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A rare case of combined central and peripheral demyelination associated with neurofascin-155 IgG antibody: Distinctive MRI findings

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Abstract

Combined central and peripheral demyelination (CCPD) is a rare neurological disorder characterized by both central nervous system (CNS) and peripheral nervous system (PNS) demyelination. Its clinical heterogeneity and overlapping features with multiple sclerosis and chronic inflammatory demyelinating polyradiculoneuropathy make diagnosis challenging. We report a 19-year-old man who presented with progressive limb numbness, sensory ataxia, tremor, and unsteady gait. Nerve conduction studies indicated sensorimotor polyneuropathy with axonal changes, and brain MRI revealed abnormal diffusion-weighted imaging signals in multiple white matter regions, with characteristic Dawson fingers on T2-weighted imaging. Serum was positive for neurofascin-155 antibodies, confirming the diagnosis of CCPD. This case highlights the importance of considering CCPD in patients with overlapping CNS and PNS demyelinating features.

Keywords: Combined central and peripheral demyelination (CCPD), neurofascin-155 (NF155) antibody, demyelinating neuropathy, chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), multiple sclerosis

INTRODUCTION

Combined central and peripheral demyelination (CCPD) is a rare and underrecognized neurological condition characterized by demyelinating lesions affecting both the central nervous system (CNS) and peripheral nervous system (PNS).[1,2] The clinical presentation of CCPD is highly heterogeneous, with overlapping features of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and multiple sclerosis (MS), making diagnosis particularly challenging.[3,4] Neurofascin-155 (NF155)-positive CCPD is typically associated with early onset, tremor, sensory ataxia, and poor response to corticosteroids.[5] Magnetic resonance imaging (MRI) findings in CCPD may mimic those of multiple sclerosis (MS), although atypical patterns can also occur. The utility of diffusion-weighted imaging (DWI) in identifying acute demyelinating lesions is of particular interest, especially when conventional T2-weighted imaging fails to reveal significant changes.[6] Here, we present a rare case of anti-NF155 antibody-positive CCPD with acute onset, demonstrating both peripheral neuropathy and CNS involvement highlighted by abnormal DWI signals in the absence of prominent T2 hyperintensities.

CASE REPORT

A 19-year-old man with no medical history was admitted to our neurology ward with progressive hand and feet numbness, unsteady gait and bilateral hand tremor for 10 days. The sensory symptoms began symmetrically in the feet and ascended to involve the hands, accompanied by an ataxic gait consistent with sensory ataxia. He also reported bilateral distal hand tremor and distal limb weakness, with relative sparing of the proximal muscles. Associated symptoms included headache, dizziness, nausea, and vomiting. There was a positive family history of hyperthyroidism on the paternal side.

A neurological examination revealed a stocking-glove distribution of sensory loss

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MNCV	Latency ms	Amplitude mV	Distance mm	CV m/s
Peroneal.R				
Ankle	**6.9**	**1.6**	370	**22**
Fibula (head)	**24.1**	**1.0**		
Tibial.R				
Ankle	**11.2**	**1.6**	370	**29**
Popliteal fossa	**23.8**	**0.6**		
Peroneal.L				
Ankle	**8.2**	**1.5**	365	**26**
Fibula (head)	**22.2**	**1.0**		
Tibial.L				
Ankle	**12.7**	**1.3**	385	**34**
Popliteal fossa	**24.1**	**1.0**		
Median.R				
Wrist	**6.1**	**2.2**	230	**28**
Elbow	**14.4**	**1.3**		
Ulnar.R				
Wrist	**4.7**	**6.0**	280	**35**
Below elbow	**12.6**	**5.5**		
Median.L				
Wrist	**6.0**	**3.7**	230	**33**
Elbow	**12.9**	**2.4**		
Ulnar.L				
Wrist	**4.9**	**4.5**	275	**37**
Below elbow	**12.3**	**3.8**		

SNCV	Onset Lat. ms	Amplitude μV	Distance mm	CV m/s
Sural.R				
Lower leg	**2.8**	**22**	140	**50**
Sural.L				
Lower leg	**2.3**	**23**	140	**61**
Median.R				
Wrist	**4.7**	**4**	140	**30**
Ulnar.R				
Wrist	**2.5**	**6**	140	**56**
Median.L				
Wrist	**4.6**	**6**	140	**31**
Ulnar.L				
Wrist	**4.4**	**6**	140	**32**

Figure 1a. Nerve conduction studies of MNCV and SNCV showed a sensorimotor polyneuropathy with diffuse demyelination and axonal changes.

affecting pinprick and temperature sensations. Joint position was impaired at both great toes, and he had an ataxic gait. He also had hyperreflexia in all four limbs with normal plantar responses.

