Neurogenic pulmonary edema due to delayed radiation necrosis


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. 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 100°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 hemitho-
rax. She was given broad -spectrum antibiotics with a
presumed diagnosis of pneumonia. Her condition con-
tinued to deteriorate with extension of the lung infiltrates
on Chest X-ray. She also developed bradycardia, hypo-
pnoea 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 admis-
sion the patient had tachycardia HR 110/minute and fe-
ver of 100°F. Examination of the chest revealed bilat-
eral widespread crepitations and fundoscopy showed bi-
lateral papilloedema. Arterial blood gas analysis showed
a respiratory acidosis (pH 7.31, PCO2 58 mm Hg); cen-
tral 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 ven-
tricular (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 pul-
monary edema.

In view of the history, papilloedema, findings on ex-
amination 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 se-
vere community acquired pneumonia (Tab
Clarithromycin 500 mg twice a day) were also instituted.
An MRI head scan done on 22 May 2003 (2
th 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 malfor-
mation. 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 ven-
tilation). The antibiotics were discontinued while main-
taining 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 instruc-
tions to continue corticosteroids and anticonvulsants.

Discussion

First described by Shanahan[5] following epileptic sei-
zures, 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 con-
flicting theories have evolved based on the haemody-
namic data and the measure of pulmonary edema fluid
protein content. Smith et al[6] have propounded the hy-
drostatic 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.[10] Animal models[6,9] where NPE has been induced
after intra-cisternal injection of veratrine 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 in-
crease 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 ar-
tery 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.\textsuperscript{[13]} Weir\textsuperscript{[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.\textsuperscript{[1]} Fontes\textsuperscript{[1]} 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 non-specific.\textsuperscript{[11]} Colice et al\textsuperscript{[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\textsuperscript{[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 intracranial 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\textsuperscript{[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.\textsuperscript{[11]}

**References**


Forthcoming ISCCM activities

9th Annual Workshop on Mechanical Ventilation
Organised by Pune Branch of ISCCM
Dates to be announced.

4th Annual Critical Care Symposium and Workshop
Organized by ISCCM (Delhi Chapter)
21st to 23rd, October, 2005
India Habitat Centre, New Delhi
Contact: Dr. Rajesh Chawla, Organizing Secretary, Room No 1007, General OPD, Gate No. 10, Indraprastha Apollo Hospitals, Sarita Vihar, Delhi-Mathura Road, New Delhi - 110044. Mobile: 09810033395

Workshop on Hemodynamic Monitoring
Organised by Bombay Branch of ISCCM
October, 2005.
Dates to be announced

Indian Society of Critical Care Medicine, Chennai Branch
1st Annual Refresher Course in Critical Care Medicine
July 9th - 10th, 2005
Chennai

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