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Clinical-evolutive particularities and therapeutic-rehabilitative approach in the rare case of acute disseminated encephalomyelitis following an episode of viral meningitis of unknown etiology

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Abstract

Acute disseminated encephalomyelitis (ADEM) is a disease mainly affecting children, however, adult cases have been also reported. The disease represents a demyelinating disorder of the central nervous system, with a monophasic evolution and mostly full recovery. Mortality is documented at only 2%, but there are risks of complications in the acute phase, mostly due to the vast number of lesions and their distribution in the cerebrum. We present the case of a 40 year-old female patient who presented with visual impairment, coordination issues with walking difficulties, hypoesthesia of the entire body, back and upper limbs paresthesia, upper limbs and torso tremor as well as speech impairment. Symptoms appeared on the same day after discharge from the Infectious Disease Hospital where she was treated for viral meningitis. MRI findings on admission described multiple demyelinating lesions located bilaterally in the white matter and in the cervical spine. The patient was started on high dose parenteral methylprednisolone 1g/day for 5 days and afterwards was switched to oral corticoids with dose tapering over a period of 40 days. Rehabilitation treatment was started during hospitalization and continued after discharge. Evolution was favorable, with almost complete recovery, the patient presenting with only minor hypoesthesia of the torso at discharge.

Key words: *acute disseminated encephalomyelitis, ADEM, meningitis, rehabilitation,*

1. Introduction

Acute disseminated encephalomyelitis (ADEM) represents a demyelinating disorder commonly believed to be immune-mediated. It mostly affects the white matter of the brain and the spinal cord and is usually preceded by an infection (1, 2).

The incidence is 0.4/100.000/year, mostly appearing in younger individuals, under the age of 20 with mean age of presentation being 5 to 8 years, however, cases have also been documented in adults ranging between the ages of 18 and 82 (2, 4). Incidence among genders is almost equal, with a slight male predominance (2). Seasonal distribution suggests only a moderate increase during winter and spring time (2). Mortality rates are currently considered to be low, at approximately 2% (2), death occurring mostly in fulminant cases (3).

The risk of developing ADEM resides in the individual's genetic composition, as well as the exposure to various microorganisms.

In most cases the disease appears after a viral or bacterial infection (4). Implicated microorganisms include CMV, EBV, herpes simplex virus, HIV, influenza, enterovirus and measles -previously considered the main virus leading to the development of ADEM (1, 5).

Clinical manifestations are comprised of multifocal neurological abnormalities, reflecting the widespread involvement of the nervous system (2). Complications, although rare, can lead to fatal consequences such as respiratory failure due to brainstem involvement (2).

The difficulty in diagnosing this particular disease is due to the lack of a specific test or laboratory finding and changes present on imagistic studies such as MRI are not pathognomonic for ADEM (1). Furthermore, differentiating from a first episode of multiple sclerosis is often times impossible.

2. Case presentation

We present the case of 40 years-old female admitted to the Neurological Emergency Department with the following complaints: visual impairment (difficulty in focusing), coordination issues with gate abnormalities, hypoesthesia of the entire body, paresthesia of the back and upper limbs, tremor of the upper limbs and speech impairment. The patient had no history of chronic pathologies, but was recently discharged from the Infectious Disease Hospital where she was successfully treated for an acute episode of viral meningitis of unknown etiology.

The symptoms started nine days prior to admission, on the same day she was discharged from the Infectious Disease Hospital with paresthesia and hypoesthesia of the back and right upper limb, after which extended to the left upper limb and was accompanied by visual impediment. The ophthalmologic consult revealed slight papillary focal edema and retinal nervous fibers edema. Five days before admission, the patient started developing both resting and intentional tremor of the upper limbs. Two days before admission was noted the debut of coordination impairment of the lower limbs with walking difficulties and the hypoesthesia engulfing the whole body. The day before admission, the patient shows muscle weakness, thus rendering independent walking impossible. On the day of admission, speech impediment in the form of dysarthria had developed.

The cerebral contrast MRI conducted describes multiple demyelinating lesions located in the with subcortical matter, periventricular bilateral, left internal capsule, right external capsule, cerebral peduncle, middle cerebellar peduncle, corpus callosum and medial spinal column. Some lesions present DWI contrast diffusion restriction (figure 1 a, b).

