

## **Atypical Presentation of Acute Disseminated Encephalomyelitis in Elder Case**

**Heyam S. Al-Rached<sup>1</sup> MD, Saleh S. Baeesa<sup>2</sup> MBChB, FRCSC, Omar M. Wazzan<sup>1</sup> MD and Yousef A. Al-Said<sup>1</sup> MBChB, FRCPC**

<sup>1</sup>*Department of Neuroscience, King Faisal Specialist Hospital and Research Center, Jeddah, Saudi Arabia*

<sup>2</sup>*Division of Neurological Surgery, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia*  
*sbaesa@kau.ed.sa*

*Abstract.* To report a 65-year-old male who presented with subacute encephalopathic syndrome without preceding triggering factors. The diagnosis of an acute disseminated encephalomyelitis was based on suggestive MRI features, and confirmed by histopathological examination. Although of a rare occurrence, and such atypical presentation in this age group, this entity should be considered in the differential diagnosis of encephalopathy in elderly.

*Keywords:* Acute disseminated encephalomyelitis, Elderly.

### **Introduction**

Acute disseminated encephalomyelitis (ADEM) is an uncommon inflammatory, immune mediated, demyelinating disease of the central nervous system (CNS)<sup>[1]</sup>. Commonly, it develops acutely or sub-acutely in a close temporal relationship to an antigenic challenge, such as infection or immunization<sup>[2]</sup>. However, it may occur without a recognizable preceding event, mainly in the elderly<sup>[3]</sup>. Multiple mechanisms of immune response may explain the pathogenesis of ADEM<sup>[4]</sup>. Its effects predominantly on children and adolescents, but it is also reported in adult population<sup>[5]</sup>. The neurological picture of ADEM

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<sup>2</sup>Correspondence & reprint request to: Dr. Saleh Baeesa  
P.O. Box 80125, Jeddah 21589, Saudi Arabia

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usually monophasic, but relapses have been reported<sup>[3,6]</sup>. Magnetic resonance imaging (MRI) scans reveal a pattern of multifocal white matter abnormalities, and the involvement of gray matter is not uncommon<sup>[7]</sup>. The classic pathological appearance is a perivascular inflammation and demyelination<sup>[8]</sup>. Currently, no therapy has been established by controlled trials, and the therapeutic modalities have been based on a presumed autoimmune etiology<sup>[9]</sup>. Early studies reported a high mortality rate and high neurological sequel, whereas recent reports suggest a more favorable prognosis<sup>[5]</sup>.

The report herein, of this 65-year-old male with atypical presentation of ADEM, and emphasize that this rare entity should be considered in the differential diagnosis of encephalopathy in elderly.

