Unusual causes of acute pulmonary oedema

The mortality of acute pulmonary oedema remains high. Pulmonary oedema is clinically defined as an excessive, diffuse accumulation of fluid in the tissues and alveolar spaces of the lung. Pulmonary oedema can be broadly divided into four categories: hydrostatic oedema, permeability oedema caused by lung injury (acute respiratory distress syndrome), permeability oedema without lung injury, and mixed hydrostatic and permeability oedema [1]. Under normal circumstances, oedema formation does not occur, because the adequate gradient of hydrostatic and osmotic forces is preserved, microvascular and alveolar barriers are intact, and liquid-clearance pathways function properly [2]. In a pathological state, excessive fluid begins to accumulate in the interstitial spaces and the alveoli. Then gas exchange becomes impaired [2,3]. The main causes of acute pulmonary oedema include cardiac disorders (e.g. left ventricular failure, acute left ventricular ischaemia, accelerated or malignant hypertension etc.), sepsis and sepsis syndrome, acid aspiration, near-drowning, pancreatitis, air or fat emboli, cardiopulmonary bypass, pneumonia, drug reaction or overdose, smoke inhalation and reperfusion injury [4,5]. In an emergency department setting, acute pulmonary oedema is most frequently associated with cardiac disease. Acute cardiogenic pulmonary oedema, in fact, is very common [6–8]. Accordingly, Edoute et al. [8] reported that acute myocardial ischaemia and cardiac arrhythmias were among the most common precipitating factors of pulmonary oedema in elderly patients hospitalized in an internal medicine department.

It is essential to bear in mind that acute pulmonary oedema is one of the most common medical emergencies and very frequently can be fatal. Thus the treatment must start as soon as the diagnosis is made. The identification of patients at risk for developing pulmonary oedema is, therefore, of critical importance. Since the primary cause of acute pulmonary oedema is cardiac disease, the physician should be careful not to misdiagnose respiratory problems in the absence of cardiac disorders. Awareness of other common or even more importantly less common underlying conditions can be a matter of life and death. The clinical assessment is frequently complicated by the fact that patients may have cardiac and other relevant disease concurrently. Furthermore, acute pulmonary oedema can start as a primary manifestation of an underlying disease or can evolve as a serious complication of an already established disease [2–4]. In this issue of the Clinical Science, Hsu and co-workers [9] discuss 18 rare cases of acute pulmonary oedema associated with Japanese B encephalitis, lymphangitis in breast carcinoma, fat embolism caused by long-bone fracture and rupture of cerebral mycotic aneurysm. The authors not only describe clinical manifestations of these disorders, but also attempt to define mechanism of pulmonary oedema development in each disease.

The rationale for this study stems from previous clinical reports and animal studies, including several from Hsu and co-workers, describing unusual causative conditions of acute pulmonary oedema [10–16]. On admission, lungs of all patients were clear (chest X-rays did not reveal any abnormalities). The patients also underwent routine in addition to specialized tests. The latter included measurements of plasma non-esterified fatty acids, cGMP, serotonin and nitrate/nitrites [9]. These factors were chosen on the basis of published observations indicating their participation in the pathogenesis of pulmonary oedema [13,14]. All patients developed dyspnoea, cyanosis, generalized weakness and heart arrest within 7 days of hospitalization, and subsequently died. Pulmonary arterial pressure was higher than normal, and post-mortem lung mass increased substantially in all patients [9]. Occurrence of pulmonary oedema associated with increased arterial pressure is well documented in both clinical and animal studies [17,18].

To my knowledge, Hsu et al. [9] are the first to describe the development of acute pulmonary oedema in patients with Japanese B encephalitis. All six patients studied had viral infection localized in the medulla [9]. The authors suggest that pulmonary oedema in the viral infections involving the lower brain stem [9,12] may be caused by excessive activation of the sympathetic system due to impairment of depressor functions in the medulla based on the earlier work from this laboratory [10,11,16].

Similarly novel is the observation that rapid development of acute pulmonary oedema in another group of patients was due to rupture of cerebral mycotic aneurysms. These patients had uncontrolled high blood pressure over a long period of time. Intracranial pressure was also significantly elevated when oedema occurred [9]. Since previous studies [10,11,16] revealed that rupture of mycotic aneurysms triggers cerebral compression which in turn causes pulmonary oedema, the authors postulate that the mechanism of oedema development in this group of patients may be similar [9].

Pulmonary oedema associated with breast carcinoma and concurrent lymphangitis has also not been described before. Two patients were included in this group, and they presented with jaundice, pleural effusion, ascites and disseminated intravascular coagulation. According to the authors, oedema formation may be triggered by blockage of lymphatics, capillaries and venules in these patients [9].

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Fat embolism is a well-recognized causative factor for pulmonary oedema [13]. However, causes of pulmonary insufficiency associated with this disease have not been thoroughly studied. Plasma levels of non-esterified fatty acids, cGMP, serotonin and nitrates/nitrites were significantly increased in all six patients with fat embolism [9]. The authors stipulate that these mediators may be involved in the pathogenesis of pulmonary oedema in fat embolism. They specifically focus on the possibility that nitric oxide may cause pulmonary oedema. Their previous study showing that nitric oxide was toxic to the lung supports this hypothesis [14].

In summary Hsu and co-workers 'bring to light' rare, but by no means not less important, cases of acute pulmonary oedema. By doing so they remind us how wide-ranging the underlying causes of acute pulmonary oedema are, and how elusive pinpointing patients at risk may be. Furthermore, the authors make effort to define causative factors for oedema. Although their observations are still preliminary, Hsu et al. [9] pave the path for other scientists in the field. The findings presented in the article give a new direction to research on mechanisms of acute pulmonary oedema of unusual causes.

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REFERENCES