Upon admission the patient presented with normal BMI, normal BP and respiratory values and urinary retention (the patient describing difficulty in coordinating urinary emission). The first neurologic examination showed normal mental status, temporally and spatially oriented, no signs of meningeal irritation. The patient presented postural, action and resting tremor located at the upper limbs, normal visual field, difficulty in visual focus, normal eye movement, hypoesthesia of the right hemiface, no sign of facial palsy, bilateral horizontal exhausting nystagmus, unsteady gait, possible only with bilateral help, decreased motor strength (4/5 in both lower limbs and 4+/5 in the upper left limb), bilateral dysmetria with hypermetria during finger to nose test and heel to shin test, exaggerated reflexes in both upper limbs, abolished abdominal reflexes, Babinski sign positive bilaterally, hypoesthesia of the whole body, paresthesia located in the back and superior limbs and dysarthria.

The patient was placed on high dose corticoid treatment, starting with 1 g a day of methylprednisolone administered intravenously for five days, followed by a dose of 16 mg po with a rate of 2-1-0 for three days, then 1-1-0 for five days and followed by further gradual tapering (30 days in total).

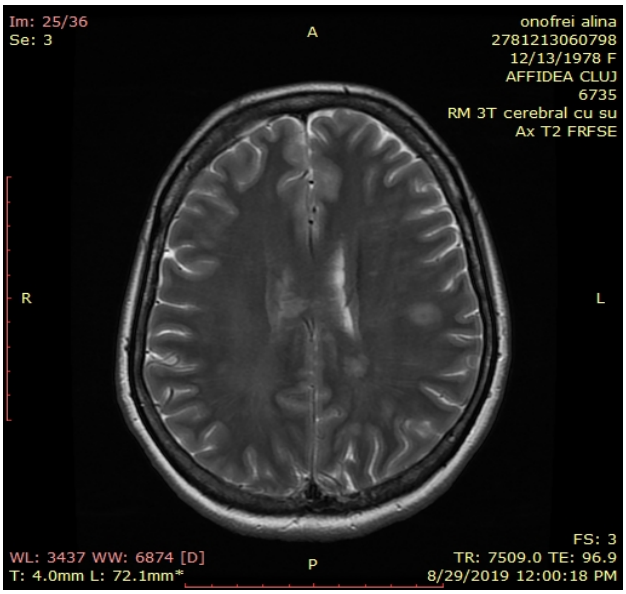

Fig. 1a: Axial T2 MRI shows lesions in the left white matter.

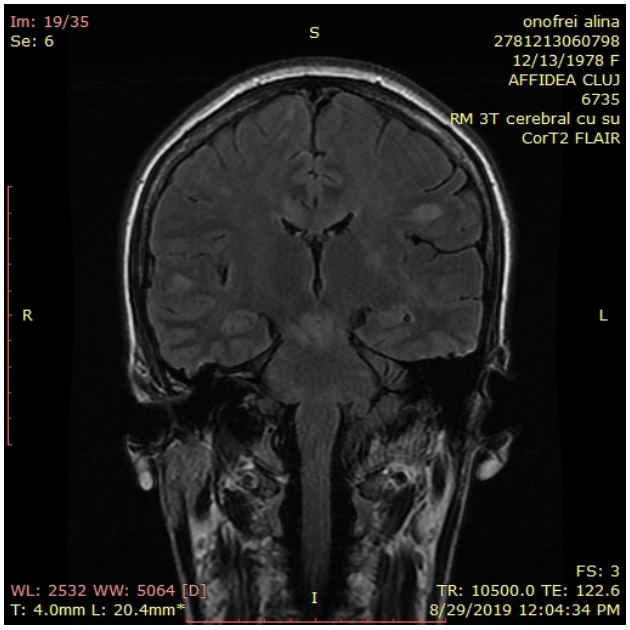

Fig. 1b: Coronal T2 FLAIR MRI shows multiple lesions.

During her stay the patient received physical and occupational therapy with emphasize on coordination and reestablishment of muscle force and walking exercises. Bed exercises where performed during the first days with both passive and active mobilization and afterwards introducing stretching exercises. Both fine and gross motor skill exercises where done daily under the surveillance of a specialist. Our aim was also to restore efficient and independent functional walking, rehabilitation being done in order to obtain a coordinated gait and increased walking distance.

