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Case Report / Olgu Sunumu

Tumefactive Brain Demyelination Accompanying Multifocal Acquired Demyelinating Sensory and Motor Neuropathy

Multifokal Edinsel Demiyelinizan Duysal ve Motor Nöropatiye Eşlik Eden Tümefaktif Beyin Demiyelinizasyonu

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Summary

Multifocal acquired demyelinating sensory and motor (MADSAM) neuropathy is characterized by asymmetric multifocal motor and sensory loss and conduction blocks in peripheral nerves. Peripheral demyelinating diseases may be accompanied by demyelination in the central nervous system (CNS). In this report, we present a patient with MADSAM who had a solitary tumefactive demyelinating lesion in the brain. Neuroimaging was performed because of a visual field defect revealed a right parietooccipital lesion, which was initially misdiagnosed as a tumor. A pathologic examination showed that it was demyelinating in nature. The patient developed peripheral nervous symptoms two years later and was then diagnosed as having MADSAM. There was a prominent clinical and electrophysiologic response to steroid treatment. Tumefactive brain involvement has not previously been reported for MADSAM neuropathy, although it has been documented in a single case of typical chronic inflammatory demyelinating polyneuropathy (CIDP). CNS involvement should therefore be considered in patients with MADSAM.
Keywords: Multifocal acquired demyelinating sensory and motor, neuropathy, tumefactive, brain, demyelination

Öz

Multifokal edinilmiş demiyelinizan duysal ve motor (MADSAM) nöropati, asimetrik motor ve duysal kayıplar ve periferik sinirlerde ileti blokları ile karakterizedir. Periferik demiyelinizan hastalıklara santral sinir sisteminde de demiyelinizasyonun eşlik edebildiği iyi bilinmektedir. Bu raporda, beyinde tümefaktif tek bir demiyelinizan lezyonun bulunduğu bir MADSAM olgusu sunulmaktadır. Yeni gelişen görme alanı defekti nedeniyle yapılan nörogörüntüleme sonucunda sağ parietooksipital bölgede başlangıçta tümör olarak yanlış tanı alan bir lezyon saptanmıştır. Patolojik inceleme sonucunda bu lezyonun demiyelinizan nitelikte olduğu anlaşılmıştır. Bu bulgudan iki yıl sonra, hastada periferik nöropatiyi düşündüren semptomlar ortaya çıkmış ve hasta MADSAM tanısı almıştır. Steroid tedavisi ile belirgin klinik ve elektrofizyolojik yanıt elde edilmiştir. Beyinde tümefaktif demiyelinizan lezyonlar, daha önce bir kronik enflamatuvar demiyelinizan nöropati olgusunda bildirilmiş olmasına karşın, MADSAM için bu tür bir bildirimde bulunulmamıştır. MADSAM olgularında da bu nedenle santral sinir sistemi tutulumu olasılığı gözden geçirilmelidir.
Anahtar kelimeler: Multifokal edinilmiş demiyelinizan duysal ve motor, nöropati, tümefaktif, beyin, demiyelinizasyon

Introduction

Multifocal acquired demyelinating sensory and motor (MADSAM) neuropathy is a variant of chronic inflammatory demyelinating polyneuropathy (CIDP), with an asymmetric multifocal pattern of motor and sensory loss, conduction blocks, and other signs of demyelination in nerve conduction studies (1,2). It is known that peripheral demyelination can accompany demyelination in the central nervous system (CNS) (3,4,5,6,7). In CIDP, symptomatic clinical involvement of the CNS occurs in up to 5% of patients

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and subclinical abnormalities can be demonstrated in 20% with electrophysiologic studies and magnetic resonance imaging (MRI) (8). The exact mechanism of this coeexistence is currently unknown. Brain involvement usually appears on MRIs as multiple small periventricular T2 hyperintense lesions, sometimes in the form of multiple sclerosis (MS) plaques (4,5,6,9,10,11). However, a large solitary steroid-responsive demyelinating brain lesion has been reported in one patient with CIDP (12). Although CNS involvement as optic neuritis, and brain and spinal cord lesions have previously been shown in multifocal demyelinating neuropathy, which is a rare clinical entity, there are no reports of a tumefactive brain lesion accompanying MADSAM neuropathy (4,10,13). Here, we present a case of a biopsy-proven solitary demyelinating lesion in the brain with evidence of multifocal demyelination in motor and sensory nerve fibers.

