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Case report

Adult onset acute disseminated encephalomyelitis: A case report ☆,☆☆

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ABSTRACT

Acute disseminated encephalomyelitis is an immune mediated demyelinating disorder of the central nervous system, it predominantly affects children in the age group between of 5-8 years. Is most widely thought to be a post-viral, post-vaccination autoimmune phenomenon.

We present a case of 40 years old Pakistani male arrived to ER agitated with decrease level of consciousness and delirium, develop tonic-clonic convulsion and it was relieved by DIAZEPAM. This is the first attack to the patient with no past medical history of similar presentation.

MRI showed supra and infratentorial white matter high T2/FLAIR signal abnormalities, involving supratentorial cortical and subcortical parito-occipital region, also to less extent at deep white matter predominantly right tempro-occipital region in asymmetric pattern. Involvement of juxta cortical and U fibers.

MRI raised the possibility of adult onset Acute disseminated encephalomyelitis, after exclusion of other causes of juxta cortical and U fibers involvement (based on imaging analysis with consideration of clinical presentation and available lab results).

Introduction

Acute disseminated encephalomyelitis (ADEM) is a monophasic inflammatory demyelinating disorder of the white matter that is often preceded by viral infection or recent vaccination [1]. ADEM is well known to be a post-infectious autoimmune encephalomyelitis [2,3]. This autoimmune phenomenon occurs in genetically susceptible individuals, resulting in a rapid inflammatory demyelination of the brain [2,3], or occurs secondary to an inflammatory response causing vascular congestion and increased permeability of central nervous system vasculature following exposure to a foreign antigen [4,5].

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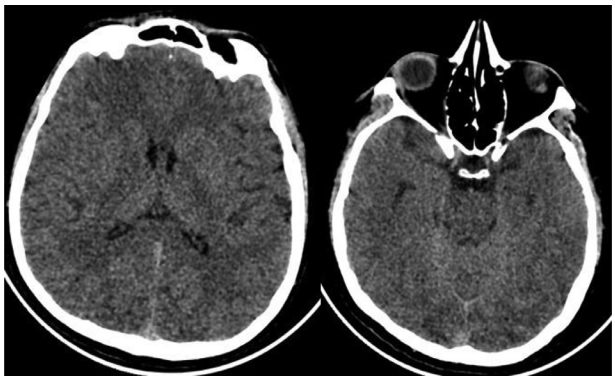

Fig. 1 – Initial non-contrast axial CT brain images (normal)

ADEM is a poorly understood neurological illness, commonly mistaken for multiple sclerosis and primary neurological infections [6].

Focal neurological deficits and encephalopathy are generally manifest 1 to 3 weeks after the primary illness with neurologic decline progressing rapidly over days to weeks. Reported incidence show that the peak of ADEM is mostly among childhood age group, although there are an increasing number of cases reported in adults and elderly [7].

Here we present a case of ADEM in an adult that recovered well after treatment with corticosteroids.

Case presentation

Forty years old Pakistani male arrived to ER agitated with decrease level of consciousness and delirium, develop tonic-clonic convulsion and it was relieved by DIAZEPAM. This is the first attack to the patient with no past medical history of similar presentation.

Upon examination the patient is afebrile, no neck rigidity, signs of meningeal irritation or rashes with normal CNS examination.

CT brain done first and it was unremarkable (Fig. 1).

Lab investigation show: Serology for human immunodeficiency virus, TB-PCR, hepatitis C antibody, Hepatitis B antigen, Brucella were negative. Blood culture was also negative.

Lumbar puncture was performed and CSF cytology show clear fluid with acellular smear and no AFB seen, Latex agglutination negative, culture show no growth. CSF analysis show elevated protein 108.4 mg/dl, no cells found, LDH 38U/L and Glucose 4.9 mmol/l.

MRI was done the same day and it shows supra and infratentorial white matter high T2/FLAIR signal abnormalities, involving supratentorial cortical and subcortical parito-occipital region, also to less extent at deep white matter predominantly right tempro-occipital region in asymmetric pattern. Involvement of juxta cortical and U fibers, particularly noted at superior frontal area bilaterally. Bilateral cerebellar hemisphere is also involved to less degree (Fig. 2, 3). Small focus of T2/FLAIR hyperintensity is also seen at right thalamus.