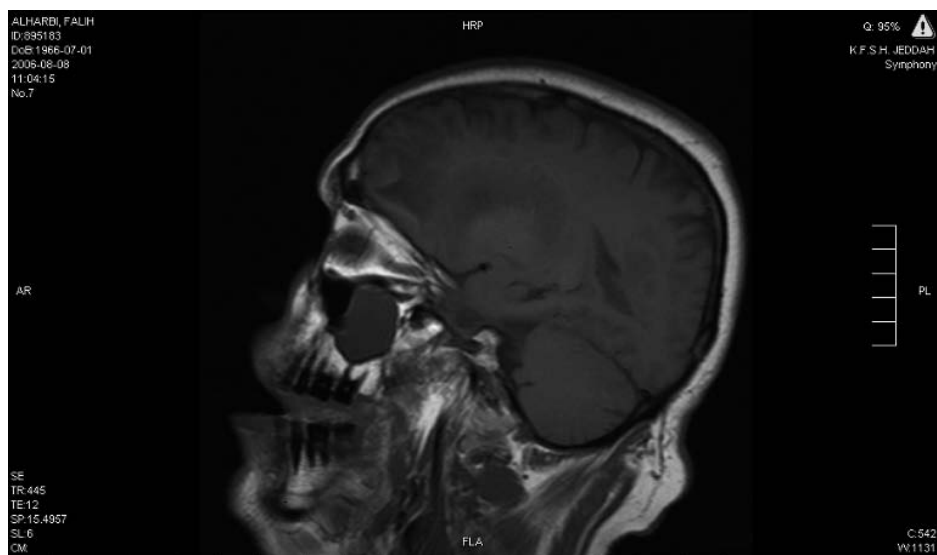
### **Case Report**

A 65-year-old man was admitted at King Faisal Specialist Hospital and Research Center (Jeddah) on August 2006, with a two-week history of progressive change in mental status. Two weeks prior to presentation, his family noticed that he became sad, less talkative, inattentive, forgetful, and acting strange. Over the following three days, he experienced further deterioration and became more confused, disoriented, irritable, agitated, and unable to recognize family members. He refused eating, and his language became incomprehensible. He also became incontinent of urine and stool. There was no history of previous complaints of headache, fever, nausea, vomiting, diarrhea, arthralgia, or weight loss. There was no incidence of recent immunization, use of alcohol or drugs, or exposure to tuberculosis. There was also no history of recent travel, or family history of multiple sclerosis.

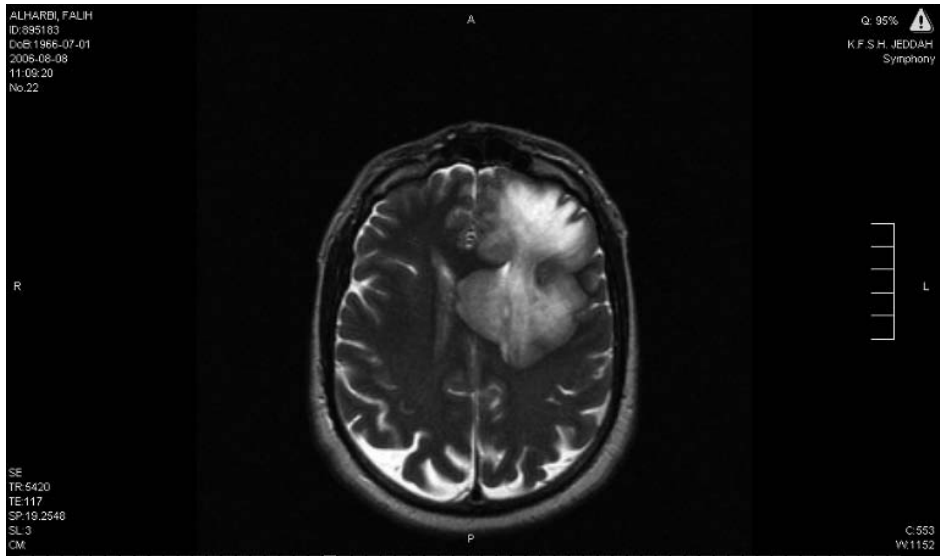
He was admitted first to a peripheral hospital where brain MRI scans revealed multiple enhancing brain lesions, which were considered as metastasis. Radiological work up for a primary malignancy, including computed tomography (CT) scans of the chest, abdomen, and pelvis, was carried out. The results of the above-mentioned CT scan were unremarkable. During his one-week stay in the referring hospital, his clinical condition steadily deteriorated, and he became diffusely encephalopathic and mute. On admission to our institution, his general examination was unremarkable and vital signs were normal. Neurological examination demonstrated that he was alternately somnolent and agitated, combative, not communicating, not understanding or obeying

commands. His pupils were symmetrical and reactive, with no detected cranial neuropathies. Although, he was uncooperative with motor examination, thus he was moving his limbs adequately without apparent weakness or in coordination. The sensation could not be assessed and the reflexes were 2+ and symmetrical. The planter response was unobtainable because of partial bilateral great toe amputation.