Case Report

A female patient aged 49 years initially developed left homonymous hemianopsia with numbness in her hand and foot. The symptoms had gradually developed over a few weeks. On cranial MRI, a T2 hyperintense lesion with contrast enhancement in the right parietooccipital region was detected (Figure 1A, 1B, 1C). We took an excisional biopy after suspecting a brain tumor. The results of a histopathologic examination revealed a demyelinating lesion, which was densely populated by macrophages and reactive astrocytes with prominent cytoplasmic processes that extended from enlarged and eosinophilic cell bodies (Figure 2A). The sharp demyelination was accentuated after myelin staining with Luxol fast blue (Figure 2B). The macrophages had abundant vacuolations in the cytoplasm (Figure 2C). Immunohistochemically, the macrophages were immunoreactive for CD68 (Figure 2D). There was a scattered lymphoplasmacytic infiltrate. After the patients was diagnosed as having demyelinating central nervous system disease, she received a course of iv methylprednisolone. Following treatment, the sensory symptoms in her extremities disappeared and contrast enhancement in the brain lesion diminished, but her hemianopsia did not recover.

Following a stable period of approximately two years, she presented to our clinic with a 5-month history of progressive numbness and tingling in all her extremities, difficulty in walking, and weakness in her feet. She had also begun to feel a burning and stabbing pain, mainly in her left arm and leg. She reported no worsening in vision loss. There was no incontinence or systemic symptoms such as weight loss, fever, joint pain, and dry mouth or eyes. She had autoimmune hypothyroidism and had been taking levothyroxine for many years. Her neurologic examination confirmed left homonymous hemianopsia with no deficit in visual acuity and no relative afferent pupil defect. There were no signs of cranial nerve involvement. However, the distal motor deficit was documented to be more prominent in the left side with a left-sided drop foot. There was distal sensory deficit in all extremities, which again was more prominent in the left side. The sense of vibration and position was absent in the left distal lower extremity. There was total loss of deep tendon reflexes with no sign of upper motor neuron lesions.

With the exception of iron deficiency anemia, her routine blood tests were unremarkable. Thyroid function tests, vitamin B12, and folate levels were normal. Anti-thyroid peroxidase antibody was positive but other autoantibodies, including antinuclear antibody, anti-double stranded DNA antibody, anti-extractable nuclear antigens, antiphospholipid antibodies, and anti-neutrophil cytoplasmic antibody were negative. Tumor markers were within normal limits. Sedimentation and C-reactive protein levels were normal. Follow-up cranial MRI (Figure 1C) showed near complete resolution of the periventricular T2 hyperintense lesion adjacent to the resection cavity; previously observable contrast-enhancement in that area had disappeared. There was no sign of a newly formed lesion when compared with previous imaging. MRI of the spine revealed contrast enhancement and mild thickening in the cauda equina nerve roots, and patchy mild increased signal intensity

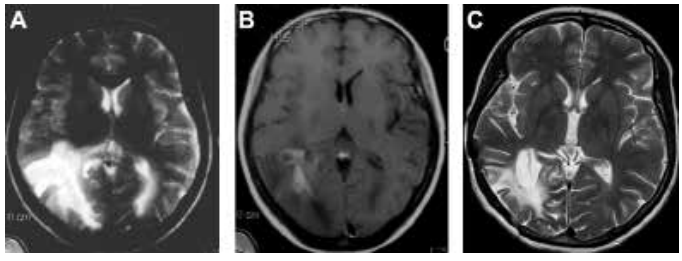

Figure 1. In cranial magnetic resonance imaging, A) Axial T2W, B) Contrast-enhanced T1W images reveal a large solitary right parietal periventricular white matter lesion with conspicuous enhancement involving the corpus callosum and left forceps major, C) Follow-up magnetic resonance imaging after treatment demonstrates near-complete resolution of the periventricular hyperintense lesion; contrast-enhancement in that area had disappeared (not shown)

