A Case of ADEM Mimicking Cerebral Adrenoleukodystrophy Based on Supratentorial MRI Findings

Supratentorial MRG Bulguları Serebral Adrenolökodistrofiye Benzeyen ADEM Olgusu

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ABSTRACT

A 9-year-old male admitted for syncope also had the complains of pain and numbness in his legs and frequent falling down. There was a history of upper respiratory tract infection 10 days before. On neurologic examination, paraparesia and fall a sleep were identified. On magnetic resonance imaging, the symmetric signal increases were seen in biparieto-occipital white matter intended to corpus callosum at T2-weighted sequences and cytotoxic edema was seen at diffusion-weighted images. Heterogeneous contrast enhancement was seen on these areas. In addition, at the C7-Th5 vertebrae levels, spinal cord had diffuse increased signal intensity and contrast enhancement. Acute disseminated encephalomyelitis was thought based on clinical and radiological findings. Steroid therapy was started. Significant improvement was shown after treatment. On 2-year follow-up, there was no recurrence. In conclusion, it must be kept in mind that acute disseminated encephalomyelitis can rarely present with biparieto-occipital involvement which extends to corpus callosum and can mimic adrenoleukodystrophy. For the differential diagnosis butterfly glioma, tumefactive demyelinating lesions or multiple sclerosis should be considered. (*Archives of Neuropsychiatry 2014; 51: 86-89*)

Key words: Acute disseminated encephalomyelitis, MRI, Leukodystrophy, Adrenoleukodystrophy, Tumefactive demyelinating lesion

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ÖZET

Bayılma nedeniyle getirilen dokuz yaşında erkek hastanın, ayrıca sık düşme, bacaklarında ağrı, uyuşukluk yakınması vardı. On gün öncesinde geçirilmiş üst solunum yolu enfeksiyonu öyküsü mevcuttu. Nörolojik muayenede, uykuya eğilim hali ve paraparezi saptandı. Manyetik rezonans görüntülemesinde T2 ağırlıklı kesitlerde korpus kallozumu içine alan biparieto-okspital simetrik sinyal artışı ve difüzyon ağırlıklı incelemede sitotoksik ödem izlendi. Aynı alanlarda heterojen kontrast tutulumu dikkati çekmekteydi. Ayrıca omurilikte C7-T5 vertebra seviyelerinde kontrast tutulumu ve diffüz sinyal artışı mevcuttu. Hasta klinik ve radyolojik bulgular ile akut dissemine ensefalomyelit olarak değerlendirildi. Steroid tedavisi başlandı. Tedavi sonrası belirgin düzelme izlendi. İki yıllık takibinde nöks görülmedi. Sonuç olarak akut dissemine ensefalomyelitin nadirde olsa korpus kallozumu içine alan biparieto-okspital tutulumla karşımıza çıkabileceği ve adrenolökodistrofi hastalığını taklit edebileceği akılda tutulmalıdır. Ayrıca tanıda "butterfly" gliom, tümefaktif demiyelinizan lezyon veya multipl skleroz da unutulmamalıdır. (*Archives of Neuropsychiatry 2014; 51: 86-89*)

Anahtar kelimeler: Akut dissemine ensefalomyelit, MRG, Lökodistrofi, Adrenolökodistrofi, Tümefaktif demiyelinizan lezyon

Çıkar Çatışması: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

Introduction

Acute disseminated encephalomyelitis (ADEM) is an immune-mediated demyelinating disease of the central nervous system. The disease has a typical onset with sudden neurological symptoms days or weeks after a viral infection or immunization. Measels, rubella, mumps and varicella have been blamed most frequently among viral agents and rabies, diphtheria, tetanus, measles, influenza and hepatitis B vaccines have been blamed most frequently among vaccines. It occurs most commonly after mycoplasma infection among bacterial infections.

The main pathological findings are perivascular inflammation, edema and demyelination in white matter (1).

