

Neurogenic pulmonary edema following acute ischemic stroke: A case report and literature review

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Abstract

Neurogenic pulmonary edema (NPE) is defined as acute pulmonary edema develops after a significant central nervous system insult. Although NPE has been recognized for a long time, it is still underdiagnosed in clinical practice. The exact mechanism remains unclear, but the activation of sympathetic nervous system and a catecholamine surge play important roles. Common clinical presentations are dyspnea, hypoxia and pink frothy sputum. The mortality rate is high, but recovery is usually good in surviving patients. Here we report a 62-year-old woman presenting with abrupt onset respiratory distress during thrombolytic therapy after acute ischemic stroke involving the left insular and fronto-temporo-parietal lobes. Diagnosis of NPE following acute ischemic stroke was made. Review of literature showed that NPE following ischemic stroke is rare, with only few cases previously reported in the literature.

INTRODUCTION

Neurogenic pulmonary edema (NPE) is a syndrome characterized by acute pulmonary edema following a significant central nervous system (CNS) insult. NPE is probably underdiagnosed and the exact incidence is unknown.^{1,2} Any acute CNS insult can lead to pulmonary edema. It has been reported in patients with subarachnoid hemorrhage, traumatic brain injury, intracerebral hemorrhage, status epilepticus, meningitis, spinal cord injury, intracranial tumors, ischemic stroke and multiple sclerosis.³⁻⁷ We describe here a case of neurogenic pulmonary edema following ischemic stroke. We also reviewed the literature and found only a few cases of NPE after acute ischemic stroke have been reported in the English literature.⁹⁻¹⁴

CASE REPORT

A previously healthy 62-year-old woman presented to the emergency department ninety minutes after developing acute onset speech difficulty and right-sided weakness. On initial presentation, the patient had a blood pressure of 133/69 mmHg, heart rate of 50 beats per minute, respiratory rate of 18 breaths per minute and temperature of 36.4 degrees Celsius. Physical examination revealed normal breath and heart sounds. Neurologic examination revealed global aphasia, right central type facial palsy and right hemiplegia. The National Institutes of Health Stroke Scale (NIHSS) was 18. Non-contrast head

computed tomography (CT) showed no significant abnormality. Computed tomography angiography (CTA) revealed absence of one branch of the M3 segment of the left middle cerebral artery (MCA) and decreased flow and caliber of the rest of left MCA branches (Figure 1). Electrocardiography (ECG) showed normal sinus rhythm and chest radiograph revealed cardiomegaly. Complete blood cell count and blood chemistry analysis were unremarkable.

After obtaining informed consent, intravenous recombinant tissue plasminogen activator (rt-PA) was administered. During the infusion, the patient suddenly experienced disturbance of consciousness accompanied by respiratory distress with copious amounts of pink frothy sputum. Given the suspicion of hemorrhagic complications, the infusion was stopped. Physical examination showed tachypnea (28/min), tachycardia (115/min), hypertension (175/100 mmHg) and reduced oxyhemoglobin saturation (67%). Chest auscultation revealed bilateral crackles and rales. She was immediately intubated and connected to a mechanical ventilator. Head CT showed sulcal effacement and parenchymal hypoattenuation in the left frontal lobe but no hemorrhage. Chest radiograph revealed generalized increased pulmonary infiltration, consistent with acute pulmonary edema (Figure 2A). Chest CT disclosed marked peripheral interlobular septal thickening and diffuse ground glass opacities mixed with consolidation in both lungs (Figure 2B). Repeat



Figure 1. Computed tomography angiography revealed absence of one branch of the M3 segment of the left middle cerebral artery and decreased flow and caliber of the rest left MCA branches.

ECG and blood tests including cardiac enzymes were within normal limits. Echocardiography showed regional wall motion abnormality and decreased left ventricular systolic function (ejection fraction=43%).

With appropriate diuresis and mechanical ventilation, the patient’s respiratory distress resolved within 48 hours. There were no more pulmonary infiltrations on repeat chest radiography. Magnetic resonance imaging of brain obtained 4 days after stroke onset showed left insula, frontal, temporal and parietal lobes infarction (Figure 3). Antiplatelet agent was

prescribed for secondary stroke prevention. She was discharged with improved NIHSS=7 without respiratory complaints.

