CASE REPORT

Neurogenic pulmonary oedema complicating a lateral medullary infarct

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SUMMARY

Neurogenic pulmonary oedema (NPO) is a rare clinical syndrome of pulmonary oedema occurring secondary to an insult of the central nervous system (CNS). The exact aetiology of this disorder is unknown. NPO can be fatal and poor awareness and identification of this entity, particularly in terms of misdiagnosis as primary pulmonary or cardiac disease, can result in suboptimal management and outcomes. We describe the presentation and management of a 68-year-old woman with an acute left lateral medullary stroke complicated by pulmonary oedema. The likely aetiology is discussed, and important learning points are highlighted.

BACKGROUND

Neurogenic pulmonary oedema (NPO) is a poorly understood entity in which pulmonary oedema occurs secondary to an insult of the central nervous system (CNS). In patients with pulmonary oedema, NPO may be overlooked as the cause of the clinical presentation, with cardiopulmonary diseases (eg, acute heart failure or pneumonia) usually considered first in the differential diagnosis.

We describe a case of NPO complicating the left lateral medullary stroke syndrome. We highlight the importance of identifying NPO in patients presenting with acute stroke and outline the management and outcome in our patient.

CASE PRESENTATION

A 68-year-old woman developed sudden onset vertigo, unsteadiness, neck ache and headache while playing golf. She managed to drive home, but her husband escorted her to a local accident and emergency department due to worsening of symptoms. Following medical assessment, the patient was suspected of having a stroke due to the classical posterior circulation stroke (PoCS) signs present. . She was immediately transferred to the hyperacute stroke centre at Salford Royal NHS Foundation Trust, arriving approximately 4.25 hours after symptom onset. She was not thrombolysed as safe completion of the prethrombolysis checklist could not be completed within the 4.5 hours thrombolysis window.

Medical history was significant only for ulcerative colitis from which the patient was suffering a recent flare. Increases to the mesalazine dose were made but were consequently reduced 3 days prior to this incident. There was no history of hypertension, ischaemic heart disease, pulmonary disease, diabetes mellitus or previous cerebrovascular disease. The patient reported alcohol consumption at 30–40 units weekly and was an ex-smoker having stopped in her mid-20s. There was family history of stroke in the patient's father, paternal grandfather and sister; as well as both siblings being treated for hypertension.

During initial assessment in the emergency department, vital signs included a blood pressure of 205/118 mm Hg with a regular heart rate of 83 beats per minute. Neurological examination revealed a mild dysarthria and subtle symmetrical dysmetria of all four limbs. Cranial nerve examination further demonstrated saccadic intrusion of horizontal pursuit eye movements and transient gaze evoked (direction changing) nystagmus on horizontal gaze to the right and left. Examination of the heart, lungs and abdomen was unremarkable.

The presentation was felt to be consistent with a PoCS, with the aetiology assumed to be vertebral artery dissection occurring in the context of the exertions of golf.

Approximately 1 hour after our initial review, the patient became significantly short of breath. Oxygen saturation dropped to 82% on room air despite normal heart rate and blood pressure. She became drowsy and had inspiratory crepitations to mid-zones of the lungs on auscultation. Oxygen therapy was commenced via a free-flow mask. A flow rate of 8 L/min improved the oxygen saturation from 82% to 94%. Further, neurological examination was performed once the patient stabilised, which identified right beating horizontal nystagmus observed in the primary position gaze, a lower motor neuron left facial palsy, more pronounced dysarthria and dysmetria of all limbs with truncal ataxia.

INVESTIGATIONS

An emergency CT brain was performed. This did not identify any acute haemorrhage or features of large-vessel infarction in arteries of the anterior or posterior circulation. Given the suspicion of vertebral artery dissection (symptoms while playing golf, neck ache, clinical signs suggestive of posterior circulation ischaemia), a CT angiogram of the extracranial vessels was performed that displayed an occlusion involving the V3 and V4 segments of the left vertebral artery, suggestive of artery dissection (figure 1). No evidence of thrombus was noted in the basilar artery.

