

Chronic inflammatory demyelinating polyradiculopathy: an atypical pediatric case complicated with phrenic nerve palsy

Muzaffer Polat, Ayşe Tosun, Gül Serdaroğlu, Engin Çağlayan, Bülent Karapınar
Sarenur Gökben, Hasan Tekgül

Department of Pediatrics, Ege University Faculty of Medicine, Izmir, Turkey

SUMMARY: Polat M, Tosun A, Serdaroğlu G, Çağlayan E, Karapınar B, Gökben S, Tekgül H. Chronic inflammatory demyelinating polyradiculopathy: an atypical pediatric case complicated with phrenic nerve palsy. *Turk J Pediatr* 2007; 49: 210-214.

An atypical form of chronic inflammatory demyelinating polyneuropathy (CIDP) complicated with phrenic nerve palsy is presented with clinical and electrophysiologic features. A seven-year-old girl had initial presentation mimicking Guillain-Barré syndrome based on electrophysiologic characteristics. Between 7-11 years of age, she had five recurrences of subacute onset of weakness which usually developed over at least 2-4 months and progressed to loss of ambulation and to respiratory insufficiency. Radiologic examinations revealed unilateral phrenic nerve palsy associated with CIDP. Our patient demonstrated the rare association of CIDP and phrenic nerve palsy, resulting in diaphragmatic paralysis and respiratory failure.

Key words: chronic inflammatory demyelinating polyradiculopathy, phrenic nerve palsy, respiratory failure, EMG, MRI.

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a diagnostic term which depends on recognition, clinical symptoms and signs, electrodiagnostic studies, cerebrospinal fluid examination, and other laboratory tests¹. Although CIDP has been recognized for many years, it remains a relatively rare cause of weakness in childhood².

Children with CIDP present with a subacute onset of symmetric proximal and distal weakness which progresses over at least two months. Initial presentations may mimic Guillain-Barré syndrome (GBS); however, a broad clinical spectrum of CIDP has been reported in a large series of adults³. Atypical features of CIDP associated with central nervous system demyelinating lesions have been reported to mimic multiple sclerosis⁴. CIDP cases with cerebellar ataxia have also been reported in the adult literature⁵.

Diagnosis of CIDP is important because immunomodulating therapies are effective^{1,6}. Here we report the clinical and electrophysiological characteristics of an atypical pediatric case of CIDP complicated with phrenic nerve palsy, which has not been reported in children before.

Case Report

An 11-year-old female admitted to the pediatric intensive care unit with respiratory insufficiency at the third month of an attack of inability to walk, weakness, fatigue and of increased frequency of seizures.

Her past history revealed clinical and electrodiagnosis of GBS with a successful response to intravenous immunoglobulin (IVIG) at seven years of age. Between 7-11 years of age she had three recurrences of weakness in the lower extremities and inability to walk with duration of two-four months. During the follow-up period, she had a possible diagnosis of the relapsing form of GBS and then of an atypical form of CIDP. All the attacks were treated with IVIG without sequelae.

She was born 3500 g at 40 weeks of gestational age by normal spontaneous vaginal delivery. Motor and mental development was normal. No similar disease was present in the family history. Weight, height and head circumference were 42 kg (75-90p), 154 cm (90p), and 53 cm (50-98p) respectively. Pulse, respiratory rate and blood pressure were 102/min, 16/min, and 100/60 mmHg, respectively.

Neurological examination revealed muscle strength of 3-4/5 in left lower and upper extremities and of 4/5 in right upper and lower extremities. Distal parts of both lower extremities were atrophic and deep tendon reflexes were diminished in all extremities. Nystagmus was present bilaterally. Sensation of vibration was moderately decreased in the feet. Pinprick, touch and position sensation were mildly decreased at the toes. She had gait ataxia with positive Romberg's sign, dysdiadochokinesis and dysmetria.

Complete blood count and routine biochemical tests were normal as well as urinary and blood amino acid chromatography, and pyruvate, lactate, aryl sulfatase and biotinidase levels.

Similarly, vitamin B12 and folate levels were normal. Cellular immune panel, levels of complement and antinuclear antibody were within normal ranges. Serological examination for viral infections was negative. Protein level in cerebrospinal fluid was 98 mg/dl.