None of these lesions showed mass effect, restriction of diffusion, hemorrhagic changes or abnormal enhancement after IV gadolinium. No identified meningeal enhancement (Fig. 4).

The patient admitted to ICU as the patient needed ventilation for 5 days, after getting better he was transferred to medical ward, then he stayed 9 days more. After that he discharged from hospital when he recovered and get better. He was started empirically on IV Ceftriaxone, vancomycine, aciclovir and Dexamethasone. The initial clinical impression was of meningoencephalitis. However, the MRI raised the possibility of adult onset ADEM, after exclusion of other causes of juxta cortical and U fibers involvement (based on imaging analysis with consideration of clinical presentation and available lab results).

Discussion

ADEM is an immune mediated demyelinating disorder of the central nervous system, is most widely thought to be a post-viral, post-vaccination autoimmune phenomenon [1–3].It's an uncommon disorder, it predominantly affects children in the age group between of 5-8 years, with a incidence of 0.6 per 100,000/y [6]. In adults it is is considerably more extraordinary, usually presenting between the age of 30 and 50 with equal sex preponderance.

ADEM have been linked to number of pathogens. Most commonly viral causes include coxsackie, cytomegalovirus, esptein-barr, coronavirus, herpes simplex, measles, rubella, varicella zoster and hepatitis A. Recent literaturs showed that non-viral organisms can be linked to ADEM including Mycoplasma pneumoniae, Borrelia burgdorferi, Leptospira, beta haemolytic streptococcus and rickettsia [2]. The work-up for ADEM includes serology shows raised inflammatory markers and CSF studies show raised protein.

Given the link to previous infections, 'molecular mimicry' hypothesis [8] is the most widely accepted hypothesis for the pathogenesis of ADEM which stated that genetically suspectable population may acquire autoimmune phenomenoa from post-infectious auto-antibodies to myelin proteins [8–10]. An alternate theory is that, vascular congestion and increased permeability of central nervous system vasculature occurs secondary to an inflammatory response to a foreign antigen [4,5]. Then demyelination, gliosis and necrosis happen as a result of the inflammatory cascade involving peri-venous haemorrhage, oedema and infiltration of inflammatory cells [4,5]. Based on these theorized mechanisms, numerous studies have determined that anti-inflammatory is the mainstay of ADEM treatment [1].

Radiologically, ADEM presents as multifocal T2 hyperintense white matter lesions that may affect both hemispheres. Usually is present with symmetrical gray matter lesions on FLAIR, involving the thalamus and basal ganglia. Spinal cord involvement occurs in up to one third [11].

Differential diagnosis is wide and includes multiple sclerosis (MS), viral encephalitides, Posterior reversible encephalopathy syndrome (PRES), progressive multifocal leukoencephaly (PML), cerebral autosomal dominant arteriopathy (CADASIL), toxic encephalopathies, and adult onset leukodystrophies. MRI studies cannot differentiate alone; therefore, the clinical data along with the other investigation is important to make the diagnosis.

