Case Report

Neurogenic pulmonary edema due to delayed radiation necrosis

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Abstract

Neurogenic pulmonary edema is oftten missed in the ICU setting as it is mistaken for pneumonia or ARDS. The case presented here illustrates how a high index of suspicion in the appropriate setting can lead to the diagnosis. The patient in this report developed acute-on-chronic cerebral edema due to radiation necrosis following gamma-knife radiation therapy for cerebral arteriovenous malformation.

Key Words: Neurogenic pulmonary edema, cerebral edema, acute pulmonary edema, subarachnoid haemorrhage, raised intracranial pressure, mechanical ventilation

Neurogenic pulmonary edema (NPE) is a recognised complication of a neurological event, commonly subarachnoid haemorrhage (SAH) and major head injuries.[1] The incidence of NPE was reported to be 6% in a series of 457 patients with SAH[2] however, the diagnosis is often missed as it is perceived to be a rare complication of acute neurological conditions[3] and, the index of suspicion is not high enough. We present a case of NPE following gamma knife irradiation of an arterio-venous malformation (AVM) of the occipital region.

Case Report

33-year-old lady was diagnosed, at another hospital to be suffering from an AVM of the right occipital lobe in September 1999, while undergoing evaluation for giddiness, nausea and vomiting. Magnetic Resonance Imaging (MRI) and digital subtraction angiography (DSA) revealed a vascular malformation in the right occipital region fed by the right internal carotid artery and a vertebral injection showed it to be draining into the transverse sinus.

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Stereotactic Gamma Knife irradiation was performed on 06/10/99 for the AVM. 99% of the AVM volume (11.9 cubic mm) was treated with a prescription dose of 25.0 Gy at 50% isodose configuration. Lens and cornea were protected using shields and plug patterns. Maximum dose at reference point was 50.0 Gy. The patient tolerated the procedure well.

Following the procedure, she developed recurrent headaches and blurring of vision. An MRI scan done six months after the procedure showed diffuse cerebral edema with features of raised intracranial pressure (ICP). She was started on corticosteroid therapy for the post-radiation cerebral edema. However, she continued to have symptoms of raised ICP in the form of blurring of vision and two episodes of focal seizures. Her compliance with medication was doubtful.

MRI head scan done in April 2002 showed a lesion in the right occipital region with mass effect and compression of the right lateral ventricle. She was continued on corticosteroid therapy for control of raised ICP. MRI head scan done in March 2003 showed persistent cerebral oedema. On 10 May 2003, she presented with features of steroid-induced cushingoid habitus, following which steroid therapy was discontinued. She was admitted 7

days later with fever, cough and breathlessness of three days' duration. At admission, she was found to be toxic, febrile 100º F with facial puffiness, dyspnoea, tachycardia and coarse crepitations over the right lung field. Other systems were essentially normal. A Chest X-ray showed bilateral diffuse infiltrates more over the right hemithorax. She was given broad -spectrum antibiotics with a presumed diagnosis of pneumonia. Her condition continued to deteriorate with extension of the lung infiltrates on Chest X-ray. She also developed bradycardia, hypoxia and respiratory acidosis, requiring endotracheal intubation and controlled mechanical ventilation. A bronchoalveolar lavage grew no organisms. The patient was shifted to this hospital on 21 May 2003. At admission the patient had tachycardia HR 110/minute and fever of 100º F. Examination of the chest revealed bilateral widespread crepitations and fundoscopy showed bilateral papilloedema. Arterial blood gas analysis showed a respiratory acidosis (pH 7.31, PCO2 58 mm Hg); central venous pressure (CVP) was 22 cm H2O; 2-D Echocardiography showed an ejection fraction (EF) of 65%, a pulmonary artery systolic pressure (PASP) of 45 mm hg, a mildly dilated right atrium (RA) and inferior vena cava (IVC) and depressed function of right ventricular (RV) function along with a normal left ventricle and left ventricular end diastolic pressure; there were no clots or vegetations. A chest X-ray showed bilateral uniform diffuse alveolar infiltrates consistent with pulmonary edema.

In view of the history, paplloedema, findings on examination of the chest and the radiological findings, we started her on anti-cerebral oedema measures in the form of hyperventilation (to achieve a PCO2 of 30 mm hg) after appropriate sedation, analgesia and paralysis; intravenous corticosteroids (Dexamethasone 4 mg iv 6 hourly), low dose Mannitol 0.25 gm / kg 8 hourly and Frusemide 20 mg iv daily. Antibiotics for presumed severe community acquired pneumonia (Tab Clarithromycin 500 mg twice a day) were also instituted. An MRI head scan done on 22 May 2003 (2nd day of admission) showed features of cerebral edema with mass effect and uncal herniation. DSA performed on the same day did not suggest recurrence of the AV malformation. Rapid and complete clearing of lung shadows occurred in the next 24 hours and the patient could be extubated on the 3rd day of admission (70 hours of ventilation). The antibiotics were discontinued while maintaining oral corticosteroids and anticonvulsants and the patient could be shifted out of the MICU on the 4th day. An uneventful recovery followed thereafter and she could be discharged from hospital on the 10th day with instructions to continue corticosteroids and anticonvulsants.