Cervical spine MRI was performed to exclude a spinal cord lesion, however the findings were unremarkable. A comprehensive myelopathy workup, including tests for TPPA, RPR/VDRL, vitamin B12, folic acid, HIV, anti-HTLV-I antibodies, and CSF TB PCR, revealed normal or negative results.

Peroneal.R	**89.6**	**30**
Tibial.R	**87.8**	**30**
Peroneal.L	**83.3**	**30**
Tibial.L	**85.1**	**40**
Median.R	**52.8**	**60**
Ulnar.R	**47.8**	**60**
Median.L	**48.5**	**60**
Ulnar.L	**47.5**	**60**

H-Wave	Lat. ms	Amp. (max) mV
Tibial.R		
H-wave:	**49.1**	**0.1**
Tibial.L		
H-wave:	**47.5**	**2.1**

Figure 1b. Nerve conduction studies of F-wave and H-reflex.

Nerve conduction studies (Figure 1) demonstrated sensorimotor polyneuropathy with diffuse demyelination and axonal involvement. CSF analysis revealed markedly elevated protein levels (240.6 mg/dL; normal <45 mg/dL), with 5 white blood cells/μL, absent oligoclonal bands, and a normal IgG index (0.5).

The acute onset and rapidly progressive course of the polyneuropathy, electrophysiological findings suggestive of a demyelinating process, albuminocytologic dissociation in CSF, and negative myelopathy findings led to a strong clinical suspicion of acute inflammatory demyelinating polyradiculoneuropathy (AIDP). The patient received intravenous immunoglobulin (IVIg) at a dose of 0.4 g/kg/day for five days, which resulted in only minimal improvement in paresthesia and gait disturbance.

The patient subsequently developed new-onset blurred vision. Workup for central demyelinating

Run	Label	N75 ms	P100 ms	N145 ms
L - VEP 3-Ch				
1.1	O1 - Fz	97.0	120.5	146.5
1.2	Oz - Fz	93.0	114.5	151.0
1.3	O2 - Fz	96.0	119.5	151.5
R - VEP 3-Ch				
1.1	O1 - Fz	105.0	133.5	150.0
1.2	Oz - Fz	104.5	129.5	142.5
1.3	O2 - Fz	107.5	131.5	147.5

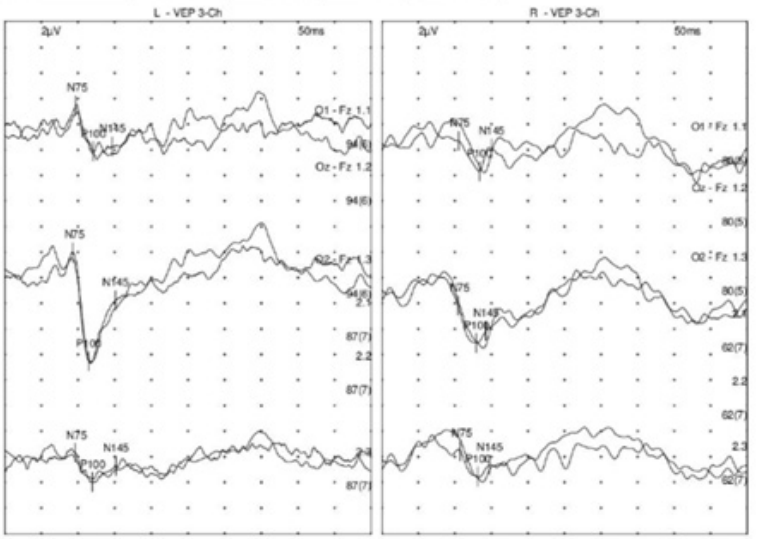

Figure 2. Visual evoked potentials (VEPs) revealed prolonged P100 latencies.

disorders including neuromyelitis optica spectrum disorder and MS was performed. Visual evoked potentials revealed prolonged P100 latencies (133 ms right eye, 120 ms left eye), indicating bilateral visual conduction pathway involvement (Figure 2). Orbit MRI was performed, which showed no evidence of abnormal T2 hyperintensity or post-contrast enhancement along the optic nerves or optic chiasm. Serum aquaporin-4 (AQP4) antibodies were negative.