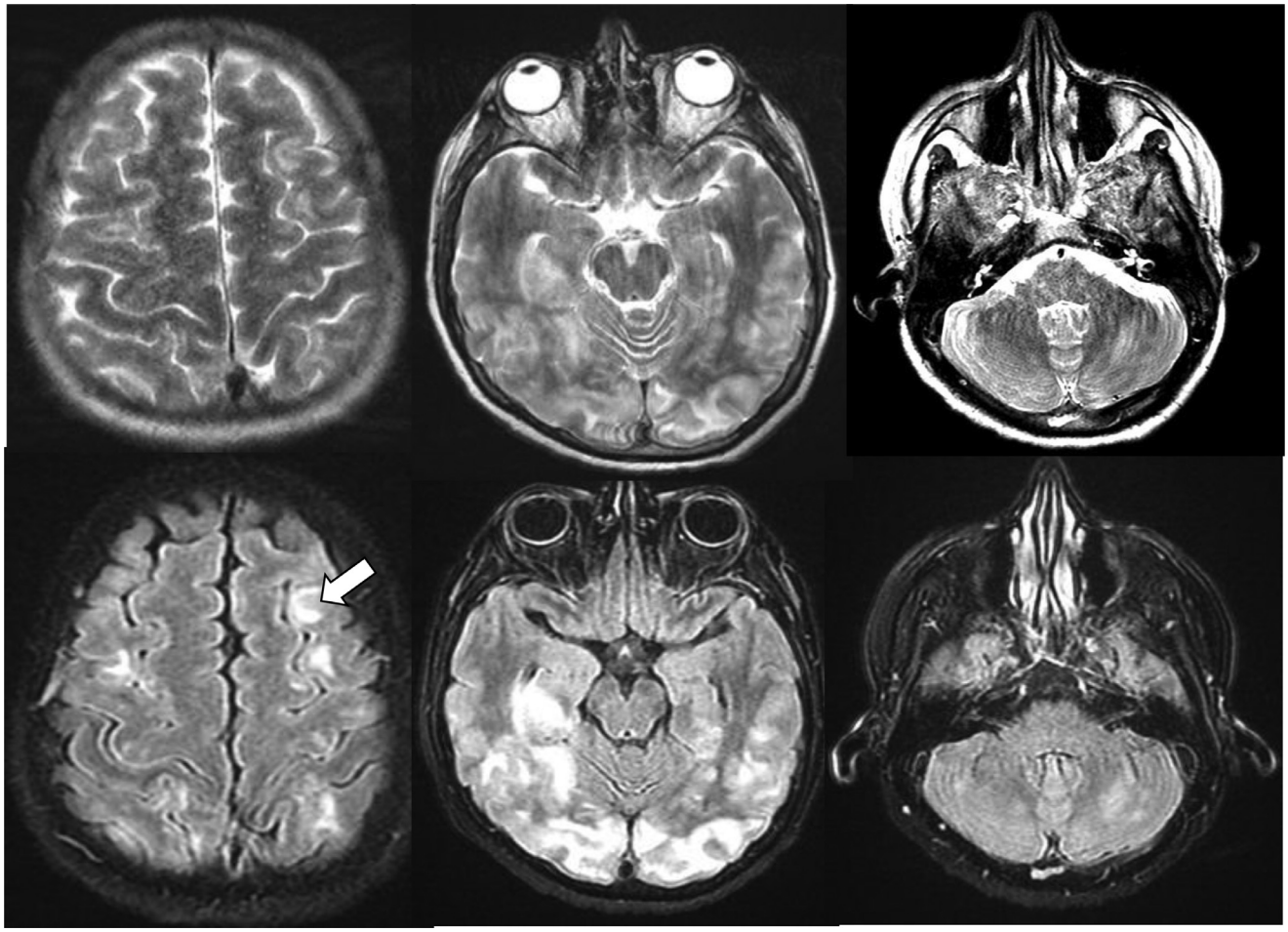

Fig. 2 – Axial magnetic resonance image T2 (first row) and FLAIR (second row) demonstrating supra and infratentorial white matter high T2/FLAIR signal abnormalities with involvement of juxta cortical and U fibers (White arrow). NB: motion artefact is noted.

