Acute pulmonary oedema: not always cardiogenic

M Bonello[1], R Pullicino[2], AJ Larner[3]

Abstract

A patient presented with fulminant pulmonary oedema and required acute intubation and ventilation. There was no history of a prior cardiac disorder. As he was weaned from sedation, following stabilisation of his pulmonary status, neurological signs suggestive of brainstem dysfunction became apparent. Investigations showed infarcts in the posterior cerebral circulation secondary to a vertebral artery dissection. Neurogenic pulmonary oedema needs to be considered in any patient with fulminant pulmonary oedema without overt evidence or history of cardiac disease.

Correspondence to:
M Bonello
Walton Centre for Neurology and Neurosurgery
Liverpool L9 7LJ
UK

Email:
michael.bonello@thewaltoncentre.nhs.uk

Keywords extracranial vertebral artery dissection, neurogenic pulmonary oedema

Declaration of interests No conflicts of interest declared

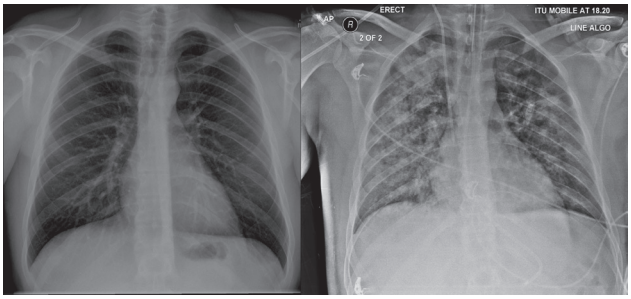
Introduction

Pulmonary oedema may sometimes have a fulminant presentation with shortness of breath, as a consequence of the movement of excess fluid into the pulmonary alveoli. This may be conceptualised as an alteration in one or more of Starling's forces: capillary hydrostatic pressure, interstitial tissue pressure, plasma colloid osmotic pressure, endothelial permeability and lymphatic function. The causes of pulmonary oedema are varied, but it is most commonly cardiogenic, due to left-sided heart disease.[1] However, occasional non-cardiogenic causes of pulmonary oedema are recognised, the correct diagnosis of which may be delayed if the possibility is not considered

Case

A previously healthy 28-year-old primary school teacher was playing football with some of his pupils. As he tried to head the ball he missed, and developed sudden onset right-sided neck pain with radiation to the back of the head, followed by sudden onset vertigo, oscillopsia and shortness of breath. He collapsed in the school playground and was admitted urgently to hospital. In the emergency department he was found to be in severe respiratory distress with type 2 respiratory failure. The patient suffered from haemoptysis and was also noted to have raised jugular venous pressure, hypotension and tachycardia. The ECG showed cor pulmonale with right heart strain. The chest radiograph (Figure 1) showed acute bilateral infiltrates consistent with pulmonary oedema. Transthoracic echocardiography confirmed mild left ventricular failure and moderate diastolic dysfunction. His blood troponin T level was raised at 1331 ng/l (normal < 14 ng/l) and his brain natriuretic peptide level was also raised

Figure 1. An incidental chest x-ray (left) acquired around a year prior to the patient's acute illness was completely normal. Chest x-ray (right) on ITU admission demonstrating bilateral peri-bronchial cuffing and pulmonary infiltrates in keeping with pulmonary oedema. The heart is not enlarged

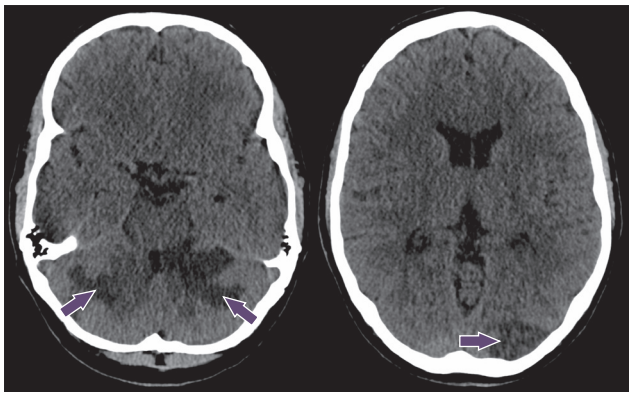


at 3655 ng/l (normal <400 ng/l). Computed tomography (CT) pulmonary angiography was normal, as was CT of the brain. He was diagnosed with acute pulmonary oedema and due to the respiratory compromise required intubation and ITU admission.

