CASE REPORT

Acute disseminated encephalomyelitis (ADEM) following a H3N3 parainfluenza virus infection in a pregnant asthmatic woman with respiratory failure

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SUMMARY

This case report relates to a 31-year-old pregnant woman, asthmatic, admitted to the intensive care unit with respiratory failure, secondary to a viral community-acquired pneumonia. A type 3 (H3N3) parainfluenza virus RNA was isolated in her throat swab. The patient developed neurological symptoms (behavioural changes, irritability, agitation and impaired consciousness) while being weaned off sedation and ventilatory support. Cerebrospinal fluid was clear with an opening pressure of 26 cm H₂O. Brain MRI showed features compatible with acute disseminated encephalomyelitis. Immune screen and EEG were normal. She was treated with intravenous methylprednisolone followed by oral prednisolone. The patient made an almost full neurological recovery within 4 weeks after starting on steroids. The patient delivered a healthy baby at 38 weeks gestation. This case highlights the importance to keep in mind rare conditions that need early recognition and prompt treatment. Brain MRI is the key to early diagnosis and treatment.

BACKGROUND

To highlight the clinical significance of the temporal relationship between an infection incident and the onset of leucoencephalopathic neurological symptoms, as well as the role of early recognition in changing the outcome of the disease.

CASE PRESENTATION

A twenty-six weeks pregnant woman, presented to accident and emergency department with worsening shortness of breath and a productive cough. A dry cough, sore throat, wheezy chest and shortness of breath started 3 days prior to hospital admission. No neurological symptoms were evident at that time. The patient's chest X-ray showed a mild haziness on the right middle lobe. Her clinical condition deteriorated rapidly in-hospital (within 24 h), requiring more oxygen supply associated with poorer gaseous exchange and tiredness. She was sedated, her trachea intubated and ventilatory support started. Antibiotics were started for a bacterial superinfection. By day 5, the patient's clinical condition improved and weaning from sedation and ventilatory support was started. In the following 48 h, the patient failed to fully wake up, making inappropriate movements which required sedation to be restarted. Nevertheless, infection markers and oxygenation were improving, it was also possible to wean her ventilatory support down

to a low pressure support. A percutaneous tracheostomy was sited to allow a better neurological assessment. Despite clear resolution of pneumonia and off sedation in the next few days, the patient was restless, non-appropriate, irritable and with fluctuating levels of consciousness. On examination there was no neck stiffness. To rule out postinfection neurological involvement a lumbar puncture and a brain MRI were conducted. Cerebrospinal fluid (CSF) examination was normal except a high opening pressure of 26 cm H₂O. MRI brain images were compatible with acute disseminated encephalomyelitis (ADEM; see figures 1A, B and 2A, B). She was treated with high-dose intravenous methylprednisolone followed by oral prednisolone and the patient made an almost full neurological recovery.

Medical history: Asthma, Arnold-Chiari malformation, panic attacks, pulmonary embolism (postdelivery).

Obstetric history: Para4 Gesta5.

Social history: non-smoker full-time mother.

Family history: nil significance.

Medications: nil regular.

INVESTIGATIONS

Brain MRI: extensive white matter signals abnormality in both the supratentorial and infratentorial brain, sparing the cortex and subcortical white matter and involving deep and callosal white matter (see figures 1A, B and 2A, B).

CSF: Clear with opening pressure of 26 cm H₂O, with negative bacterial or viral cultures.

Negative PCR for herpes simplex virus (HSV) 1&2, cytomegalovirus (CMV), varicella virus, human herpes virus type 6, Epstein-Barr virus (EBV), enterovirus and parainfluenza.

Protein concentration and cell count within normal range. Negative oligoclonal bands.

Throat Swab: Type 3 H3N3 parainfluenza virus.

Blood cultures: Negative.

Sputum: No growth.

Immune screen: Negative for antinuclear antibody, antineutrophil cytoplasmic antibody, rheumatoid factor (RAF), anti-Sm antibody, venereal disease research laboratory (VDRL), Lyme disease IgG, ACE serum, tuberculosis (TB) and anticardiolipin antibodies.

DIFFERENTIAL DIAGNOSIS

ADEM, with its protean clinical manifestations and lack of specific biological markers, raises serious problems of differential diagnosis outlined below:

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Figure 1 (A) Axial diffusion-weighted image of brain MRI (B1000), showing areas of restricted diffusion in the white matter and corpus callosum. (B) Axial diffusion-weighted image of brain MRI (apparent diffusion coefficient map), showing areas of restricted diffusion in the white matter and corpus callosum.

1. *Microbial infections*: bacterial meningitis, Lyme meningitis, syphilitic meningitis, tuberculous or cryptococcal meningitis; as well as meningoencephalitis caused by HSV, CMV, EBV, HIV enterovirus or influenza viruses H1N1.^{1 2}
2. *Vasculitis*: Should be considered such as primary central nervous system (CNS) angiitis or systemic lupus erythematosus.
3. *Other inflammatory demyelinating diseases*: Where multiple sclerosis (MS) is perhaps the condition that most closely resembles ADEM, particularly the multiphasic ADEM variants.

MRI is very reliable to differentiate between the lesions of ADEM and MS. There are differences in the lesions sites; ADEM lesions tend to be more in the deeper white matter than MS (see [figures 1A, B, and 3A, B](#)). Most of the lesions in ADEM have often poorly defined margins whereas MS lesions have well-defined 'plaque-like' margins (see [figure 2A, B](#)).

Figure 2 (A) Coronal fluid-attenuated inversion recovery image of brain MRI, showing diffusely increased signal in the white matter of both cerebral hemispheres (A) and of both cerebellar hemispheres (B).

