypical variants of CIDP, which can be misdiagnosed because of the clinical heterogeneity and lack of a uniformly present confirmatory tests.

Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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