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Double Filtration Plasmapheresis in the Treatment of a Case with Acute Disseminated Encephalomyelitis

Akut Dissemine Ensefalomiyelitli Vakanın Çift Filtrasyon Plazmaferez ile Tedavisi

Mehmet Uğur Çevik, Mehmet Guli Çetinçakmak*, Sefer Varol*, Eşref Akıl*
Department of Neurology, Faculty of Medicine, Dicle University, Diyarbakır, Turkey
*Department of Radiology, Faculty of Medicine, Dicle University, Diyarbakır, Turkey

Summary

Acute disseminated encephalomyelitis (ADEM), is a monophasic autoimmune demyelinating disease of the central nervous system. Although high-dose steroid management has been considered the mainstay of treatment for ADEM, some patients are unresponsive to steroid therapy. We report the case of a 44-year-old woman with ADEM who did not respond to steroid therapy, but who showed a noticeable improvement with double filtration plasmapheresis (DFPP). To the best of our knowledge, this is the first case report of ADEM in literature treated with DFPP. *(Turkish Journal of Neurology 2013; 19:63-5)*

Key Words: Acute disseminated encephalomyelitis, corticosteroids, double filtration plasmapheresis

Özet

Akut dissemine ensefalomiyelit (ADEM), merkezi sinir sisteminin monofazik otoimmün demiyelinizan hastalığıdır. Temel tedavi yönteminin yüksek doz steroid uygulaması olmasına rağmen bazı olgular bu tedaviye yanıt vermemektedir. Kırkdört yaşında, yüksek doz steroid tedavisinden fayda görmeyen, ancak başarıyla uygulanan çift filtrasyon plazmaferez (ÇFP) tedavisi ile belirgin düzelme gösteren ADEM'li kadın hastayı sunduk. Bildiğimiz kadarıyla, bu olgumuz literatürde ADEM'de ÇFP tedavisi uygulanan ilk olgudur. *(Türk Nöroloji Dergisi 2013; 19:63-5)*

Anahtar Kelimeler: Akut dissemine ensefalomiyelit, kortikosteroid, çift filtrasyon plazmaferez

Introduction

Acute disseminated encephalomyelitis (ADEM) is a monophasic autoimmune demyelinating disease of the central nervous system that usually follows a febrile infection or immunization (5). High-dose intravenous methylprednisolone (IVMP), intravenous immunoglobulin (IVIG), plasmapheresis or combinations of these are established as medical treatments in ADEM (8), and the principal medical treatment is accepted to be high dose IVMP (3). Plasmapheresis is an extracorporael method used to rapidly decrease the circulating immune complex and abnormal immunoglobuline levels (10) and is administered via continous plasma exchange (CPE) or double filtration plasmapheresis (DFP) methods. In the DFP method two membranes are used, namely plasma separator and plasma fractionator, that selectively filtrate larger molecules such as immunoglobulins. Plasma separator separates plasma from cellular elements, whereas plasma fractionator separates semi-selectively immunoglobulins from plasma (13,15). Our 44-year old female patient, resistant to high-dose IVMP (1 gram/day) treatment had clear clinical benefit from DFP treatment. CPE is shown in literature as a plasmapheresis technique in ADEM (3). We present this case as it is the first case administered DFP treatment in ADEM in literature.

Cese Report

Forty-four year old female patient presented in the emergency room with high fever, nonsensical speaking, not recognizing close friends and family, complaints that started 2 weeks after a severe upper respiratory infection that started one month ago. Physical examination revealed that body temperature (axillary) was 38°C. Neurological examination showed confusion and limited cooperation, impaired spatial, temporal and personal orientation. Muscle strength was 4/5 in upper and lower right extremities. She had trouble maintaining her balance while walking. Complete

