Inflammatory Demyelinating Diseases of Childhood: Case Report and Literature Review

Çocukluk Çağında İnflamatuar Demiyelinizan Hastalıklar: Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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ABSTRACT
Multiple sclerosis (MS) and acute disseminated encephalomyelitis (ADEM) are demyelinating inflammatory diseases, considered to have a striking pathophysiological resemblance. However, due to the differences in both clinical course and clinical approaches, it is important to differentiate between the two conditions, to plan further investigations and therapy protocols. These diseases have similar but also distinct clinical, radiological and cerebrospinal fluid (CSF) findings. ADEM is typically a monophasic disease of children. MS occurs generally in adult age, but uncommonly may develop in childhood with variable features. Our case is a 14-year-old girl, presented with a three-month history of left hemiparesis, followed by right hemiparesis, cerebellar signs, myelitis and cortical visual disturbances. Based on the clinical follow-up, MR and CSF findings, our patient was diagnosed with relapsing tumefactive multiple sclerosis. Steroid treatment was not significantly effective, however the patient has benefited from plasmapheresis clinically and radiologically. Our patient is still being followed under the disease modifying therapy without any relapse. (Archives of Neuropsychiatry 2014; 51: 74-78)

Key words: MS, ADEM, childhood, tumefactive MS

Conflict of interest: The authors reported no conflict of interest related to this article.

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Multiple sclerosis (MS) and acute disseminated encephalomyelitis (ADEM) are demyelinating inflammatory diseases, considered to have a striking pathophysiological resemblance. However, due to the differences in both clinical course and clinical approaches, it is important to differentiate between the two conditions, to plan further investigations and therapy protocols. These diseases have similar but also distinct clinical, radiological and cerebrospinal fluid (CSF) findings. ADEM is typically a monophasic disease of children. MS occurs generally in adult age, but uncommonly may develop in childhood with variable features. Our case is a 14-year-old girl, presented with a three-month history of left hemiparesis, followed by right hemiparesis, cerebellar signs, myelitis and cortical visual disturbances. Based on the clinical follow-up, MR and CSF findings, our patient was diagnosed with relapsing tumefactive multiple sclerosis. Steroid treatment was not significantly effective, however the patient has benefited from plasmapheresis clinically and radiologically. Our patient is still being followed under the disease modifying therapy without any relapse. (Archives of Neuropsychiatry 2014; 51: 74-78)

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Introduction

Multiple sclerosis (MS) and acute disseminated encephalomyelitis (ADEM) are inflammatory demyelinating diseases which have similar pathophysiological properties, but generally show different clinical, radiological and cerebrospinal fluid findings. Typical MS is a recurring disease characterized with attacks in young adults. However, ADEM is frequently known as a monophasic disease of the prepubertal childhood (1). Although treatment of both diseases in the acute phase is similar, the necessity of long-term administration of immunomodulator agents and planning a follow-up program in MS which is a chronic progressive process renders differentiation of MS from ADEM important. However, many investigators have reported that it is difficult to differentiate acute MS and ADEM and to predict transformation to MS in the first attack (1,2,3,4,5). In this article, the difficulties in diagnosis, differential diagnosis and treatment in acute inflammatory processes are reviewed in the light of the literature information by presenting a 14-year-old girl.

Case

A 14-year old girl presented with weakness in the right arm and leg, imbalanced gait and inability to urinate. There was no pathology in her personal history and familial history except for
third-degree of consanguinity between parents. 4/5 level motor hemiparesia accompanied by sensory defect developed on the left side 1.5 months before the patient presented to our clinic. It was learned that she was diagnosed with ADEM based on brain and cervical spinal MR (Figure 1,2) imagings in the center where she was evaluated in that period, she received 1 g methyl prednisolone intravenously (IVMP) for 9 days and the findings improved completely. However, new complaints developed in the patient 15 days after this treatment was completed. The patient was evaluated in the center where she was initially followed up at this stage and found to have 3/5 level right motor hemiparesia, bilateral cerebellar findings and deep sensory defect. She was discharged with partial recovery after a second IVMP treatment given with the same dose for the same time period. Neurological examination of the patient who presented to our clinic in that period revealed bilateral paleness in the temporal regions on fundoscopic examination, right central facial paralysis, triparesia (right upper and bilateral lower extremities) (3-4/5 level), bilateral pyramidal findings, sensory defect at the T7 level, bilateral complete deep sensory loss, appendicular and truncal ataxia and sphincter control defect. The neurological findings observed in the patient were associated with medulla spinalis lesion and cranial lesions during that period were thought to be asymptomatic. On cranial MR examinations repeated to determine the general status of the patient, hypointense lesions creating edema effect with no contrast uptake were observed in T1-weighted sections in bilateral occipital regions extending to the parietal and temporal areas and occipital cortex. It was noted that the cervical lesions with contrast enhancement on previous MR imagings had no contrast enhancement. MR spectroscopy performed to elucidate the lesions was found to be compatible with active demyelination. Examination of CSF revealed no cells, normal protein level, increased IgG index (0.78) and negative oligoclonal band (OCB). Since the cervical lesions exceeded the height of 3 vertebral corpi, NMO was tested to exclude neuromyelitis optica and found to be negative.

