CASE REPORT / OLGU SUNUMU

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Acute Disseminated Encephalomyelitis Following Completion of Pneumococcal Meningitis Treatment: A Case Report and Review of the Literature

Pnömokokal Menenjit Tedavisinin Tamanlanmasını Takiben Gelişen Akut Dissemine Ensefalomiyelit: Olgu Sunumu ve Literatür Taraması

Ayşe Serra ÖZEL[1], Lütfiye Nilsun ALTUNAL[1], Zakir SAKCI[2], Ece Aslı YILMAZ[3], Mesut YILMAZ[3], Ayten KADANALI[4]

[1]*University of Health Sciences Turkey, Ümraniye Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, İstanbul, Turkey*

[2]*University of Health Sciences Turkey, Ümraniye Training and Research Hospital, Clinic of Radiology, İstanbul, Turkey*

[3]*İstanbul Medipol University, International School of Medicine, Department of Infectious Diseases and Clinical Microbiology, İstanbul, Turkey*

[4]*İstanbul Biruni University, International School of Medicine, Department of Infectious Diseases and Clinical Microbiology, İstanbul, Turkey*

Abstract

Acute disseminated encephalomyelitis (ADEM) is an immune-mediated inflammatory disease of the central nervous system (CNS) and is commonly seen in children. It has seasonal peaks in winter and spring, consistent with its infectious etiologies, and it rarely occurs as a reaction to vaccination. ADEM is less common in adults and progresses with a more severe clinical course. Cases diagnosed with ADEM by CNS demyelination after streptococcal meningitis have rarely been reported in adult patients. In this report, we present a rare case of a 31-year-old female diagnosed with ADEM following pneumococcal meningitis treatment and treated successfully with low-dose methylprednisolone.

Keywords: Acute disseminated encephalomyelitis, ADEM, meningitis, *Streptococcus pneumoniae*

Öz

Akut dissemine ensefalomiyelit (ADEM), merkezi sinir sistemini etkileyen immün sistem ilişkili enflamatuvar bir hastalık olup sıklıkla çocuklarda görülür. Enfeksiyöz etiyolojiler ile ilişkili olması sebebiyle sonbahar ve kış dönemlerinde mevsimsel pik yapmakta olup nadiren aşılara karşı bir reaksiyon olarak da görülmektedir. Akut dissemine ensefalomiyelit erişkinlerde daha nadir görülmekte ve daha ağır bir klinik tabloya sebep olmaktadır. Erişkin hastalarda nadiren streptokoksik menenjit sonrası merkezi sinir sistemi demiyelinizasyonu ile ADEM tanısı konulan olgular bildirilmiştir. Bu yazıda pnömokokal menenjit tedavisini takiben ADEM tanısı alan ve düşük doz metilprednizolon ile başarılı bir şekilde tedavi edilen 31 yaşında bir kadın olgu sunulmuştur.

Anahtar Kelimeler: Akut dissemine ensefalomiyelit, ADEM, menenjit, *Streptococcus pneumoniae*

Introduction

Acute disseminated encephalomyelitis (ADEM) is a rare monophasic idiopathic inflammatory disease of the central nervous system (CNS). It is commonly seen in children following bacterial infection, viral infection, and vaccination. Acute disseminated encephalomyelitis is difficult to diagnose because it has characteristics similar to those of other clinically isolated

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Address for Correspondence/Yazışma Adresi: Ayşe Serra ÖZEL MD, University of Health Sciences Turkey, Ümraniye Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, İstanbul, Turkey
Phone: +90 216 632 18 18 (1627) **E-mail:** aserra.ozel@gmail.com **ORCID ID:** orcid.org/0000-0003-2111-1183
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syndromes and is often considered in the differential diagnoses of clinically isolated syndromes[1]. Because of the absence of a clear-cut diagnosis of ADEM, diagnosis by exclusion is still the accepted method of diagnosis. Multifocal CNS disturbances with suspected demyelinating tissue, encephalopathy, brain magnetic resonance imaging (MRI) abnormalities during the acute period (three months), and no progression or new MRI findings after the acute period remain the ADEM diagnostic criteria. Along with acute onset encephalopathy and multifocal neurological deficits, prodromal symptoms such as headache, fever, nausea, vomiting, somnolence, and malaise may precede[2].

Few cases of ADEM after bacterial infection have been reported in the literature. Pneumococcal meningitis is the most common cause of bacterial meningitis in adults and peaks seasonally. Vaccination programs are important in preventing pneumococcal diseases, especially in people with immunosuppression and splenectomy.

As ADEM is uncommon, we should take the disorder into consideration while proceeding with the differential diagnoses. This report presents a case of an adult female with pneumococcal meningitis associated with ADEM, highlighting the difficulties of diagnosis.

