

## Case report

## Acute disseminated encephalomyelitis in an older adult following prostate resection

Ceronie B.<sup>a,\*</sup>, Cockerell O.C.<sup>b</sup><sup>a</sup> National Hospital for Neurology and Neurosurgery, London, UK<sup>b</sup> The London Clinic, London, UK

## ARTICLE INFO

## Keywords:

Acute disseminated encephalomyelitis  
Encephalopathy  
Demyelination  
Multiple sclerosis

## ABSTRACT

Acute disseminated encephalomyelitis (ADEM) is an uncommon, autoimmune, demyelinating disorder of the central nervous system. It is rare in adults beyond 65 years. Here, we describe a novel presentation following urological surgery. Using illustrative features from our case study, we describe some of the clinical features, aetiologies, diagnostic uncertainties and pathogenic mechanisms of the disease. A 69 year old gentleman underwent transurethral resection of the prostate. He then developed confusion, unsteadiness, behavioural disturbance and left-sided hemiparesis. On admission he was febrile with left hemiplegia and ataxia. Neuroimaging showed multifocal, posterior-predominant semi-confluent lesions. Autoimmune serology and virology were negative. Cerebrospinal fluid revealed mildly elevated protein. Brain biopsy confirmed a diagnosis of ADEM. ADEM is a predominantly a childhood disorder and rare in older adults. It is precipitated by vaccinations, viral, bacterial or parasitic infections. It is rarely described after surgical intervention. Differential diagnosis is wide and includes multiple sclerosis (MS), encephalitides and encephalopathies. Treatment is with corticosteroids, plasma exchange, intravenous immunoglobulin or cyclophosphamide. Up to a quarter will experience recurrence and 10% progress to MS. Further study is needed to determine its pathogenic and immunological characteristics.

## 1. Introduction

Acute disseminated encephalomyelitis (ADEM) is an uncommon, immune-mediated, demyelinating disorder of the central nervous system (CNS) [1]. It is rarely seen in older adults beyond 65 years. It is mostly precipitated by infections and vaccinations, with few reports after surgery. We describe a novel presentation following prostate resection.

## 2. Case report

A 69 year old gentleman underwent a transurethral resection of the prostate. He had a background of benign prostatic hypertrophy, hyperthyroidism, and seborrheic dermatitis.

Several days later he developed malaise, myalgia and headache. In the following week, he suffered emotional lability, unsteadiness and left-sided weakness, presenting to the emergency department. On examination he was febrile, with a left-sided hemiparesis, normal tone and reflexes and reduced left-sided coordination.

Erythrocyte sedimentation rate was raised at 74 mm/h with a c-reactive protein of 9 mg/L. Creatine kinase was raised at 650 U/L and

fibrinogen 424 mg/dL. Autoimmune serology including rheumatoid factor, anti-nuclear and extractable nuclear antibodies, anti-neuronal, anti-N-methyl D-aspartate (NMDA) and voltage-gated potassium channel complex (VGKCC) antibodies were negative. Serology for human immunodeficiency virus (HIV), herpes simplex (HSV), Epstein-Barr (EBV), varicella zoster and John Cunningham (JC) viruses, Lyme disease and syphilis was negative.

Computed tomography (CT) showed multifocal, posterior-predominant semi-confluent lesions. Magnetic resonance imaging (MRI) confirmed high signal lesions on T2 and fluid attenuated inversion recovery (FLAIR), with restricted diffusion (Fig. 1). Cerebrospinal fluid (CSF) protein was raised at 73 mg/dL with normal white cell count and glucose, with no oligoclonal bands (OCBs). No organisms were detected, including tests for tuberculosis, cryptococcus, listeria and viral polymerase chain reaction.

He was started on empirically on IV ceftriaxone and aciclovir. He initial impression was of posterior-reversible encephalopathy syndrome (PRES). He was started on IV methylprednisolone. He then developed confusion, seizures and deteriorated to coma. There was no response to corticosteroids and he underwent several cycles of plasma exchange without improvement. An electroencephalogram showed generalised

\* Corresponding author at: 3 Roman Farm, Nettleleden HP13DA, UK.