During hospitalization a number of tests where ordered, starting with routine blood test which showed high cholesterol, iron deficiency anemia (Hb – 11,3 g/dl – NV: 12 – 15,5 g/dl, iron blood value – 22 ug/dl – NV: 60 – 180 ug/dl), elevated markers of inflammation (mostly due to corticoid treatment) and low folic acid. Multiple paraclinical tests were conducted (electroneurographic examination, visual evoked potentials, ophthalmological examination, internal medicine and cardiological consults, echocardiography, abdominal echography and pulmonary radiography) – all proving to be within normal margins.

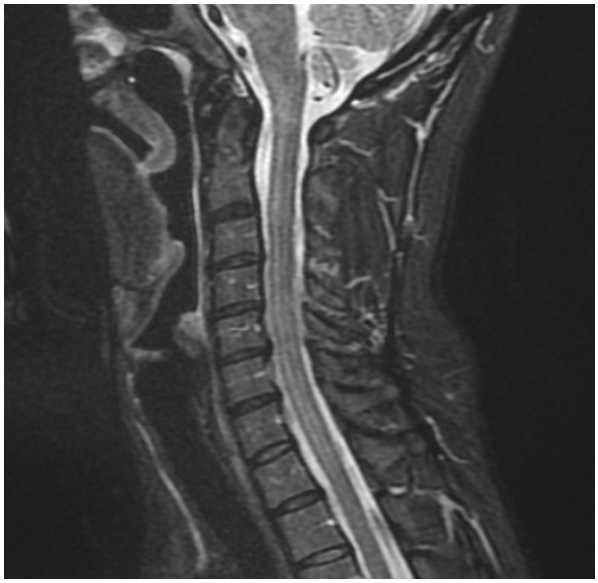

Fig. 2a: Sagittal T2 - cervical spine

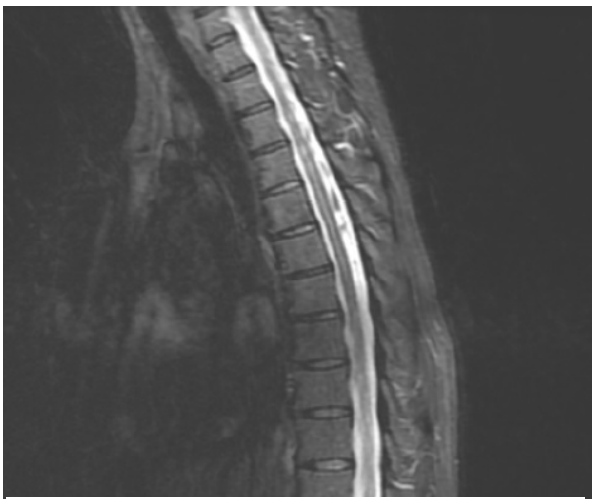

Fig. 2b: Sagittal STIR dorsal spine

MRI of the cervical and dorsal spine was conducted which showed millimetric contrast enhancing lesions located posterior to the C2 and C7-T1 vertebrae (figure 2a, b).

Lumbar puncture was already done during the previous admission in the Infectious Disease Hospital, which showed elevated *CSF* total *protein* (7,3), lymphocytic pleocytosis and no bacterial growth. Testing for various microorganisms was also already conducted, with no positive test (E. coli, H. influenzae, Listeria monocytogenes, N. meningitidis, Streptococcus agalactiae, Streptococcus pneumoniae, CMV, Enterovirus, Herpes simplex virus 1,2 and 6, Cryptococcus neoformans, Parechovirus and Varicella Zoster Virus).

During her stay, the patient's symptoms slowly regressed, with improvement in coordination and the regained ability to stand and walk independent. Paresthesia almost disappeared and only minor hypoesthesia of the back still being present at the time of discharge.

The patient was discharged with the following recommendations: continue corticoid treatment (methylprednisolone 16 mg po) with tapering until discontinuation with association of a proton pump inhibitor, iron and folic acid substitution, Neurossen Injekt 1-0-0 intramuscular injections for seven days and continuation of physical rehabilitation.

