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CASE REPORT

An Unusual case of adult-onset Acute Disseminated Encephalomyelitis

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A 57 year old gentleman presented to our emergency department with a ten day history of progressive loss of balance, left-sided weakness and gait disturbance. CT brain showed bilateral subcortical hypodensities in the parietal lobes with right sided cortical involvement. Subsequent MRI of the neuro-axis showed symmetrical high FLAIR signal in the parietal lobes bilaterally, suggestive of Acute Disseminated EncephaloMyelitis (ADEM), while excluding cord lesions. CSF and serum analysis excluded alternative diagnoses. He was treated with high dose IV methylprednisolone followed by an oral steroid taper, with rapid clinical response aided by physical and occupational therapy.

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CASE PRESENTATION

A 57-year-old gentleman presented to our emergency department with a ten-day history of evolving neurological symptoms. He initially noted numbness of the fourth and fifth fingers of his left hand, but gradually developed worsening left-sided weakness in both his upper and lower limb, together with gait imbalance. There was no history of preceding injury or systemic illness. No recent history of vaccination. His past medical history was notable for hypertension, gastro-oesophageal reflux and benign prostatic hyperplasia. He suffered from chronic osteomyelitis in the right tibia originating from an injury in 1987 that had been managed with multiple courses of antibiotics and hyperbaric therapy over the years. He was taking amlodipine 10mg, omeprazole 20mg and tamsulosin 400mg daily. No known drug allergies. He worked as a carer, did not smoke and drank alcohol moderately. There was no family history of neurological or autoimmune disorders.

On examination, he was apyrexial, parameters were normal, HGT 9.2 mmol/L Systemic examination was normal. ECG and chest X-ray were normal. Patient was alert and orientated to time, place and person. Visual acuity (corrected) and fields were normal. Fundoscopy was normal as was the rest of his cranial nerve assessment. Left sided pronator drift was present. Power was uniformly decreased across all left upper limb muscles and the left hip flexors (MRC 4/5). Tone was increased in his left arm and leg and sustained clonus was present at both ankles (>10

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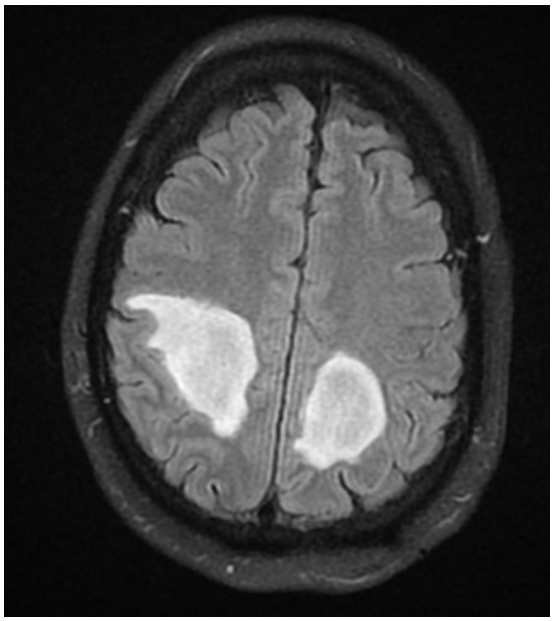

Figure 1 MRI images in T2 Flair sequence taken prior to treatment showing a fairly symmetrical open-ring enhancement pattern in both parietal lobes

