

Mechanisms of disease/hypothesis: Neurogenic left ventricular dysfunction and neurogenic pulmonary oedema

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Hypothese: Neurogen-induzierte linksventrikuläre Funktionsstörung und neurogenes Lungenödem

Zusammenfassung. Grundlagen: Das Auftreten kardiovaskulärer Funktionsstörungen kann durch eine akute Störung des zentralen autonomen Nervensystems verursacht werden. Die Inselregion, der laterale Hypothalamus sowie der Hirnstamm stellen wichtige Schaltzentralen innerhalb des zentralen autonomen Netzwerkes dar. Der Hirnstamm spielt eine entscheidende Rolle in der Kontrolle und Regulation des Funktionszustandes des autonomen Nervensystems.

Patienten und Methodik: Fallberichte.

Ergebnisse: Unsere beiden Fallberichte zeigen die innigen Verbindungen zwischen dem kardiovaskulären und pulmonalen System einerseits und dem zentralen Nervensystem andererseits. Bei einem 13-jährigen Mädchen mit einer okzipital lokalisierten zerebralen Angiomasose kam es nach einer Blutung im Bereich der Pons zum plötzlichen Einsetzen einer hochgradigen linksventrikulären Funktionseinschränkung mit konsekutivem Lungenödem. Ein 5-jähriges Mädchen entwickelte ein neurogen-induziertes Lungenödem im Rahmen eines Status epilepticus.

Schlussfolgerungen: Diese beiden Kasuistiken deuten darauf hin, dass eine zentral ausgelöste linksventrikuläre Funktionsstörung und das neurogen-induzierte Lungenödem keine separaten Krankheitsentitäten sind, sondern möglicherweise zwei verschiedene Erscheinungsformen einer zentral ausgelösten Funktionsstörung des autonomen Nervensystems darstellen.

Schlüsselwörter: Autonomes Nervensystem, linksventrikuläre Funktionsstörung, neurogen-induziertes Lungenödem, Reanimation

Summary. Background: Acute onset of cardiovascular dysfunction may be the result of insults to the central nervous and autonomic system. Several cerebral regions (insular cortex, lateral hypothalamus, and brain stem) have been identified as part of the “central autonomic network”. The brain stem plays an integral role in controlling and mediating autonomic tone.

Patient and methods: Case reports.

Results: These two case reports demonstrate the intimate connectivity between the cardiovascular/pulmonary system and the central nervous system in a 13-year-old girl with occipital angiomasosis, but no history of heart disease who developed profound left ventricular dysfunction and pulmonary oedema following pontine haemorrhage, and in a 5-year-old girl who developed severe pulmonary oedema after suffering from status epilepticus.

Conclusions: The two case reports suggest that cardiovascular dysfunction secondary to central nervous insults and neurogenic pulmonary oedema are not two separate clinical entities, but may very well encompass two different presentations of central autonomic disturbances.

Key words: Autonomic nervous system, left ventricular dysfunction, neurogenic pulmonary oedema, resuscitation

Introduction

Acute cerebrovascular disease may alter cardiovascular and autonomic function [1]. Clinical studies have shown that acute cerebral lesions (stroke, haemorrhage, etc.) may induce changes in cardiac function including hypertension, arrhythmias, myocardial necrosis and sudden death [2, 3]. Moreover, experimental and clinical studies indicate that damage to the insular cortex, the amygdala, lateral hypothalamus, and the

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brain stem is likely to cause disturbances in either sympathetic or parasympathetic autonomic function with subsequent cardiac compromise [4–6].

Here we report on two patients with cardiopulmonary dysfunction following a cerebral insult: A 13-year-old adolescent developed acute and profound cardio-circulatory compromise and pulmonary oedema because of pontine haemorrhage secondary to extra- and intracranial angiomas with extension into the brain stem; a 5-year-old girl suffered severe pulmonary oedema following status epilepticus.

Case reports

Case 1: A 13-year-old, previously healthy girl with a long-standing history of an extra- and intracranial occipital angiomas extending into the brain stem (Fig. 1) developed an acute, first ever episode of cardiovascular dysfunction requiring prolonged out-of-hospital cardiopulmonary resuscitation. On physical examination, the patient had bilateral rales, and large amounts of secretions were suctioned through the endotracheal tube. On admission to our hospital, the patient was severely bradycardic (19 bpm), and hypotensive (blood pressure not measurable) despite repetitive doses of epinephrine and atropine. Blood gas analysis demonstrated severe combined metabolic and respiratory acidosis (pH: 6.9; pCO₂: 83 mmHg, pO₂: 54 mmHg; base excess: 17 mmol/l; serum lactate: 133.9 mg/dl (normal: <20 mg/dl). Oxygen saturation was 78% with FiO₂ of 100%. The findings on chest X-ray were compatible with pulmonary oedema.