The clinical and characteristic magnetic resonance imaging (MRI) findings were identified by the International Pediatric Multiple Sclerosis (MS) Working Group (2). Accordingly, the major clinical characteristics include encephalopathy and polysymptomatic neurological findings and acute or subacute onset demyelinating disease. On MRI, bilateral, asymmetrical, multifocal lesions with a size of larger than 1-2 cm are observed in the supratentorial or infratentorial white matter. Grey matter and especially basal ganglia and thalamus may also be involved.

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In addition to brain imaging findings, confluent, intramedullary lesions may be observed in the medulla spinalis (2). In this article, a case of ADEM with symmetrical involvement in the parieto-occipital, periventricular deep white matter including the corpus callosum is presented.

Case

A 9-year-old male patient presented with the complaint of fainting. It was learned that he had a sudden seizure as generalized tonic contraction accompanied by fixation of the eyes at a constant point and loss of consciousness which lasted approximately for 15 minutes. He had the complaints of pain and numbness in the legs and frequent falling for the last three days. It was learned that he had a history of upper respiratory tract infection with nasal discharge, sore throat and cough accompanied by non-purulent sputum which he recovered without treatment about ten days ago. He had no history of vaccination. He had no pathology in his personal and familial history. On neurological examination, his consciousness was open and he had mild stupor. His fundoscopic examination and examination of the cranial nerves were found to be normal. Muscle strength was found to be 3/5 in bilateral lower extremities. Deep tendon reflexes were bilaterally lively. No accompanying pathological reflex was found. On examination of the cerebellar system, dysmetria and dysdiadochokinesia were found. The Romberg test was found to be positive. Tandem gait was found to be disrupted.

Laboratory tests revealed normal serum electrolytes, hepatic and renal function tests and blood count. C-reactive protein and erythrocyte sedimentation rate were found to be normal. Blood and urine cultures were found to be negative.

On cerebrospinal fluid examination performed to differentiate possible central nervous system infections, the CSF was found to be clear and no cells were observed on direct examination. No microorganism was found on gram staining and on examination for acid-resistant bacteria. Glucose was found to be 72 mg/dl (simultaneous serum glucose 118 mg/dl), protein was found to be 26 g/dl and chlor was found to be 108 mg/dl. Oligoclonal band was not observed. CSF bacterial culture was found to be negative and brucella and viral serological tests were found to be negative.

On brain MRI, increased signals were observed in the adjacent areas of the lateral ventricle occipital horns involving deep and partly subcortical white matter bilaterally and symmetrically on the fluid-attenuated inversion recovery (FLAIR) and T2-weighted images. The lesion also included the isthmus and splenium of the corpus callosum. The lesions were mildly hypointense on the T1-weighted images. Following intravenous contrast material injection, diffuse and mildly heterogeneous contrast enhancement was observed in these areas (Figure 1). On diffusion weighted images (DWI), increased signal intensity secondary to diffusion restriction was observed on b:1000 images and decreased signal was observed on ADC images (Figure

Figure 1. Bilateral and symmetrical signal increases in the parieto-occipital white matter on the axial FLAIR (A) and axial T2-weighted (B) images. The lesion also includes the isthmus and splenium of the corpus callosum on sagittal T2-weighted images. The lesion area is mildly hypointense on axial T1-weighted image (D). Diffuse, mildly heterogeneous contrast enhancement is observed following intravenous injection of contrast material on axial (E) and sagittal (F) T1-weighted images.

Figure 2. Increased signal intensity on b: 1000 images secondary to diffusion restriction on DWI (A), decreased signal on ADC images (B)

Figure 3. Diffuse signal increase and edema continuing from the level of the 7th cervical vertebrae to the level of the 5th thoracic vertebrae in the spinal cord on sagittal T2-weighted image (A). Patchy contrast enhancement is observed in these areas following intravenous injection of contrast material on the sagittal image (b).

2). In addition, diffuse signal increase, edema and contrast enhancement were observed extending from the seventh vertebral level to the 5th thoracic vertebrae (Figure 3).