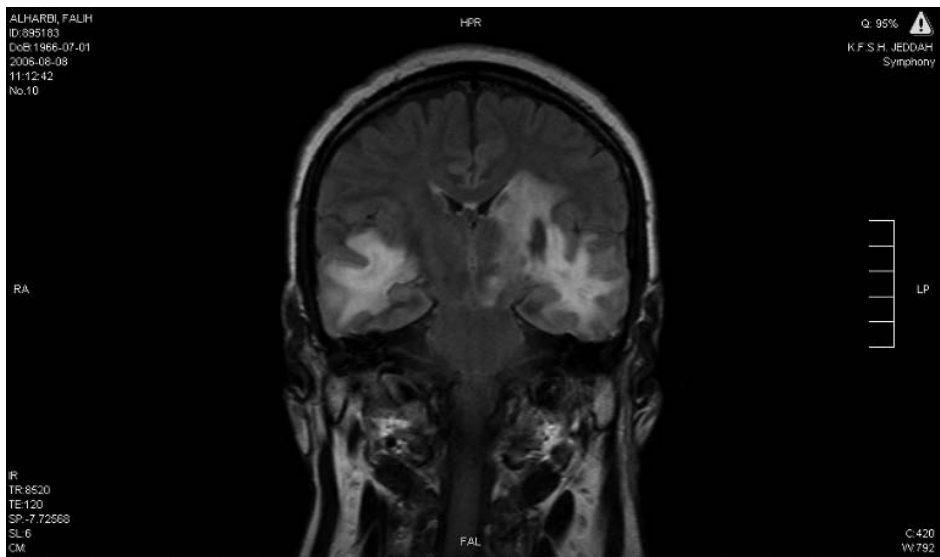
Laboratory investigations including, Complete Blood Count and Differential, coagulation, renal, electrolyte, hepatic, thyroid profiles, and vitamin B12 level, were within normal limits. HIV serology was negative. Echocardiogram was unremarkable and electroencephalogram (EEG) showed diffuse disturbance of cerebral activity with no epileptiform discharges. A clear Cerebrospinal fluid (CSF) was obtained through lumbar puncture with an opening pressure of 130 mm of water. CSF examination revealed 1 RBC, 7 WBCs (90% lymphocytes), glucose was 4 mmol/L (glucose blood level, 7 mmol/L), protein level was 720 mg/L (normal up to 400 mg/L), and the bacterial and fungal cultures were negative. CSF serology for oligoclonal proteins and polymerase chain reaction for acid-fast bacilli and herpes were negative. MRI brain scans (Fig. 1A-D) revealed multiple areas of abnormal increased signal intensity in T2-weighted images, and a low signal intensity in T1-



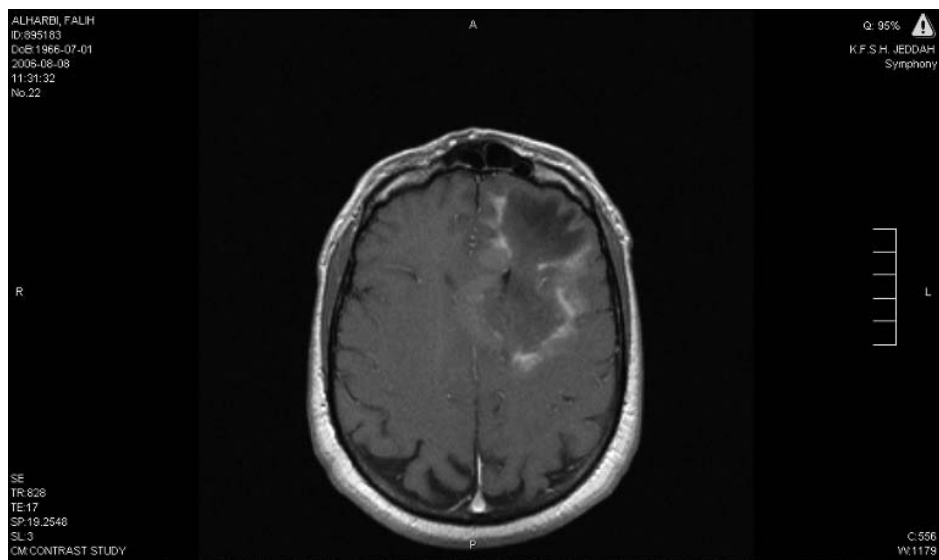
**Fig. 1A.** A sagittal T1-weighted image shows multiple areas of low signal intensity involving frontal and temporal areas.