Brain MRI revealed DWI abnormalities in bilateral deep white matter, periventricular regions, corpus callosum, corticospinal tracts, cerebral peduncles, brainstem, and right cerebellum (Figure 3a). T2-weighted images showed hyperintense lesions with a stripe-like pattern in the periventricular white matter. Sagittal views demonstrated linear and ovoid T2 hyperintensities perpendicular to the lateral ventricles, suggestive of Dawson fingers (Figure 3b).

Serological testing revealed positive NF155 IgG antibodies, confirming the diagnosis of CCPD.

DISCUSSION

CCPD is a rare disease characterized by demyelinating lesions affecting both the CNS and PNS.[1,2,4] The clinical manifestations are highly variable, making accurate diagnosis challenging.[3,4] There are currently no well-defined diagnostic criteria for CCPD.[2] Cortese *et al*.[3] reported that approximately 74% of CCPD patients fulfilled the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) diagnostic criteria for CIDP, and that 46% of cases fulfilled the 2010 McDonald criteria for MS. In our case, the clinical, electrophysiological, and CSF findings met the EFNS/PNS criteria for CIDP.[7] However, spinal and cranial MRI findings were limited to DWI abnormalities and did not fulfill the 2017 McDonald criteria.[8]

CCPD can present as acute, subacute, or chronic onset.[1-3] Our patient presented with acute onset. A previous study reported a male-to-female ratio of 1:2.6[1], with a mean age of onset around 32 years (range: 8–59 years).[1] The clinical course of CCPD can be monophasic, relapsing-remitting, or chronic progressive, with the relapsing-remitting form being most common.[1,3] CNS and

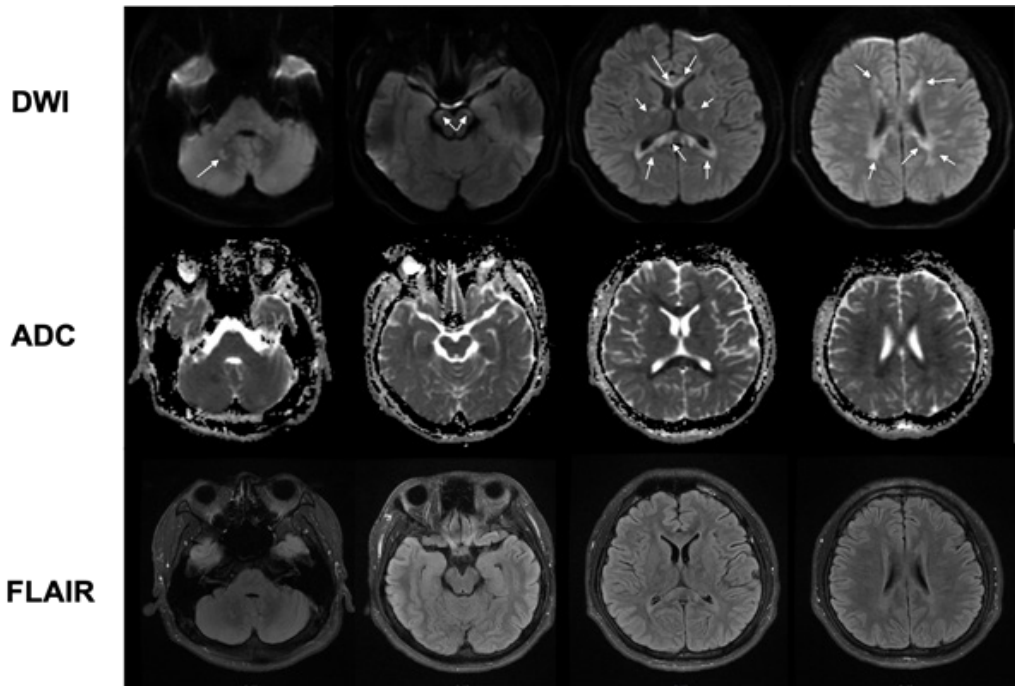

Figure 3a. Axial diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) showing abnormal signals at bilateral deep white matter, periventricular regions, corpus callosum, corticospinal tracts, cerebral peduncles, brainstem, and right cerebellum.