The patient's respiratory status was stabilised over several days. When sedation was withdrawn he complained of vertigo and unsteadiness on sitting up. Neurological examination showed broken saccadic eye movements with jerky nystagmus, bilateral upper limb intention tremor, truncal ataxia and dysdiadochokinesia. The CT brain scan (Figure 2) now showed extensive bilateral low density change in the cerebellum as well as in the left occipital lobe, appearances consistent with subacute infarction. A CT angiogram (Figure 3) demonstrated a reduction in calibre in the V3 segment of the right vertebral artery. Magnetic resonance brain imaging showed a dissection flap and intramural haematoma at the atlantic or extradural segment of the right vertebral artery on

[1]SpR in Neurology, [2]SpR in Neuroradiology, [3]Consultant Neurologist, Walton Centre for Neurology and Neurosurgery, Liverpool, UK

Figure 2. Unenhanced CT of the brain demonstrating bilateral cerebellar and left occpital infarcts in keeping with posterior circulation strokes (see arrows)



T1 Spectral Presaturation with Inversion Recovery (SPIR) (fat suppressed) sequences (Figures 4 and 5).

Hence a final diagnosis of neurogenic pulmonary oedema secondary to extracranial vertebral artery dissection with multiple posterior circulation embolic infarctions was made. The patient was treated with intravenous heparin and then converted to warfarin. He was subsequently transferred for neurorehabilitation. Three months post event his only residual neurological deficit was some mild incoordination.

Discussion

Neurogenic pulmonary oedema was first described by Brown-Séquard in the Lancet in 1871, following experimental injuries to the base of the brain in guinea pigs.[2] It was further characterised in the 1950s by MacKay who reported pulmonary oedema secondary to traumatic brain injury,[3] and multiple case reports have since been added to the literature.

Neurogenic pulmonary oedema characteristically presents within minutes of a severe central nervous system insult, especially to the medulla oblongata. Bilateral lesions in the nucleus of the solitary tract, area postrema and lesions in the A1 and A5 noradrenergic neurones have been shown in animal models to cause systemic hypertension and pulmonary oedema.[4,5] Patients usually present with acute dyspnoea that may be associated with haemoptysis. Examination shows tachypnoea, tachycardia and pulmonary rales. Neurogenic pulmonary oedema may have a fulminant onset, as in our case, and urgent treatment is required in such situations.

Neurogenic pulmonary oedema has been reported in the context of various neurological disorders, including epilepsy,[6] subarachnoid haemorrhage,[7] bulbar multiple sclerosis,[8] and brainstem infarcts,[9] although we have identified only one previous case associated with vertebral artery dissection.[10] The medulla seems to be invariably involved. Brown-Séquard had observed in 1871 that 'oedema…principally appears after an injury to the medulla oblongata'.[2]

Figure 3. CT angiogram demonstrating a reduction in calibre (arrow) in the V3 segment of the right vertebral artery when compared to its counterpart