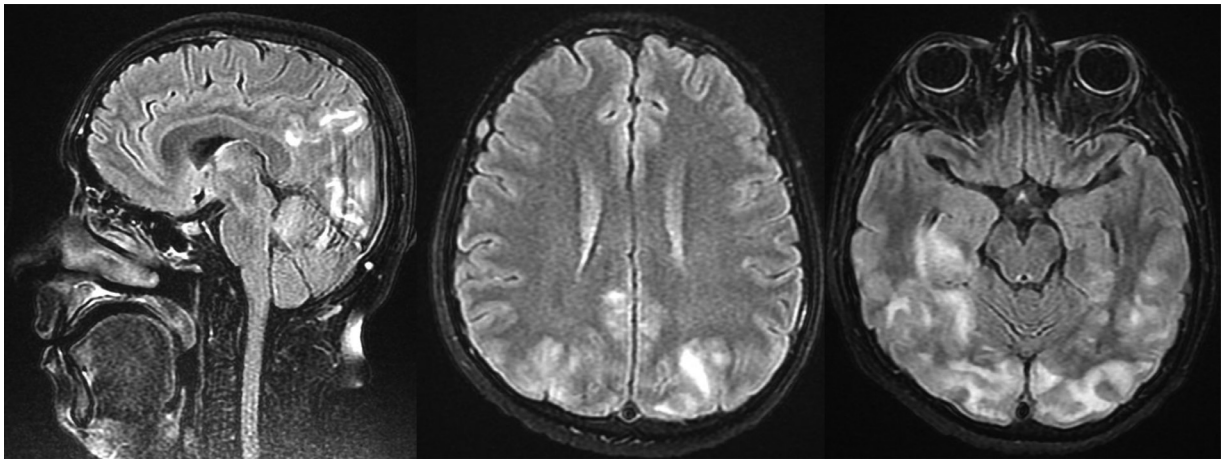

Fig. 3 – Sagittal and axial magnetic resonance FLAIR image demonstrating the lesions, mainly at prito-occipital and frontal region with no periventricular involvement.

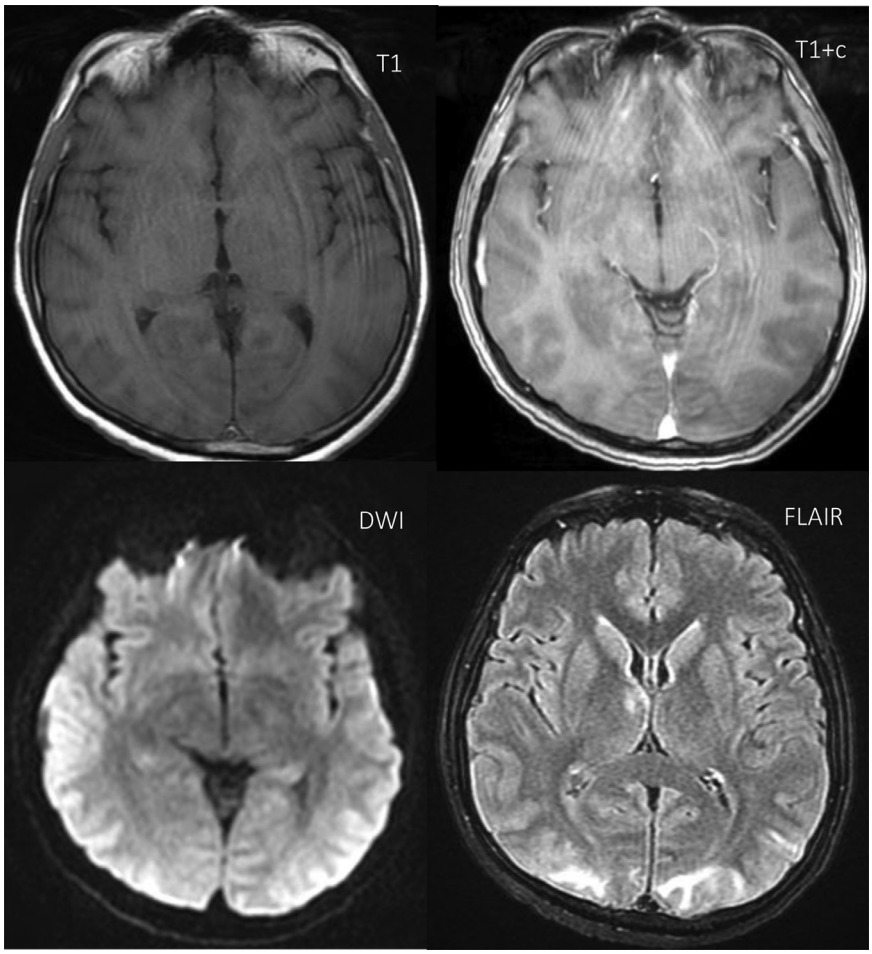

Fig. 4 – Axial magnetic resonance image demonstrating small hyperintensity seen at right thalamic without notable restriction and diffusion seen nor enhancement. No identified meningeal enhancement seen.

