An 8-yr-old, 20-kg girl was scheduled to undergo dental restorations and extractions as an outpatient. The patient had a history of seizures and multiple ischemic strokes secondary to Moyamoya disease. She had undergone three previous operations during general anesthesia, without anesthesia-related difficulties.

At the preoperative visit, she was aphasic and drooling. Significant left lower extremity weakness and diffuse fine motor deficits were also present, but the patient was ambulatory.

The patient received 10 mg midazolam via G-tube as premedication. After application of electrocardiogram leads and pulse oximetry, inhalational induction with 70% nitrous oxide in oxygen and halothane was begun. Within seconds after the start of induction, vigorous hiccups, which were accompanied by tracheal tugging, developed in the patient. Pulse oximetry showed a stable arterial saturation of 99-100% throughout induction, and capnography did not show impairment of gas exchange. Therefore, inhalational induction was continued, with the child breathing spontaneously. The strong hiccups never ceased during approximately 10 min of induction.

Finally, intravenous access was obtained and 20 mg rocuronium was administered intravenously. As neuromuscular blockade occurred, spontaneous ventilation and the hiccups stopped, and positive-pressure ventilation of the lungs was applied without difficulty. The trachea was intubated with an uncuffed 5.5-mm nasotracheal tube. Subsequently, the patient underwent mechanical ventilation with 1% isoflurane in an air-oxygen mixture. Fentanyl, 2 μg/kg, and 0.1 mg glycopyrrolate were administered intravenously, and the table was turned 90° for the dental procedure.

During the next 20 min, blood pressure readings by Dinamapp (Critikon, Tampa, FL) were erratic. The Dinamapp intermittently displayed unexpectedly high pressures between 165/100 and 130/100 mmHg but eventually failed after prolonged cycling. Peripheral pulses could not be palpated, but a Doppler probe placed over the left posterior tibial artery finally gave reproducible systolic readings between 90 and 120 mmHg. During the period of hemodynamic lability, increased oxygen requirements developed in the patient. Repeated chest auscultations revealed no evidence of wheezing or decreased or asymmetric breath sounds. The capnogram remained unchanged with end-tidal carbon dioxide values of 36-40 mmHg. After the oxygen requirements reached 100%, the dental procedure was interrupted. Endotracheal suction revealed more than 100 ml frothy pink fluid. Chest radiography confirmed moderate pulmonary edema with a central pattern and normal heart size (fig. 1B). No effusions or focal consolidations were present. Intraoperative transthoracic echocardiography showed good biventricular function but mild mitral regurgitation (+1) and mild pulmonary insufficiency.

The patient was administered a second dose of 15 mg rocuronium, and reintubation was performed with a cuffed tube. The patient was sedated with 2 mg lorazepam and 60 μg fentanyl and transferred to the intensive care unit for postoperative ventilation with positive end-expiratory pressure. No inotropic or vasoactive agents were administered at any time. A total volume of 800 ml lactated Ringer's solution was infused over 4 h. The patient was extubated on the first postoperative day. Chest radiography showed almost complete resolution of the pulmonary edema and no focal areas of consolidation. The inspiratory oxygen requirement normalized. A neurologic examination did not show new deficits. Follow-up echocardiography showed resolution of all intraoperative abnormalities. Results of an allergy workup were negative for latex and ethylene oxide, but a skin-prick test showed a mild reaction to a 1:100 dilution of rocuronium (roc 1+, histamine 3+).

**Discussion**

This child presented with fulminant pulmonary edema that was most likely postobstructive and related to vigorous hiccups during inhalation induction.

Negative-pressure pulmonary edema (NPPE) occurs
soon after relief of acute or chronic obstruction of the upper airway. It is commonly reported after laryngospasm during induction or emergence from anesthesia. Markedly negative intrapleural pressures during airway occlusion cause increased venous return and increased left ventricular afterload. The increased hydrostatic pressure gradient in the pulmonary capillaries leads to transudation of fluid into the alveoli. Hypoxemia and a hypoxia-induced hyperadrenergic state further promote edema formation.

In this patient, the rapid appearance and resolution of edema with supportive respiratory therapy alone make NPPE likely. Lack of acidity of the suctioned fluid (pH 7.0) and the centrally and bilaterally symmetric pattern of the edema on the chest radiograph argue against any significant aspiration of gastric contents. The initial hypertensive phase and the complete absence of wheezing and other signs of anaphylaxis are inconsistent with an allergic reaction. In addition, results of the allergy workup for latex were negative and a second dose of rocuronium before reintubation was tolerated well.

The most important differential diagnosis to NPPE in this patient seems to be neurogenic pulmonary edema. Moyamoya disease is characterized by symmetric narrowing of the anterior and middle cerebral arteries and the formation of hemodynamically insufficient collateral networks. We were initially concerned that the hemodynamic lability in this patient with intracranial malformations could have caused cerebral edema and subsequent neurogenic pulmonary edema. Intraoperative hypertension in the absence of strong surgical stimuli has been described in patients with Moyamoya disease. Neurogenic pulmonary edema, however, usually has a prolonged course with high mortality, and our patient did not show any deterioration in neurologic status or evidence of cerebral edema after extubation.

However, the observed hemodynamic instability with peripheral vasoconstriction may be explained by a hyperadrenergic state that is associated with the development of postobstructive pulmonary edema. Hypoxia of the central nervous system is an important mediator for this reaction, and some central nervous system tissue hypoxia may have been present in this patient because Moyamoya disease impairs cerebral blood circulation.

Negative-pressure pulmonary edema has been described without any clinical evidence of airway obstruction, which suggests that obstructive events can be subtle. Our patient had vigorous hiccups during 10 min of spontaneous breathing that only ceased with neuromuscular blockade. Hiccups are brief, powerful inspiratory efforts synchronous with glottic closure. Studies in cats have shown that hiccups can cause negative intrathoracic pressures that are four times greater than during normal inspiration. Because NPPE can develop even after minor airway obstruction, we suggest that, in our patient, the continuous, forceful hiccups were sufficient to cause NPPE.
We believe this is the first reported case of NPPE associated with hiccups during inhalational induction of anesthesia. It is likely that more cases of unexplained perioperative hypoxemia are related to unrecognized NPPE. We suggest that prolonged vigorous hiccups in anesthetized, spontaneously breathing patients who are not intubated may not always be benign.

References