At the onset of breathlessness, an emergency portable anteroir-posterior (AP) chest X-ray (CXR)

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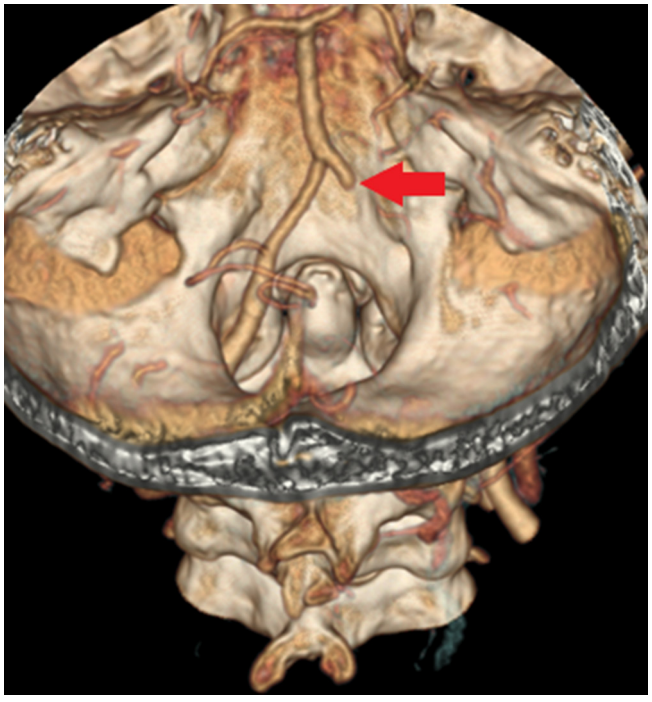

Figure 1 CT angiogram demonstrating occlusion of the left vertebral artery.

was performed that demonstrated bilateral interstitial oedema and blunting of the right costophrenic angle (figure 2A).

ECG was performed, which showed sinus rhythm with some left ventricular hypertrophy and slightly prolonged corrected QT interval of 493 ms. An arterial blood gas on room air soon after the onset of breathlessness showed: pH 7.35, Po_2 11.3, PCo_2 6.0, base excess −1.2, lactate 0.9.

DIFFERENTIAL DIAGNOSIS

In patients with severe breathlessness, the following diagnoses should be considered, depending on what is found on examination:

- Wheeze: Asthma, chronic obstructive pulmonary disease.
- Stridor: Anaphylaxis, acute epiglottitis, foreign body.
- Crepitations: Pneumonia and pulmonary oedema.
- Clear chest on auscultation: pulmonary embolism, hyperventilation, metabolic acidosis, severe asthma.

In the context of this case and history, the combination of acute respiratory distress and stroke led to concern about the possibility of NPO. Given the significant hypertension, cardiogenic pulmonary oedema secondary to hypertensive crisis was also considered.

TREATMENT

After the CT brain scan, 300 mg of aspirin was administered and hypertension was managed with a glyceryl trinitrate infusion with the dose titrated to 6 mg/hour. This was stopped after around 15 min as the blood pressure fell to 140/80 mm Hg. The blood pressure subsequently remained within the normal range without additional treatment.

Breathlessness developed after the blood pressure had come under control. At this point, 40 mg of intravenous furosemide was administered. Over the next hour, the patient's condition stabilised. Over the next 24 hours, no further neurological symptoms developed and there was gradual improvement noted from a respiratory perspective, with resolution of breathlessness and normalisation of oxygen saturations.

OUTCOME AND FOLLOW-UP

An MRI brain performed 24 hours after symptom onset demonstrated an acute infarction within the posterolateral medulla on the left side, consistent with the clinical presentation (figure 3). At this time, the CXR (also AP) was repeated, demonstrating near complete resolution of the previously demonstrated oedema (figure 2B). No further respiratory distress of oxygen desaturation occurred.

Five days after the presentation of stroke, the patient continued to demonstrate focal neurological deficits. Past pointing was evident in the left upper limb accompanied by reduced power (Medical Research Council [MRC] scale 4/5), with an additional mild dysmetria in the left lower limb. No sensory deficit was identified. At this time, the patient was repatriated to her local district general hospital for stroke rehabilitation.

