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Enhancement of hypoxemia by right-to-left atrial shunting in severe asthma

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Abstract. We report two cases of severe hypoxemia due to right-to-left shunt in acute asthmatic patients. During acute asthma, the transmural right atrial pressure can be higher than left atrial pressure during inspiration and then induce a right-to-left shunt through inter-atrial communication leading to hypoxemia. Contrast echography as well as Doppler analysis can easily confirm the diagnosis.

Key words: Right-to-left shunt – Patent foramen ovale – Asthma

A patent foramen ovale (FO) has been associated with severe hypoxemia in critically ill patients [1, 2]. Increased right atrial pressure may stretch the inter-atrial septum, reopen the FO and induce a right-to-left shunt. This can occur in clinical situations such as primary pulmonary hypertension [3], pulmonary embolism [4], mechanical ventilation with PEEP [5] or chronic respiratory insufficiency [6]. Similarly, left-to-right shunt through an inter-atrial communication can be reversed to right-to-left shunt if right atrial pressure becomes higher than left atrial pressure. Then it can induce hypoxemia. To our knowledge such a mechanism has not been previously reported to explain hypoxemia during severe asthma.

Case reports

Patient 1

A 33-year-old woman was admitted for status asthmaticus requiring intubation and mechanical ventilation. Her blood gas analysis on FIO_2 0.40 showed: pH = 7.33, PaO_2 = 17.3 kPa, $PaCO_2$ = 6.0 kPa. After sedation with flunitrazepam and fentanyl and curarization with pancuronium bromide, peak airway pressure was about 50 cmH_2O with a 7 ml/kg tidal volume. With aminophylline, terbutaline and corticosteroids, her condition rapidly improved and sedation could be discontinued. On the 4th day after admission, clinical examination was normal. Peak airway pressure was 25–35 cmH_2O. However, arterial blood gas analysis showed severe hypoxemia: PaO_2 = 7.6 kPa on FIO_2 = 0.40. Chest X-ray was normal (Fig. 1). On the 5th day hypoxemia worsened and neither an increase FIO_2 to 1 nor a rapid 500 ml colloid infusion improved PaO_2 as shown on Table 1. Pulmonary angiography was performed with the hypothesis of pulmonary embolism. During the procedure, the catheter easily crossed to the left atrium. After repositioning of the catheter pulmonary angiography was normal. Right cardiac pressure were not recorded. Despite persisting hypoxemia, the patient was weaned from the ventilator on the 7th day. Three days later PaO_2 returned to normal values. One month later a hemodynamic study was performed with a Swan-Ganz catheter, showing normal pressures and normal cardiac output. During the procedure the catheter moved into the left atrium.

Patient 2

A 20-year-old woman was admitted for a severe and persisting asthmatic crisis. She had a long history of asthma, but no crisis since one year without any treatment before admission. Initial examination showed

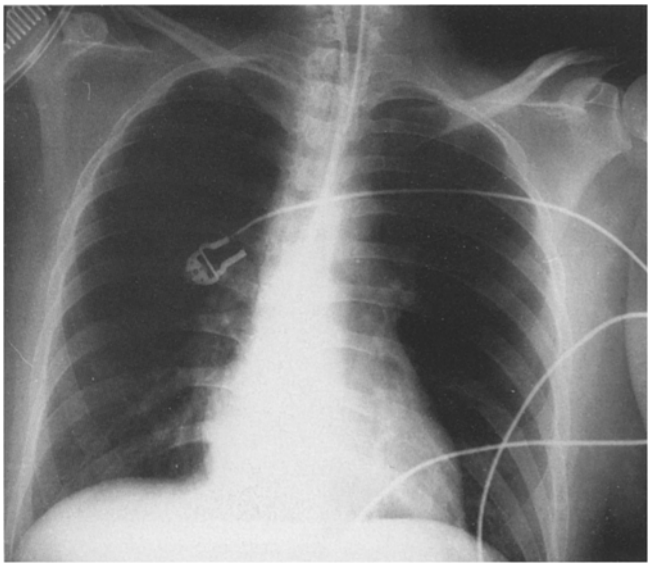

Fig. 1. Chest X-ray at Day 4 showing no abnormality whereas severe hypoxemia occurred

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Table 1. Blood gases after rapid 500 ml colloid infusion and with $FIO_2 = 1$ in patient