ADEM was considered with the present clinical and radiological findings. 25 mg/kg methyl prednisolone was administered for 5 days. Muscle strength was evaluated to be 5/5 on the 7th day of treatment. Partial improvement was observed in the cerebellar findings. The patient was discharged with oral prednisolone treatment. Oral steroid treatment was tapered and discontinued in the sixth week. The neurological examination performed at the first year was evaluated to be normal. On the follow-up MRI, signal increases were found to be markedly regressed in the FLAIR and T2-weighted series and contrast enhancement was not observed (Figure 4). The appearances were considered sequela changes. No spinal cord lesions were found. The patient was followed up for 2 years and clinical or radiological recurrence was not observed.

Discussion

Acute disseminated encephalomyelitis lesions are evaluated by MRI. However, the MRI findings of the disease are not specific. Typically, bilateral, asymmetrical, homogenous or mildly non-homogenous and patchy signal intensities are observed on FLAIR and T2-weighted images (3,4). The lesions may involve many cerebral and cerebellar regions. In one study, the localizations of ADEM lesions were found to be as follows: frontal region 100%, parietal region 93%, temporal region 8% and occipital region 6%. In the same study, 93% involvement was found in the subcortical white matter, 80% involvement was found in the gray matter, 60% involvement was found in the periventricular white matter and 7% involvement was found in the corpus callosum (5). In acute disseminated encephalomyelitis, involvement of the medulla spinalis is observed with a lower rate compared to involvement of the brain. Involvement of medulla spinalis was reported with a rate of 53% in one study (6).

Generally, restricted diffusion is observed in the acute phase and free diffusion is observed in the subacute phase in lesions of acute disseminated encephalomyelitis (7). On diffusion-weighted images, differentiation of cytotoxic and vasogen-

ic edema is possible. This differentiation is important in terms of prognosis. In one study in which cytotoxic edema was found in two patients, mortality was reported in the patient who had brainstem involvement and cortical blindness was reported in the patient who had parieto-occipital involvement (8). In our patient, diffusion restriction compatible with cytotoxic edema was observed in the acute phase on diffusion-weighted images. However, the fact that the patient had no sequela is significant in terms of demonstrating the significance of early diagnosis and treatment.

As known, MS is the most compelling differential diagnosis for ADEM. In the literature, symmetrical involvement in the parieto-occipital region including the corpus callosum was reported in Schilder's disease which is a subform of MS (9). Since some of the patients described by Schilder had adrenoleukodystrophy, Schilder's disease is controversial in the literature (10). In addition, bilateral occipital involvement including the corpus callosum was reported in a patients with tumefactive MS in the literature (11). MRI findings of the lesions of our patient are very similar to these cases. However, this morbidity was excluded during the diagnostic process and follow-up, since the patient had a history of upper respiratory tract infection, no disease attack occurred in the last 2 years and oligoclonal band was negative in the CSF.

Neuromyelitis optica may be considered in the differential diagnosis because of presence of medulla spinalis involvement exceeding 3 vertebral segments in our patient. The diagnostic criteria of neuromyelitis optica were published by Wingerchuk in 2006 after revision. Accordingly, optic neuritis and acute myelitis should definitely be present. It generally has a mono-symptomatic onset, but sometimes myelitis and optic neuritis may be observed simultaneously. Supportive criteria have been reported to include brain MRI findings which are insignificant in terms of MS, spinal cord lesion involving three or more spinal segments and neuromyelitis optica IgG seropositivity (12). Neuromyelitis optica is characterized with attacks with a rate of more than 85% and the attacks are severe. In addition, there is no history of infection or immunization (13). Absence of clinical or radiological findings of optic neuritis and presence of history of upper respiratory tract infection enabled us to exclude the diagnosis of neuromyelitis optica. In addition, response to treatment was very good.