The patient has remained clinically well during follow-up with no further admissions or medical issues to note. Referral and management by the physiotherapists and orthoptists have aided

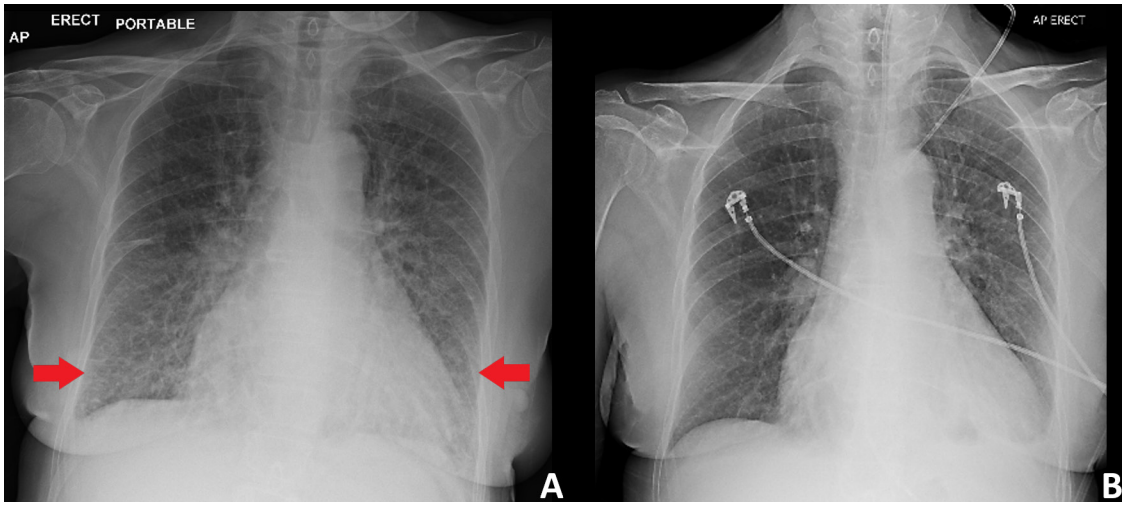

Figure 2 (A) Anterior-posterior (AP) portable chest X-ray demonstrating bilateral interstitial oedema and blunting of the right costophrenic angle. (B) AP chest X-ray demonstrating resolution of interstitial oedema, although blunting of left costophrenic angle now evident.

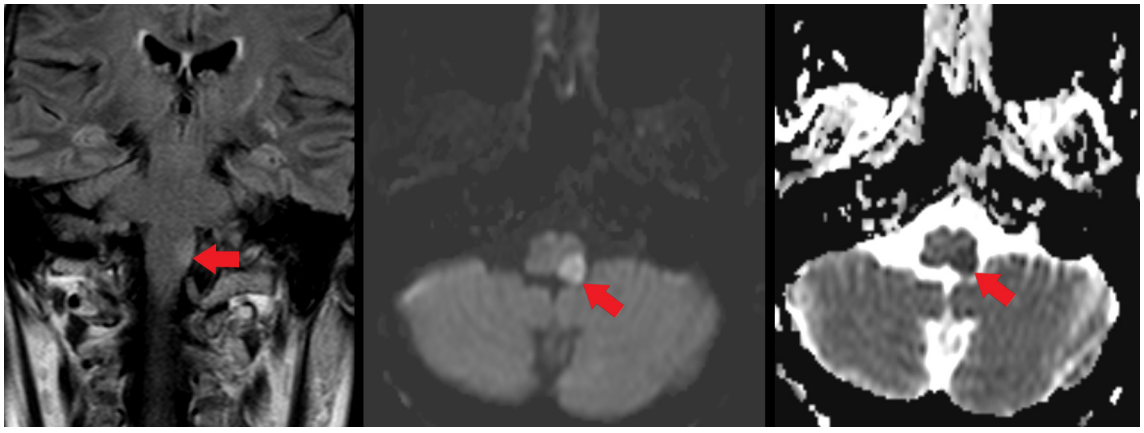

Figure 3 MRI demonstrating an infarct in the left posterior lateral aspect of the medulla (left: coronal fluid attenuation inversion recovery sequence; middle: axial diffusion weighted imaging; right: accompanying apparent diffusion coefficient image).

the patient in returning to undertake her normal daily activities. The patient has also returned to playing golf.

