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Case Report

Chronic inflammatory demyelinating polyradiculoneuropathy associated with Sjögren's syndrome in a child

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ABSTRACT

Background. Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a peripheral nervous system disease associated with polyautoimmunity.

Case. We report a previously healthy 13-year old boy who was referred to our outpatient clinic with gait disturbance and distal lower limb weakness that had been increasing for six months. The patient had decreased deep tendon reflexes in the upper extremities and absence in the lower extremities, reduced muscle strength in the distal and proximal lower extremities, muscle atrophy, drop foot, and normal pinprick sensations. The patient was diagnosed with CIDP as a result of clinical findings and electrophysiological studies. Autoimmune diseases and infectious agents were investigated in terms of triggering CIDP. Although there was no clinical sign other than polyneuropathy, he was also diagnosed with Sjögren's syndrome due to positive antinuclear antibodies and antibodies against Ro52, and with autoimmune sialadenitis. After six months of monthly intravenous immunoglobulin and oral methylprednisolone treatments, the patient was able to dorsiflex his left foot and walk without support.

Conclusions. To our knowledge, our case is the first pediatric case with the coexistence of Sjögren's syndrome and CIDP. Therefore, we suggest investigating children with CIDP in terms of underlying autoimmune diseases such as Sjögren's syndrome.

Key words: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), neuropathy, polyautoimmunity, Sjögren's syndrome.

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a peripheral nervous system disease associated with an immune-mediated response.[1] The prevalence of CIDP in children is 0.22 per 100,000 and is rarer than in adults.[2,3] Environmental and genetic factors may contribute to the autoimmunity of CIDP.[4] It is characterized by symmetric weakness and sensory dysfunction in limbs, lasting at least eight weeks. Moreover, autonomic nervous system involvement, cranial nerve palsy and neuropathic pain may occur less frequently.[5] Invaluable findings for the diagnosis of CIDP include the absence or decreased deep tendon reflexes (DTR) in neurological examination, and demyelination in electrophysiological studies. Diagnostic criteria including clinical, laboratory, electrophysiological, and laboratory findings for all age groups were updated in 2021 by the European Academy of Neurology/Peripheral Nerve Society.[6] However, diagnosis of pediatric CIDP is difficult due to the inadequacy or misinterpretation of electrophysiological studies.[3]

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According to the literature, CIDP may be associated with some autoimmune diseases such as systemic lupus erythematosus (SLE), myasthenia gravis (MG), multiple sclerosis (MS), Sjögren's syndrome (SS), Hashimoto's thyroiditis, rheumatoid arthritis (RA), type 1 diabetes mellitus (T1D), vitiligo, Graves' disease, primary biliary cholangitis, and autoimmune hepatitis.[4] However, only SLE, MG, MS, T1D, Graves' disease and autoimmune hepatitis have been reported to be associated with CIDP in childhood.[7-15] We aim to present the first pediatric case with the coexistence of CIDP and Sjögren's syndrome.

Case Report

A 13-year-old boy presented with progressive gait disturbance and distal lower extremity weakness for six months. The medical history was uneventful except for a history of 30-week prematurity. He was born after an uneventful pregnancy and delivery, to non-consanguineous parents. His developmental milestones were reported as normal. The patient had a cousin with a history of Guillain–Barré syndrome.

On neurological examination at admission, DTRs were found as decreased in the upper extremities and absent in the lower extremities. Moderate muscle atrophy and reduced muscle strength were observed in the bilateral distal more than proximal lower extremities. He had bilateral drop-foot and no dorsiflexion of either feet. He could walk with support. He had normal pinprick sensations in his limbs and trunk.

Cranial and spinal magnetic resonance imaging (MRI), and genetic analysis for Charcot Marie Tooth variants were normal. Electromyography

Table I. The results of nerve conduction study, needle electromyography findings, and F waves of the patient with CIDP associated with Sjögren's syndrome.

