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CASE REPORT

# Respiratory failure, rapidly progressive paralysis and an abnormal computed chest radiograph: acute disseminated encephalomyelitis

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**We report on rapidly progressive respiratory failure in a 62-year-old female patient, who was initially diagnosed with pneumonia and metastatic brain abscesses. On further evaluation, however, ventilatory pump failure caused by acute disseminated encephalomyelitis (ADEM) was diagnosed. Impaired coughing and pre-existing chronic obstructive pulmonary disease had precipitated atelectasis. Her clinical course was protracted but eventually favourable after methylprednisolone was administered. We discuss this unusual case, and the use and limitations of the alveolar gas equation to differentiate ventilatory pump failure and respiratory failure due to pulmonary dysfunction. Finally we briefly review the diagnostic criteria, differential diagnosis and management of ADEM in adults.**

Respiratory failure may result either from ventilatory pump failure due to neuro-muscular impairment or thoracic cage abnormalities or from lung failure, usually as the result of severe ventilation-perfusion mismatch, or severely reduced diffusion capacity for oxygen. The usual processes of lung failure include pneumonia, acute lung injury, congestive cardiac failure, and diffuse alveolar haemorrhage, but occasionally local airway obstruction caused by tumours or foreign bodies may also result in respiratory failure. The alveolar gas equation may help in differentiating extra-pulmonary causes – i.e. ventilatory pump failure – from pulmonary causes [1] as the calculated difference between alveolar $pO_2$ and arterial $pO_2$ would only be increased (>>2kPa) if the lung is injured. Here we show how this approach to solving a clinical problem can sometimes be inconclusive.

## Case Report

A sixty-two-year-old woman was admitted by a cardiologist for analysis of episodes of loss of consciousness. Her medical history revealed that she had had tension headache for several years, had undergone hysterectomy 15 years earlier and that she was a heavy smoker (approximately 40 pack years). Over the preceding few months she had gradually developed dizziness, headache behind her right ear and a gradual decrease in visual acuity. Six weeks earlier she had started to have episodes of syncope for which she was evaluated by her cardiologist, who could find no explanation for it. This unexplained syncope caused the cardiologist to transfer her to the neurology ward for further analysis but on transfer, her clinical condition deteriorated rapidly. She could not move her arms properly, her face looked slightly twisted, the right hand corner of her mouth was drooping, and she became confused. The next morning she was found unconscious and in respiratory failure; while receiving supplemental oxygen by face mask ($fiO_2$, estimated - 60%) arterial blood gas analysis showed pH 7.29; $pCO_2$ 49 Hg = 6.5 kPa; $pO_2$, 265 mmHg = 35.3 kPa; sodium bicarbonate, 23 mmol/l; base excess, - 3.9 mmol/l (normal range). The hospital emergency team was alerted. She was orotracheally intubated and transferred to the ICU. Using the alveolar gas equation, the $D(A\text{-}a)O_2$ was later estimated at around 13 kPa. Bronchoscopy was performed and respiratory secretions that were blocking the left lower lobe bronchus were evacuated. From these secretions, *Haemophilus influenzae* and *Streptococcus pneumoniae* were isolated. An antibiotic regimen of amoxicillin combined with clavulanic acid, and ciprofloxacin was started. After sedation was stopped, both her arms appeared paralytic and a Babinski plantar extension reflex was now noted at her right foot. The second day, $fiO_2$ was tapered to 0.4, and arterial blood gas analysis showed pH 7.47; $pCO_2$, 40 mmHg = 5.3 kPa; $pO_2$, 115 mmHg = 15.3 kPa; sodium bicarbonate, 28 mmol/l. $D(A\text{-}a)O_2$ was now around 16 kPa.

A CT scan of her brain showed no abnormalities that could explain the neurological deficits. A second CT two days later showed a lesion in the posterior fossa on the right side. The follow-up CT scan showed lesions with low attenuation in the white matter. The radiologist considered the possibility of a brain abscess. The chest radiograph (Fig 1a) and the CT scan of the chest (fig 1b) showed collapse of the left lower lobe with pleural effusion. Lumbar puncture was performed; chemistry and cell counts of the CSF were normal.