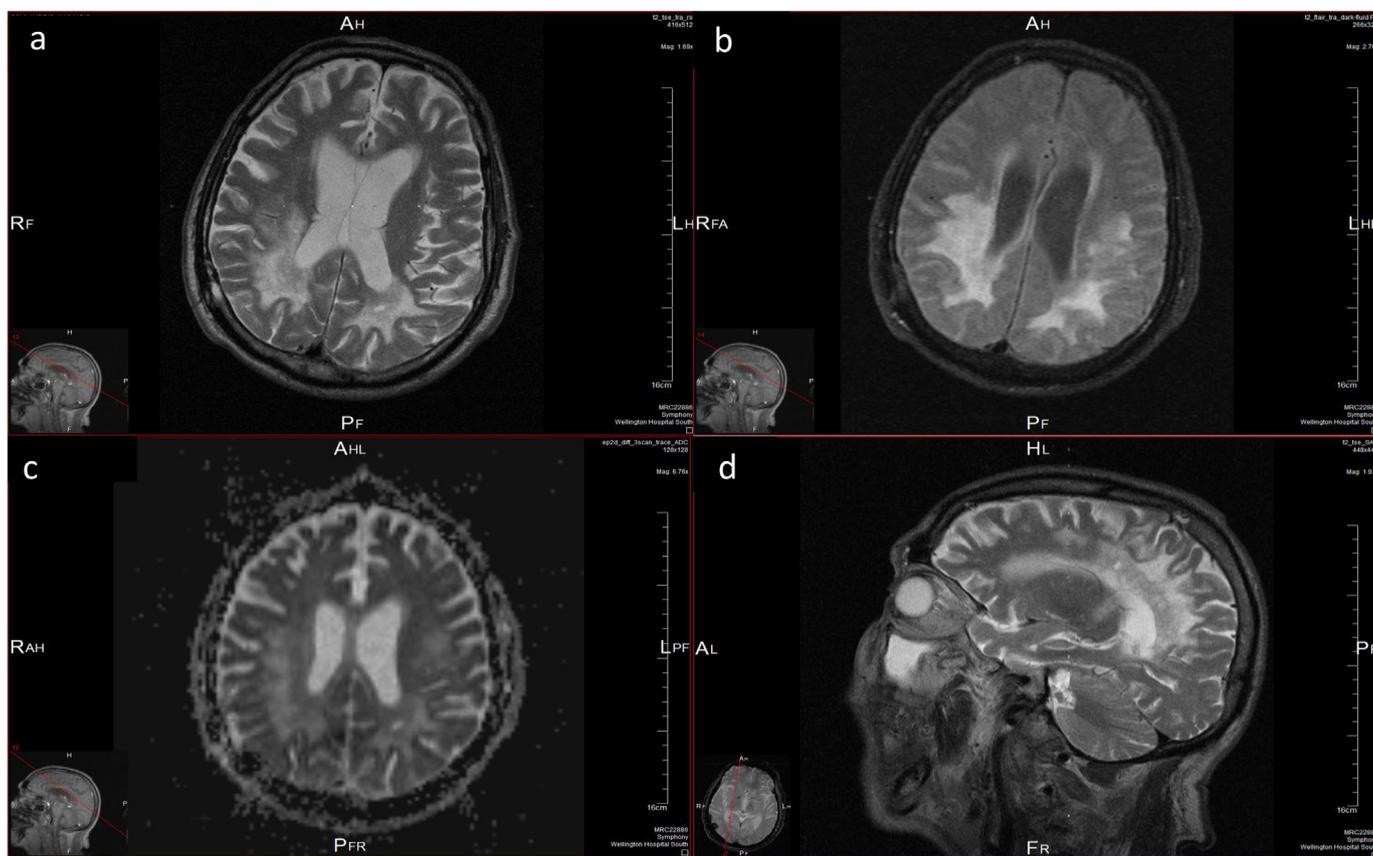
E-mail address: [bryan.ceronie@nhs.net](mailto:bryan.ceronie@nhs.net) (B. Ceronie).

<https://doi.org/10.1016/j.ensci.2018.11.006>

Received 13 November 2018; Accepted 17 November 2018

Available online 22 November 2018

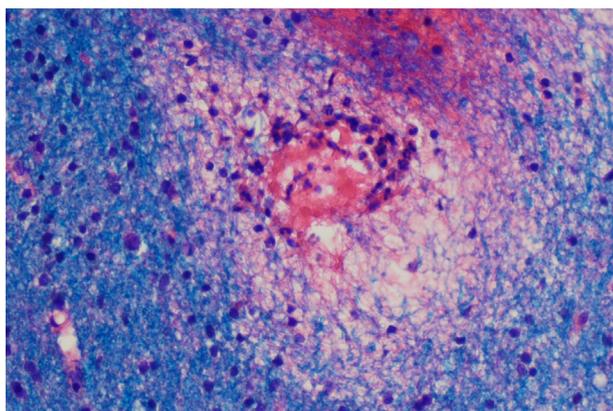
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**Fig. 1.** T2 axial turbo spin echo (TSE) (a), fluid-attenuated inversion recovery (FLAIR) (b) and diffusion weighted imaging (DWI) (c), showing multifocal, posterior-predominant, semi-confluent lesions, with restricted diffusion. (d) T2 sagittal TSE imaging showing semi-confluent lesions of the occipital and parietal lobes.

slow wave activity, consistent with encephalopathy.

He proceeded to brain biopsy, which demonstrated prominent pallor of myelin staining in perivascular region with perivascular mononuclear cell infiltration with possible fibrinoid necrosis of the vessel wall and fresh haemorrhage, consistent with a diagnosis of ADEM (Fig. 2). As intravenous immunoglobulin was not available, he was started on IV cyclophosphamide. To this he made limited recovery and was transferred to a neurorehabilitation unit.