Case Report

A 31-year-old female veterinarian presented to the emergency department with complaints of fever and headache for the past four days with a change in consciousness and meaningless speech. She underwent a splenectomy due to trauma at the age of five years, and her history of pneumococcal vaccination was unknown.

On physical examination, she was confused and agitated, with symptoms of nuchal rigidity and mydriasis of the left pupil with no light reflex. Laboratory tests revealed the following results: hemoglobin 10 g/dl, leukocyte count 23.000/mm^3, platelet count 90.000/mm^3, and C-reactive protein 20 mg/dl (0-0.5). A biochemical workup revealed normal serum transaminases and kidney function tests.

A lumbar puncture was performed with an initial diagnosis of meningitis that revealed a cerebrospinal fluid (CSF) leukocyte count of 160/mm^3 with 80% granulocytes and 22% bands, a protein concentration of 416 mg/dl, and a glucose concentration of <1 mg/dl (simultaneous serum glucose level was 117 mg/dl). Based on these findings, the patient was diagnosed with acute bacterial meningitis and treated with vancomycin 1 g IV q12h and ceftriaxone 2 g IV q12h. In addition, prednisolone 60 mg/day IV was given for six days (60 mg/day for two days, 40 mg/day for two days, and 20 mg/day for two days). The diagnosis was confirmed as CSF culture revealed *Streptococcus pneumoniae*. As the patient developed hearing loss and tinnitus during the early phases of treatment, cranial computed tomography confirmed left-sided mastoiditis. After completing a four-week course of antibiotic treatment, she was given a conjugate pneumococcal vaccine, *Haemophilus influenzae* vaccine, and meningococcal vaccine and discharged with total hearing loss in her left ear.

The patient was readmitted to the hospital with a fever two days following discharge. Cranial MRI revealed multiple T2 and fluid-attenuated inversion recovery hyperintense foci in the left frontal region, the pericallosal area, the corpus callosum, the bilateral periventricular area, and the centrum semiovale. The findings were consistent with demyelinating plaques and were reported in favor of secondary contrast enhancement to active plaques (Figure 1). The cranial diffusion MRI showed that loss of airway and collection in bilateral mastoid cells, defused inflammatory changes in the paranasal sinuses, and mucosal thickening in the maxillary and ethmoid sinuses was detected. In the periventricular areas of the left centrum semiovale and basal ganglion and the posterior of the corpus callosum, diffusion-restricted areas were detected in the occipital region at a high convexity level (Figure 1).

Acute disseminated plaques were detected on cranial MRI, and neurological examination was unremarkable. ANA, AMA, PR3 ANCA, P-ANCA, anti-ds DNA, anti-SS-A/B, anti-Scl70, anti-histone, anti-Sm, anti-Jo 1, anti-Sm/Rnp, anti-Ssa/52, anti-nucleosome, anti-cardiolipin, beta-2 glycoprotein, C 3/4, anti-ribosomal P, and Lupus anticoagulant were tested negative, and protein electrophoresis was normal. Thus, we excluded autoimmune, paraneoplastic, infectious, and rheumatoid diseases. Lumbar puncture was repeated, and CSF was negative for oligoclonal bands. Because the patient is a veterinarian, a broad range of zoonotic infections, including *Bartonella*, leptospirosis, rickettsiosis, Q fever, and brucellosis, were tested and excluded. Finally, the patient was diagnosed with ADEM, and prednisolone 60 mg/day IV (60 mg/day for two days, 40 mg/day for two days, and 20 mg/day for two days) was commenced for six days as treatment. Her fever regressed in one week, and a

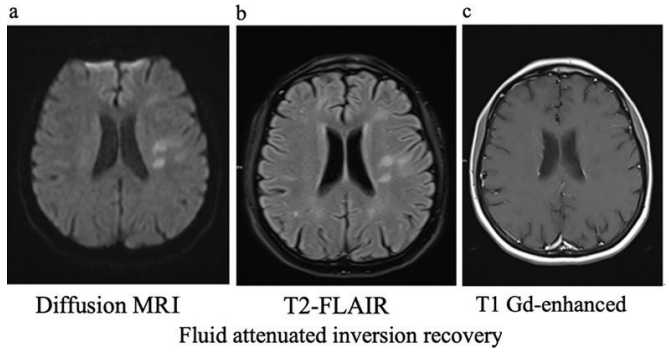

Figure 1. MRI scan two days after readmission

MRI: Magnetic resonance imaging

control cranial MRI showed regression of demyelinating plaques (Figure 2). The patient had no complaints three months after discharge, and hearing loss did not improve.