PNS involvement may occur simultaneously or sequentially, and may originate from either the CNS or PNS.[1,3,4] In our case, the symptoms of headache, dizziness, nausea, vomiting, hyperreflexia, and blurred vision indicated CNS involvement, while sensory deficits and motor weakness suggested PNS involvement.

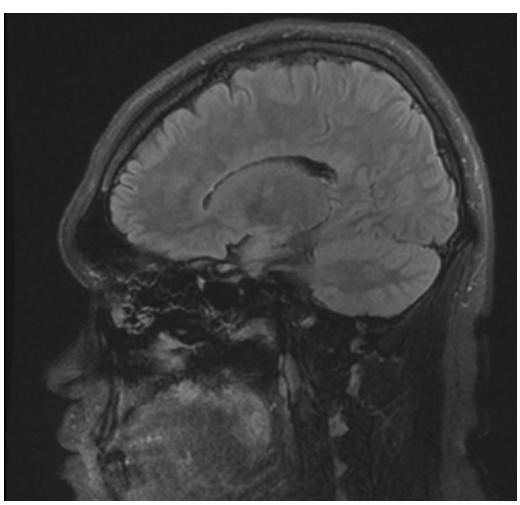

Figure 3b. Sagittal T2-weighted image, high signal lesion perpendicular to the body of the lateral ventricles, suggestive of Dawson fingers.

The presence of hyperreflexia in a patient with polyneuropathy should prompt consideration of concomitant CNS involvement.

Anti-NF155 antibodies were first identified in CCPD by Kawamura *et al*.[5] NF155 is expressed in both the PNS and CNS, which may explain the simultaneous demyelination in both systems. A nationwide Japanese survey reported NF155 antibody positivity in 45% of CCPD cases.[2] Key features of NF155-positive CCPD include: 1) CNS and PNS involvement either simultaneously or sequentially; 2) peripheral demyelination indistinguishable from CIDP; 3) CNS lesions that may mimic typical MS or display atypical diffuse cerebral white matter involvement; 4) absence of CSF oligoclonal IgG bands despite elevated CSF protein levels; and 5) limited response to corticosteroids, while IVIg and plasma exchanges are beneficial for both CNS and PNS lesions.[1,5] In our case, the patient tested positive for anti-NF155 antibodies, and his clinical course progressed from peripheral symptoms (numbness, motor weakness, ataxia, tremor) to CNS symptoms (cranial neuropathy). Testing for NF155 antibodies should be considered in patients with suspected CCPD, especially when nerve conduction studies are abnormal and CSF lacks oligoclonal bands.

MRI findings in CCPD may include T2-weighted hyperintensities or contrast-enhancing lesions in the brain, cerebellum, brainstem, optic nerve, and spinal cord.[2,4] Several case reports have described CCPD patients with brain MRI findings that resemble those typically seen in MS.[9] In our case, DWI abnormalities were observed in bilateral deep white matter, periventricular areas, brainstem, and right cerebellum, with minimal corresponding changes on T2-weighted imaging.

DWI may serve as a sensitive marker for early demyelinating lesions, with restricted diffusion potentially appearing in the early stages of lesion development, often preceding contrast enhancement or overt T2 changes.[6,10] The DWI abnormalities in our case likely represent early-stage demyelination.

The most frequently used treatment for CCPD patients is intravenous or oral corticosteroids, followed by IVIG and plasmapheresis. Rituximab, a monoclonal antibody targeting CD20-positive B cells, may be effective in patients unresponsive to standard therapies.[1]

In summary, CCPD is a rare disorder involving demyelination of both the CNS and PNS. It can present with variable onset and clinical course. Diagnosis remains challenging due to the lack of established diagnostic criteria and its overlap with MS and CIDP. This case highlights the diagnostic complexity and clinical heterogeneity of CCPD, the diagnostic value of DWI in identifying early CNS involvement, and the importance of anti-NF155 antibody testing in patients with atypical demyelinating syndromes. Early recognition of CCPD and appropriate treatment is essential for improving outcomes. Further research is needed to refine the diagnostic criteria and guide management strategies for this rare but increasingly recognized disorder.

DISCLOSURE

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Conflicts of interest: None

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