**Fig. 2.** Brain biopsy stained with haematoxylin and eosin with luxol fast blue for myelin. It shows prominent pallor of myelin staining in perivascular region with perivascular mononuclear cell infiltration, possible fibrinoid necrosis of the vessel wall and fresh haemorrhage. There is no evidence of vasculitis, viral inclusions or microglial nodules. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

### 3. Discussion

ADEM is an uncommon, immune-mediated, demyelinating disorder of the central nervous system. It predominantly affects children of 5–8 years, with a incidence of 0.6 per 100,000 per year [1]. In adults it is even rarer, usually presenting between 30 and 50 years with equal sex preponderance. There are few cases in adults beyond 65 years.

The most common precipitants are viruses [2] and vaccinations, especially influenza. It is also associated with bacterial infections, toxoplasmosis and malaria. There are few documented cases following therapy (Table 1). In surgery, it most commonly follows solid organ or stem cell transplantation, although it is reported after intracranial aneurysmal coiling [3] and appendectomy [4]. There are no previous reports following urological intervention.

The exact pathogenesis of ADEM is unknown, but some mouse models of experimental experimental autoimmune encephalitis (EAE) resemble its monophasic, demyelinating pattern [5]. These are

**Table 1**  
Reported precipitants of ADEM in adults.

Cause	Examples
Viral	Influenza A or B, Hepatitis A or B, HSV, Human Herpes Virus 6, EBV, Cytomegalovirus, HIV, Dengue, Zika
Bacterial	Mycoplasma pneumonia, Chlamydia, Legionella, Campylobacter, Streptococcus,
Parasitic	Malaria, Toxoplasma
Vaccinations	Influenza, Rabies
Medication	Gold therapy
Toxic	Synthetic cannabinoids, intravenous herbal remedies
Surgery	Renal, liver, heart-lung or stem cell transplantation, appendectomy, intracranial aneurysmal coiling

characterised by the infiltration of pro-inflammatory T helper (Th)1 lymphocytes, secreting pathogenic cytokines interferon gamma and interleukin (IL)-12, and Th17 cells, secreting IL-17, IL-23 and granulocyte-macrophage colony-stimulating factor [6]. Peripheral T cells may be activated by an infectious antigen which has some similarity to a CNS antigen (mimicry), leading to activation of Th1 and Th17 cells and crossing of the blood brain barrier into the CNS. This leads to antigen presentation and further recruitment of autoreactive T cells and myelin-activated macrophages. The presence of antibodies against myelin oligodendrocyte protein (MOG), myelin basic protein (MBP) and aquaporin-4 in some cases may also suggest an important B cell-mediated humoral response.

This case presented characteristically with an flu-like prodrome followed in 4–12 days by encephalopathy with focal neurological deficits and seizures. Other presentations include optic neuritis, transverse myelitis and peripheral neuritis [7]. A hyperacute variant, acute hemorrhagic leukoencephalitis (AHL), is associated and hemorrhagic lesions on MRI and rapid deterioration to coma, although whether this is part of the same disease remains controversial [1].

The work-up for ADEM includes serology shows raised inflammatory markers. Antibodies to MBP and MOG may be raised [8]. CSF studies typically show mild lymphocytosis with raised protein. Oligoclonal bands (OCBs) are generally negative, as in this case. Radiologically, ADEM presents as multifocal T2-hyperintense white matter lesions that may affect both hemispheres. There are often symmetrical gray matter lesions on FLAIR, involving the thalamus and basal ganglia. Spinal cord involvement occurs in up to one third [9]. The posterior white matter predominance in this case was unusual, initially pointing to an alternative working diagnosis. Histopathology reveals perivascular zones of demyelination with relative axonal sparing. The may also be lymphocytic and neutrophilic infiltration, as well as perivascular oedema.

Differential diagnosis is wide and includes multiple sclerosis (MS). MRI studies alone cannot differentiate ADEM from MS, and therefore diagnosis may rest on the clinical syndrome. Other differentials include vasculitis, PRES, progressive multifocal leukoencephaly, viral encephalitis, neurosarcoidosis, systemic lupus erythematosus, toxic encephalopathies and adult onset leukodystrophies.

Treatment is with intravenous methylprednisolone. If this fails then plasma exchange, intravenous immunoglobulin or cyclophosphamide may be considered. Rarely, patients who develop raised intracranial pressure have been treated with decompressive craniectomy.

Prognosis is generally good with up to 80% of paediatric patients experiencing complete recovery and 20% suffering residual

neurological deficit. In adults, up to a quarter will experience a recurrence of the disease, termed multiphasic disseminated encephalomyelitis. If multiple episodes occur the syndrome is considered a chronic, relapsing disorder, potentially consistent with MS or neuromyelitis optica spectrum disorder (NMOSD). Indeed, up to 10% will progress to develop clinically definite MS, and 4% will be diagnosed with NMOSD [1]. It is clear that ADEM occupies an important part of the CNS inflammatory demyelinating disease spectrum. Further study is needed to determine pathogenic and immunological characteristics of the disease.

#### Disclosures

Dr. Ceronie has nothing relevant to declare.

Dr. Cockerell has nothing relevant to declare.

#### Consent

Informed consent was obtained from the patient's next of kin.

#### Acknowledgements

Dr. Angharad Davis for her in work identifying the case.

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