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Οι φλεγμονώδεις απομυελινωτικές παθήσεις συμπεριλαμβάνουν πολλά διαφορετικά σύνδρομα με κοινό χαρακτηριστικό την καταστροφή της μυελίνης με ή χωρίς συνοδό αξονική βλάβη, μέσω της ενεργοποίησης του ανοσοποιητικού συστήματος. Το περιστατικό που ακολουθεί αναφέρεται σε μία σπάνια περίπτωση μετα-λοιμώδους, συνδυασμένης κεντρικής και περιφερικής απομυελίνωσης σε γυναίκα ασθενή 69 ετών που προκάλεσε τη μακρά νοσηλεία της και οδήγησε τελικά σε μόνιμο μηχανικό αερισμό αυτής. Η διαφορική διάγνωση των απομυελινωτικών παθήσεων είναι πολλές φορές δυσχερής λόγω της έλλειψης ειδικών βιολογικών δεικτών. Οι ασθενείς με συνδυασμένη απομυελίνωση κεντρικού και περιφερικού νευρικού συστήματος έχουν άσχημη πρόγνωση, και επί του παρόντος δεν υπάρχει αιτιολογική, αποτελεσματική θεραπευτική επιλογή.

• • : Φλεγμονώδεις απομυελινωτικές παθήσεις, συνδυασμένη απομυελίνωση κεντρικού και περιφερικού νευρικού συστήματος

A POST-INFECTIOUS COMBINED CENTRAL AND PERIPHERAL DEMYELINATION IN A 69-YEAR-OLD FEMALE LEADING MECHANICAL VENTILATION

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Abstract

Inflammatory demyelinating diseases include various disorders characterized by Immune-mediated myelin damage, often accompanied by axonal loss. We present a rare case of a post-infectious combined central and peripheral demyelination (CCPD) of a 69-year old female patient which led to long-term hospitalization in an Intensive Care Unit and a permanent need for mechanical ventilation. Differential diagnosis of demyelinating diseases is a difficult issue due to the lack of specific biological marker. Patients with CCPD show a worse prognosis, and there is currently a lack of effective treatment.

Key words: Inflammatory demyelinating diseases, combined central and peripheral demyelination

Background

Inflammatory demyelinating diseases include various disorders characterized by immune-mediated myelin damage, often accompanied by axonal loss. Acute Disseminated EncephaloMyelitis (ADEM) is a heterogeneous syndrome with diverse etiologies and presentation (1). Guillain-Barré syndrome, on the other hand, is an acute inflammatory polyradiculopathy characterized by rapidly progressive, relatively symmetric limb weakness, areflexia, with or without the involvement of respiratory muscles or cranial nerve- innervated muscles (2). It is supposed to be the most frequent cause of acute flaccid paralysis. The simultaneous occurrence of Combined Central and Peripheral Demyelination (CCPD) is rare and data are limited (3). Patients with CCPD show a worse prognosis and a higher relapse rate compared to central nervous system (CNS) restricted variants (4). A documented infection preceded CCPD onset in 65% of cases, suggesting a triggering mechanism of the subsequent autoimmune process (3).

Case Report

A 69 years old female patient was transferred from a provincial hospital to the Neurological EmeRgencies (NER) as a probable Guillain-Barré syndrome. Regarding her medical history, she had a recent (five days ago) respiratory infection with fever, productive cough and rhinorrhea. She received antibiotic treatment (clarithromycin) at home, and three days later, she also presented diarrhea. The patient was admitted to the hospital. Physical examination revealed limb weakness and impaired bladder function, for which a catheter was induced. Then she was transferred to G.H. «Agios Pavlos».

Medical History: Breast Cancer operated in 2007, followed by radiotherapy and chemotherapy, hypertension, dyslipidemia, hypothyroidism

During her examination in NER, she presented fatigue, no fever and low blood pressure (80/60 mmHg), and was fully oriented to time and place. She had a left upper motor neuron type facial nerve palsy while the rest cranial nerves examination was normal, mild inarticulacy, lower limb weakness (muscle strength of lower limbs 3/5, upper limbs 4+/5), normal flexor plantar reflexes and mild symmetrical Tendon Reflexes (DTRs).

The emergency Brain Computed Tomography (CT) which was performed without intravenous contrast agent to rule out hemorrhage and space-occupying lesion, was normal. A lumbar puncture was performed, and the results showed a mild protein increase (64,5 mg/dl) and a modest increase in cell count (< 100 cells/ μL), polymorphonuclear type (see Table 1). Cerebrospinal Fluid (CSF) culture was sterile. She was treated with empirical antibiotic therapy: Ampicillin – Sulbactam, Ceftriaxone, Metronidazole. Unfortunately, the amount of CSF was not enough for further investigation for antibodies and PCR for viral DNA of common neurotropic viruses to be performed.