Discussion

First described by Shanahan[4] following epileptic seizures, the pathogenesis of NPE remains controversial. Hypoxia results from an increase in extra vascular lung water (EVLW), which correlates with the magnitude of intra pulmonary shunt and degree of hypoxia. Two conflicting theories have evolved based on the haemodynamic data and the measure of pulmonary edema fluid protein content. Smith et al[5] have propounded the hydrostatic mechanism for pulmonary edema in humans. The findings of a low edema fluid to plasma protein ratio in some patients in addition to frequently present LV dysfunction support the concept of pulmonary venous and alveolar capillary hypertension as a cause of NPE.[5,6] On the other hand, some patients have edema fluid with a high protein level suggesting increased permeability of the alveolar capillary wall. In addition, indices of LV performance (PCWP, CVP and Cardiac Index) may be normal.[7] Animal models[8,9] where NPE has been induced after intra-cisternal injection of veraterine have shown a pronounced sudden rise in pulmonary arterial and left atrial pressures. This is thought to be due to a massively increased sympathetic discharge causing a sudden increase in pulmonary artery pressures which have been recorded in acute SAH[10] The pulmonary edema in this situation is of hydrostatic origin. However, disruption of alveolar capillaries because of the high pressure may cause a subsequent exudative pulmonary edema.

Our patient had a moderately elevated pulmonary artery systolic pressure of 42 mm Hg with a normal left ventricle size and LVEDP, thus ruling out a cardiogenic cause. This patient had evidence of delayed radiation necrosis and cerebral edema requiring corticosteroid therapy from time to time. Just prior to this presentation, her corticosteroids were tapered off to minimize adverse effects.

To the best of our knowledge no case of neurogenic pulmonary oedema following Gamma knife irradiation of tumors of the brain has been described so far in the literature.[1-3,11,12]

Incidence of NPE has been reported as an unusual complication of neurogenic events.[13] Weir[14] reported an incidence of a pathological diagnosis of pulmonary edema in 71% of 78 cases of fatal subarachnoid haemorrhage, out of these 31% had a clinical diagnosis of pulmonary edema prior to death. Neurogenic pulmonary edema is a recognized complication of a neurological event, commonly subarachnoid haemorrhage and major head injuries.[1] Fontes[11] reported the most common underlying neurological pathology with NPE is subarachnoid haemorrhage following aneurysm rupture (42.9%). Other causes include phenothiazine overdose (14.3%), head trauma and tumors (9.5%) and epilepsy, primary medullary haemorrhage, multiple sclerosis, medullary lesion, and intraparenchymal haematoma (4.8%).

Clinical features of NPE have been described as nonspecific.[11] Colice et al[15] have described two patterns for the development of NPE. These are acute (minutes to hours after the insult) or several days after the precipitating event. Two cases have been described where NPE preceded neurological events[16,17] both had a dissection of an intracerebral artery with slow subarachnoid bleeding.

Our patient differs distinctly from the patients described in the literature with respect to the acute-on-chronic setting of raised intracranial pressure being present prior to the onset of NPE.

The precipitating event was presumably a rise in intra cranial pressure as evidenced by the presence of uncal herniation on MRI head scan following stereotactic gamma irradiation. The striking feature in our patient is the evidence of chronic raised intracranial pressure in the period prior to the acute event. It is possible, therefore, that acute rise in ICP may be the underlying event that triggers off NPE. Acute rise in intracranial pressure could be the underlying trigger in the several neurological conditions implicated in the development of NPE. This possibility is further supported by the quick resolution of NPE following control of intracranial pressures with anti-edema measures in the case described. Fontes et al[11] in their excellent review of literature have found that therapeutic measures were mostly supportive. Patients received appropriate measures for their precipitating neurological problems, including increased intracranial pressure requiring endotracheal intubation (76%), diuretics (38.1%) and corticosteroids (19%), all measures that may decrease intracranial pressure.

Conclusions

A case of neurogenic pulmonary edema resulting from delayed necrosis after gamma knife irradiation of cerebral arterio-venous malformation is described, where a quick resolution of bilateral alveolar opacities occurred with anti-cerebral edema measures. The pathophysiological mechanisms of NPE have remained obscure.[11]

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