Address for Correspondence/Yazışma Adresi: Mehmet Uğur Çevik MD, Department of Neurology, Faculty of Medicine, Dicle University, Diyarbakır, Turkey
Gsm.: +90 412 248 80 16/4510 E-mail: mehmetugur.cevik@gmail.com
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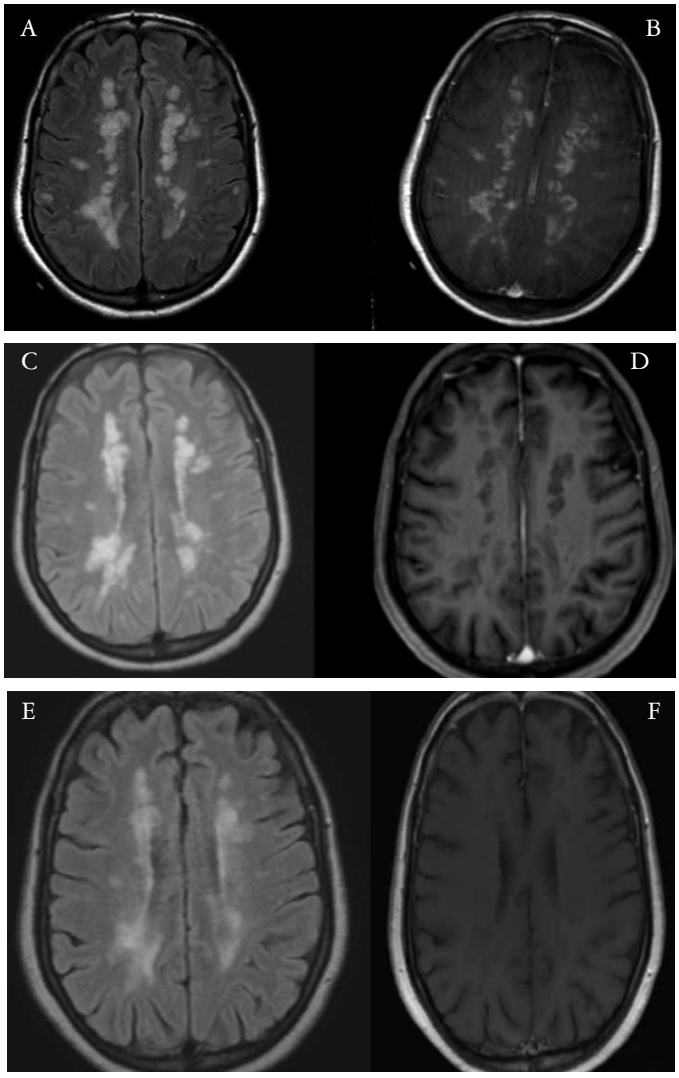

Image 1: Imaging findings of 44-year old female patient, pre- and post-plasmapheresis, and follow-up approximately 4 and 9 months following plasmapheresis. 1A-B: In acute stage, hyperintense multiple lesions with a tendency to confluence are seen in periventricular and subcortical white matter at centrum semiovale in FLAIR weighted axial sequences (1A); all lesions in T1-weighted sequences (1B) show concentrated heterogenous contrast material uptake. 1C-D: In follow-up scans (4 months later) there is decrease in the dimensions of the lesions in FLAIR weighted axial sequences (1C); contrast material uptake has completely disappeared in all T1-weighted sequences (1D). 1E-F: In follow-up scans (9 months later) no new lesions are seen, the dimensions of lesions have decreased in FLAIR weighted axial sequences (1E) and there is no contrast material uptake in T1-weighted sequences (1F).

(VDRL) test, blood and urine culture, Epstein-Barr virus (EBV), herpes simplex virus (HSV), rubella and toxoplasma investigation, hepatitis markers, antiphospholipid antibodies and brucella tube agglutination tests were all negative. There were no cells in her cerebrospinal fluid (CSF) examination, and protein was 29 mg/dL and glucose was 78 mg/dL. CSF culture and oligoclonal band was negative. In the brain magnetic resonance imaging (MRI) scan taken the day after she was hospitalized, hyperintense multiple lesions with tendency to confluence were seen in the periventricular and subcortical white matter in centrum semiovale level in fluid attenuated inversion recovery (FLAIR) weighted sequences (Image 1A). All lesions showed concentrated heterogenous contrast material uptake (Images 1A, B) in T1-weighted sequences (Image 1B). There were no demyelinating lesions in cervical and thoracal MRI scans. Slow delta waves were seen in 3-4 Hz frequency and theta waves in 4-6 Hz frequency in bilateral temporo-occipital regions throughout the recording in electroencephalography. These findings suggested a diagnosis of ADEM, and high-dose IVMP 1 gram/day was initiated. When there was no response to steroid treatment after five days, this treatment was extended to 10 days, with no improvement in the clinical picture. Five sessions of DFP treatment every other day was planned. Following the second administration, there was decrease in confusion, and clear improvement in spatial, temporal and personal orientation. The patient was administered oral prednisolone 1 mg/kg/day for six weeks following the 5th and last plasmapheresis session. The neurological examination at discharge did not reveal any pathologic findings. Neurological examination at four and 9 month follow-up was normal. There was decrease in dimensions of the lesions in FLAIR weighted sequences in follow-up MRI scans at these time points (Images 1C-E) and contrast material uptake had completely disappeared in all lesions in T1-weighted sequences (Images 1D-F).