Laboratory results revealed normocytic normochromic anemia, increased Erythrocyte Sedimentation Rate (ESR), a mild increase in C-reactive protein, low serum sodium and normal procalcitonin (PCT). The admission chest X-ray was normal.

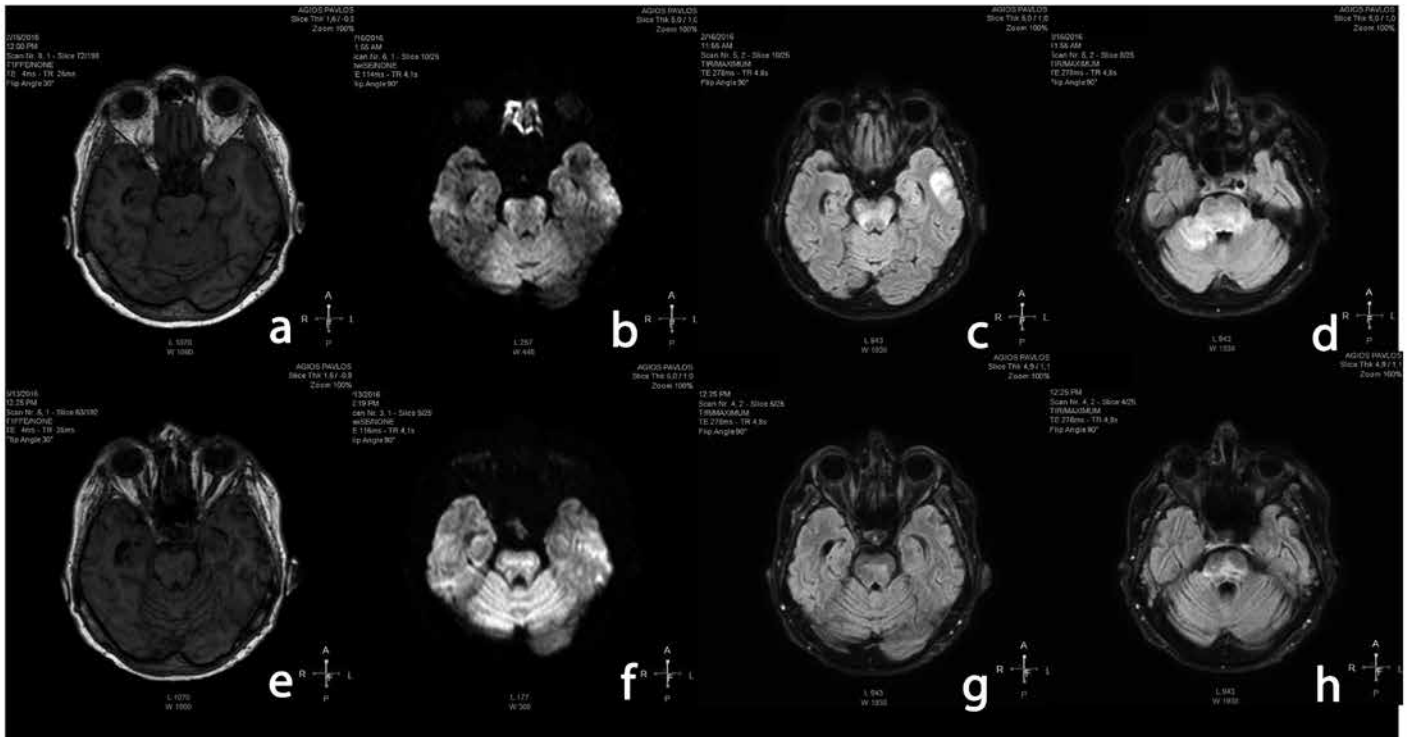
Brain Magnetic Resonance Imaging (MRI), performed the day after her admission (see Figure 1), revealed abnormal signal intensity in the pons and right cerebellar peduncle, as well as in left temporal lobe cortically and subcortically, with diffusion deterioration. Differential diagnosis of ischemia or encephalitis was not possible by the imaging findings. Heart ultrasonography (Transthoracic and transesophageal) was performed to exclude infectious endocarditis. CT of thorax, superior, inferior abdomen and retroperitoneum was performed to exclude paraneoplastic syndrome, due to patient's medical history of breast cancer.