Ultrasound of the heart revealed hypokinesia of the interventricular septum and slightly impaired left ventricular contractility, but was otherwise unremarkable, and congestive heart failure was ruled out as a cause of her respiratory failure. The patient was now suspected of having a brain abscess complicated by a respiratory tract infection that did not improve on antimicrobial treatment. As the attending physicians were uncertain about their diagnosis, the patient was transferred to the Medical Intensive Care Unit in the referral institution, five days after intubation.

After transfer, she appeared conscious but paralytic, and she was unable to communicate. Haemodynamic and gas exchange parameters were all in the acceptable range. An MRI of the brain showed multifocal hyperintense lesions in the thalamus next to the chorioideal plexus of the right ventricle on both sides of the corpus callosum, and diffusely in the pons. Multiple focal ring-like enhancements in the right cerebellum were seen on the MRI. Lesions were noted both in the white and in the grey matter (Fig 2).

CSF cell count, glucose, protein, IgG index, lactate and isoelectric focus were normal. Microbiological screening tests of the patient's blood and CSF did not reveal any current infection. Serological screening for collagen-vascular disease (i.e. complement factors, anti-nuclear

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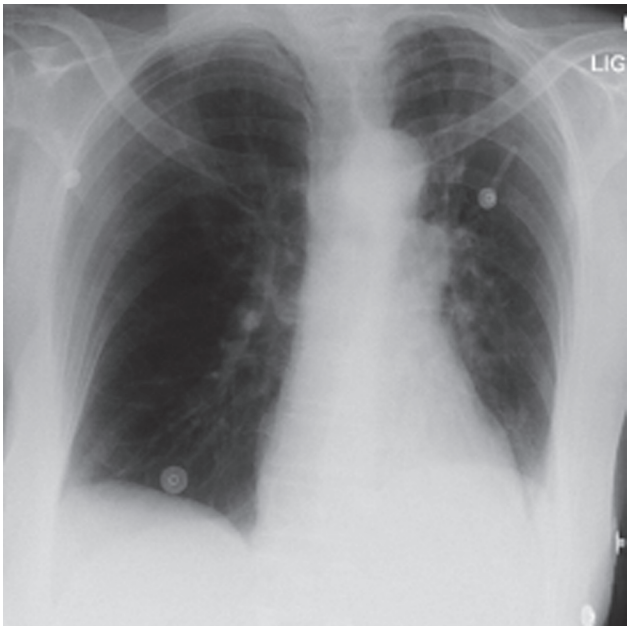

Fig 1a: chest radiograph on admission showing left lower lobe atelectasis

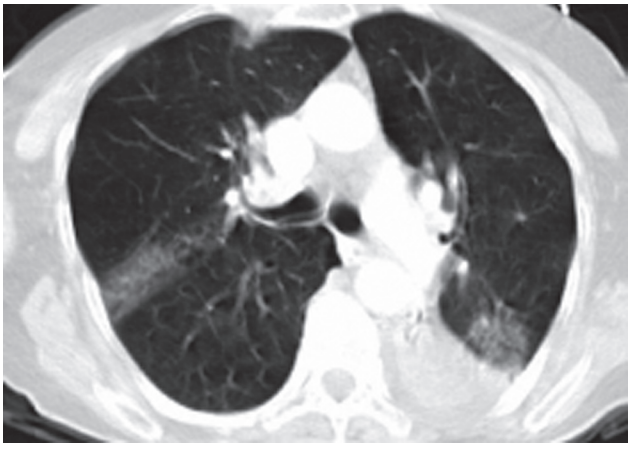

Fig 1b: chest CT after orotracheal intubation confirms collapse of the left lower lobe, and shows slight pleural effusion; and bilateral infiltrative changes

antigen, anti-neutrophil cytoplasmic antigen, lupus anticoagulant, anti double-stranded DNA) as well as all routine blood tests, were normal. Based on the rapidly progressing symptoms and the MRI results and by excluding other syndromes, the favoured diagnosis was therefore acute disseminated encephalomyelitis. The rapid onset suggested that this diagnosis was more likely than glioma, or multiple sclerosis which would be the second most likely diagnosis. As there were no signs of current infection, antibiotic therapy was stopped. The diagnosis was now acute disseminated encephalomyelitis, with ventilatory pump failure whereby the pulmonary abnormalities could be attributed to atelectasis due to retention of bronchial secretions with impaired coughing and chronic obstructive pulmonary disease (COPD).