**Fig. 1B.** Axial T2-weighted image shows areas of abnormal increased signal intensity in left frontal with minimal mass effect and surrounding vasogenic oedema.



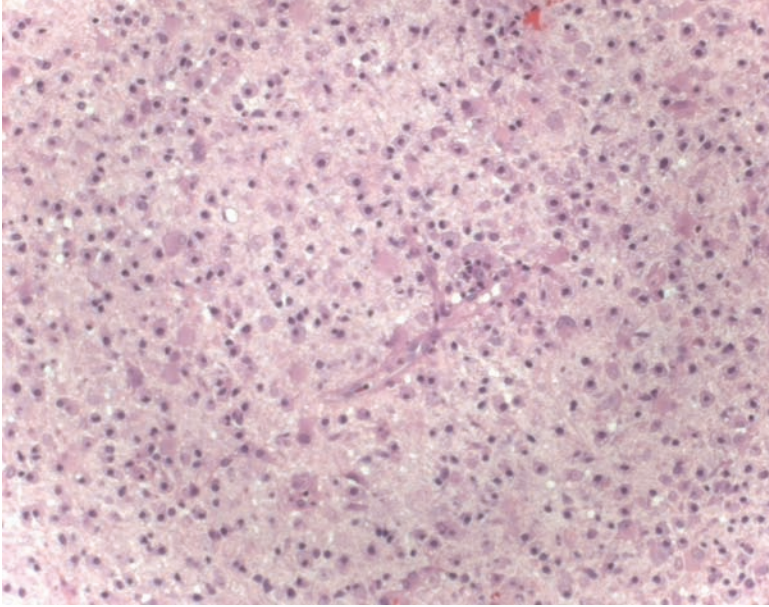
**Fig 1C.** Coronal fluid-attenuated inversion recovery show areas of abnormal increased signal intensity in left frontal, left basal ganglia, bilateral temporal, and left occipital lobe, with extensive surrounding vasogenic oedema, and minimal mass effect.



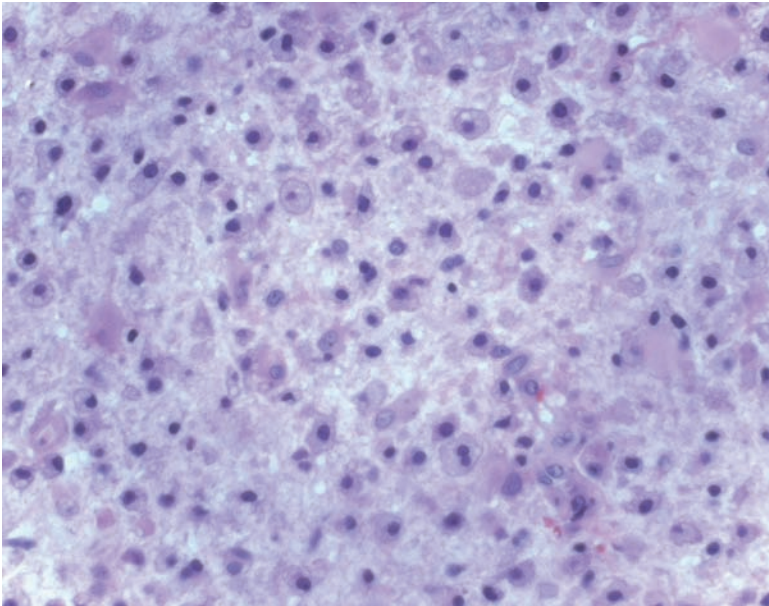
**Fig. 1D.** Axial contrast-enhanced T1-weighted images show an irregular nodular peripheral enhancement of the lesions.

weighted images involving the left frontal lobe extending inferiorly to the basal ganglia.