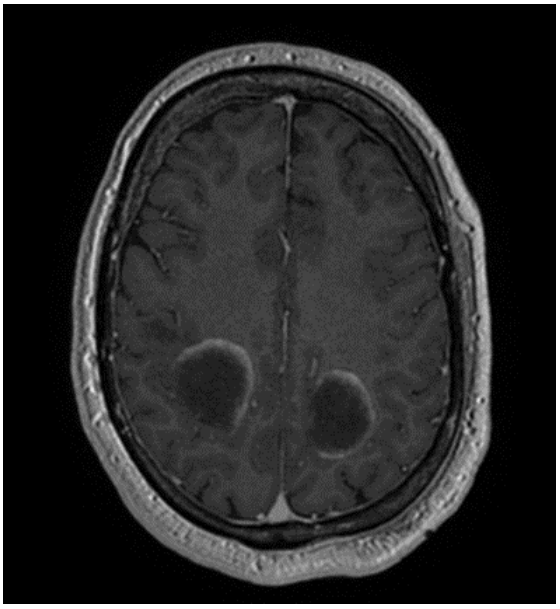

Figure 2 MRI images in T1 post contrast taken prior to treament

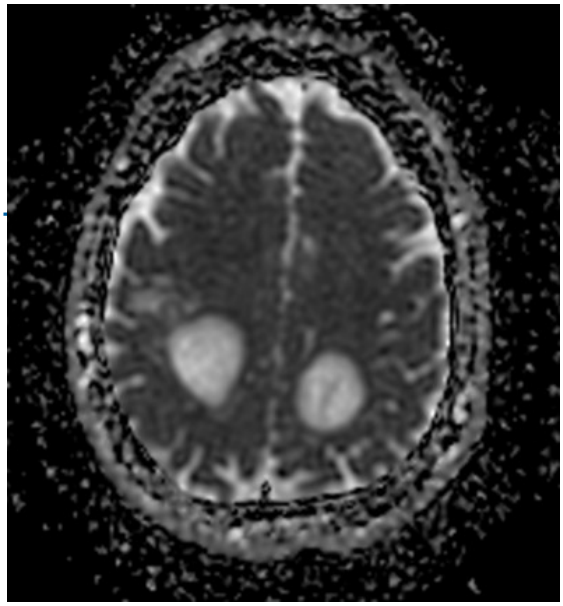

Figure 3 MRI images in DWI showing restricted diffusivity at the edges of the lesions prior to treatment

beats). There was no sensory neglect on examination. Sensory testing revealed reduced light touch perception in the left fourth and fifth fingers. He struggled significantly to stand from a seated position, and when helped up to walk, he had a broad-based gait, his usual gait due to the chronic osteomyelitis.

CT of the neck excluded disc herniation or canal stenosis. CT of the brain identified bilateral subcortical hypodensities in the parietal lobes with cortical involvement on the right. MRI brain showed symmetrical high FLAIR signal in the parietal lobes bilaterally with corresponding subcortical T1 hypointense foci. There was a separate similar lesion posterior to the right sylvian fissure in the right parietal lobe. All three lesions demonstrate an open-ring enhancing pattern and restricted diffusivity at the edges (Figures 1 - 3). Changes were in keeping with actively demyelinating lesions. The symmetrical appearance of the identified changes was highly suggestive of acute disseminated encephalomyelitis (ADEM). A lumbar puncture for CSF analysis and a panel of blood tests were taken to exclude possible differential diagnoses (See Tables 1-5).

Table 1 Cerebrospinal fluid analysis results

Cerebrospinal fluid analysis	
Opening pressure (cm H_2O)	23.5
Colour	Colourless
Turbidity	Clear
Supernatant	Clear
Coaglum	Absent
Protein (mg/L)	536
Globulins	Negative
Glucose (mmol/L)	6.12
Chloride (mmol/L)	121
Erythrocytes ($x10^{12}$/L)	0.000
Nucleated cell count ($x10^{12}$/L)	0.001
Polymorphonuclears ($x10^{12}$/L)	0.000
Lymphocytes/ Mononuclear ($x10^{9}$/L)	0.001
PCR	Negative for enterovirus, herpes simplex, mumps, parechovirus, varicella zoster

**CSF oligoclonal bands was sent but unfortunately sample leaked in transit. It was decided not to repeat lumbar puncture in view of rapid patient improvement.*

Table 2 Serology results

Serology	
White blood cells (x10⁹/L)	9.01
Neutrophils (x10⁹/L)	6.85
Lymphocytes (x10⁹/L)	1.28
Monocytes (x10⁹/L)	0.61
Eosinophils (x10⁹/L)	0.01
Basophils (x10⁹/L)	0.07
Haemoglobin (g/dL)	15.7
Mean cell volume (fL)	86.6
Mean cell Hb (pg)	29.2
Mean cell Hb concentration (g/dL)	33.7
Platelets (x10⁹/L)	302

Table 3 Biochemistry results

Biochemistry	
Urea (mmol/L)	7.0
Creatinine (umol/L)	105
Potassium (mmol/L)	4.10
Sodium (mmol/L)	138
C-reactive protein (mg/L)	15

Table 4 Serology results

Immunology	
EBV IgG	Positive
EBV IgM	Negative
CMV IgG	Negative
CMV IgM	Negative
Syphilis	Negative
ANCA	Negative (<1/10)
ANA	Negative (<1/100)
Complement 3	2090
Complement 4	375
Aquaporin 4 antibodies	<1:10
Myelin oligodendrocytes glycoprotein antibodies	<1:10
COVID-19 PCR	Not Detected