In the period when the patient was followed up without treatment, it was observed that motor hemiparesia regressed,
deep sense normalized in the upper extremities and sensory impairment showing level and syphincter defect improved. However, an increase was observed in the patient’s truncal ataxia. While the diagnosis was being reviewed, sudden visual defect developed 2.5 months after the initial complaints. On examination, the papilla borders were found to be mildly pale in the fundus, altitudinal visual field defect was present on the right side and concentric visual field defect was present on the left side, the right eye could count fingers at a distance of 1 m and the left eye could count fingers at a distance of 50 cm. Other neurological findings were not found to be different. On repeated cranial MR imaging, bilateral occipitoparietal lesions with no contrast enhancement and with increased dimensions when compared with the previous imaging were observed (Figure 3) and the cervical spinal lesions were found to be regressed (Figure 4). Visual evoked potential (VEP) examination revealed involvement which severely disrupted conduction in both visual pathways with predominance on the right side. The patient’s visual defect was associated with the cortical lesions. Clinical improvement was not observed after IVMP treatment administered at a dose of 1 g/day for ten days. Afterwards, it was decided to administer 7 courses of plasmapheresis and IVMP at a dose of 1 g/day weekly in combination with oral steroid at a dose of 32-24 mg/day. Although there was no change in the neurological picture right after plasmapheresis treatment, clinical improvement was observed after one week. The patients visual acuity increased to 1.6/10 bilaterally. The pyramidal and cerebellar findings improved almost completely and posterior cord findings improved partially. It was decided to administer 1 g IVMP monthly and interferon beta as prophylactic treatment in the follow-up period. It was planned to repeat the visual field, VEP, cranial and cervical spinal MRI examinations with regular intervals. Afterwards, attacks did not recur and it was observed that the visual field and VEP examination findings improved and the MR lesions regressed. It was observed that the second attack developed 2.5 months after the initial complaints in our patient. It has been reported that imm

**Discussion**

When we reviewed the current approaches and controversial aspects of pediatric MS, it was noted that MS occurred more rarely in the population below the age of 16 years (with a frequency of approximately 4-5%) (6,7). Incomplete maturation of the immune system, better repair capacity of the central nervous system (CNS) in children compared to adults and differences in tolerance to drugs affect the prognosis and treatment response (2). It has been reported that it is difficult to detect newly emerging visual defects and somatosensory defects in clinical practice in contrast to adult-onset MS and concentration difficulty and fatigue may be associated with attention deficit or non-organic causes in this age group. It has been proposed that myelitis, sphincter impairment, vestibular symptoms or pure motor hemiparesis are observed more rarely, but ataxia, encephalopathy and epileptic seizures which are the classical findings of ADEM develop more frequently in pediatric MS (2,6). However, most of these results have been obtained from retrospective studies.

In our patient, predominance of involvement of the medulla spinalis and lack of encephalopathy findings were primarily compatible with MS. No consensus related with the time between the attacks have been made in pediatric MS. Generally, the interval between the initial two attacks has been reported to be long in cases where the disease onset occurs below the age of 10 years and 1-2 years in cases where the disease onset occurs above the age of ten years similar to adults (8). Some authors reported that this period was shorter compared to adults and some others reported that it was longer (9,10). It was observed that the second attack developed 2.5 months after the initial complaints in our patient. It has been reported that im-

**Figure 5.** Cranial MRI, FLAIR, axial: Reduction in the dimensions of the lesion is observed on cranial MR examinations repeated 1 month and 6 months after visual defect which developed 2.5 months after the initial complaints of the patient.

