



Case Report

Combined Central And Peripheral Nervous System Demyelination: A Case Report

İlay Hilal KILIÇ, Can Emre ERDOĞAN, İsa AYDIN, Figen GÖKÇAY, Ayşe Nur YÜCEYAR

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

Abstract

Combined central and peripheral nervous system demyelination (CCPD) is a fairly new concept and our knowledge is restricted to several case series and case reports. We aimed to contribute to the literature with our experiences in the management of a patient representing both chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and multiple sclerosis (MS) features. A 32-year-male patient presented with neuropathic complaints for one year and recent onset of optic neuritis with central demyelinating lesions. Clinical, electrophysiological and radiological response was achieved with corticosteroid treatment and relapsed after cessation. His second simultaneous CCPD exacerbation did not respond on intravenous immunoglobulins (IVIG) but responded well on intravenous high dose corticosteroid. Previous studies reported inadequate responses to high-dose corticosteroids and IVIG in the majority of patients with CCPD. It's estimated to be a unique disease beyond MS and CIDP with heterogenous features. We suggest that awareness of this steroid-dependent condition may improve our knowledge in the pathophysiology and management strategies.

Keywords: Chronic inflammatory demyelinating polyneuropathy; Multiple sclerosis; Combined central and peripheral demyelination; Optic Neuritis

Kombine Santral Ve Periferik Sinir Sistemi Demiyelinizasyonu: Bir Olgu Bidirimi

Özet

Kombine santral ve periferik sinir sistemi demiyelinizasyonu (CCPD), oldukça yeni bir kavramdır ve bu konudaki bilgilerimiz az sayıdaki olgu serileri ve olgu bildirimlerine dayanmaktadır. Amacımız hem kronik inflamatuvar demiyelinizan polinöropati (CIDP) hem de multipl skleroz (MS) bulguları olan bir olgunun yönetimindeki deneyimlerimizle literature katkı sağlamaktır. 1 yıldır nöropatik şikayetleri olan 32 yaşında erkek hasta yeni gelişen optik nörit ve eşlik eden santral demiyelinizan lezyonlarla başvurdu. Kortikosteroid tedavisiyle klinik, elektrofizyolojik ve radyolojik yanıt sağlandı ve kesilmesiyle birlikte relaps gözlemlendi. İkinci eş zamanlı CCPD hecmesi intravenöz immunglobulin (IVIG) tedavisine yeterli yanıt vermemekle birlikte intravenöz yüksek doz kortikosteroidden belirgin yarar gördü. Önceki çalışmalarda CCPD olgularının çoğunda ne IVIG ne de yüksek doz kortikosteroidlerle tatmin edici sonuçlar elde edilemediği bildirilmektedir. CCPD'nin MS ve CIDP'nin ötesinde, heterojen özelliklere sahip, ayrı bir hastalık olduğu düşünülmektedir. Bu steroid bağımlı tabloya yönelik farkındalığın hastalığın patofizyolojisi ve tedavi stratejileri hakkındaki bilgilerimize katkı sağlayabileceğini düşünüyoruz.

Anahtar Kelimeler: Kronik inflamatuvar demiyelinizan polinöropati; Multipl skleroz; Kombine santral ve periferik sinir sistemi demiyelinizasyonu; Optik nörit

INTRODUCTION

Recent immunologic studies are supporting that combined central and peripheral nervous system demyelination (CCPD) is a distinct entity with a different pathophysiology, rather than a coincidence of multiple sclerosis (MS) and chronic inflammatory demyelinating polyneuropathy (CIDP) or central nervous system involvement in the CIDP course (1). CCPD may differ from MS and CIDP, in terms of clinical course, management strategies and treatment response, and needs a unique approach. In this paper we describe a patient featuring both, central and peripheral nervous system demyelination and share our experience in the management.

CASE PRESENTATION

A 32 year old male patient presented with acute blurred vision on the left eye for about 10 days and was admitted to the neurologic inpatient station. He had no antecedent infection or vaccination. He also complained of progressive tingling and numbness sensation in his hands and feet for about a year and weakness in the distal parts of the extremities for 3 months, causing difficulty in walking and carrying heavy objects in the hand.

