Acute disseminated encephalomyelitis: recognition in the hands of general paediatricians

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Acute disseminated encephalomyelitis will often present to the general paediatrician as an acute polysymptomatic encephalopathy, and initially the diagnosis may not be clear. A brain MRI scan is essential in establishing the diagnosis and so enabling appropriate advice and treatment to be given. Multicentre clinical audit of outcome and controlled therapeutic trials are needed to secure an evidence base for current practice.

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ADEM has also been reported following immunisation for measles, rubella, meningitis A and C, influenza, Japanese B encephalitis, smallpox, BCG, and rabies. Consideration of the number of immunisations given, ADEM following immunisation is rare. Usually no infectious agent is identified.

INVESTIGATIONS

There is evidence of inflammation in children with ADEM. Elevation of the white cell count, particularly the lymphocyte count, is common. The erythrocyte sedimentation rate and C reactive protein may also be raised. CSF examination may show a lymphocytosis. CSF protein concentrations are frequently raised, and although most are in the range 0.4–0.6 g/l,¹ seven can be as high as 2.7 g/l. Frequently the CSF examination is normal. Oligoclonal bands in the CSF, indicating intrathecal immunoglobulin synthesis, can also be found, but less commonly than in established multiple sclerosis (MS). Serological testing for Epstein-Barr virus, mycoplasma, herpes, varicella, influenza A and B, mumps, cytomegalovirus, and rubella is rarely positive.

The electroencephalogram (EEG) may show an excess of background slow wave activity consistent with the encephalopathy or encephalitic picture. Rarely the EEG may show focal epileptic activity. Visual evoked potentials may show attenuation with degradation and delay in waveform, particularly if there is clinical evidence of bilateral optic neuritis.

NEUROIMAGING

A cranial CT scan of the brain may be normal, so is often not helpful in establishing a diagnosis. However, MRI of the brain may show early subtle features of the disseminated CNS demyelination associated with ADEM (fig 1). MRI T2 weighted, and FLAIR images show the abnormalities more readily than T1 weighted images. These changes are usually distinguishable from MS.¹⁹ Involvement of the deep and subcortical white matter is almost universal, whereas grey matter lesions are seen less often, and only in addition to the more characteristic white matter lesions. Involvement of the thalami and basal ganglia is a typical finding in ADEM, but unusual in MS and may be a useful marker in its differentiation.¹³ In ADEM supratentorial lesions tend to be asymmetrical, whereas thalamic and basal ganglia lesions are often symmetrical. Spinal cord lesions are relatively common too. Additionally the lesions may be extensively distributed.

Follow up MRI scans will show evidence of partial or complete resolution of the lesions and may be useful in differentiating monophasic from multiphasic disease. New lesions or relapses, especially those that occur after six months, may indicate the development of MS⁰ or relapsing ADEM, which may be considered a special case of MS (see later).

Other techniques not widely available, but helpful in supporting the diagnosis of ADEM, are gadolinium diethylenetriamine penta-acetic acid (Gd-DTPA) enhancement of the lesions on MRI, and areas of increased activity on single photon emission computed tomography.²⁰

TREATMENT

As most children present with meningism, fever, and an acute encephalopathy, with evidence of inflammation in blood and CSF, they should be covered initially with cefotaxime or other appropriate antibiotic and acyclovir until a diagnosis can be established. Once the diagnosis of ADEM is established, treatment usually commences with 3–5 days of intravenous methylprednisolone (20–30 mg/kg/day), with or without a following course of oral prednisolone, commencing at 2 mg/kg/day and tapering over 4–6 weeks, depending on resolution of clinical signs. In children who have early relapses or in whom there has been a delay in diagnosis, we have used a tapering course of intravenous methylprednisolone over two weeks after the initial course; for example, single dose intravenous methylprednisolone 10 mg/kg, one week after the last dose, followed by another single dose of 5 mg/kg a week later.

Other treatment options include dexamethasone, intravenous immunoglobulins,²⁰ and plasmapheresis,²⁰ but little evidence exists for their effectiveness.

ADEM, MULTIPHASIC ADEM, RELAPSING ADEM, AND MULTIPLE SCLEROSIS

With the absence of a biological marker the distinction between ADEM and MS cannot be made with absolute certainty at the time of first presentation. New lesions or relapses, especially those that occur after six months, may indicate the development of MS.¹⁵ If the relapse occurs in the months following the initial ADEM, for example during or shortly after steroid withdrawal, the diagnosis of multiphasic acute disseminated encephalomyelitis should be considered. The demyelination can be considered to belong to one multiphasic episode. MS has not yet developed and may or may not develop in the future, with the advent of further episodes of CNS demyelination disseminated in time and space.¹⁷ ¹⁸ ¹⁹ ²⁰ ²¹

A minority will relapse more than six months later. By operational definition this is a type of MS, fulfilling the criteria of Poser and colleagues²⁴ or McDonald and colleagues,²⁵ but may be better classified as relapsing acute disseminated encephalomyelitis, a special type of MS. Ancodatal evidence suggests that if relapses are ADEM in character—polysymptomatic clinically and multifocal on MRI—the prognosis may be better than relapsing remitting MS in general.

In trying to differentiate between ADEM and MS, several pointers may be helpful. ADEM is often associated with a prodromal viral illness. At presentation there may be fever and meningism. These would be unusual in MS. ADEM is typically a monophasic illness producing widespread CNS disturbance, with coma or drowsiness. Conversely MS usually presents as a monosymptomatic syndrome such as optic neuritis or a
subacute myelopathy, and typically develops a relapsing remitting course. Ataxia is common in ADEM but is rarely a presenting feature in childhood MS.

On reviewing the MRI, ADEM is often associated with a higher lesion load, with larger bilateral but asymmetrical white matter lesions. Plaques in MS are usually smaller and lie in the deep white matter. In ADEM there is thalamic involvement in up to 40% of cases, while this is rare in MS. The lesions in ADEM are usually of the same age, whereas in MS lesions of different ages (spread in time and space) will be seen. However, complete differentiation between the two diseases is impossible on a single MRI examination. A few typical ADEM cases will later evolve to typical MS with separate episodes of monosymptomatic demyelination over time. Some will relapse with further polysymptomatic ADEM-like demyelination (relapsing acute disseminated encephalomyelitis). In Dale’s series, five of 40 cases presenting with ADEM later had a diagnosis of MS, after a variable follow up of a mean of five years; 10–15% of cases of ADEM later had a diagnosis of MS, after a variable follow up with a mean of five years; 10–15% of cases of ADEM are usually of the same age, whereas in MS lesions of different ages (spread in time and space) will be seen. However, complete differentiation between the two diseases is impossible on a single MRI examination.

A minority of children are left with a neurological impairment that can range from mild to severe. This can include motor disability, visual impairment, cognitive impairment, behavioural impairment, and epilepsy. Any neurological impairment will need to be addressed, and appropriate coordinated multiagency rehabilitation organised.

PROGNOSIS

Most children with ADEM present with an acute aggressive encephalopathy with multifocal neurological deficits. Most make excellent progress over the following days, weeks, or months with no subsequent neurological impairment. Spontaneous remission can occur, although it seems likely that the current practice of active treatment with steroids is usually beneficial. A minority of children are left with a neurological impairment which can range from mild to severe. This can include motor disability, visual impairment, cognitive impairment, behavioural impairment, and epilepsy. Any neurological impairment will need to be addressed, and appropriate coordinated multiagency rehabilitation organised.

REFERENCES