Serial EMG studies revealed the following features: (1) significantly slowing motor conduction velocity, (2) conduction block, and (3) prolonged distal latencies on motor nerves. Follow-up EMG revealed that the peripheral nerves were unresponsive to stimuli of long duration and high voltage (Table I).

Diagnosis of CIDP was essentially confirmed by a progressive or relapsing sensory, motor or sensorimotor dysfunction of peripheral nerves,

Table I. Nerve Conduction Velocities and Needle Electromyography of the CIDP Patients

		1999 7-years-old	2003 11-years-old	2003 11 years and 3 months old (at the PICU)
EMG time from onset				
Motor conduction				
Median nerve	Normal value			
Distal latency (msec)	2.73±0.44	3.36	5.28	EI
Amplitude (mV)	12.37±4.79	1.17	1.69	EI
CV (m/sec)	57.32±3.35	44.6	47.8	EI
Ulnar nerve				
Distal latency (msec)	1.98±0.21	3.54	3.57	EI
Amplitude (mV)	2.73±1.09	3.74	1.39	EI
CV (m/sec)	58.92±9.7	45.2	58.9	EI
Posterior tibial nerve				
Distal latency (msec)	3.6±0.67	ND	9.75	EI
Amplitude (mV)	12±4.68	ND	0.2	EI
CV (m/sec)	52.4±4.19	ND	24	EI
Fibular motor nerve				
Distal latency (msec)	3.01±0.43	8.65	8.3	EI
Amplitude (mV)	7.01±4.76	0.65	0.59	EI
CV (m/sec)	56.14±4.96	25.4	28.4	EI
Sensory conduction				
Median nerve				
Latency (msec)		2.20	1.91	2
Amplitude (µV)	36.1±8.82	13.7	24.7	9
CV (m/sec)	42.9±3.78	54.5	52.4	60
Ulnar nerve				
Latency (msec)		ND	2.28	EI
Amplitude (µV)	14.2±2.72	ND	13	EI
CV (m/sec)	47.7±6.75	ND	50.4	EI
Sural nerve				
Latency (msec)		ND	2.6	EI
Amplitude (µV)	26.75±6.59	ND	4.5	EI
CV (m/sec)	53.85±4.19	ND	49.2	EI
Needle EMG				
		Fibs/PSW positive	Chronic neurogenic MUPs	Chronic neurogenic MUPs
F-waves				
Latency (msec)	19.4±1.5	21	26	Absent

PICU: Pediatric intensive care unit. EMG: Electromyography. Fibs: Fibrillation potentials. PSW: Positive spike and waves. CV: Conduction velocity. MUP: Motor unit potentials. EI: Electrically inexcitable. ND: Not done.

an association with hypo or areflexia for at least two months, and the EMG findings described above. These features were essentially based on the research criteria established by the Ad Hoc Subcommittee of the American Academy of Neurology AIDS Task Force¹.

After the fifth attack of weakness, the patient received IVIG (400 mg/kg) for five days with the diagnosis of CIDP. Complex partial seizures were treated with carbamazepine. Frequency of convulsions decreased during follow-up and muscle strength recovered. The patient received intermittent IVIG treatment every three weeks as well as steroid treatment at a dose of 60 mg/day. Respiratory depression requiring ventilatory support developed despite IVIG and steroid treatments approximately three months after the initiation of the respiratory symptoms. She was lost due to sepsis and multiorgan failure that developed as a result of infection.

Somatosensory evoked potentials (SEP) revealed bilateral sensorial block in fasciculus gracilis and cortical hyperexcitability. Electronystagmography was consistent with central

nystagmus (Table II). Cranial magnetic resonance imaging (MRI) was normal. Electroencephalography (EEG) revealed an epileptic focus at the parietal lobe.

Chest X-ray revealed unilateral elevation of the hemidiaphragm suggesting phrenic nerve palsy. Spiral computerized tomography revealed eventration of left diaphragm (Table II).

Sural nerve biopsies demonstrated demyelination reflected by the reduction of the myelinated nerve fiber density and intra-fascicular edema.