Table 5 Urinalysis results

Urinalysis	
White blood cells	Negative
Nitrites	Negative
Proteins	Negative
Erythrocytes (uL)	25

He was started on intravenous methylprednisolone 1000mg daily for three days followed by an oral steroid taper (prednisolone 50mg daily for 7 days tailing down 10mg each week). Physiotherapists and occupational therapists were involved for rehabilitation. Physiotherapy focused on postural re-education and stepping. Occupation therapist helped with proprioception, motor coordination and stereognosis. He experienced a rapid improvement in his symptoms and signs such that he was discharged after 10 days.

By this time, he had residual left arm drift and left sided incoordination on finger-to-nose testing due to reduced proprioception, tone was normal, no sensory neglect, and power on the left side was normal. He continued to receive physiotherapy and occupational therapy input on an outpatient basis. Follow up MRI brain after 3 months showed that the previously described T2 hyperintense lesions in the parietal lobes were much less conspicuous and had decreased slightly in size in the interim (Figures 4 - 6). When last reviewed after 3 months, his neurological examination was intact, and he had restarted working and driving.

DISCUSSION

Acute disseminated encephalomyelitis is a monophasic demyelinating condition caused by an autoimmune process affecting the central nervous system. This entity is seen more frequently in children rather than adults, mostly preceded by an infection or vaccination. Patients most often present with acutely multifocal neurological deficits progressing rapidly with encephalopathy.

Classically ADEM, due to the acute and rapid progression of motor deficits with encephalopathy, requires admission to hospital. Motor deficits can vary from single limb involvement to quadriparesis.[1,4] Sensory deficits as well oculomotor deficits and dysarthria may be present if brainstem is involved..[1] Other symptoms and signs may include

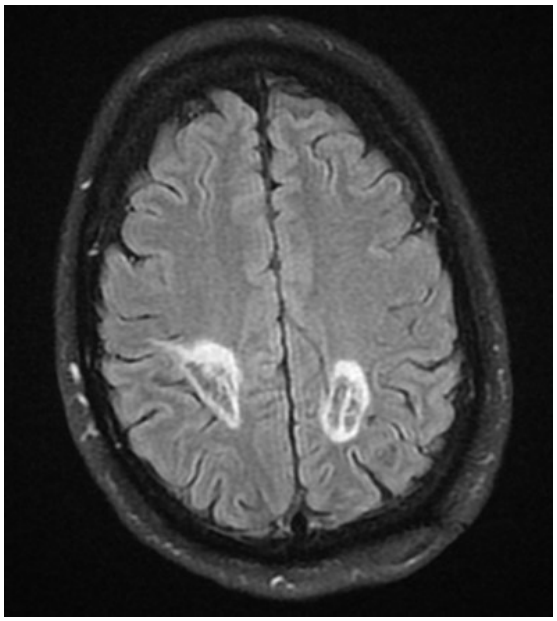

Figure 4 MRI images in T2 Flair sequence taken three months post treatment showing a decrease in size in both parietal lobe lesions

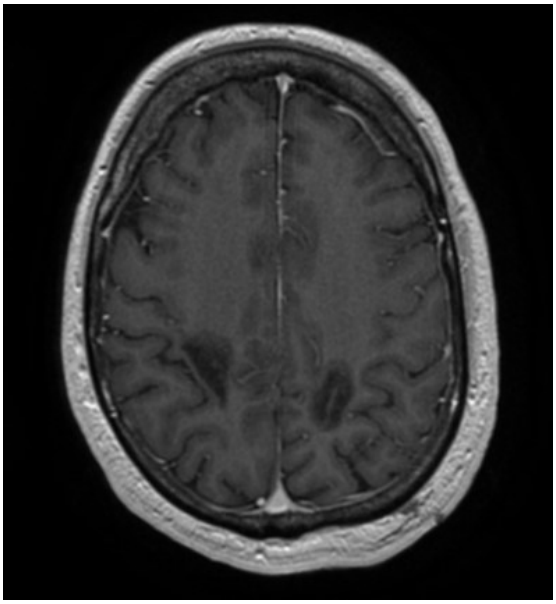

Figure 5 MRI images in T1 post contrast sequence taken three months post treatment

