J Forensic Sci, July 2007, Vol. 52, No. 4
doi: 10.1111/j.1556-4029.2007.00495.x
Available online at: www.blackwell-synergy.com

Commentary on: Tuemer AR, Dener C. Diagnostic dilemma of sudden deaths due to acute hemorrhagic pancreatitis. J Forensic Sci 2007;52:180–2.

Sir:

In a recent review of autopsy cases, 11/12 patients with sudden death due to acute hemorrhagic pancreatitis were found to have pulmonary edema as an associated finding (1). The authors concluded that forensic pathologists should consider pulmonary damage in such cases. Pancreatitis is associated with hypercytokinemia (2). It recently emerged that conditions associated with a severe systemic inflammatory response due to hypercytokinemia and without primary pulmonary focus may be associated with pulmonary edema. Pulmonary edema has thus been associated with blood transfusions following a severe trauma not involving the lung (3), diabetic ketoacidosis (4,5), meningococcal septicemia (6) and the direct stimulation of T cells by a monoclonal antibody releasing large amounts of cytokines (7).

The mechanism of pulmonary edema induction involves the down regulation of the expression and function of alveolar epithelial cystic fibrosis transmembrane conductance regulator (CFTR) chloride channel, epithelial sodium channels (ENaC), and sodium potassium ATPase (Na/K ATPase) which mediate ion and associated fluid transport in the lung, by cytokines like tumor necrosis factor and interleukin-1 (8). CFTR, ENaC, and Na/K ATPase mediate transport of sodium and chloride into the basolateral compartment of alveolar epithelia where water follows the osmotic gradient through paracellular pathways and aquaporin channels.

It is important that pathologists are aware that any condition with a severe systemic inflammatory response may potentially be associated with life threatening pulmonary edema which may be a prominent finding on autopsy and otherwise difficult to explain.

References

1. Tümer AR, Dener C. Diagnostic dilemma of sudden deaths due to acute hemorrhagic pancreatitis. J Forensic Sci 2007;52:180–2.
2. Browne GW, Pitchumoni CS. Pathophysiology of pulmonary complications of acute pancreatitis. World J Gastroenterol 2006;12:7087–96.
3. Silliman CC. The two-event model of transfusion-related acute lung injury. Crit Care Med 2006;34:124–31.
4. Dixon AN, Jude EB, Banerjee AK, Bain SC. Simultaneous pulmonary and cerebral oedema, and multiple CNS infarctions as complications of diabetic ketoacidosis: a case report. Diabet Med 2006;23:571–3.
5. Hoffman WH, Burek CL, Waller JL, Fisher LE, Khichi M, Mellick LB. Cytokine response to diabetic ketoacidosis and its treatment. Clin Immunol 2003;108:175–81.
6. Eisenhut M, Wallace H, Barton P, Gaillard E, Newland P, Diver M, et al. Pulmonary edema in meningococcal septicemia associated with reduced epithelial chloride transport. Pediatr Crit Care Med 2006;7:119–24.
7. Suntharalingam G, Perry MR, Ward S, Brett SJ, Castello-Cortes A, Brunner MD, et al. Cytokine storm in a phase 1 trial of the anti-CD28 monoclonal antibody TGN 1412. N Engl J Med 2006;355:1018–28.
8. Eisenhut M. Changes in ion transport in inflammatory disease. J Inflamm (Lond) 2006;3:5.

Michael Eisenhut, M.D.
Luton & Dunstable Hospital NHS Foundation Trust
Lewsey Road
Luton LU 4 O DZ
U.K.
E-mail: michael_eisenhut@yahoo.com