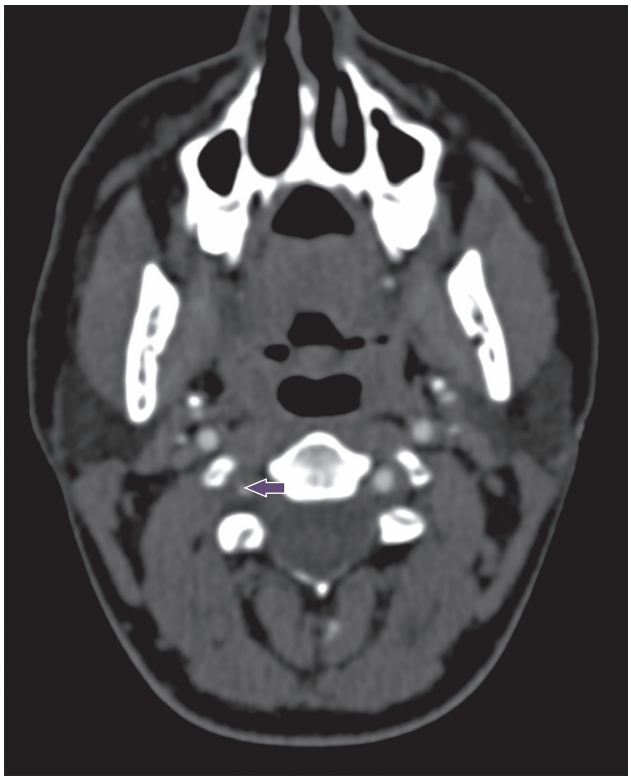
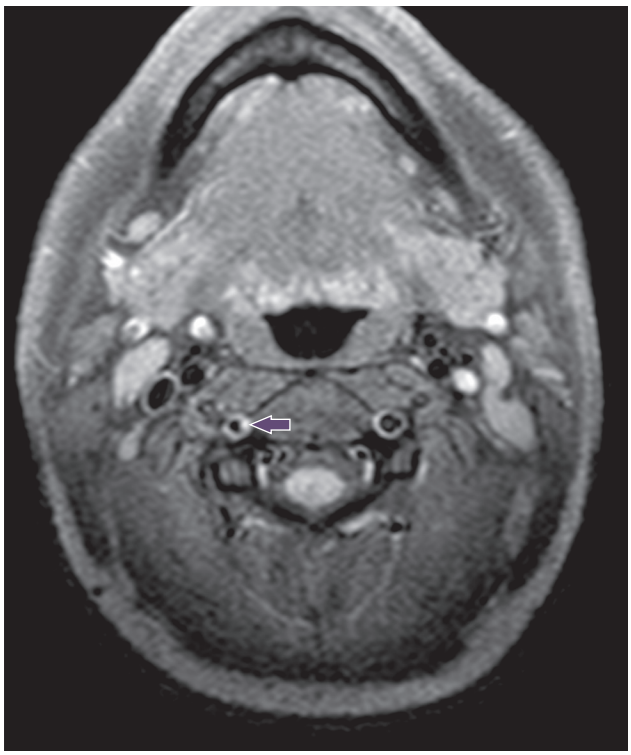


Figure 4. T1-SPIR sequence demonstrating a dissection flap and intra-mural haematoma (arrow) in the right vertebral artery in keeping with dissection



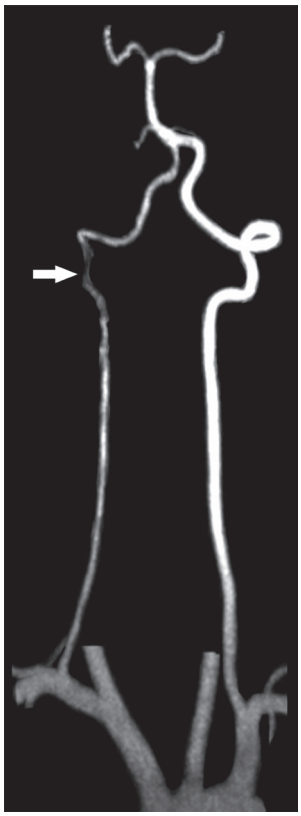


Figure 5. Formated magnetic resonance angiography desmonstrating dissection and a reduction in calibre of the V3 segment (arrow) of the right vertebral artery

The mechanism of neurogenic pulmonary oedema, suggested from various animal models,[4,5] is thought to involve the sympathetic component of the autonomic nervous system. An insult in the medulla may thus acutely alter capillary hydrostatic pressure, one of Starling's forces, causing pulmonary veno-constriction,[11,12] excessive systemic veno-constriction resulting in an increase in venous return,[13] and impaired left ventricular contraction due to myocardial stunning.[14] The fact that neurogenic pulmonary oedema may be prevented by alpha adrenergic blockade[15,16] supports this theory.