Review of the Literature

Parainfectious ADEM commonly occurs after bacterial and viral upper respiratory tract infections such as *Mycoplasma* spp., *Borrelia* spp., *Chlamydia* spp., *Haemophilus influenzae*, and *Legionella* spp.[4-8]. Post-infectious ADEM following pneumococcal meningitis has rarely been reported in the literature[9-13]. In the literature, patients aged 50 years and older were diagnosed with ADEM after pneumococcal meningitis treatment and treated with pulse corticosteroid therapy[9,10]. Additionally, a 39-year-old man clinically improved after pulse steroid treatment after four days of pneumococcal meningitis treatment[11]. A previous report presented a case of a 61-year-old woman with a history of splenectomy diagnosed with ADEM two days after the appropriate treatment of pneumococcal meningitis, which is similar to our case[12].

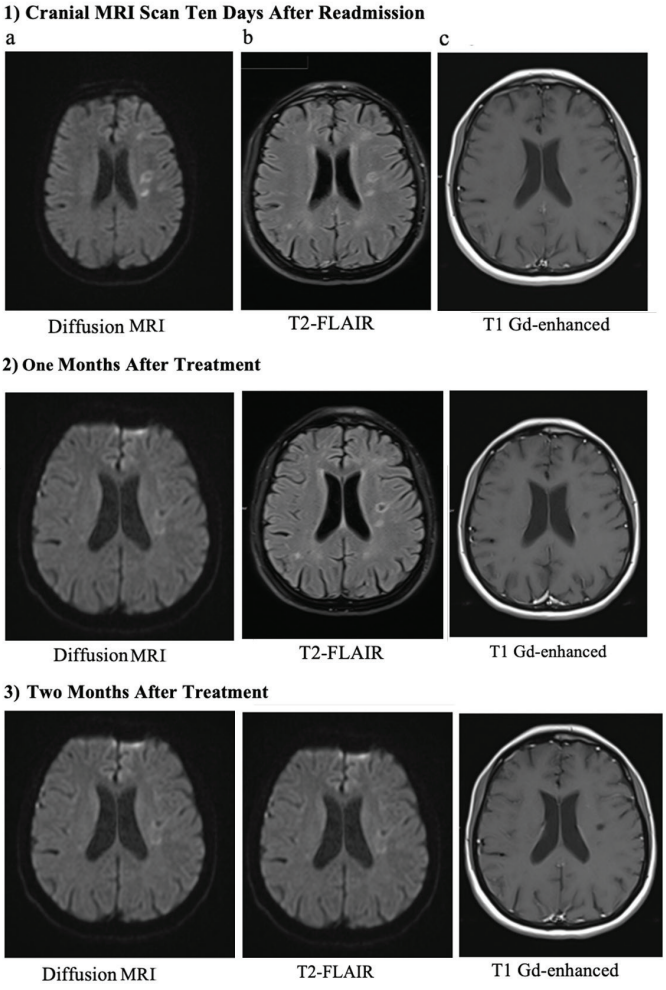

Figure 2. Cranial MRI imaging, follow-up
MRI: Magnetic resonance imaging

Discussion

We reported a rare case diagnosed with ADEM following pneumococcal meningitis treatment. In the reported cases, ADEM was diagnosed after cranial imaging with the onset of neurological symptoms following pneumococcal meningitis[9-13]. In our case, ADEM was diagnosed by detecting white matter lesions on cranial imaging concurrently with mastoiditis detected by refractory fever developing two days after meningitis treatment. Using especially lumbar puncture and gadolinium-enhanced MRI of the brain and spinal cord as we did for both diagnoses of pneumococcal meningitis and ADEM, respectively, will help distinguish between diseases with very similar clinical characteristics[14]. Additionally, CNS vasculitis and multiple sclerosis were ruled out with autoimmune markers and CSF biochemical evaluation, which was in the differential diagnosis in our case.

ADEM is a disease characterized by monophasic inflammation that frequently develops following systemic infections involving the CNS. It is more likely to occur in childhood, 7 to 10 days (range: two days-four weeks) after infection or, rarely, after vaccination[3]. Due to the association between infectious etiologies, ADEM has seasonal peaks in the winter and spring and begins with symptoms like fever, headache, nausea, and vomiting as well as neurologic findings like neck stiffness, ataxia, hemiparesis, and cranial nerve involvement[4]. Because the symptoms of ADEM and meningoencephalitis tend to be similar, both illnesses could be misdiagnosed.

There are no clear data on the dose and duration of steroids for ADEM treatment. Hunh et al.[12] presumed that starting high-dose corticosteroid therapy, even if the patient is septic, is safe unless it is within the first 14 days following a bacterial meningitis diagnosis and the CSF leukocyte count has regressed with meningitis treatment. Other cases treated with pulse steroid therapy (1 gr/day) showed radiological and clinical responses[9-12]. Although there is no standard treatment for ADEM, prednisolone therapy is used in most cases. A previous study showed that prednisolone treatment is more effective than dexamethasone[15]. Other reports showed that intravenous immunoglobulin with high-dose steroid therapy was proven successful[16].