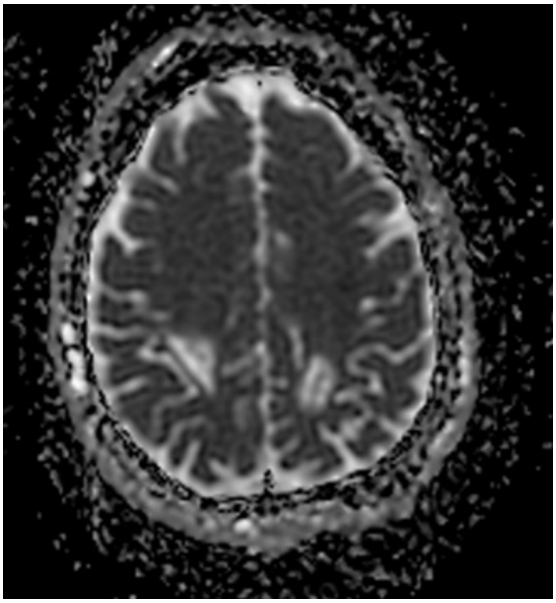

Figure 6 MRI images in DWI taken three months post treatment

ataxia, headache, malaise, meningism, aphasia, optic neuritis, nystagmus and extrapyramidal symptoms.[1,2,4]

Patients with suggestive clinical history and examination need investigation to support the diagnosis of ADEM and eliminate other differential diagnosis (Tables 6,7). MRI of the brain usually shows asymmetric poorly marginated lesions in both hemispheres.[5] Most patients have deep and subcortical white matter involved by demyelination. These usually appear as hyperintense lesions on fluid attenuated inversion recovery (FLAIR) and T2-weighted sequences. Infratentorial lesions involvement may be present as well.[1,4] Lumbar puncture is done for CSF testing. This is done to rule out inflammation and infections. Changes seen in ADEM are non-specific for the condition. These include lymphocytic pleocytosis with a CSF white blood cells of less than 100 cells/mL and mildly elevated CSF protein.

Mainstay treatment for ADEM is immunosuppression. Initial therapy involves high dose glucocorticoids.[6] Methylprednisolone intravenously 1000mg daily for three to five days can be given then switched to oral formulation and tapered over a few weeks.

Table 6 Differential Diagnosis to Acute Disseminated Encephalomyelitis in adults

Differential Diagnosis
Multiple Sclerosis
Chronic autoimmune demyelinating disease
Recurrent attacks separated in time and space
MOG antibody associated disorder
Central nervous system demyelination
IgG serum antibodies directed against MOG
Neuromyelitis optica spectrum disorder
Severe immune mediated demyelination and axonal damage
Positive for aquaporin 4 antibody
Infectious meningoencephalitis
Fever, headaches, meningism
Sarcoidosis
Autoimmune disorder affecting multiple organs
Cranial mononeuropathy, focal or multifocal encephalopathy, myelopathy, myopathy

Table 7 Differences between Acute Disseminated Encephalomyelitis and Multiple Sclerosis

	ADEM	Multiple Sclerosis
Clinical picture	Widespread CNS dysfunction fever headache	Focal signs Motor deficit cranial nerve palsies optic neuritis
Precedent viral infection	Common	No association
Course	Acute, non-progressive	Chronic Mostly relapsing & remitting
MRI	Bilateral lesion Poorly marginated Uniform appearance Diffuse	Predominantly unilateral Well marginated Variable appearance Periventricular white matter involvment
Follow up MRI	Complete/partial resolution of lesions	New lesions
Sequelae	Uncommon	Common

When there is inadequate response to glucocorticoid therapy, intravenous immunoglobulins (IVIg) or plasma exchange may be given to achieve the desired effect. IVIg are usually started after assessing the response of the disease with five-day glucocorticoid therapy. If there is poor response, one might switch to IVIg therapy.[7] Studies have shown that patients with poor response to glucocorticoids fared well with IVIg therapy with regards to clinical improvement with respect to peripheral nervous system involvement.[8] Plasma exchange has been used but data is still limited.

When comparing the clinical course of ADEM in children with that in adults, although the disease is more frequent in children, literature suggests that the clinical course in the adult population is more severe. Adults required admission to intensive care units with longer hospitalization stays. Furthermore, outcome also was worse, fewer adults achieve complete motor recovery and the condition is more frequently fatal.[5]

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