TREATMENT

Short course (5 days) of high-dose intravenous methylprednisolone followed by a tapering dose of oral prednisolone.

OUTCOME AND FOLLOW-UP

The patient was discharged to the ward 19 days after intensive care unit (ICU) admission. She stayed in the hospital for an additional 2 weeks undergoing neurorehabilitation therapy for an acquired ICU-related myopathy before been discharged home. She had a follow-up ultrasonography scan at 32 weeks gestation, which showed normal fetal growth and movements. Fetal MRI was performed before delivery and failed to show any abnormalities. The patient had an uncomplicated spontaneous vaginal delivery at 38 weeks gestation. A healthy baby boy was born, with normal Apgar scores and his weight was 3.100 kg. One year after the event, the patient has fully recovered from her ICU-acquired myopathy. No sensory or motor deficits were present. She is totally independent in her daily life activities.

Figure 3 Axial T2 weighted image of brain MRI, showing diffuse bilateral confluent changes in the white matter at the level of basal ganglia (A) and at the level of corona radiata (B).

Nevertheless she notices that her short-term memory is affected since this acute illness.³

DISCUSSION

In recent years, a number of observational studies with relatively large numbers of patients and follow-up time have been conducted.^{4–6} Although the majority focused on children, one study enrolled adults.⁷ Regarding our particular case report, only a few cases of ADEM secondary to parainfluenza virus have been reported and mainly in children.

ADEM is a rare disorder which usually occurs following viral illness but may occur after bacterial or parasitic infection, immunisation,⁸ or administration of drugs and serum. It is an immune-mediated disorder producing multifocal inflammation and subsequent demyelination lesions within the CNS. The incidence rate is about 8 in 1 000 000. It can occur at any age but more common in children and adolescents with an average age of 5–7 years.⁹ Patients present with non-specific symptoms and with neurological symptoms such as confusion, altered level of consciousness or irritability.

Diagnosis is made by exclusion as neither the clinical nor paraclinical tests allow a specific and unequivocal diagnosis of ADEM.¹⁰ Diagnosis should be readily considered if there is a close temporal relationship between an infection or vaccination and the onset of neurological symptoms—such as headaches, confusion, altered level of consciousness or irritability.¹⁰ In this case, the persistence of irritability, fluctuation of levels of consciousness and inappropriate behaviour despite the resolution of infection and lack of sedation made us suspect a postinfectious neurological impairment. Regarding additional tests, MRI is the most widely applied diagnostic tool. MRI can be normal in the early course of disease progression. It is important to keep in mind that taking a ventilated patient to MRI is not without risk, therefore it is essential to rule out clinically if the abnormal behaviour changes, irritability and impaired level of consciousness are not due to hypoxia, acidosis, delirium or withdrawal syndromes and drugs.

A lumbar puncture is typically performed as patients present initially with non-specific symptoms such as headaches, fever and lethargy to exclude viral, bacterial or parasitic meningoencephalitis. CSF is analysed to help identify the pathogen and make the diagnosis.

Regarding differential diagnosis, three main groups are considered: infection-related meningoencephalitis, inflammatory demyelinating diseases and vasculitis. Infectious meningoencephalitis of viral, bacterial and parasitic origin was investigated in our patient. CSF cultures were negative for bacteria or virus. Herpetic meningoencephalitis was excluded as CSF HSV 1&2 PCR was negative as well as there was clinical improvement with a high dose of corticosteroids and no antiviral treatment given. The rest of the septic screen including Lyme disease antibodies, VDRL and TB as well as blood cultures were all negative. A type 3 H3N3 parainfluenza virus was cultured from a throat swab, which together with the MRI brain findings (see figures 1A, B and 2A, B), the close relationship between the onset of infection and the neurological symptoms and the good response to the IV corticosteroids made the diagnosis ADEM secondary to this virus. With regard to inflammatory demyelinating diseases, where MS is perhaps the condition that most closely resembles ADEM, particularly the multiphasic ADEM variants,¹⁰ MRI is reliable to differentiate between the lesions of ADEM and MS. Most of the lesions in ADEM have often poorly defined margins whereas MS lesions have well-defined ‘plaque-like’ margins.¹¹ There are also differences in the lesion’s sites; ADEM lesions tend to be in the deeper white matter, as it was present in our patient’s brain MRI (see figures 1A, B and 2A, B). Our patient’s brain MRI findings were very suggestive of ADEM, also the lack of oligoclonal banding in the CSF made the diagnosis of MS unlikely. Vasculitis, mainly primary CNS angiitis and systemic lupus erythematosus were investigated. These diagnoses were found to be unlikely after the immune screen came back negative.

The first-line treatment is high-dose methylprednisolone (20–30 mg/kg/day maximum 1 g/day) for 3–5 days followed by

tapered oral prednisolone for 4–6 weeks. Plasma exchange is recommended if patient shows poor response or if high-dose corticosteroids use is contraindicated, then intravenous immunoglobulin at a dosage of 2 g/kg is a therapeutic option. Most severe cases may require plasmapheresis. Patients with ADEM with intracranial hypertension may require decompressive craniotomy.¹² Mortality from ADEM is around 5%. Up to 50–75% do recover fully, 70–90% recover with residual neurological abnormalities. The average time to recover is approximately up to 6 months.

Learning points

- ▶ To keep in mind the temporal relationship between infection incident and the onset of leucoencephalopathic neurological symptoms to suggest the clinical diagnosis of acute disseminated encephalomyelitis.
- ▶ Rare disease can be easily missed if not investigated properly.
- ▶ Brain MRI is the gold standard investigation.
- ▶ Timely treatment can avoid complications.

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Competing interests None.

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