Discussion

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a DP of proximal and distal muscle involvement which has a progressive or relapsing course^{2,6,7}. Although most cases have typical clinical picture of CIDP, with a symmetrical, predominantly motor polyradiculoneuropathy and proximal and distal weakness associated with hyporeflexia or areflexia over at least two months, the initial presentation in some children may mimic GBS.

Table II. Electrophysiologic and Radiologic Features of the CIDP Patients

	1999 7-years-old	2003 11-years-old	2003 11-years and 3-months-old (at the PICU)
Electrophysiology			
SEP		bilateral sensorial block in fasciculus gracilis	
BAEP		normal	
ENG		bilateral horizontal gaze-evoked nystagmus (central nystagmus)	
EEG	not done	sharp wave activity in the bilateral parietal area	right parietal focus
Radiology			
Cranial MRI	normal	normal	
Spinal MRI	normal	normal	
Chest X-ray			left diaphragmatic elevation
US			left diaphragmatic paralysis
HRCT			left diaphragmatic elevation

SEP: Somatosensory evoked potentials. BAEP: Brain-stem auditory evoked potentials. ENG: Electronystagmography. EEG: Electroencephalography. MRI: Magnetic resonance imaging. US: Ultrasonography. HRCT: High resonance computerized tomography.

This presented case had also been initially diagnosed as GBS based on the electrophysiological findings. The clinical follow-up and electrophysiologic studies provided the diagnosis of CIDP based on the research criteria set by the Ad Hoc Subcommittee of the American Academy of Neurology.

Association with atypical features, including central nervous system demyelination, prominent cranial nerve dysfunction and cerebellar ataxia, was reported in a recent large series of adults with CIDP³. Some atypical presentations have also been documented in a few children. An atypical form of CIDP with prominent axonal involvement was reported in a 12-year-old child after an initial diagnosis of myasthenia gravis at two years of age⁸.

Here we present an additional atypical case of CIDP including ataxic neuropathy and involvement of unilateral phrenic nerve palsy. Involvement of the dorsal column was documented with SEP analysis. The patient also showed four-limb and truncal ataxia with bilateral horizontal gaze-evoked nystagmus in both directions. Neurophysiologic studies (SEP and electronystagmography) indicated bilateral horizontal gaze-evoked nystagmus was caused by spinocerebellar damage. Cranial and spinal MRI examinations, which were performed to assess the evidence of probable central nervous system demyelination, were normal. It is also reported that evoked potentials have superiority to MRI in patients with CIDP⁹. Since the main features of CIDP are distal dominant motor and sensory disturbances, little attention has been focused on the ataxic form of CIDP. Therefore, the precise incidence of the ataxic form among CIDP patients remains unclear^{5,10-13}. To our knowledge, this is the first case report associated with dorsal column involvement in the childhood population.

Partial seizures were noticed during the third attack of the patient. Seizures were controlled with dual therapy (carbamazepine and phenytoin). EEG examination revealed right parietal focus. Central nervous system involvement has been reported in a few patients with CIDP^{4,5,14}. However, MRI examination did not reveal any lesion which might be related to the electrophysiologic abnormality in the right parietal area. The pathophysiology of seizures and epileptogenesis is not clear in

the patients with CIDP. Only a single case has been reported so far¹⁴. This causal relationship needs clarification with additional reports.

Diaphragmatic paralysis may result from abnormalities at any of several different sites, but most frequently arises from diseases affecting the phrenic nerve or its parent motor neurons, disorders of the neuromuscular junctions, or myopathies¹⁵. Phrenic nerve palsy had rarely been reported in association with CIDP¹⁶⁻¹⁸. Although phrenic nerve palsy is rare in patients with CIDP, it is important to take notice of this condition, because phrenic nerve palsy is critical when it occurs bilaterally or when it develops in patients who have suffered from respiratory diseases. Unilateral phrenic nerve palsy was documented in the presented case with radiologic examinations before the pediatric intensive care unit period. We thought that unilateral phrenic nerve palsy associated with the progression of CIDP may have accelerated the respiratory insufficiency of our patient.

In conclusion, as we begin to understand the more subtle and complicated presentation of CIDP, systematic neurophysiologic evaluation of the phrenic nerve and pulmonary function tests should be performed in pediatric patients with respiratory insufficiency.