His physical examination showed a relative afferent pupillary defect on the left side, symmetrical profound distal weakness, glove and stocking hypoesthesia, bilateral thenar atrophy and absence of deep tendon reflexes. Power was +4/5 (MRC ;Medical Research Council) proximally, and 3/5 distally in the upper and lower limbs. His visual acuity was 1.0 on the right side and 0.5 (with pinhole) on the left side ; color vision was 21/21 on the right side and 10/21 on the left side. Complete blood

count, fasting glucose concentration, glycosylated hemoglobin concentration (Hb A1c), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), hepatic and renal function tests, serum vitamin B-12 and folate concentrations, and thyroid function tests were within normal range.

Nerve conduction studies showed proximal conduction block and abnormal temporal dispersion in bilateral median, left ulnar motor, peroneal motor and posterior tibial nerves, with a reduction in conduction velocity in the peroneal and posterior tibial motor nerves, more than %30 below lower limit of normal values. He was diagnosed as CIDP based on clinical, electrophysiological findings and symptoms lasting for more than a year. Serum protein and immunofixation electrophoresis, tumor markers were normal. Antibodies against hepatitis C virus (HCV), hepatitis B virus (HBV) and human immunodeficiency virus (HIV) were negative. Chest x-ray and abdominal ultrasonography were normal. Visual Evoked Potentials (VEP) were concordant with demyelinating optic neuropathy in the left eye with subclinical involvement in the right eye. We investigated the patient for accompanying central nervous system involvement with magnetic resonance imaging (MRI) studies. His spinal MRI was normal but cranial MRI showed asymptomatic demyelinating lesions in the right middle cerebellar peduncle and right basal ganglia (Fig.1). The patient refused to undergo a lumbar puncture. He recieved 1gr/day intravenous metilprednisolone for 7 days and oral prednisolone 80 mg daily as maintenance therapy . His weakness improved significantly after pulse corticotherapy, with a muscle strength of 5/5 in proximal and +4/5 in distal extremities. His visual acuity also

improved to 0,9⁻¹ in the left eye on discharge.

He regained normal muscle strength under steroid therapy that was slowly tapered to 60 mg/d within a month. After 7 months on prednisolone 25 mg every other day treatment, repeated nerve conduction studies resulted within normal range. Neuroophthalmologic evaluation revealed a visual acuity of 1.0 in the right eye and 1.0⁻³ in the left eye. Pattern reversal visual evoked potential (VEP) P100 latency was 108 milisecond in the right eye, and 118.8 milisecond in the left eye. His control cranial MRI showed remarkable regression of the demyelinating lesions.

The patient went very well for about 1,5 years. But then he was diagnosed for coronary artery disease and underwent a coronary artery stent implantation. Steroid treatment was tapered and stopped as the cardiologist advised. After 2 months of steroid discontinuation, the patient showed up with paresthesias in the hands and feet, and blurred vision in the left eye. He was hospitalized for his second attack. His physical examination showed no apparent weakness but he complained of paresthesia in the hands and feet and additionally a right hemipoesthesia beyond the third thoracic vertebral level. Deep tendon reflexes were absent, Babinski sign was bilateral positive. The former blood tests were repeated and were within normal range. But his current MRI showed a focal T2w hiperintens lesion of the posterolateral spinal cord, at the level of 1.-2. cervical

vertebra (Fig.2). This contrast enhancing lesion suggested an active demyelinating plaque. Cranial MRI showed regression of the previously mentioned lesions. Orbita MRI showed T2w hyperintense and contrast enhancing lesion in the intraorbital part of the left optic nerve, suggestive for acute demyelinating optic neuropathy without clinical evidence of vision deterioration. Nerve conduction studies showed decreased motor conduction velocities and proximal motor conduction blocks. Cerebrospinal fluid (CSF) analysis showed slightly increased protein levels (microprotein:47mg/dl, normal range:15-45mg/dl) without pleocytosis and type 3 oligoclonal bant positivity. Because of his metabolic problems, we preferred a treatment course of 2gr/d intravenous immunoglobulin (IVIG) for 4 days, instead of intravenous pulse methylprednisolone. But the patient did not benefit, therefore he was started on prednisolone 15mg/d therapy at discharge. After three weeks on prednisolone 15mg/d treatment he still did not show any improvement, thus he was put on 500mg/d IV methylprednisolone treatment for three days and 60mg/d prednisolone as maintenance therapy. His paresthetic symptoms diminished within days. Steroid dose was slowly tapered within 2 months and Azathioprine (AZA), was added to the treatment. The patient is still on AZA 50mg twice a day and prednisolone 5mg every other day treatment for 12 months and is doing well, without any new central or peripheral nervous system involvement.