DISCUSSION

NPO was considered the most likely explanation of the acute shortness of breath in this patient given the presentation with a PoCS and the absence of prior cardiorespiratory disease. Whilst most often described in association with subarachnoid haemorrhage (SAH), in this case NPO occurred secondary to suspected vertebral artery dissection, presumably caused by the physical exertions of golf. Vertebral artery dissection causing NPO has also been described in other case reports, including one instance occurring after playing tennis.[1 2]

After an insult to the CNS, the possibility of complicating NPO should always be considered when there is a rapid respiratory decompensation. NPO was first described in 1871 by Brown-Séquard, who published details of pulmonary oedema occurring after injury to the medulla in non-human studies.[3] A case series and literature review of 14 cases by Fontes *et al* 2003 focused on patients diagnosed with SAH.[4] The authors indicated that cardinal clinical features of NPO include pink frothy airway fluid, dyspnoea and cyanosis, and mortality estimated at 10%. In patients suffering from a severe CNS injury, the prevalence of NPO has been estimated between 40% and 50%, although the overall prevalence with other CNS insults is unknown.[5]

Two hypotheses regarding the pathology of NPO are described. The first includes a massive sympathetic discharge, and associated release of large amounts of catecholamines triggered by the underlying neurological insult. This generates severe systemic vasoconstriction, shifting blood from the systemic circulation into that of the pulmonary blood volume.[6] The second involves increased pulmonary vascular permeability facilitated by the increased sympathetic microvascular stimulation causing micropores to increase in number and size, allowing more fluid into the alveoli.[6] Permeability is further increased by release of neurohumoral factors.[7 8] These factors facilitate an increased hydrostatic pressure driving the oedematous process within the lung parenchyma.[9] Suspected trigger zones for NPO include the hypothalamus and the medulla.[10] Other triggers of NPO are reported, including seizures, multiple sclerosis and trauma.[11–14] NPO may present at any time up to 12 hours after the neurological insult and may be classified as subclinical or fulminant.[15]

The hypertension observed in this case suggests that a massive sympathetic discharge, triggered by the lateral medullary infarct, may be the mechanism causing pulmonary oedema. While it is possible that a hypertensive crisis from alternative cause and resultant cardiac failure might be implicated as the cause of breathlessness in this case, this appears less likely given the co-occurrence of stroke, the lack of cardiac background and the patients' blood pressure stabilising before the onset of the pulmonary oedema.

Treatment of NPO is supportive with the emphasis on ensuring the causative factor is identified and reversed where possible. Future areas of research include use of alpha adrenergic blockade to counteract the sympathetic overactivity, with animal studies showing its benefit in progression and ultimate severity of NPO.[16 17] Predictors of NPO in patients with intracranial insult are not well researched or validated. In patients with non-traumatic intracranial haemorrhage treated in an intensive care unit, Junttila *et al* described increased risk of NPO in those with Acute Physiology and Chronic Health Evaluation II scores ≥20 and plasma interleukin 6 concentrations >40 pg/mL.[18] Further work is required to investigate the relevance of these findings and what measures might be taken in those patients felt to be at high risk of developing NPO.

Learning points

- Neurogenic pulmonary oedema (NPO) should be considered in a patient presenting with a central nervous system (CNS) event and concomitant respiratory compromise.
- Key clinical features of NPO include: pink frothy sputum, acute dyspnoea with rapidly dropping oxygen saturations.
- From our experience and limited literature available, use of diuretics appears to have benefit, alongside a focus on managing the primary CNS insult.

Contributors HMR: drafted and updated the manuscript in response to author and patient comments. AVH: reviewed neuroradiology and provided images for publication, critically reviewed manuscript. KP: reviewed patient (consultant in charge), critically reviewed manuscript. JBL: Reviewed patient (on-call registrar), had the original idea and oversaw the project and critically reviewed and finalised the manuscript. All authors have reviewed the final version of the manuscript and agree with its contents.

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