Discussion

We presented the first case in literature where DFP is administered in ADEM. Immunopathogenesis in ADEM includes demyelination of white matter in the central nervous system and perivascular inflammatory infiltration. İnflammation is caused by lymphocytes, plasmocytes and macrophages via autoimmune mechanisms (16). ADEM may be caused by viral and bacterial infections, as well as immunizations including rabies, diphteria, tetanus, or poliomyelitis. It is thought that antibodies developing against these pathogens cause cross reactions due to molecular similarities to myelin basic protein (MBP) in the white matter (6). T celss isolated from ADEM patients are found to react with MBP 10 times more compared with controls (1,7). Serum antibodies against myelin oligodendrocyte glycoprotein (MOG) were found in ADEM patients (4). Anti-MBP and anti-MOG are immunoglobulin G ve IgM type antibodies (1). Significant decrease in plasma levels of IgG, IgA, IgM, C3 and C4 were shown post-DFP compared to pre-DFP (9). Immunoadsorpsion (IA), an improved technique compared to DFP, is a method of plasma exchange where special adsorption columns are used, with binding capacity for the substance to be removed from circulation. This method helps selectively remove from plasma, for example, antibodies developing agains acetilcholine receptors in myastenia gravis (17). Special adsorption columns against anti-MBP and anti-MOG have not yet been manufactured. One of the limitations of DFP can be said to be lack of selectiveness for antibody types as in IA administration. DFP has some advantages over CPE. A replacement solution (fresh frozen plasma, albumin) is not required during DFP, and neither is investigating ABO blood types. Therefore, exposure to probable risks including infections and allergies arising from extrinsic replacement solutions is

prevented. In addition, DFP is less expensive than CPE, as there is no need for a replacement solution (9,13). DFP can cleanse the immunoglobulins in the serum autologously and semi-selectively, whereas CPE cleanses immunoglobulins non-selectively. However, anaphylactic reactions may develop in patients using angiotensin converting enzyme inhibitors, due to the membranes used (13). ADEM is diagnosed based on clinical signs, and CSF and MRI findings (11). It is usually seen in childhood (2). Although it is more commonly seen in children than adults, it is noteworthy that our patient is 44-year old. In a study performed in 40 adult ADEM patients, the average age of onset for ADEM was found to be 33 years (11). Multiple sclerosis (MS) is the main differential diagnosis in ADEM (5). Clinical signs in ADEM are polysymptomatic inclyding fever, change in consciousness, headache, ataxia, brain stem signs, hemiparesis, and loss of balance, whereas they are usually monosymptomatic in a MS attack (8, 11). The polysmptomatic encephalopathy picture in our patient, with hemiparesis and imbalanced gait was consistent with ADEM. Fever and change in consciousness is seen in ADEM patients at a rate of 19% and 15%, respectively, while these symptoms are not expected to be seen at onset in MS patients (11). Old lesions are expected to stabilize or regress in follow-up MRI scans in ADEM patients, and no new lesions are expected (5). Cranial MRI lesions being of the same age, showing a tendency of confluence, no new lesions in the follow-up MRI scans taken 4 and 9 months later, no new attack, ie, monophasic disease course all suggested ADEM rather than MS in our patient (5). Although CSF examination usually reveals lymphocytic pleocytosis and increase in protein levels in ADEM, 20% of CSF findings may be normal, as in our patient (5, 11). CPE is successfully used in severe cases of ADEM resistant to high-dose IVMP (3). Our patient did not respond to high-dose IVMP and benefited clearly from DFP treatment. Iniatiating plasmapheresis treatment early prevents severe central nervous system damage. Usually, as in our patient, plasmapheresis is administered following high-dose IVMP treatment. Prognosis in ADEM patients is 60=80% full recovery in 1-6 months and usually monophasic disease course (5). In this case presentation we showed that DFP treatment is effective in a patient resistant to high-dose IVMP treatment. Literature review shows that CPE is a therapeutic plasmapheresis technique in ADEM (12). DFP has been administered in acute episodes of MS (9). As far as we know, our case is the first to be administered DFP treatment in ADEM in literature. DFP may be considered as an effective treatment option in steroid resistant ADEM patients.

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