The effectiveness of specific medical treatments in neurogenic pulmonary oedema is not definitively proven. However in a recent case report administration of phentolamine demonstrated rapid improvements in oxygenation.[15] Unopposed alpha adrenergic antagonists may precipitate systemic hypotension and thus further evidence is required before their use in clinical practice can be advocated. Most patients require mechanical ventilation, supplemental oxygen, and maintenance of low cardiac filling pressures. The outcome of patients with neurogenic pulmonary oedema normally depends on the degree of the neurological insult. Independent predictors include the severity of disease as calculated by the APACHE II score and higher interleukin-6 levels.[17] Higher one-year mortality but not poorer functional status was found comparing intensive care unit-treated non-traumatic intracranial haemorrhage patients with and without neurogenic pulmonary oedema.[17]

Conclusion

Neurogenic pulmonary oedema may have a fulminant presentation, as in our case, and thus needs to be considered in the differential diagnosis of acute pulmonary oedema, particularly if there is no suggestion of an underlying primary cardiac disorder. The fact that the patient had such a dramatic presentation requiring urgent ventilator support meant that clinical signs pointing to medullary dysfunction might have been initially missed. This case highlights the importance of assessing the whole patient in context especially if all the clinical findings cannot be explained by one diagnosis. Early treatment of an underlying neurological disorder may potentially improve long term outcome.

References

1 Morrell NW, Firth JD. Pulmonary oedema. In: Warrell DA, Cox TM, Firth JD, editors. *Oxford Textbook of Medicine*. 5th ed. Oxford: Oxford University Press; 2010. p.2992–3001.
2 Brown-Séquard CE. On the production of haemorrhage, anaemia, oedema and emphysema in the lungs by injuries to the base of the brain. *Lancet* 1871; i: 6.
3 MacKay KE. Experimental pulmonary edema. IV. Pulmonary edema accompanying trauma to the brain. *Proc Soc Exp Biol Med* 1950; 74: 695–7.
4 Blessing WW, West MJ, Chalmers J. Hypertension, bradycardia, and pulmonary edema in the conscious rabbit after brainstem lesions coinciding with the A1 group of catecholamine neurons. *Circ Res* 1981; 49: 949–58.
5 Chen HI, Chai CY. Integration of the cardiovagal mechanism in the medulla oblongata of the cat. *Am J Physiol* 1976; 231: 454–61.
6 Zhao H, Lin G, Shi M et al. The mechanism of neurogenic pulmonary edema in epilepsy. *J Physiol Sci* 2014; 64: 65–72.
7 Yamagishi T, Ochi N, Yamane H et al. Neurogenic pulmonary edema after subarachnoid hemorrhage. *J Emerg Med* 2014; 46: 683–4.
8 Plummer C, Campagnaro R. Flash pulmonary edema in multiple sclerosis. *J Emerg Med* 2013; 44: e169–72.
9 Probasco JC, Chang T, Victor D et al. Isolated pulmonary edema without myocardial stunning in brainstem strokes. *J Neurol Transl Neurosci* 2014; 2: 1040.
10 L'e Orme RM, McGrath NM, Rankin RJ et al. Extracranial vertebral artery dissection presenting as neurogenic pulmonary oedema. *Aust N Z J Med* 1999; 29: 824–5.
11 Macmillan CS, Grant IS, Andrews PJ. Pulmonary and cardiac sequelae of subarachnoid haemorrhage: time for active management? *Intensive Care Med* 2002; 28: 1012–23.
12 Kadowitz PJ, Joiner PD, Hyman AL. Influence of sympathetic stimulation and vasoactive substances on the canine pulmonary veins. *J Clin Invest* 1975; 56: 354–65.
13 Sedý J, Zicha J, Nedvidková J et al. The role of sympathetic nervous system in the development of neurogenic pulmonary edema in spinal cord-injured rats. *J Appl Physiol* 2012; 112: 1–8.
14 Bahloul M, Chaari AN, Kallel H et al. Neurogenic pulmonary edema due to traumatic brain injury: evidence of cardiac dysfunction. *Am J Crit Care* 2006; 15: 462–70.
15 Davison DL, Chawla LS, Selassie L et al. Neurogenic pulmonary edema: successful treatment with IV phentolamine. *Chest* 2012; 141: 793–5.
16 Lu WH, Hsieh KS, Lu PJ et al. Different impacts of α- and β-blockers in neurogenic hypertension produced by brainstem lesions in rat. *Anesthesiology* 2014; 120: 1192–204.
17 Junttila E, Ala-Kokko T, Ohtonen P et al. Neurogenic pulmonary edema in patients with nontraumatic intracerebral hemorrhage: predictors and association with outcome. *Anesth Analg* 2013; 116: 855–61.