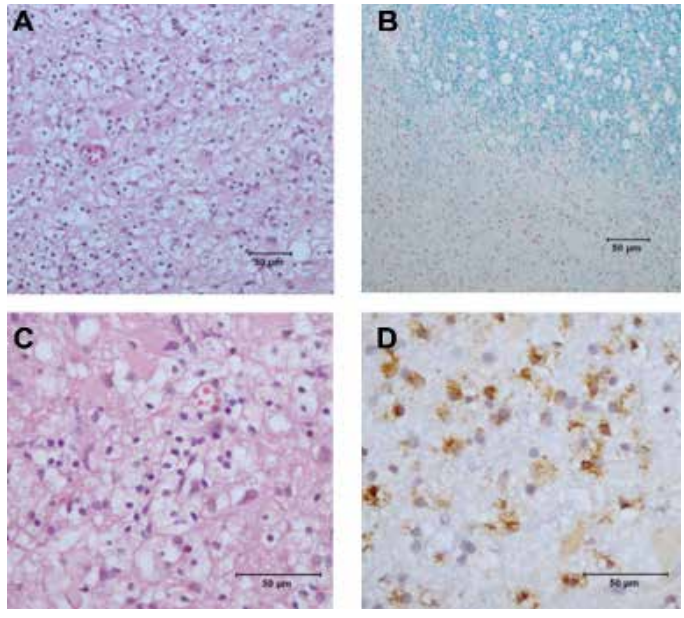

Figure 2. A) Histopathologic examination revealed a lesion that was densely populated by macrophages with reactive astrocytes, B) Luxol fast blue staining shows well circumscribed loss of blue staining in demyelinated areas (lower left), C) Macrophages with vacuolated cytoplasm were present, D) Macrophages were identified through their immunohistochemical reactivity for CD68

of lumbar plexuses, which suggested peripheral nervous system involvement (Figures 3A and 3B). Following MRI, a lumbar puncture was performed. Cerebrospinal fluid (CSF) protein was elevated (59 mg/dL), with 50 lymphocytes/mm^3. The IgG index was normal (0.5) and oligoclonal bands were negative. Lyme, brucella, syphilis, and toxoplasmosis, rubella, cytomegalovirus, herpes simplex, HIV (TORCH) tests were negative in the CSF. A cytologic examination of the CSF was negative for malignant cells.

Electrophysiologic Studies

There was a mild bilateral prolongation of P100 wave latencies. Nerve conduction studies demonstrated significantly decreased motor conduction velocity in the left median-, right ulnar-, and right peroneal nerves along with conduction blocks and loss of sensory potentials (Figure 4A and 4B). Motor and sensory nerve conduction in the right median- and left sural nerves were relatively preserved. These findings were compatible with asymmetrical and multifocal motor and sensory involvement with evidence of demyelination, which was suggestive of MADSAM neuropathy.

Treatment and Follow-up

The patient received a 5-day course of iv methylprednisolone, followed by oral deflasocort in alternating doses. Pregabalin 300 mg/day and duloxetine 60 mg/day was started for the neuropathic pain. The patient's motor deficits significantly improved in the 3-month follow-up period. She had no drop-foot and most of the sensory deficits, mainly the absent position and vibration sense in left foot, had recovered. However, there was no improvement in her left homonymous hemianopsia. Repeat nerve conduction studies demonstrated improvement in conduction blocks (Figure 4C).

Discussion

The case presented here is a unique example of CNS involvement in MADSAM neuropathy in the form of a single demyelinating lesion. The nature of the initial symptoms, visual field defect and numbness, suggested that central and peripheral lesions started at the same time. The brain lesion was initially regarded as a tumor; however, a definite demyelinating process was documented during a pathologic examination. Although her initial peripheral symptoms benefited from steroid treatment, probably because of the extent of the destructive lesion in the right parietooccipital area, her main symptom, left homonymous hemianopsia, remained stable over time. There was no another episode of CNS involvement and no additional lesions formed. However, 2 years after the initial attack, the patient had another episode of peripheral symptoms, which caused major disability. There was once again a significant response to intravenous and oral steroid therapy, and improvement in peripheral nerve lesions, both clinically and electrophysiologically.

MADSAM neuropathy should be differentiated from CIDP, although both conditions are regarded as chronic acquired demyelinating polyneuropathies. Typical CIDP is characterized by symmetric involvement, weakness, sensory symptoms in hands and feet, and loss of deep tendon reflexes (2,14). Symptoms may begin asymmetrically, but over time they progress to symmetric involvement, with characteristic elevated CSF protein (15,16). In contrast, MADSAM neuropathy is distinguished from CIDP with asymmetric weakness and conspicuous asymmetric multiple nerve involvement in electrophysiologic studies. Persistent conduction blocks in motor and sensory fibers are typical. Similar to CIDP, there is a favorable response to plasmapheresis, steorids or intravenous immunoglobulin (IVIg), and CSF protein is increased in 60-80% of patients with MADSAM neuropathy (1,17). Our patient demonstrated the definitive clinical and electrophysiologic picture of MADSAM neuropathy, along with elevated CSF protein, contrast enhancement in cauda equina, and significant response to steroids.