High dose steroid therapy was started – methylprednisone 1000 mg, for five days. There was no improvement and intravenous immunoglobulin 50 g IV was administered for the next five days .

She received intensive nursing care, and her condition was explained to her and her family. Gradually her airways started to clear, and she was able to be weaned from the ventilator; she was extubated three weeks after transfer. She was able to move her head a few centimetres and could move her right lower leg a little on request. After yet another ten days, she was transferred to the ward where she made a slow recovery. She started rehabilitation therapy, and she gradually gained weight and her muscle strength improved.

## Comment

### *Gas exchange*

Gas exchange parameters alone may help in analysing the cause of respiratory failure [1]. Using the gas exchange equation, it is possible to differentiate gas exchange deficit – suggesting a pulmonary lesion – from ventilatory pump failure with normal gas exchange. Gas exchange is best estimated by calculating the alveolo-arterial oxygen difference or $D(A\text{-}a)O_2$ . If $D(A\text{-}a)O_2 >> 2$ kPa, one may conclude that severe ventilation-perfusion mismatch or severe reduction in diffusing capacity for oxygen is the cause of respiratory failure. The limitation of this estimate is obvious in patients with pre-existing pulmonary function deficit. This may go unnoticed in patients who gradually develop chronic pulmonary dysfunction as they develop chronic obstructive pulmonary disease over the course of time. Moreover, mechanically ventilated patients often have atelectasis and increased dead space ventilation making it difficult to use the gas equation to differentiate between primary gas exchange problems and primary hypoventilation caused by a neuro-muscular condition. Our patient's gas exchange may indeed have been compromised by atelectasis and possibly, COPD, as a result of her smoking habit, and this could have caused the medical team in the referring hospital to reach their conclusion that the patient was suffering from a pulmonary infection and not a neurological condition.

### *ADEM*

Acute disseminated encephalomyelitis (ADEM) is an immune-mediated demyelinating disorder of the central nervous system, typically occurring after an infection or vaccination [2-5]. It can be differentiated from multiple sclerosis (MS) by the rapid progression that is much more common in ADEM than in MS. Although both conditions may respond to high-dose steroids, the response in ADEM is much more profound than in MS. ADEM is defined as a monophasic disease with a much more favourable prognosis [6]. It is most frequently seen in children or adolescents, but occasionally adults and even the elderly may be affected [7-9].

The typical clinical course is a rapidly developing unilateral or multifocal neurological syndrome occurring after infection or vaccination [2-5]. In ADEM, several cytokines and chemokines appear upregulated in blood and CSF. In one study, mean CSF concentrations of CXCL7, CCL1, CCL22, and CCL17 were higher in ADEM than in MS, whereas those of CCL11 were lower in MS than in ADEM and healthy controls [10] suggestive of an immune response that could be triggered by any infectious process [3]. Presently however, no CSF criteria have been developed or validated to differentiate ADEM from MS.

In the less typical cases, the diagnosis of ADEM can be challenging as MRI findings of white matter disease with ring-like enhancements have a broad differential diagnosis [11;12]. The differential diagnosis includes processes with Th2 preponderance like tuberculosis and schistosomiasis. Abscesses, tuberculomas, toxoplasmosis, histoplasmosis, metastases, multiple sclerosis, gliomas, resolving haematomas, and vascular malformations are all among the differential diagnoses [9;13]. Occasionally, and especially in cases in which the differential diagnosis includes tumours (small cell lung cancer metastasis; non-Hodgkin's lymphoma of the brain) and infections requiring specific treatment