On initial echocardiography, a structurally normal heart was seen. Left ventricular end-diastolic diameter

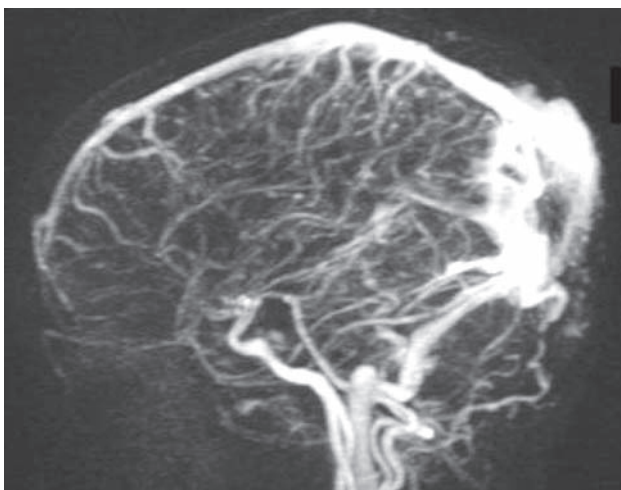


Fig. 1: Angiography showing extensive occipital angiomas (patient 1)

(LVEDD) was at the upper limit for age (44–48 mm) with marked depression of left ventricular function (shortening fraction: 10%). The velocity time integral (VTI) of the ascending aorta was low (15–18 cm). The left atrium was enlarged with poor pulmonary venous return and pulmonary venous dilatation. On echocardiography, no signs of pulmonary hypertension (tricuspid valve regurgitation) were noted. In addition, she suffered from pulmonary oedema secondary to left ventricular depression with low cardiac output syndrome. ECG recordings showed sinus rhythms without ST-segment elevation, Q-waves or QT-prolongation. Laboratory studies (troponin T, CK, LDH) did not confirm the diagnosis of myocardial infarction. After the administration of epinephrine, norepinephrine and dobutamine arterial blood pressure normalised.

On MRI studies an intracranial haemorrhage was noted within the brain stem (Fig. 2) as the most likely cause of the sudden onset of cardiac dysfunction; a cerebral herniation and intracranial hypertension were excluded. As the occipital angiomas had remained unchanged for several months prior to this acute episode, it is unlikely that the vascular malformation itself caused left ventricular dysfunction. A myocarditis by cardiotropic viruses (German measles, measles, cytomegaly virus, herpes simplex virus, Epstein-Barr virus, varicella virus, parvo virus B19, adeno virus, and enterovirus) were excluded by serological and PCR studies), myocardial infarction as well as other medical conditions possibly causing left ventricular dysfunction (e.g., toxic, electrolyte imbalances) were ruled out by adequate means (serum chemistry and toxicological examination

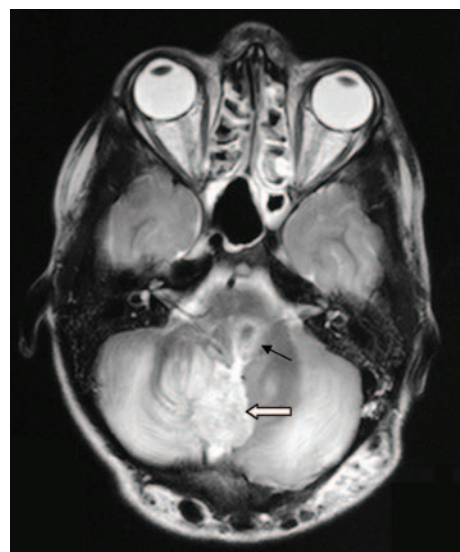


Fig. 2: MRI demonstrating occipital extra- and intra-cranial angiomas (patient 1) extending into the brain stem (white arrow) and pontine hemorrhage (black arrow)

of blood and urine). Initial coagulation studies were normal except for an INR of 1.62.

Five days after admission the inotropes could be weaned; two weeks later the patient was extubated. On follow-up echocardiography (after 5 days), left ventricular contractility was normal. After resolution of the haemorrhage the patient suffered from spastic tetraplegia and dysphagia.

Case 2: A 5-year-old girl who was born as a premature infant with a history of an intracranial haemorrhage and left-sided hemiparesis developed a focal seizure with secondary generalization. Despite repetitive administration of diazepam by an emergency physician the seizure progressed to status epilepticus. After approximately 45 min. seizure activity had ceased. However, the patient developed respiratory insufficiency and the trachea had to be intubated. Following intubation, large amounts of blood-stained secretions (approximately 500 ml) had to be suctioned through the endotracheal tube. There was no evidence for pulmonary aspiration. The patient developed cardio-circulatory failure requiring the administration of epinephrine and norepinephrine. On conventional chest radiographs, bilateral pulmonary oedema was noted (Fig. 3). Prior to commencing inotropes echocardiography demonstrated moderate depression of left ventricular function with a shortening fraction of 20%. LVEDD and pulmonary venous return were normal. After continuing intensive care treatment, including positive pressure ventilation and administration of inotropes, the patient's clinical condition improved rapidly, and she