In our patient MS have been ruled out because the majority of lesions are in cortical and subcortical regions with mild involvement of deep periventricular white matter. PML strongly associated with immunosuppressed states, and primary PML developing in an immunocompetent patient is very rare, also there is no restriction of diffusion or abnormal enhancement in our case. PRESS have an association with severe hypertension, toxicity and chronic morbidity disease which our patient doesn't have, the distribution of lesions are primarily in parieto-occipital region which is common in PRESS, however the infratentorial involvement is not typical. CADASIL can have U fibers and juxta cortical involvement later in the disease, however there is no classic involvement of anterior temporal lobe (86%), external capsule (93%) or periventricular white matter, also our patient presentation does not fit a diagnosis of CADASIL. Toxic encephalopathies have been excluded because commonly it has symmetric involvement and favoring basal ganglia region rather than cortical /subcortical location like our case. And finally meningoencephalitis was ruled out because of lack of meningeal enhancement on MRI and negative results of WBC in lumbar puncture analysis.

Intravenous methylprednisolone is the first-line drug for 3-5 days are being used (Class IV) [7,12,13]. Methylprednisolone-treated patients had significantly better outcome with respect to disability status when compared with those treated with dexamethasone [14]. However, these regimens are not based on controlled randomized trials.

Along with the initial steroid treatment, empiric antimicrobial cover is recommended until infectious causes have been ruled out [1,2]. Vaccination should be avoided during the first 6 months following recovery [15].

In patients showing a poor response or failure of high dose glucocorticoids, IVIG therapy 5-7 days has been recommended [1]. Recent studies show that approximately half of patients with ADEM that fail a trail of high dose glucocorticoids will respond to IVIG [1,2]. The final line in management of is plasma exchange; however, the optimum regiment and benefit are still poorly defined in the literature.

Myelin oligodendrocyte glycoprotein (MOG) is a candidate target antigen abstract in demyelinating central nervous system diseases, including ADEM, neuromyelitis optica, and multiple sclerosis. MOG is primarily encountered in children and young adults [16]. It may give prognostic information regarding monophasic or recurrent course. During the first episode of ADEM it has been shown to be positive in high titers and rapidly decreasing to undetectable limits after recovery. If per-

sistent MOG antibodies detected this considered as a predicting factor for multiple sclerosis, optic neuritis relapses, and incomplete recovery of ADEM [17].

Prognosis is generally good among paediatric patients, complete recovery up to 80% and up to 20% suffering residual neurological deficit [18], 10% of children with an initial diagnosis of ADEM experience another ADEM attack, typically within the first 2-8 years after the initial attack [19]. On the other hand, adults 15% will experience a recurrence of the disease, termed multiphasic disseminated encephalomyelitis. 25% of patients will develop multiple sclerosis within 5 years of initial presentation of ADEM but the majority of individuals do not progress beyond 3 months [18].

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.

Conclusion

ADEM is a mono-phasic inflammatory demyelinating disorder of the white matter that is often preceded by viral infection or recent vaccination. It is a disease of childrens; the mean age is 5-8 year. Although ADEM is rare to occur in adults group, it should be in the differential diagnosis as it is commonly mistaken for multiple sclerosis and primary neurological infections.

MOG is a candidate target antigen abstract in demyelinating central nervous system diseases, including ADEM, neuromyelitis optica, and multiple sclerosis.

MOG antibodies should be searched in ADEM cases. During the first episode of ADEM it has been shown to be positive in high titers and rapidly decreasing to undetectable limits after recovery.

Patient consent

Informed consent was obtained from the patient for their anonymized information to be published in this article. This report does not contain any personal information that could lead to the identification of patient. The authors declared no potential Conflict of interest with respect to the research, authorship, and/or publication of this article.

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