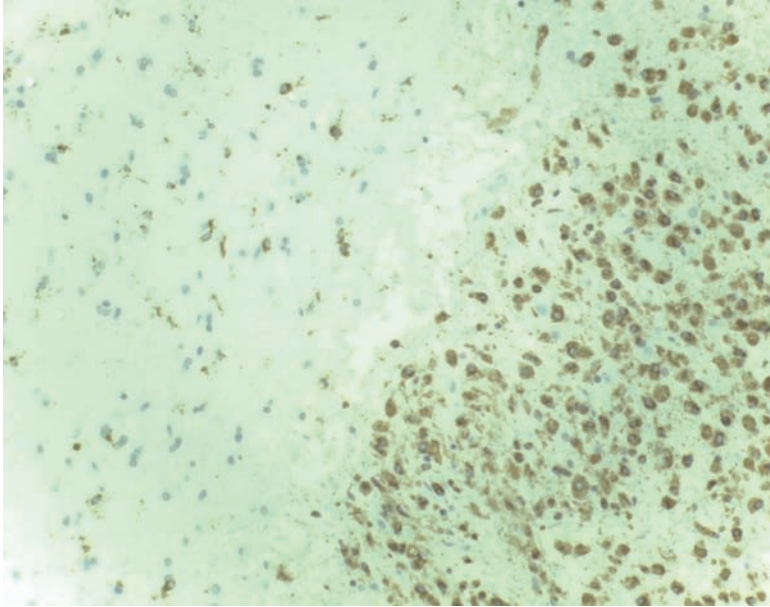
There were areas of almost symmetric distribution involving both, temporal and occipital lobes which appear of low signal intensity in T1-weighted images and bright in T2-weighted images with no involvement of the corpus callosum. These lesions showed extensive surrounding vasogenic edema with no definite mass effect. Following gadolinium administration, those lesions demonstrated an irregular nodular peripheral enhancement. MR spectroscopy was inconclusive. Final diagnosis was achieved through stereotactic biopsy of left frontal lesion. Histopathological examination revealed areas with large number of histiocytes that intermixed with some lymphocytes, particularly around blood vessels, focal gliosis and disruption of myelin in these areas with relative preservation of axons. No definite neoplasia was identified and special staining for acid-fast bacilli and fungi were negative (Fig. 2A-E). The patient had uneventful postoperative period, and he was started on intravenous injection of methylprednisolone for 5 days. He showed slight cognitive improvement and became more cooperative. He started to follow up few simple commands, and to have normal oral intake. He was discharged home with tapering oral doses of prednisolone over 10 days.



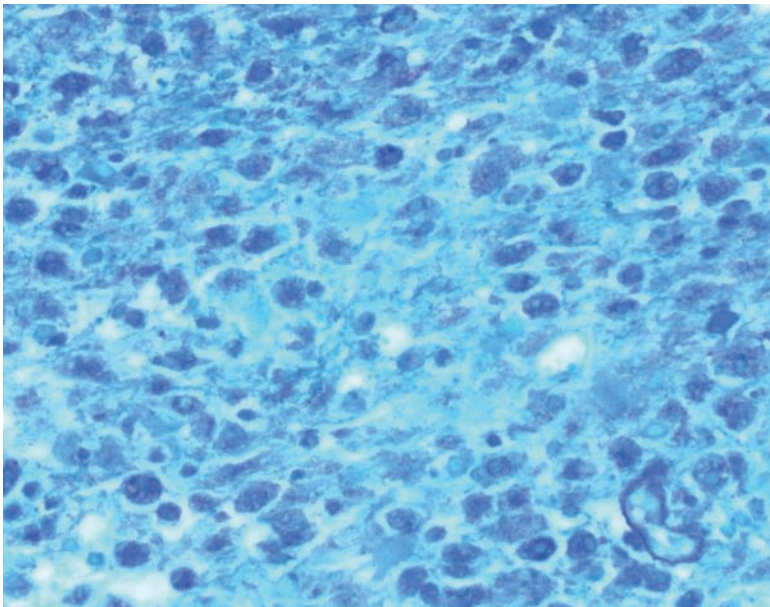
**Fig. 2A.** Biopsy specimen of the lesion in the left frontal lobe (Hematoxylin and Eosin,  $\times 200$ ). The cerebral white matter is replaced by macrophages, with perivascular inflammation.