Nerve	Left			Right		
Motor Nerve	MCV (m/s)	CMAP (mV)	Distal latency (ms)	MCV (m/s)	CMAP (mV)	Distal latency (ms)
Median nerve	36.5	6.22	4.7	30.2	4.79	5.3
Ulnar nerve				43	11.6	3.1
Peroneal nerve	No response	No response	No response	No response	No response	No response
Sensory nerve	SCV (m/s)	SNAP (μV)	Distal latency (ms)	SCV (m/s)	SNAP (μV)	Distal latency (ms)
Median nerve	39.2	9.30	3.32	45.2	10.8	3.1
Ulnar nerve				41	17	3.8
Sural nerve	No response	No response	No response	No response	No response	No response
F wave conduction velocity						
Ulnar nerve				35		

Muscle	Left				Right			
	Interference	Fibrillation	Positive sharp waves	MUAP	Interference	Fibrillation	Positive sharp waves	MUAP
Biceps brachii muscle	Normal	Negative	Negative	Normal	Normal	Negative	Negative	Normal
Extensor digitorum communis muscle	Normal	Negative	Negative	Normal	Normal	Negative	Negative	Normal
Tibialis anterior muscle	No action	++	Negative	No action	No action	++	Negative	No action
Gastrocnemius medialis muscle	Reduced	Negative	Negative	High amplitude	Reduced	Negative	Negative	High amplitude

CMAP: compound motor action potential, MCV: motor conduction velocity, MUAP: motor unit action potential, SCV: sensory conduction velocity, SNAP: sensory nerve action potential.

and nerve conduction studies were performed (Table I). In the upper extremity, distal latencies were detected as prolonged, motor conduction velocities were found as decreased, and there was also a conduction block. Despite using supramaximal stimulation, motor and sensory nerve conductions could not be obtained in the lower extremity. Neurogenic motor unit action potentials (MUAPs) were observed in the lower extremity muscles. These electromyoneurography (EMNG) findings were consistent with sensory and motor demyelinating polyneuropathy with predominant demyelination, severe in the lower extremities, mild in the upper extremities, and accompanied by loss of axons in the lower extremities.

The cerebrospinal fluid (CSF) evaluation revealed increased protein levels (97 mg/dl, normal reference: 15-45 mg/dl). The IgG index (CSF/serum ratio for IgG) was found as 0.7 (normal reference: 0-0.77). Infectious markers, erythrocyte sedimentation rate (11 mm/h, normal reference limit 0-15 mm/h), anti-ganglioside antibodies, neurofascin 155 and 186 were all unremarkable. Based on these clinical and neurophysiological findings, he was diagnosed with CIDP and was treated with monthly intravenous immunoglobulin (IVIg, 2 g/kg in 5 days). Serum autoantibodies were analyzed in terms of underlying autoimmune diseases. Antinuclear antibody (ANA; 1:80 arbitrary units (AU), normal reference limit <1:40 AU), thyroid autoantibodies [thyroid peroxidase antibody (anti-TPO):153 IU/ml, normal reference limit 0-34 IU/ml; thyroglobulin antibody (anti-TG):155 IU/ml, normal reference limit 0-115 IU/ml], and antibodies against Ro52 were found to be positive. However, rheumatoid factor (RF), anti-double-stranded DNA (anti-dsDNA), anti-Ro/SSA, and anti-La/SSB antibodies were found negative. Unfortunately, antibodies against Ro60 could not be tested. These autoantibody tests were repeated and confirmed two more times within three months. The thyroid ultrasonography (USG) and thyroid function tests were unremarkable. The Schirmer's test was considered abnormal because of the result of 35 mm/5 minutes. The salivary gland biopsy showed an inflammatory focus exceeding 50 lymphocytes (>1 focus/4mm^2), consistent with autoimmune sialadenitis and supportive of Sjögren's syndrome. He was diagnosed with definitive Sjögren's syndrome, according to the Japan Pediatric Sjögren's syndrome clinical practice guideline, by getting seven points serologically, two points from the exocrine gland score and 0 points from the lacrimal gland score.[16]

Based on the clinical and electrophysiological findings, we suggested that the patient had coexistence of CIDP and Sjögren's syndrome. We administered pulse intravenous methylprednisolone (1g/day for 3 days) and then continued with oral methylprednisolone (1 mg/kg/day) with monthly IVIg (total 1-2 g/kg in 2-5 days). The patient was able to dorsiflex his left foot and walk without support at the 6th month of his first admission.