In acute disseminated encephalomyelitis, the brain lesions are generally localized in the white matter and asymmetrical. Symmetrical involvement is usually observed at the level of thalamus and basal ganglia. Bilateral symmetrical white matter lesions have also been reported (3,14). In this case, leukodystrophies should be considered in the differential diagnosis (15). In the literature, a case of ADEM which was confused with leukodystrophy was reported (16). However, adrenoleukodystrophy has not been mentioned in the differential diagnosis of ADEM until the present time in the literature. In our patient, the localization of involvement was very similar to adrenoleukodys-

Figure 4. Marked improvement is observed in the lesion areas on axial FLAIR (A) and sagittal T2-weighted (B) images.

trophy. The lesion was symmetrical and included the isthmus and splenium of the corpus callosum. The classical brain MRI findings of adrenoleukodystrophy most frequently include involvement of deep parieto-occipital white matter, corpus posterior and splenium of the corpus callosum including the visual and auditory pathways. Prolongation in T1 and T2 relaxation times is present in these areas. Peripheral contrast enhancement may be observed in the white matter lesions on contrast enhanced T1-weighted images. Spinal cord lesions are also observed in adrenomyeloneuropathy which is another form of adrenoleukodystrophy occurring in adults. In adrenoleukodystrophy, involvement of corticospinal tract, medial geniculate body, inferior colliculus and lateral lemniscus is observed in addition to involvement of parieto-occipital white matter and corpus callosum (17). In our patient, pathological signals were not observed at these levels and intensive contrast enhancement was present in the lesion areas on the initial MRI. These findings were significant in terms of differential diagnosis. In addition, the diagnosis of adrenoleukodystrophy was excluded because of acute clinical picture, normal long-chain fatty acids in the serum and rapid response to treatment.

"Butterfly" lesions should also be kept in mind in bilateral symmetrical lesions including the corpus callosum. Glioma is the most common one among these lesions. In this morbidity, contrast enhancement is observed according to the stage of the tumor. In the literature, a case of demyelinating disease which was confused with high grade "butterfly" glioma was reported (18,19). In our patient, glioma was excluded because of rapid response to steroid treatment and wide spinal cord involvement. "Butterfly" lesions have also been reported in lymphoma, metastasis, toxoplasmosis, granulocytic sarcoma and neuronal ceroid lipofuscinosis (20,21,22,23).

Although classical brain involvement in acute disseminated encephalomyelitis are in the form of asymmetrical lesions, it should be kept in mind that it may present with biparieto-occipital involvement including the corpus callosum and mimic adrenoleukodystrophy. "Butterfly" glioma, tumefactive demyelinating lesions and multiple sclerosis should also be kept in mind in the differential diagnosis.