The patient clinical condition gradually deteriorated the next 72 hours. She presented bilateral lower mo-

Table 1. CSF biochemical tests and culture

Examination	1st LP	2nd LP	Normal values
CSF Glucose	67	79	50-60% of serum glucose
CSF LDH	< 30	58	1/10 of serum U/L
CSF protein	64,5	1015,9	14-15 mg/dl
CSF cells	55/mm ^{3}	22/mm ^{3}	Adults 0-5 cells
Cell type	Polymorphonuclear	Polymorphonuclear	
Gram stain	Negative	Negative	
Koch culture	Negative	Negative	

Figure 1. First Brain MRI (upper row): a. Axial brain T1w, b. Axial Brain Diffusion-weighted imaging, c,d. Fluid attenuation inversion recovery (FLAIR): Abnormal signal in left temporal lobe cortically and subcortically Abnormal signal intensity in the pons and right cerebellar peduncle with diffusion deterioration. Second Brain MRI four months after hospital admission (lower row): e. Axial brain T1w, f. Axial Brain Diffusion-weighted imaging g, h. Fluid attenuation inversion recovery (FLAIR): Decrease of the pathologic area in the left temporal lobe.There are gliotic lesions in the pons and right cerebellar hemisphere



tor neuron type facial palsy, horizontal, torsional and vertical nystagmus in upper gaze, muscle strength 4/5 in upper limbs and 1/5 in lower limbs, absent plantar reflex bilaterally and absent DTR in lower limbs, right arm ataxia, impaired sensation in lateral aspect of the calf and plantar aspect of foot bilaterally. Impaired vocalization (volume lowering), difficulty in swallowing although preserved elevation of the soft palate. The patient complained about fatigue and weakness. The arterial blood gasses were within normal, but she was assessed by intensivists due to her easy fatigue even with breathing and talking. Her condition rapidly deteriorated, and finally, she was intubated, under mechanical ventilation and transferred to the ICU.

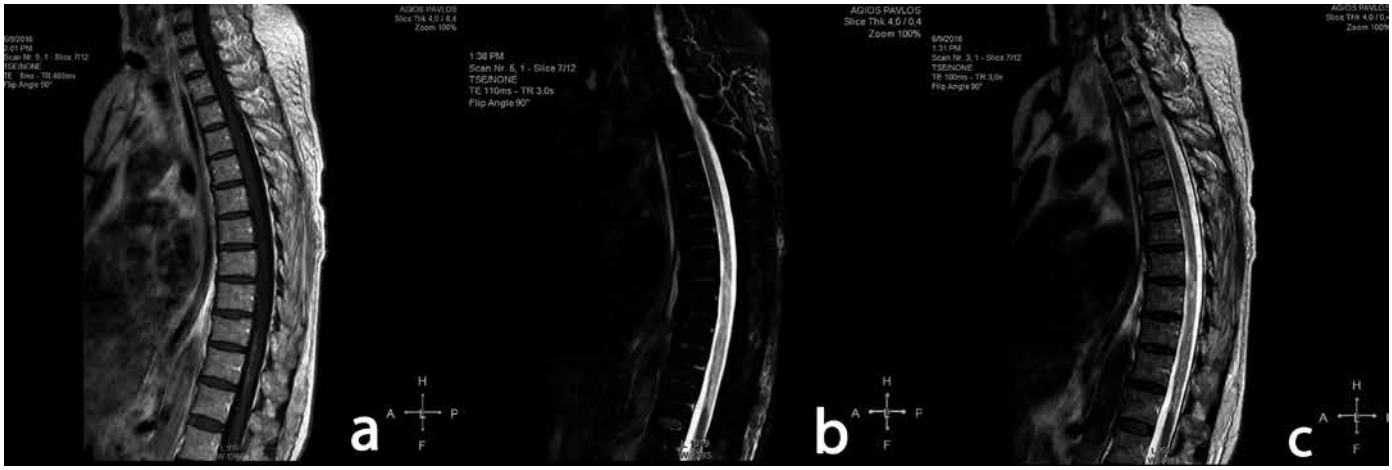
In ICU, she remained sedated, in mechanical ventilation. When she regained consciousness, she was fully oriented to place and time but with flaccid tetraplegia. A second lumbar puncture was performed (Table 1), on the eleventh day admission, which showed high protein levels and a decrease in the initial cell number. She was treated with intravenous immune globulin (IVIG) in three five-day courses (26/2-1/3, 21/3-25/3, 25/4-29/4) resulting in gradual improvement of upper limbs mobility.