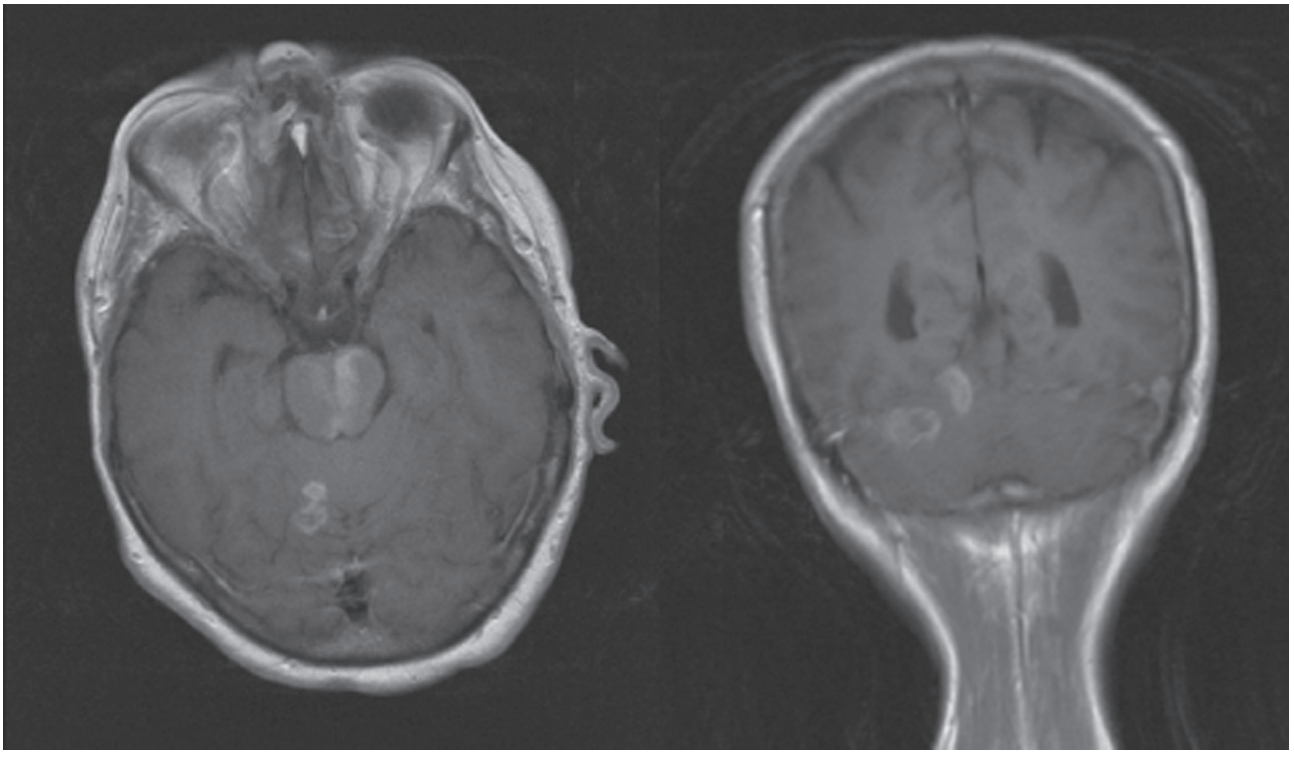

**Figure 2: MRI of the brain showing multifocal ring-like hyperintense lesions**

like tuberculosis, toxoplasmosis, blastomycosis, cryptococcosis, coccidioidomycosis, schistosomiasis and neurocysticercosis, a stereotactic needle aspiration or brain biopsy may required [9].

Our patient was not a typical case. The absence of any obvious recent infection or vaccination and her age did not suggest the diagnosis, and the initial imaging was inconclusive. Clearly, MRI imaging is superior in detecting and differentiating white matter lesions [5;12]. The MRI images and the sudden onset of her symptoms supported the diagnosis of ADEM, but even histopathology may not differentiate between a first episode of MS and ADEM [4;5;9]. Her rapid response to methylprednisolone treatment, together with the two year follow-up with no recurrent disease episodes, strongly suggests that ADEM was the correct diagnosis.