**Figure 6.** Improvement is observed in the evaluation of the visual field repeated 3 weeks and 3 months after treatment.
In recurrent and multiphasic ADEM, a new attack should develop at least 3 months after the onset of an attack or at least one month after the end of steroid treatment to make the diagnosis (27). Biphasic ADEM is defined with presence of 2 attacks, recurrent ADEM is defined with presence of sterotypical attacks and multiphasic ADEM is defined with presence of multiple attacks characterized with new findings and lesions. Because of the difficulty of differentiation of recurrent ADEM concept and MS, some authors state that the differential diagnosis can only be made retrospectively (28). It has been proposed that MS, vasculitis or granulomatous diseases should be considered in cases where more than 3 attacks develop similar to our case (1).

In our patient, attacks which suggested different clinical localizations (firstly left hemiparesia, then right hemiparesia), cerebellar findings, superficial and deep sensory loss, sphincter defect and visual defect related with bilateral occipital cortex involvement developed in a period of 3 months. Absence of a history of infection and vaccination, findings related with brain involvement, marked awareness defect and epileptic seizures and presence of examination findings suggesting partial involvement of the medulla spinalis primarily suggested acute MS attack. However, cases of ADEM which are characterized only with hemiparesis have also been reported in the literature (17). These attacks compatible with different clinical localizations which could not be explained by a single anatomic localization not accompanied by awareness defect and seizures characterized with new clinical findings primarily suggested the diagnosis of recurrent MS rather than ADEM.

When the radiological findings were evaluated, it was observed that the asymmetrical, annular contrast enhancement lesions found on the initial cranial imaging suggested ADEM and the patient was followed up with a diagnosis of ADEM in the center where she was evaluated during that period. Presence of the lesions involving cortical grey matter, brainstem and thalamus and exceeding the length of 3,5 vertabral corpi in the medulla spinalis on MR imaging repeated during the follow-up supported this diagnosis. On the other hand, these cranial lesions are compatible with tumefactive MS in contrast to classical MS defined. Brain MR spectroscopy performed because of this confirmed that the lesions had inflammatory, demyelinating character and thus other causes were excluded (central nervous system lymphoma etc.). In addition, accompaniment of cervical lesions to the picture radiologically and their appearance supported the diagnosis of demyelinating disease. It was observed that the lesions had no contrast enhancement, but increased in size on examinations repeated in the acute worsening period during which complaints of visual defect developed. This shows that radiological findings may not necessarily be compatible with clinical attacks. In addition, visual defect related with occipital involvement is not a common finding in classical recurrent MS; however, it was thought that the clinical and VEP findings of the patient could be explained with tumefactive lesions in the occipital regions (5).

When the CSF findings were examined, OCB positivity was found with a rate of 0-58% (29), but OCB was found to have be-
come negative in the period of remission. However, studies have reported that OCB is negative in the initial CSF examination, but becomes positive in the following period in cases which are characterized with relapses (30). In these patients, intrathecal IgG synthesis has been found in 3-30% of the cases (24,31,32) and pleocytosis in CSF has been found in 55% of the cases (30). The CSF findings of our patient (presence of IgG synthesis and absence of pleocytosis and increased protein) supported the diagnosis of MS rather than ADEM.

Inflammatory demyelinating disease was considered and the other possibilities were excluded in our patient. This patient is a good example which shows that necessity of treatment is determined by the clinical picture, though radiological findings compatible with objective clinical findings or contrast enhancement in the lesions are absent.

In conclusion, it was thought that all these clinical and laboratory findings could be compatible with recurrent tumefactive MS. Prophylactic treatment was initiated in the patient considering presence of frequent and severe attacks, requirement for frequent use of high dose steroid treatment, the negative effects of this treatment on growth and development and the controversial effects of plasmapheresis and intravenous immunoglobulin. Repeated imaging was planned for the follow-up period.

This study demonstrates that a meticulous assessment and follow-up process is required to reach a definite diagnosis in pediatric demyelinating diseases as stated in the current diagnostic criteria and marked clinical improvement can be provided by an appropriate treatment approach which will be specified as a result of this process.

References