References

- Noorbakhsh F, Johnson RT, Emery D, Power C. Acute disseminated encephalomyelitis: clinical and pathogenesis features. *Neurol Clin* 2008; 26:759-780.
- Lee YJ. Acute disseminated encephalomyelitis in children: differential diagnosis from multiple sclerosis on the basis of clinical course. *Korean J Pediatr* 2011; 54:234-240.
- Lim KE, Hsu YY, Hsu WC, Chan CY. Multiple complete ring-shaped enhanced MRI lesions in acute disseminated encephalomyelitis. *Clin Imaging* 2003; 27:281-284.
- Kawashima S, Matsukawa N, Ueki Y, Yamada K, Sakurai K, Yamawaki T, Ojika K. Predicting the motor outcome of acute disseminated encephalomyelitis by apparent diffusion coefficient imaging: Two case reports. *J Neurol Sci* 2009; 280:123-126.
- Murthy SN, Faden HS, Cohen ME, Bakshi R. Acute disseminated encephalomyelitis in children. *Pediatrics* 2002; 110:e21.
- Lu Z, Zhang B, Qiu W, Kang Z, Shen L, Long Y, Huang J, Hu X. Comparative brain stem lesions on MRI of acute disseminated encephalomyelitis, neuromyelitis optica, and multiple sclerosis. *PLoS One* 2011; 6:e22766.
- Balasubramanya KS, Kovoov JM, Jayakumar PN, Ravishankar S, Kamble RB, Panicker J, Nagaraja D. Diffusion-weighted imaging and proton MR spectroscopy in the characterization of acute disseminated encephalomyelitis. *Neuroradiology* 2007; 49:177-183.
- Donmez FY, Aslan H, Coskun M. Evaluation of possible prognostic factors of fulminant acute disseminated encephalomyelitis (ADEM) on magnetic resonance imaging with fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging. *Acta Radiol* 2009; 50:334-339.
- Büyükkaya R, Dikici S, Uzun H, Büyükkaya A, Erdoğan B, Yazgan S, Yazgan Ö. Nadir Bir Olgu: Simetrik Tutulumlu Schilder hastalığı. *Düzce Tıp Dergisi* 2011; 13:70-72.
- Ferrer I, Pujol A. Mini-symposium: X-linked adrenoleukodystrophy. Foreword. *Brain Pathology* 2010; 815-816.
- Yamada S, Yamada SM, Nakaguchi H, Murakami M, Hoya K, Matsuno A, Yamazaki K, Ishida Y. Tumefactive multiple sclerosis requiring emergent biopsy and histological investigation to confirm the diagnosis: a case report. *J Med Case Rep* 2012; 6:104.
- Wingerchuk DM, Lennon VA, Pittock SJ, Lucchinetti CF, Weinshenker BG. Revised diagnostic criteria for neuromyelitis optica. *Neurology* 2006; 66:1485-1489.
- Wingerchuk DM, Lucchinetti CF. Comparative immunopathogenesis of acute disseminated encephalomyelitis, neuromyelitis optica, and multiple sclerosis. *Curr Opin Neurol* 2007; 20:343-350.
- Alves-Leon SV, Velutini-Pimentel ML, Gouveia ME, Malfetano FR, Gaspareto EL, Alvarenga MP, Frugulhetti I, Quirico-Santos T. Acute disseminated encephalomyelitis: clinical features, HLA DRB1*1501, HLA DRB1*1503, HLA DQA1*0102, HLA DQB1*0602, and HLA DPA1*0301 allelic association study. *Arq Neuropsiquiatr* 2009; 67:643-651.
- ale RC, de Sousa C, Chong WK, Cox TC, Harding B, Neville BG. Acute disseminated encephalomyelitis, multiphasic disseminated encephalomyelitis and multiple sclerosis in children. *Brain* 2000; 123:2407-2422.
- Kaya A, Acikgoz M, Ustyol L, Avcu S, Sal E, Okur M, Caksen H. A case of acute disseminated encephalomyelitis mimicking leukodystrophy. *Kurume Med J* 2010; 57:85-89.
- Kim JH, Kim HJ. Childhood X-linked adrenoleukodystrophy: clinical-pathologic overview and MR imaging manifestations at initial evaluation and follow-up. *Radiographics* 2005; 25:619-631.
- Bower RS, Burrus TM, Giannini C, Erickson BJ, Meyer FB, Pirko I, Mauermann ML. Teaching Neurolmages: demyelinating disease mimicking butterfly high-grade glioma. *Neurology* 2010; 75:1-4.
- Scozzafava J, Johnson ES, Blevins G. Neurological picture. Demyelinating butterfly pseudo-glioma. *J Neurol Neurosurg Psychiatry* 2008; 79:12-13.
- Agrawal A. Butterfly glioma of the corpus callosum. *J Cancer Res Ther* 2009; 5:43-45.
- Chaudhari VV, Yim CM, Hathout H, Lai A, Donovan SM. Atypical imaging appearance of toxoplasmosis in an HIV patient as a butterfly lesion. *J Magn Reson Imaging* 2009; 30:873-875.
- Kei PL, Kok TY, Linn YC, Padhy AK. Butterfly lesion of the corpus callosum: an unusual case of extramedullary myeloid sarcoma (granulocytic sarcoma). *Clin Nucl Med* 2011; 36:365-366.
- Hammersen S, Brock M, Cervós-Navarro J. Adult neuronal ceroid lipofuscinosis with clinical findings consistent with a butterfly glioma. Case report. *J Neurosurg* 1998; 88:314-318.