Few published cases of ADEM with elderly-age onset and no history of recent infection or vaccination have been reported in the English literature in the Western hemisphere [7;8]. In patients presenting with a focal or multifocal encephalopathy, the diagnosis ADEM should however be considered, even in the absence of obvious recent infection or vaccination. In our patient, an exacerbation of COPD might have gone unnoticed, while non-specific respiratory infections are among the most common infections triggering ADEM [4].

Finally, patients with rare or unusual disorders might benefit from transfer to another institution for a second opinion. The risks of health hazards incurred by the transfer itself should be balanced against the potential benefits [14;15].

**References**


1. van der Werf TS, Mook GA, Zijlstra JG. Respiratoire insufficiëntie: bereken de oorzaak. Ned Tijdschr Geneeskd 1996; 140: 2381-2384.
2. Bennetto L, Scolding N. Inflammatory/post-infectious encephalomyelitis. J Neurol Neurosurg Psychiatry 2004; 75 Suppl 1: i22-i28.
3. Marchioni E, Ravaglia S, Piccolo G, Furione M, Zardini E, Franciotta D, Alfonsi E, Minoli L, Romani A, Todeschini A, Uggetti C, Tavazzi E, Ceroni M. Postinfectious inflammatory disorders: subgroups based on prospective follow-up. Neurology 2005; 65: 1057-1065.
4. Menge T, Hemmer B, Nessler S, Wiendl H, Neuhaus O, Hartung HP, Kieseier BC, Stuve O. Acute disseminated encephalomyelitis: an update. Arch Neurol 2005; 62: 1673-1680.
5. Tenembaum S, Chitnis T, Ness J, Hahn JS. Acute disseminated encephalomyelitis. Neurology 2007; 68: S23-S36.
6. Orrell RW. Grand rounds--Hammersmith Hospitals. Distinguishing acute disseminated encephalomyelitis from multiple sclerosis. BMJ 1996; 313: 802-804.
7. Wang PN, Fuh JL, Liu HC, Wang SJ. Acute disseminated encephalomyelitis in middle-aged or elderly patients. Eur Neurol 1996; 36: 219-223.
8. Schwarz S, Mohr A, Knauth M, Wildemann B, Storch-Hagenlocher B. Acute disseminated encephalomyelitis: a follow-up study of 40 adult patients. Neurology 2001; 56: 1313-1318.
9. Ravin P, Hedley-Whyte ET. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 34-2002. A 55-year-old man with cognitive and sensorimotor findings and intracranial lesions. N Engl J Med 2002; 347: 1433-1440.
10. Franciotta D, Zardini E, Ravaglia S, Piccolo G, Andreoni L, Bergamaschi R, Romani A, Tavazzi E, Naldi P, Ceroni M, Marchioni E. Cytokines and chemokines in cerebrospinal fluid and serum of adult patients with acute disseminated encephalomyelitis. J Neurol Sci 2006; 247: 202-207.
11. Singh S, Prabhakar S, Korah IP, Warade SS, Alexander M. Acute disseminated encephalomyelitis and multiple sclerosis: magnetic resonance imaging differentiation. Australas Radiol 2000; 44: 404-411.
12. Tan HM, Chan LL, Chuah KL, Goh NS, Tang KK. Monophasic, solitary tumefactive demyelinating lesion: neuroimaging features and neuropathological diagnosis. Br J Radiol 2004; 77: 153-156.
13. Denes E, Magy L, Pradeau K, Alain S, Weinbreck P, Ranger-Rogez S. Successful treatment of human herpesvirus 6 encephalomyelitis in immunocompetent patient. Emerg Infect Dis 2004; 10: 729-731.
14. Kreeftenberg HG, Jr., Ligtenberg JJ, Arnold LG, van der Werf TS, Tulleken JE, Zijlstra JG. Condition on arrival of transferred critically ill patients. Neth J Med 2000; 57: 180-184.
15. Ligtenberg JJ, Arnold LG, Stienstra Y, van der Werf TS, Meertens JH, Tulleken JE, Zijlstra JG. Quality of interhospital transport of critically ill patients: a prospective audit. Crit Care 2005; 9: R446-R451.