Written informed consent was obtained from both the parents and the participant of the study after the treatment for the publication of this case report.

Discussion

Based on the current clinical features and electrophysiological findings, the patient was diagnosed with CIDP according to the latest European Academy of Neurology/Peripheral Nerve Society guidelines.[6] Demonstration of increased protein in CSF and partial recovery with IVIg therapy are supportive findings for the diagnosis of CIDP in our patient. Other supportive findings, according to the latest guidelines, are the use of USG and MRI, and nerve biopsy. Median nerve segments and brachial plexus imaging with USG are not recommended in the pediatric population, and are used in possible CIDP diagnostic criteria in adults.[6] Magnetic resonance imaging may detect enlargement or hyperintensity of the nerve roots, but it was normal in our patient.

Since nerve biopsy is not recommended in cases with a definite diagnosis of CIDP, it was not performed on our patient.

The patient was evaluated for possible underlying infectious, autoimmune, and genetic etiologies. The findings which support Sjögren's syndrome such as high autoantibody levels including ANA, anti-Ro-52, anti-TPO, anti-TG, and the autoimmune sialadenitis which was demonstrated by salivary gland biopsy were defined. A single anti-Ro test combining anti-Ro-60 and anti-Ro-52 antibodies in solid-phase immunoassays was found to be negative in our patient. However, separately performed assays for anti-Ro-60 and anti-Ro-52 are more useful.[17] Accordingly, these findings fulfilled the definitive diagnostic criteria for Sjögren's syndrome according to the Japan Pediatric Sjögren syndrome clinical practice guidelines.[16]

As is known, neurological involvement, such as polyneuropathy, often occurs much earlier than classical Sjögren's syndrome findings, such as dry eyes, dry mouth.[18] Seeliger et al.[19] suggested that this association can be called neuro-Sjögren, and when they evaluated their patients with neuro-Sjögren retrospectively in their study, they noticed that most of the patients met the diagnostic criteria for atypical CIDP, which shows that the association of CIDP and Sjögren's syndrome is significant.

The association between CIDP and Sjögren's syndrome was first reported in an 83-year-old woman in Taiwan.[20] Subsequent studies also showed that female gender predominance was higher than male gender in patients with pure CIDP.[3,21-23] In a comparative study in the adult population, Seeliger et al.[24] suggested that female gender predominance and cranial nerve involvement may be red flags for an additional Sjögren's syndrome in patients with CIDP. On the other hand, a significant difference between CIDP with and without Sjögren's syndrome in terms of clinical, electrophysiological and CSF findings was not observed.[24] However, the validity of these findings need to be confirmed in further studies.

The patient is currently receiving monthly IVIg and oral methylprednisolone therapy, and clinically moderate improvement in muscle strength has been observed. In addition, some clinicians recommend adding rituximab to treatment in the coexistence of CIDP and Sjögren's syndrome or the presence of IVIg and corticosteroid resistance.[25]

To our knowledge, our case is the first pediatric case with the coexistence of Sjögren's syndrome and CIDP. This report expands on the comorbidities of CIDP and suggests that CIDP may present with Sjögren's syndrome in childhood. Therefore, we suggest investigating children with CIDP in terms of underlying autoimmune diseases such as Sjögren's syndrome. Further case series are needed to identify a potential correlation between CIDP and Sjögren's syndrome.

Ethical approval

Ethical approval was waived by the local Ethics Committee of Ankara University in view of the retrospective nature of the study and all the procedures being performed were part of the routine care. The study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from both the parents and the participant of the study.

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: NYS, ATK, MY, ŞE; interpretation of results: FA, ZBÖ, ÖB, ST; draft manuscript preparation: NYS, MY. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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