DISCUSSION

Neurogenic pulmonary edema is a syndrome characterized by acute pulmonary edema following a CNS insult. Any acute CNS insult can lead to pulmonary edema.^{1,2} The severity and acuity of the insult may play an important role.¹ Ischemic stroke is a rare cause of NPE. Only a few cases of NPE after acute ischemic stroke have been reported in the English literature (Table 1).⁹⁻¹⁴

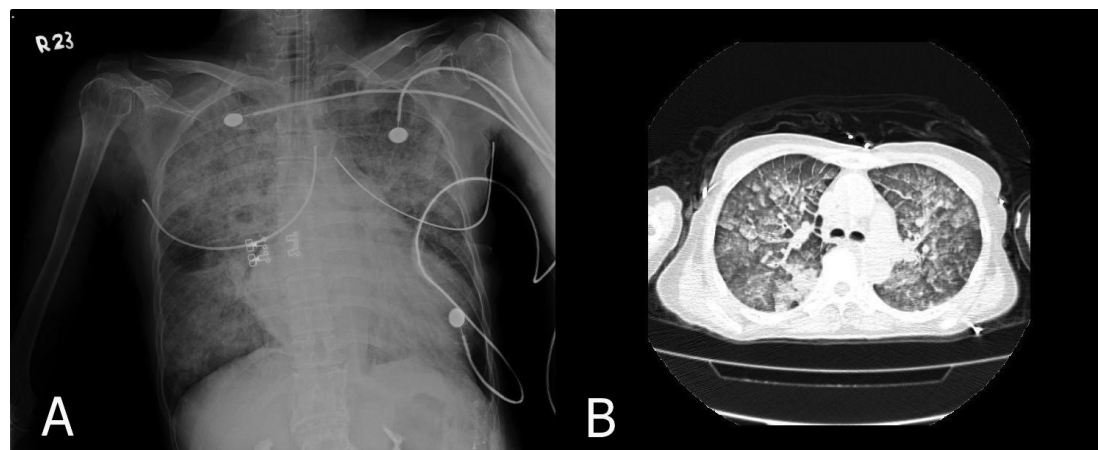


Figure 2. (A) Chest radiography showed generalized increased pulmonary infiltration. (B) Chest computed tomography showed marked peripheral interlobular septal thickening and diffuse ground glass opacities mixed with consolidation in both lungs

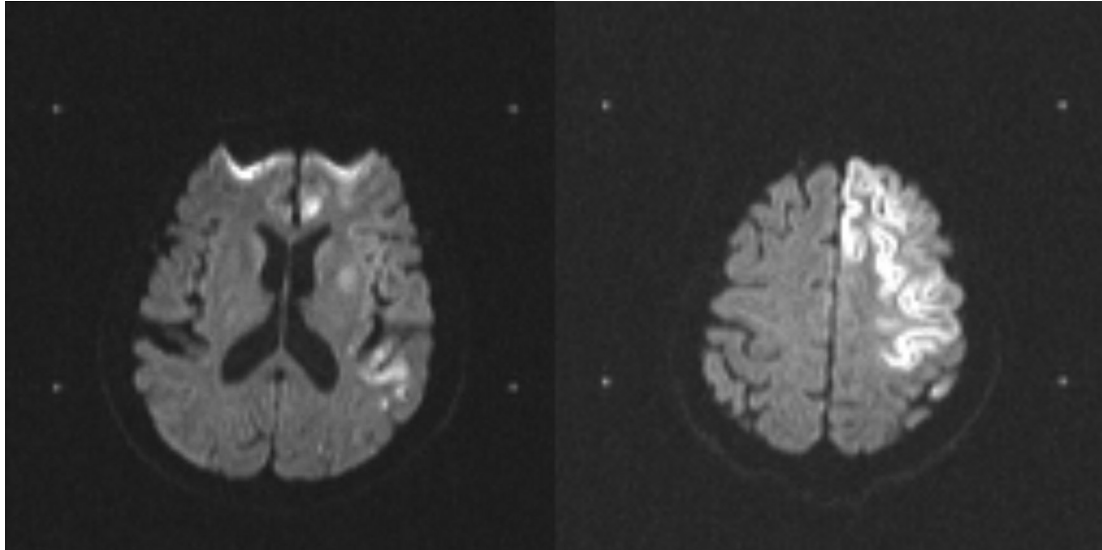


Figure 3. Diffusion-weighted magnetic resonance imaging of brain revealed left insula, frontal, temporal and parietal lobes infarction.