In our case, cranial lesions regressed, and fever response was obtained after low-dose IV prednisolone treatment was given for six days. The absence of neurological findings other than fever in our case may also contribute to the benefit of low-dose steroid therapy.

Conclusion

Pneumococcal immunization is necessary to prevent the development of meningitis, especially in patients with

splenectomy, alcohol use, and skull base fractures. Acute disseminated encephalomyelitis diagnosis should be considered in patients who develop encephalopathy after meningitis treatment.

Ethics

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.S.Ö., A.K., Concept: L.N.A., M.Y., Design: L.N.A., M.Y., A.K., Data Collection or Processing: A.S.Ö., Analysis or Interpretation: Z.S., E.A.Y., Literature Search: Z.S., E.A.Y., Writing: A.S.Ö., A.K.

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References

1. Pohl D, Alper G, Van Haren K, Kornberg AJ, Lucchinetti CF, Tenembaum S, Belman AL. Acute disseminated encephalomyelitis: Updates on an inflammatory CNS syndrome. Neurology. 2016;87(9 Suppl 2):S38-45.
2. Young NP, Weinshenker BG, Lucchinetti CF. Acute disseminated encephalomyelitis: current understanding and controversies. Semin Neurol. 2008;28:84-94.
3. Sonneville R, Klein I, de Broucker T, Wolff M. Post-infectious encephalitis in adults: diagnosis and management. J Infect. 2009;58:321-8.
4. Stonehouse M, Gupte G, Wassmer E, Whitehouse WP. Acute disseminated encephalomyelitis: recognition in the hands of general paediatricians. Arch Dis Child. 2003;88:122-4.
5. van Assen S, Bosma F, Staals LM, Kullberg BJ, Melchers WJ, Lammens M, Kornips FH, Vos PE, Fikkers BG. Acute disseminated encephalomyelitis associated with Borrelia burgdorferi. J Neurol. 2004;251:626-9.
6. Beleza P, Ribeiro M, Pereira J, Ferreira C, Jordão MJ, Almeida F. Probable acute disseminated encephalomyelitis due to Haemophilus influenzae meningitis. Dev Med Child Neurol. 2008;50:388-91.
7. Heick A, Skriver E. Chlamydia pneumoniae-associated ADEM. Eur J Neurol. 2000;7:435-8.
8. Spieker S, Petersen D, Rolfs A, Fehrenbach F, Kuntz R, Seuffer RH, Fetter M, Dichgans J. Acute disseminated encephalomyelitis following Pontiac fever. Eur Neurol. 1998;40:169-72.
9. Ueda M, Kanamori A, Mihara T, Hara H, Mutoh T. [A case of acute disseminated encephalomyelitis (ADEM) following treatment for pneumococcal meningoencephalitis]. Rinsho Shinkeigaku. 2009;49:96-9.
10. Kureshiro J, Kusumoto Y, Komatsu H, Kusunoki S. Acute meningoencephalitis caused by Streptococcus pneumoniae, mimicking acute disseminated encephalomyelitis. Rinsho Shinkeigaku. 2008;48:255-8.
11. Ohnishi H, Sawayama Y, Ariyama I, Yamaji K, Furuya N, Hayashi J. Acute disseminated encephalomyelitis (ADEM) onset during meningitis and sepsis. Kansenshogaku Zasshi. 2007;81:577-81.
12. Huhn K, Lee DH, Linker RA, Kloska S, Huttner HB. Pneumococcal-meningitis associated acute disseminated encephalomyelitis (ADEM) - case report of effective early immunotherapy. Springerplus. 2014;3:415.
13. Alonso A, Etminan N, Krebs J, Szabo K, Platten M, Förster A. Fulminant Cytotoxic Edema in a Patient with Pneumococcal Meningoencephalitis. J Clin Neurol. 2019;15:575-7.
14. Tenembaum S, Chitnis T, Ness J, Hahn JS; International Pediatric MS Study Group. Acute disseminated encephalomyelitis. Neurology. 2007;68(16 Suppl 2):S23-36.
15. Sakakibara R, Hattori T, Yasuda K, Yamanishi T. Micturitional disturbance in acute disseminated encephalomyelitis (ADEM). J Auton Nerv Syst. 1996;60:200-5.
16. Repić-Buličić A, Filipović-Grčić P, Jadrijević E, Jurinović P, Titlić M. Successful Treatment of Acute Disseminated Encephalomyelitis (Adem) by Prompt Usage of Immunoglobulins - Case Report and Review of the Literature. Acta Clin Croat. 2019;58:173-9.