**Fig. 2B.** Many macrophages in the affected area with some lymphocytes (Hematoxylin and Eosin stain,  $\times 400$ ).



**Fig. 2C.** CD68 immunohistochemistry stain highlighting the markedly increased number of macrophages (right) ( $\times 200$ ).



**Fig. 2 D.** Luxol fast blue (LFB) stain for myelin showing myelin debris (blue) within macrophages ( $\times 400$ ).

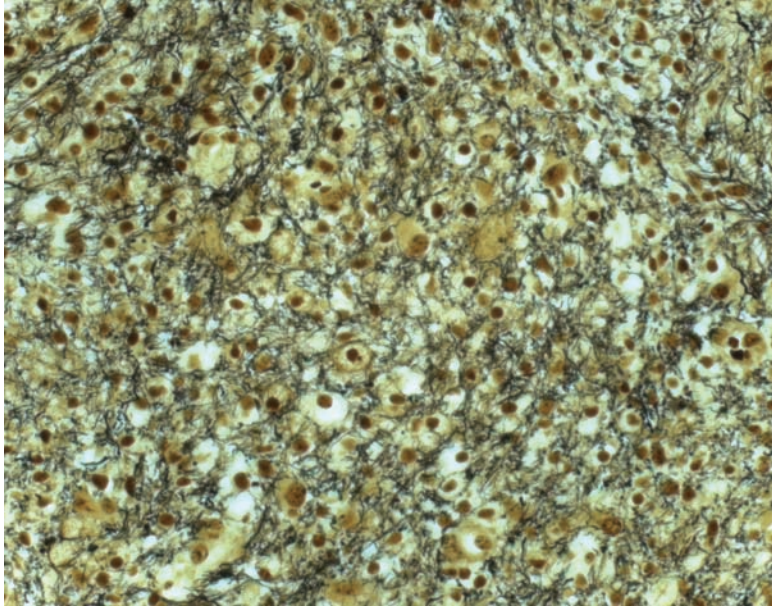


Fig. 2E. Bielschowsky stain for axons (black) showing relative preservation of axons ( $\times 400$ ).

### Discussion

Although, ADEM affects most commonly on children and adolescents, rare cases in middle-aged and elderly patients have been reported<sup>[3,5,7]</sup>. Also, it is typically antedated by infection or immunization, but it may affect adults without preceding evident of infection or antigenic challenge, as in our patient, and some etiologies remained unrecognized<sup>[1,8,10]</sup>. Typical clinical presentation is sudden onset of multifocal neurological symptoms, accompanied by generalized complaint of fever, headache, and disturbance of consciousness that may vary in severity from irritability to a coma<sup>[1,4]</sup>. Most adult patients clinically present, somewhat similar to the clinical presentation in children, with the exception of the relatively infrequent occurrence of headache, fever, and meningismus. Optic neuritis is also rare in adults presenting with ADEM<sup>[5]</sup>. Atypical presentation with acute purely psychiatric symptoms of psychosis, anxiety, and depression, have been reported in the literatures<sup>[1,12,13]</sup>. The frequency of psychiatric symptoms was more prevalent in the elderly<sup>[3]</sup>. Although, regarded as monophasic illness, relapsing disease could exist<sup>[2,6]</sup>.