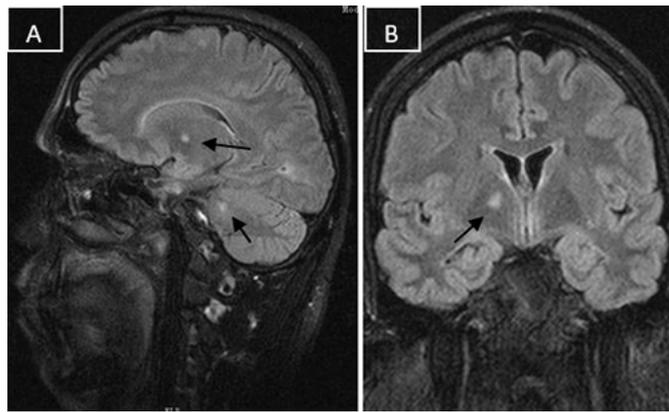


Fig 1: Brain MRI sagittal FLAIR sequence (A), coronal FLAIR sequence (B) showing signal intensity within the right middle cerebellar peduncle and right basal ganglia.

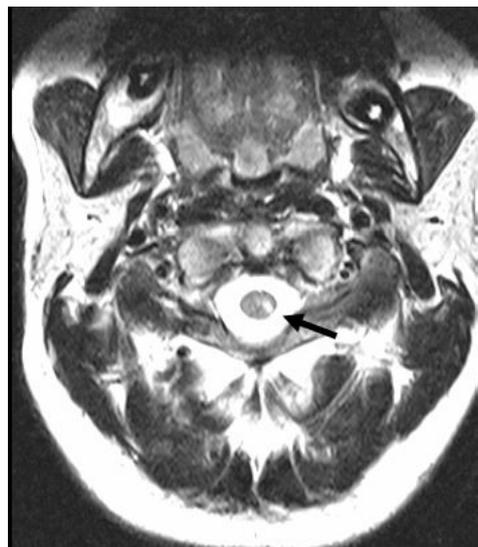


Fig 2: Cervical MRI axial T2w sequence showing signal intensity within the posterolateral spinal cord, at the level of 1.-2.cervical vertebra.

DISCUSSION

Our patient presented with distal weakness three months prior to an optic neuritis attack. He fulfilled clinical and electrodiagnostic criteria for CIDP, according to European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) guideline (2).

MS like demyelinating non-contrast enhancing lesions in the right cerebellar peduncle and right basal ganglia detected on MRI disappeared in seven months after corticotherapy for optic neuritis. His clinical signs and symptoms and electrophysiological findings of CIDP also responded very well to corticosteroids. But after a steroid discontinuation for 2 months, he relapsed with symptoms of polyneuropathy and spinal cord syndrome suggesting simultaneous combined central and peripheral nervous system demyelination. Based on clinical attacks and follow up MRI findings (new lesions in the spinal cord, optic nerve and in temporal region with former supratentorial and infratentorial lesion) he fulfilled the revised McDonald criteria for MS(3). His acute symptoms most apparently benefit from high dose steroid treatment rather than intravenous immunoglobulins (IVIG). Simultaneous central and peripheral demyelinating exacerbation after cessation of oral steroid indicates that CCPD may have a steroid dependant character similar to neuromyelitis optica. In a study published in 2016, where data of 31 patients with CCPD were analyzed retrospectively; 23 patients (74%) fulfilled the electrodiagnostic criteria for CIDP and 11 patients (46%) had spatial dissemination of demyelinating lesions fulfilling the 2010 McDonald criteria for MS. Two thirds of the patients were found to be inadequately responsive to high-dose corticosteroids and IVIG. But the authors are stating that "CCPD has heterogeneous features and current

diagnostic criteria for MS and CIDP may not fully encompass the spectrum of possible manifestations of CCPD"⁴.The pathophysiology of CCPD is still unknown. But there is increasing data suggesting that this condition may be caused by an autoimmune process against common epitopes expressed both in central and peripheral nervous system(1).

CONCLUSION

Central nervous system (CNS) involvement in CIDP patients has been reported in previous studies⁵. But recent studies showed some differences in the disease course and treatment response in this group 4. The notion of CCPD as a unique entity beyond CIDP and MS is also emerging. Despite the growing interest in CCPD, the pathophysiology is still unclear and our knowledge is restricted to several case series and case reports. A detailed neurologic examination and our awareness may increase the number of CCPD diagnosis and improve our management as well as our understanding of the pathophysiology.

Correspondence to:

İlay Hilal Kılıç

E-mail: ilayhilalkilic@hotmail.com

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