There are previous reports of multifocal sensory or sensorimotor demyelination accompanying evidence of CNS demyelination, which were demonstrated with evoked potential studies or MRI findings (4,13). There is large group of patients with CIDP who have CNS lesions. In the most common form, radiographic involvement of CNS demonstrates symptomatic or asymptomatic multiple, small lesions in periventricular white matter. It is still unknown whether the pathophysiology of concurring peripheral nervous system and CNS demyelination share a common immunologic mechanism. Tumefactive demyelinating CNS lesions usually occur in patients with MS (18,19). However, a case of tumefactive central demyelination associated with CIDP has been reported (12). CNS demyelinating lesions associated with CIDP may respond to steroids or IVIg (7,12).

In our patient, a diagnosis of MS was not feasible because there was no evidence of dissemination in time in relation with the

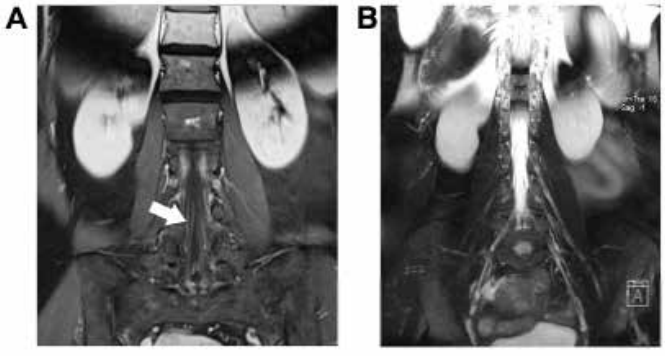

Figure 3. A) Sagittal fat-supressed contrast-enhanced T1W image shows smooth enhancement and mild thickened of the cauda equina nerve roots (arrow), B) Reconstructed by maximum intensity projection coronal fat-supressed T2W image of the lumbar spine reveal symmetric, mild patchy high signal intensity of lumbar plexus

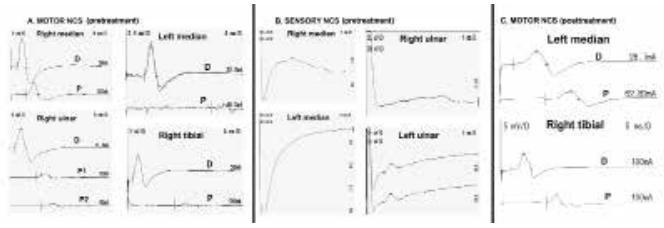

Figure 4. A) Pretreatment nerve conduction studies demonstrated motor conduction blocks more prominently in the right ulnar-, left median-, and right tibial nerves. Asymmetrical loss of sensory potentials in the right ulnar- and left median nerves are noted, B) Nerve conduction studies performed after 3 months of treatment showed partial resolution of conduction blocks in the left median- and right tibial nerves

brain lesion. Although VEP findings accompanying visual field defect could be regarded as dissemination in space, CSF findings characteristic for MS, such as high IgG index or oligoclonal bands were normal or negative. There were no plaques in the brain or spinal cord typical of the radiologic criteria for MS. Therefore, the single parietooccipital lesion and visual-evoked potential findings were evaluated as tumefactive CNS involvement of MADSAM neuropathy, a previously unreported observation. The presence of autoimmune thyroiditis in this patient would be far more than a coincidence because there are reports of autoimmune syndrome complexes involving Hashimoto's thyroiditis, CIDP or CNS demyelination (20). CNS or peripheral demyelination can occur even though thyroid involvement is asymptomatic.

The patient was very reponsive to steroids. It would be useful to continue with a tapered dose of oral steroids to prevent further relapses. However, the patient's hemianopsia did not benefit from steroid treatment, probably because of the extent of the parietooccipital lesion and reactive gliosis in the area. A lack of significant contrast enhancement within the lesion, apart from linear enhancement in the surgical border, would predict this unresponsiveness to steroids. Surgical damage to the parietooccipital area would be another factor in the persistence of the visual field defect. This case, although unique for MADSAM neuropathy, once again reminds us to be cautious of CNS lesions in patients with acquired demyelinating polyneuropathy.

Informed Consent: The patient has given written consent for presentation of medical information, **Concept:** Aslı Tuncer Kurne, **Design:** Şefik Evren Erdener, Aslı Tuncer Kurne, **Data Collection or Processing:** Şefik Evren Erdener, Çağrı Mesut Temuçin, Figen Söylemezoğlu, Rahşan Göçmen, **Analysis or Interpretation:** Şefik Evren Erdener, Aslı Tuncer Kurne, **Literature Search:** Şefik Evren Erdener, Aslı Tuncer Kurne, **Writing:** Şefik Evren Erdener, Aslı Tuncer Kurne, **Peer-review:** Externally peer-reviewed, **Conflict of Interest:** No conflict of interest was declared by the authors, **Financial Disclosure:** The authors declared that this study has received no financial support.

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