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 conscious. 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-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-a)O$_2$ was now around 16 kPa.

A CT scan of her brain showed no abnormalities that could explain the neurologic 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 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 choroidal plexus of the right ventricle on both sides of the corpus callosum, and diffusely in thepons. 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...
or D(A-a)O2 is best estimated by calculating the alveolo-arterial oxygen difference from ventilatory pump failure with normal gas exchange. Gas exchange to differentiate gas exchange deficit – suggesting a pulmonary lesion – respiratory failure [1]. Using the gas exchange equation, it is possible Gas exchange parameters alone may help in analysing the cause of gas exchange problems and primary hypoventilation caused by a neuromuscular 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 predominance like tuberculosis and scotosomiasis. Abscesses, tuberculosis, toxoplasmosis, histoplasmosis, metastases, multiple sclerosis, gliomas, resolving haematomas, and vascular malformations are all among the differential diagnoses [9,12]. 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...
like tuberculosis, toxoplasmosis, blastomycosis, cryptococcosis, coccidioidomycosis, schistosomiasis and neurocysticercosis, a stereotactic needle aspiration or brain biopsy may be 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 recurrence 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