Most cases reported have large or brainstem infarction. With proper and timely management, the recovery is good in the majority of surviving patients.

The exact mechanism of NPE is not clear. Neurologic insults that cause sudden and severe intracranial pressure (ICP) elevation pose the greatest risk. Elevated ICP leads to neuronal compression or ischemia, activation of the sympathetic nervous system, and the release of catecholamines that can lead to cardiopulmonary dysfunction.^{1,2} Certain brain regions have been implicated in the genesis of sympathetic hyperactivity, including insular cortex, hypothalamus, and medulla.^{1,15} Insular cortex lesion is associated with both NPE and cardiac abnormality (stunned myocardium) while hypothalamus and medulla lesions are more likely to cause isolated NPE.¹⁵ In our case,

the elevated ICP caused by MCA infarction and the involvement of the insular cortex most likely resulted in the both NPE and cardiac abnormality.

The pathogenic mechanisms is believed to occur at the level of pulmonary vascular endothelium but remains unclear. Several theories have been proposed, such as direct myocardial injury caused by a surge in catecholamines (Neuro-cardiac NPE); direct pulmonary vascular bed injury caused by massive sympathetic discharge (Pulmonary venule adrenergic hypersensitivity); indirect left ventricular failure caused by increased systemic and pulmonary pressures after catecholamine surge (Neuro-hemodynamic NPE); and high hydrostatic pressure and pulmonary endothelial injury caused by catecholamine surge (Blast theory).¹

Table 1: Summary of studies reporting neurogenic pulmonary edema after acute ischemic stroke

Study	Year	Age	Gender	Stroke location	Outcome
L'e Orme <i>et al.</i> ⁹	1999	34	Male	Bilateral cerebellum and right medulla (VA dissection)	resolved
Tan <i>et al.</i> ¹⁰	2007	57	Female	Right MCA	resolved
Seow <i>et al.</i> ¹¹	2007	52	Male	Left hemisphere (ACA+MCA)	mortality
Marshall <i>et al.</i> ¹²	2009	41	Female	Pons, cerebellum and bilateral PCA (BA dissection)	resolved
Gupta <i>et al.</i> ¹³	2012	48	Female	Left cerebellum	resolved
Devos <i>et al.</i> ¹⁴	2012	44	Female	Right hemisphere	mortality

VA, vertebral artery, MCA, middle cerebral artery, ACA, anterior cerebral artery, PCA, posterior cerebral artery, BA, basilar artery

NPE usually occurs within minutes to hours after a CNS insult. Clinical symptoms and signs of NPE are non-specific; although dyspnea, tachypnea, tachycardia, cyanosis, pink frothy sputum, basal pulmonary crackles and rales are common features of NPE.^{1,2} Chest radiograph typically shows bilateral diffuse alveolar infiltrates. With appropriate treatment, NPE often resolves within 48 to 72 hour.^{1,2} The initial management should focus on treating the underlying neurological insult. Most NPE patients require supplemental oxygen or mechanical ventilation. Several medications such as alpha adrenergic blockers have been used to treat NPE but their efficacy has not been established.^{16,17} The role of rt-PA in our case is unclear. The follow-up magnetic resonance angiography (MRA) showed recanalization of the left MCA branches. The thrombolytic therapy may have helped to reduce the intracranial pressure, and hereby improve recovery.

Diagnosis of NPE is difficult because of its relatively unpredictable nature and lack of specific signs and diagnostic tests. Differential diagnoses include aspiration pneumonia, congestive heart failure, acute respiratory distress syndrome and ventilation-induced lung injury.^{1,2} In the present case, complications of thrombolytic therapy that may cause disturbance of consciousness and respiratory distress like intracranial hemorrhage, systemic hemorrhage, and severe orolingual angioedema should also be excluded.^{18,19} Physical examinations, prompt imaging, laboratory studies and a high index of suspicion can help to establish the correct diagnosis. Our patient presented with typical NPE symptoms and signs without evidence of congestive heart failure, fluid overload, aspiration pneumonia or other systemic cause for the pulmonary edema.

In conclusion, NPE is a rapidly developing and sometimes life-threatening complication of CNS insult. Physicians should remember this clinical entity when caring for patients with acute respiratory distress following neurologic events to avoid misdiagnosis and unfavorable outcomes.

DISCLOSURE

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