The patient was advised to enroll in a specialized program which combined functional rehabilitation with physical procedures. The duration and difficulty of daily exercises will be slowly increased given the fact that the patient still presented fatigue at discharge. Therefore, daily rehabilitation will consist of coordination, balance and walking exercises as well as stretching and relaxation techniques. The patient will also undergo aerobic training, and exercises which will strengthen all group muscles with emphasize on the lower limbs.

Approximately one month after the initial debut of symptoms, another cerebral Gadolinium contrast MRI was conducted revealing almost complete resolution of lesions – in number and size (figure 3 a, b, c).

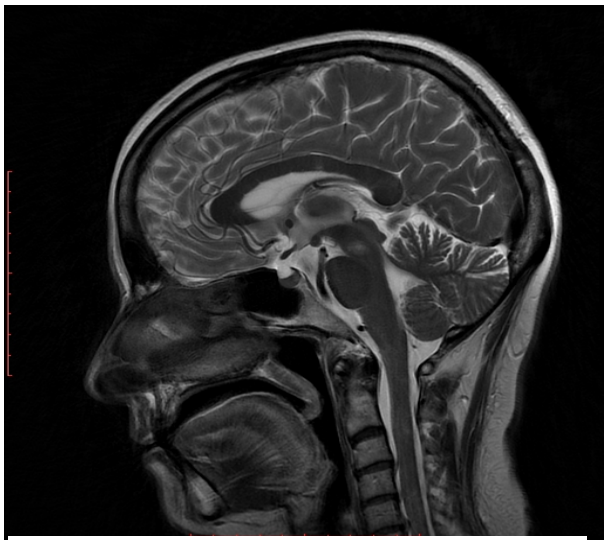

Fig. 3a: Sagittal T2 – one lesion in the brainstem

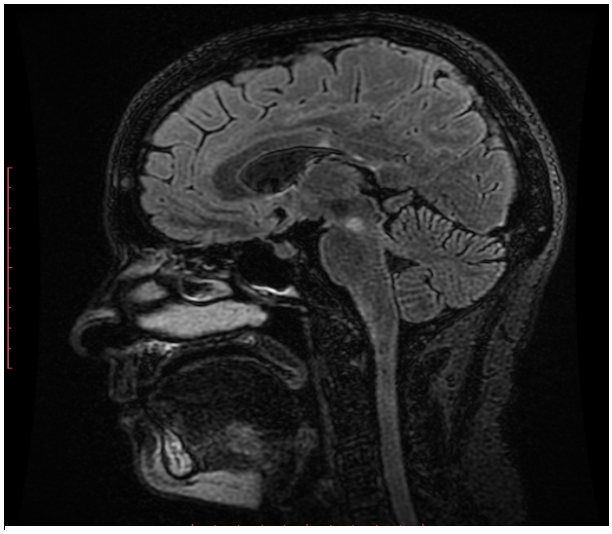

Fig. 3b: Sagittal FLAIR – shows the same unique brainstem lesion

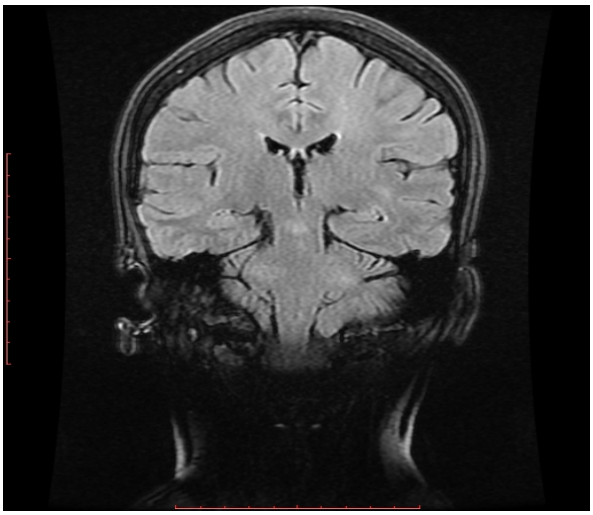

Fig. 3c: Coronal T2 FLAIR – lesion in the brainstem

3. Discussions

Patients with ADEM usually have an excellent outlook, as they can look forward to a complete recovery or to the persistence of only mild deficits (1). Our patient's symptoms regressed almost in full at discharge, with only minor sensory deficits of the back still being present. Routine follow up is mandatory for the control of appropriate diagnosis, efficacious treatment and the surveillance of developing MS, as the long-term risk is approximately 25% (1). Features that have been found to predict relapses include female sex and absence of encephalopathy at presentation (7).