REFERENCES

1. Subcommittee of the American Academy of Neurology AIDS Task Force. Research criteria for diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP). *Neurology* 1991; 41: 617-618.
2. Simmons Z, Wald JJ, Albers JW. Chronic inflammatory demyelinating polyradiculoneuropathy in children: I. Presentation, electrodiagnostic studies, and initial clinical course, with comparison to adults. *Muscle Nerve* 1997; 20: 1008-1015.
3. Rotta FT, Sussman AT, Bradley WG, Ram Ayyar D, Sharma KR, Shebert RT. The spectrum of chronic inflammatory demyelinating polyneuropathy. *J Neurol Sci* 2000; 173: 129-139.
4. Rodriguez-Casero MV, Shield LK, Coleman LT, Kornberg AJ. Childhood chronic inflammatory demyelinating polyneuropathy with central nervous system demyelination resembling multiple sclerosis. *Neuromuscul Disord* 2003; 13: 158-161.
5. Ozawa E, Fujimoto T, Motomura M, Shirabe S, Yoshimura T, Tanaka K. [A case of CIDP with horizontal gaze-evoked nystagmus and ataxia]. *Rinsho Shinkeigaku* 2002; 42: 221-226.
6. Uncini A, Parano E, Lange DJ, De Vivo DC, Lovelace RE. Chronic inflammatory demyelinating polyneuropathy in childhood: clinical and electrophysiological features. *Childs Nerv Syst* 1991; 7: 191-196.

7. Dyck PJ, Lais AC, Ohta M, Bastron JA, Okazaki H, Groover RV. Chronic inflammatory polyradiculoneuropathy. *Mayo Clin Proc* 1975; 50: 621-637.
8. Kimura K, Nezu A, Kimura S, et al. A case of myasthenia gravis in childhood associated with chronic inflammatory demyelinating polyradiculoneuropathy. *Neuropediatrics* 1998; 29: 108-112.
9. Pakalnis A, Drake ME Jr, Barohn RJ, Chakeres DW, Mendell JR. Evoked potentials in chronic inflammatory demyelinating polyneuropathy. *Arch Neurol* 1988; 45: 1014-1016.
10. Dalakas MC. Chronic idiopathic ataxic neuropathy. *Ann Neurol* 1986; 19: 545-554.
11. Gorson KC, Allam G, Ropper AH. Chronic inflammatory demyelinating polyneuropathy: clinical features and response to treatment in 67 consecutive patients with and without a monoclonal gammopathy. *Neurology* 1997; 48: 321-328.
12. Bouchard C, Lacroix C, Plante V, et al. Clinicopathologic findings and prognosis of chronic inflammatory demyelinating polyneuropathy. *Neurology* 1999; 52: 498-503.
13. Oh SJ, Joy JL, Kuruoglu R. "Chronic sensory demyelinating neuropathy": chronic inflammatory demyelinating polyneuropathy presenting as a pure sensory neuropathy. *Neurol Neurosurg Psychiatry* 1992; 55: 677-680.
14. Ohtake T, Komori T, Hirose K, Tanabe H. CNS involvement in Japanese patients with chronic inflammatory demyelinating polyradiculoneuropathy. *Acta Neurol Scand* 1990; 81: 108-112.
15. Wilcox PG, Pardy RL. Diaphragmatic weakness and paralysis. *Lung* 1989; 167: 323-341.
16. Kawakami T, Sekijima Y, Tokuda T, Yamazaki M, Yanagisawa N. [A case of chronic inflammatory demyelinating polyradiculoneuropathy complicated by phrenic nerve palsy]. *Rinsho Shinkeigaku* 1998; 38: 118-121.
17. Stojkovic T, De Seze J, Hurtevent JF, Fourrier F, Vermersch P. Phrenic nerve palsy as a feature of chronic inflammatory demyelinating polyradiculoneuropathy. *Muscle Nerve* 2003; 27: 497-499.
18. Macia F, Le Masson G, Rouanet-Larriviere M, et al. A prospective evaluation of phrenic nerve conduction in multifocal motor neuropathy and chronic inflammatory demyelinating polyneuropathy. *Muscle Nerve* 2003; 28: 319-323.