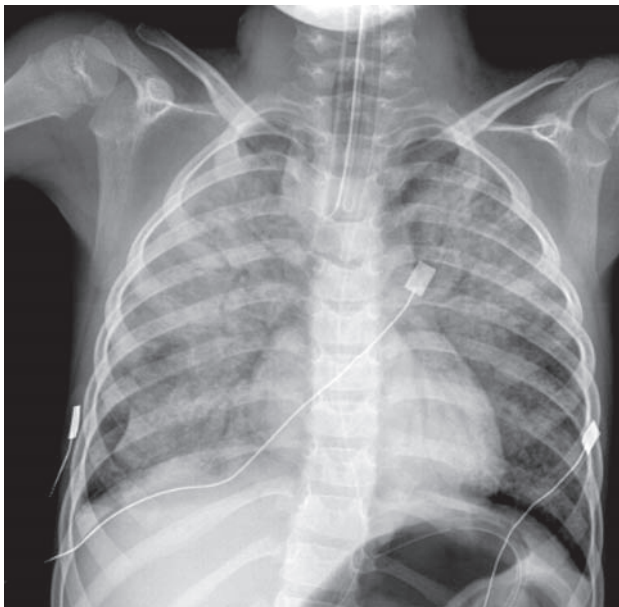


Fig. 3: Chest X-ray showing bilateral pulmonary oedema requiring positive pressure ventilation (patient 2)

was extubated on day 2. LV function had normalized with a shortening fraction of 42%. On MRI studies, an intracranial hemorrhage, cerebral infarction and an infectious etiology was ruled out. Microbiology testing (including cerebrospinal fluid) was unremarkable. As in case 1, other possible causes for left ventricular dysfunction were excluded by adequate means (for detail please compare patient 1).

Discussion

There is a growing body of evidence from animal and clinical studies that cerebrovascular disease alters cardiovascular and autonomic function [1]. Several investigations in humans have shown that acute cerebral lesions (stroke and hemorrhage) may induce changes in cardiac autonomic control which in turn may cause hypertension, arrhythmias, myocardial necrosis and even sudden death [2, 3]. Distinct cerebral regions have been implicated in the genesis of the pathological activation of the autonomic nervous system [4]. Experimental data indicate that the insula, the amygdala, lateral hypothalamus, and the brain stem play a crucial role in the autonomic control of the heart [5]. Cardio-autonomic dysfunction is mediated either directly via modulation of the sympathetic activity or by alterations of the parasympathetic activity with a reciprocal shift in sympathetic function. Experimental studies have so far yielded contradictory data, and are not conclusive [6].

An important differential diagnosis that has to be taken into account in our patients is primary neurogenic pulmonary oedema with concomitant cardiovascular dysfunction. Neurogenic pulmonary oedema is usually defined as an acute pulmonary oedema occurring shortly after a central neurologic insult [7]. It has been reported in various injuries of the central nervous system (stroke, hemorrhage, seizures, etc.) in both adults and children, but remains poorly understood because of the complexity of its pathophysiologic mechanisms, involving both hemodynamic and inflammatory aspects. The hemodynamic mechanism is usually referred to as the "blast theory". A sudden increase in intracranial pressure induces a α -adrenergic catecholaminergic response with transient but substantial increases in both pulmonary and systemic vasoconstriction in the veins or arteries [7]. The subsequent increase in pulmonary vascular pressure induces an alteration of the Starling forces in the lungs, with a shift of fluids into the pulmonary alveoli and the interstitial spaces. Hydrostatic oedema usually develops when the transmural pressure

exceeds 40 mmHg, initially resulting in damage to the pulmonary capillary endothelium, followed by injury to the basement membrane of the alveolar capillaries and, finally, injury to the alveolar epithelium, resulting in a leakage of red blood cells and proteins into the alveolar spaces [8]. The changes in pulmonary circulation may be associated with a simultaneous cardiac insult in susceptible individuals, especially in patients with pre-existing heart disease [7]. However, the differential diagnosis of neurogenic pulmonary oedema in patient 1 seems less probable as an intracranial hypertension was excluded, and the patient did not have a previous history of heart disease. Conversely, in patient 2 the diagnosis of neurogenic pulmonary oedema seems more likely as the initial presentation was pulmonary oedema followed by moderate cardiovascular dysfunction. However, a clear-cut distinction between primary cardiac and pulmonary dysfunction seems somewhat arbitrarily. As a matter of fact, these two case reports may reflect two different presentations of one distinct clinical entity.

In summary, our case reports illustrate the intimate connectivity between the brain and the cardiovascular and respiratory system. It is important to consider insults to the central nervous system (an intracranial hemorrhage, cerebral infarction, seizure, etc.) as a cause for acute onset of cardio-circulatory and respiratory compromise (neurogenic pulmonary oedema) even in

young patients. These complications are attributed to damage to the central autonomic network [1–6]. The treatment is largely supportive, and includes positive pressure ventilation and the administration of inotropes as required.

Conflict of interest

The authors declare that there is no conflict of interest.

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