The onset of ADEM occurs in the immediate wake of a febrile illness (1) between two days and four weeks after it's resolution (2), with a general rule of having at least one afebrile day between the two diseases (1).

Clinical symptoms include specific neurologic manifestations such as encephalopathy (represented by change in mental status ranging from lethargy to coma), meningeal signs, muscular weakness, ataxia, cranial nerves palsies, loss of visual acuity, seizures, impairment of speech, paresthesia, and is usually accompanied by nonspecific symptoms such as fever, lethargy and vomiting (2, 4).

Paraclinical studies usually include imagistic exams and biological testing.

MRI is executed in helping to distinguish ADEM from other demyelinating disorders. T1, T2, FLAIR and T1 postcontrast sequences are mostly used to determine the disease's activity. Typical lesions seen on MRI are usually asymmetrical, bilateral with slightly inhomogeneous increased signal on T2 and FLAIR and with greater size than in MS, rounding up at approximately 4 cm. Some lesions may be even larger and confluent. (6).

Cerebrospinal fluid findings are unspecific, including lymphocytic pleocytosis and mildly elevated *CSF* total *protein* (as is the case of our patient) (6). Testing for oligoclonal bands and immunoglobulin elevation is conducted in need of differentiating ADEM from multiple sclerosis, as these markers are mostly elevated in the second disease (1).

Blood work is mostly unspecific, with platelet counts seen elevated in some cases and high values of sedimentation rate appearing in 30% of patients (1).

Diagnosis criteria proposed by IPMSSG (International Pediatric Multiple Sclerosis Study Group) are generally used in children, but can be

correlated in adult ADEM. According to IPMSSG, four criteria are required in making the diagnosis of ADEM (table 1) (5,8). In our patients' case 3 out of the 4 criteria where established, with the three month MRI still is awaiting to be conducted.

Treatment for acute disseminated encephalomyelitis often represents administration of high-dose intravenous corticoids, usually using methylprednisolone 20 – 30 mg/kg/day (maximum dose of 1g/day) for 3 – 5 days (1). This approach is followed by oral medication with tapering the dose of corticoid over a period of 14 to 21 days (2).

The main alternative is administering immune globulin at a dose of 2 g/kg intravenous over the course of 3 – 5 days (1).

Some clinicians prefer the approach of combining the two medications, but there is no convincing evidence of any advantages to such measures (1).

In our case, corticoid treatment was used, with evident improvement of the patient.

The main problem in approaching ADEM or any form of demyelinating disease is establishing the diagnosis. Various monophasic and relapsing illnesses must be considered as there are a broad spectrum of symptoms that overlap over numerous diseases. Clinical features and imaging findings must be closely analyzed (2).The most challenging disease to differentiate is multiple sclerosis. Certain clinical features may be used in support of the diagnosis: history of a recent viral illness and widespread central nervous system signs and symptoms with or without encephalopathy usually suggest ADEM (3). Imaging findings can also be used as ADEM presents with more lesions than MS and also larger and more poorly defined (3).

Table 1. IPMSSG diagnosis criteria (8)

Multifocal, clinical CNS event with presumed inflammatory demyelinating cause;
Encephalopathy that cannot be explained by fever, sysstemic illness or post-ictal fever;
No new clinical and MRI finding 3 months or more after onset;
Brain MRI is abnormal with changes consistent with demyelination during the acute, 3 month phase.

4. Conclusions

Acute disseminated encephalopathy is an auto-immune demyelinating disease, mostly appearing after an infection or immunization. Even though the evolution is usually monophasic and benign with symptoms resolving almost completely, there are risks of fatality if certain regions of the cerebrum are involved. The main problem is in successful diagnosis, treatment in order to decrease the risk of residual deficits and progressive early passive and active exercise therapy. It is pertinent to emphasize the difficulty and importance of differentiating ADEM from other diseases of the central system, demyelinating or not.

Informed consent

An informed consent was obtained from the patient participating in the study.

Declaration of conflict of interests

The authors declare that there was no conflict of interest regarding the publication of this paper.

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