The pathogenesis of ADEM is suspected to be a T-cell mediated autoimmune response to the myelin, triggered by an antigenic molecular mimicry<sup>[4]</sup>. Cerebral spinal fluid (CSF) examination is not of great help in the diagnosis, because it may be normal or may show mild leukocytosis, with mildly elevated protein. Oligoclonal immunoglobulin (IgG) bands can be present acutely, in 25% of cases<sup>[14]</sup>. Brain MRI is regarded as the investigation of choice, and T2-weighted images are more sensitive than T1-weighted images, because of the findings it may be clearly abnormal on the former and completely normal in the later images. The MRI findings consist of lesions with acute edema, inflammation, and demyelination, rather than tissue loss or gliosis, as in our patient. In comparison with multiple sclerosis (MS), ADEM radiological abnormalities are typically disseminated more peripherally, without predilection for periventricular and pericallosal areas, and are often located in the rim of occipital and parietal regions<sup>[15]</sup>. They tend to be large, confluent, and asymmetric, and they involve gray matter areas such as basal ganglia and thalami, 40% of ADEM; in exceedingly rare in MS and may have a mass effect that usually enhance with gadolinium. An extensive perifocal edema may be seen and tumor-like lesions may also occur<sup>[15,16]</sup>.

Biopsy allows a definite diagnosis, however it is rarely necessary. The pathologic findings are predominantly white matter disease, with periveinular inflammation and demyelination. Microscopically, there is mononuclear cellular infiltration along small veins, with occasional neutrophils, surrounded by demyelination<sup>[4]</sup>. Histologic staining for myelin basic protein (MBP) and myelin oligodendrocytes glycoprotein (MOG) demonstrates loss of these myelin proteins, with relative preservation of the axons. Later, these areas of demyelination are infiltrated with lipid-laden macrophages.

No therapy has been established by controlled trials for treatment of ADEM, but two studies published are consistent with earlier reports that support that corticosteroids are useful<sup>[3,5]</sup>. High dose of intravenous immunoglobulin, cytostatic drugs, and plasmapheresis are alternative treatment options, if high dose of corticosteroids fails<sup>[17,18]</sup>. The patient was treated with IV Methylprednisolone one month after the onset of the symptoms, which is considered late because of the late referral and the difficulty establishing the diagnosis without biopsy.

## Conclusion

Although of a rare occurrence in elderly with atypical presentation in this age group, ADEM should be considered in the differential diagnosis of leukoencephalopathy in elderly. A delay in diagnosis and inappropriate management may unfavorably affect the outcome of this disease.

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## التهاب الدماغ والنخاع المنتثر الحاد غير النموذجي عند الكهول

هيام صالح الراشد<sup>١</sup>، وصالح سالم باعيسى<sup>٢</sup>، وعمر موفق وزان<sup>١</sup>،  
و يوسف علي السيد<sup>١</sup>

<sup>١</sup> قسم العلوم العصبية، مستشفى الملك فيصل التخصصي ومركز الأبحاث،  
و <sup>٢</sup> شعبة جراحة المخ والأعصاب، كلية الطب، جامعة الملك عبد العزيز،  
جدة - المملكة العربية السعودية

المستخلص. نثبت في هذا التقرير حالة مريض عمره خمسة وستون عاماً، أدخل إلى المستشفى بمتلازمة الاعتلال الدماغى تحت الحاد، دون وجود أي عوامل مؤهلة لذلك، وتم تشخيص الحالة على أنها التهاب الدماغ و النخاع المنتثر الحاد، وذلك اعتماداً على الموجودات الشعاعية في تصوير الدماغ المرئاني، وتأكد التشخيص بالتشريح المرضي النسجى لخزعة الدماغ. صحيح أن حدوث مثل هذه الحالات غير النموذجية نادر في هذه الفئة العمرية، ولكن يجب أن توضع في التشخيص التفريقي لمتلازمة الاعتلال الدماغى عند الكهول. التهاب الدماغ، والنخاع المنتثر الحاد، الكهولة.