During her three-month staying in ICU, she had multiple infectious/ septic incidents which were treated according to cultures and antibiograms. Despite the multiple efforts, the patient was incapable of weaning from the ventilator, as could not use the intercostal muscles. She was transferred to a neurologic clinic with a mechanical ventilator (MV PSV IPAP 24, PEEP, F_1O_2 0.29, V_T ~500ml, RR ~18/mm) while being hemodynamically stable, having a large, painless, coccyx pressure ulcer.

The new neurological examination revealed a fully oriented patient, with left hypoglossal palsy, right horizontal nystagmus and vertical at the upper gaze, diplopia at left gaze (upper, middle, lower) and mild, upper motor neuron type, left facial palsy. Plantar reflexes were absent bilaterally, muscle strength: lower limbs 0/5, upper limbs 4-/5. DTRs were absent in lower limbs, decreased in upper limbs. Sensation of pain, light touch, and temperature till T6 dermatome, as well as joint position sense and vibration were absent.

Nerve conduction study revealed prolonged distal latencies, decreased motor conduction velocity, great decrease of motor potentials, most prominent in lower limbs, absence of sensory potentials, delayed

Figure 2. Thoracic Spine four months after hospital admission. a. Sagittal T1w post gadolinium b. Sagittal T2w-SPAIR, c. Sagittal T2w-TSE. There is a patchy high T2 signal from T6 to the middle of T12. There is also a mild enhancement of the lower segment of the spinal cord



F- wave without Chrono- dispersion. Electromyography revealed active neurogenic lesion in both upper and lower limbs, distally.

A new MRI of brain and thoracic spinal cord was performed due to the level of hyposensation. The examination revealed gliotic lesions in the pons and right cerebellar hemisphere, decrease of the pathologic area in left temporal lobe (see Figure 1). The spinal cord had a patchy high T2 signal from T6 to the middle of T12 and a mild enhancement of the lower segment of the spinal cord (see Figure 2). These findings combined with the medical history and clinical presentation led to the diagnosis of post-infectious encephalomyelitis.

Discussion

Differential diagnosis of demyelinating diseases is a difficult issue due to the lack of specific biological markers. In our case, a respiratory infection preceded. The CSF in admission was positive for CNS inflammation (55 polymorph nuclear cells, and mildly elevated protein) and the MRI presented multifocal lesions with impaired diffusion predominantly in white matter. However, the patient's intact consciousness and orientation level were inconsistent with the diagnosis of encephalitis. The gradual deterioration with the symmetrical lower limb weakness and areflexia, the almost intact sensation at first and the cranial nerve involvement came along with the diagnosis of the Guillain-Barré syndrome. This syndrome usually presents with low serum sodium and the characteristic CSF albumin cytologic dissociation, which was present in the second lumbar puncture of the patient. Nerve conduction study/electromyography showed prolonged distal latencies, decrease of motor conduction velocity, delayed F- wave without Chrono- dispersion, and electromyography revealed active neurogenic lesion in both upper and lower limbs, distally, findings, also consistent to polyradiculoneuritis.

The patient did not suffer from pain or paresthesia in the beginning or after the admission in ICU which would be expected in ADEM and Guillain-Barré syndrome respectively. The only hint of myelitis was the early impairment of urination, covered by catheterization.

We also believe that Critical Illness Neuropathy (CIN) involved partially in our patient's prognosis. She remained three months in ICU, faced various septic episodes while being under essential sedation and received corticosteroids when it was necessary. However, we are confident that CIN was a cofactor to another underlying inflammatory demyelinating condition as MRI and CSF findings revealed.

Unfortunately, our patient was unable to wean off the mechanical ventilation, due to thoracic spinal cord myelitis and the resulting intercostal muscle weakness. She partially responded to multiple IVIG courses, regaining the mobility of the upper limbs. The large, painless, coccyx pressure ulcer, was unlikely to heal, and her total prognosis was poor. She died fifteen days after hospital discharge, at home, by cardiac arrest.

Our case, presents a rare (31 known cases) (3), severe combined central and peripheral demyelination, probably triggered by a virus (negative PCT), which required ICU admission and resulted in flaccid paraplegia and mechanical ventilation. The second MRI which was performed three months later, despite the partial resolution of imaging changes was not followed by similar clinical recovery.

Disclosure statement

The authors report no actual or potential conflict of interest. This paper is not under consideration by any other journal, and it has not previously published. The corresponding author takes full responsibility for the data, the analyses and interpretation and the conduct of the research, as well as access to all of the data. All authors have seen and agreed with the contents of the manuscript.

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