	$FIO_2 = 0.4$	$FIO_2 = 0.4 +$ fluid infusion	$FIO_2 = 1.0$
PaO_2 (kPa)	6.3	6.1	6.9
$PaCO_2$ (kPa)	4.88	4.85	4.38
pH	7.45	7.44	7.47
HCO^3 (mmol/l)	27	25	24

tachypnea, mild cyanosis, heart rate of 130 beats/min, and diffuse wheezing. Arterial blood gas analysis on room air showed: $PaO_2 = 6.8$ kPa, $PaCO_2 = 4.03$ kPa, and pH = 7.41. With terbutaline 0.5 mg/h IV and methylprednisolone 240 mg/day IV the clinical situation rapidly improved. However, severe hypoxemia persisted: $PaO_2 = 6.5$ kPa with 10 l/min of nasal oxygen administration. A rapid 500 ml colloid infusion did not modify hypoxemia. Four days later hypoxemia progressively and spontaneously decreased and the patient was discharged from the ICU. Echography showed normal right atrium and ventricle; left-to-right shunt was demonstrated by bubble contrast injection showing a filling defect inside the right atrium close to the FO; furthermore Doppler analysis showed a typical high-frequency flux through the inter-atrial septum (Fig. 2).

Retrospective analysis of 54 consecutive cases of severe acute asthma revealed unexplained persisting hypoxemia in 4 other cases. However, no cardiac echography was performed and we cannot conclude to right-to-left shunt in these patients.

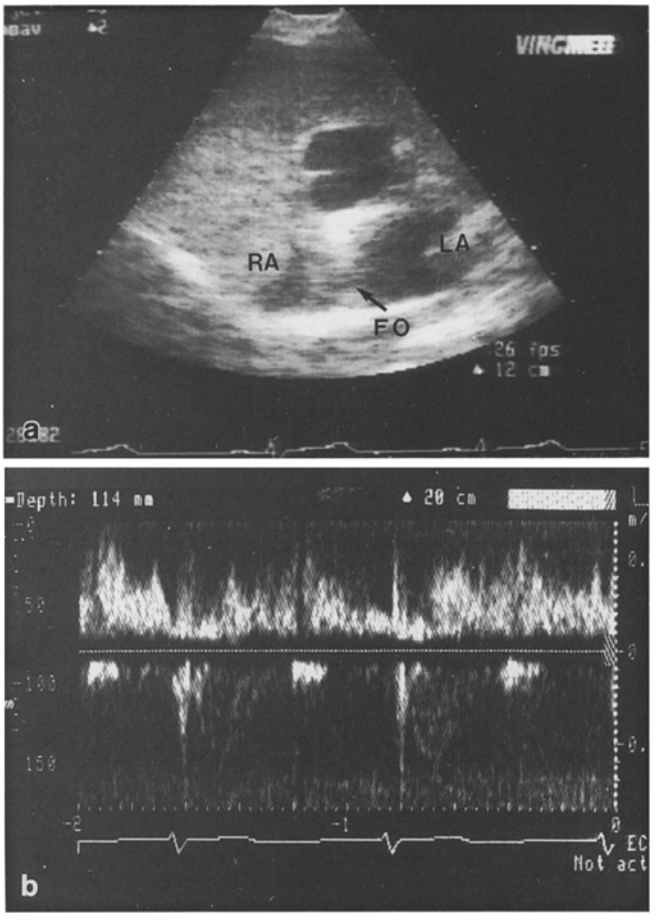

Fig. 2. **a** Contrast echography showing microbubbles and filling defect inside the right atrium close to the foramen ovale (*FO*). *RA*, right atrium; *LA*, left atrium. **b** Doppler showing high-frequency flux through the inter-atrial septum

Discussion

Persisting patent FO was found in about 30% of patients in autopsy studies [7]. In normal volunteers echography with bubble contrast study and sensitization by Valsalva maneuver or cough showed a patent FO in 10–18% [8–10]. This lower incidence could be due to a persisting left atrial pressure higher than the right atrial pressure, even during the Valsalva maneuver. The opening of FO could be responsible for paradoxical embolism [10] and right-to-left shunt with hypoxemia. This latter condition has been described in clinical situations with pulmonary hypertension, i.e. primary pulmonary hypertension [3], pulmonary embolism [4], cardiac transplantation [11], pulmonary hypertension associated with chronic respiratory insufficiency [6, 12], right ventricular infarction [13] or after lung resection [14]. In patients with patient FO, the aggravation of the deleterious effects of mechanical ventilation with PEEP have also been reported [1, 5]. A small atrial septal defect normally induces left-to-right shunt, however, this shunt can be reversed to right-to-left when right atrial pressure becomes higher than left atrial pressure thus inducing hypoxemia.

To our knowledge, hypoxemia due to right-to-left shunt and particularly to a patent FO has never been described previously in patients with severe asthma. During acute asthma, hypoxemia is mainly due to ventilation-perfusion mismatch [15]. β2 agonists could worsen hypoxemia by increasing pulmonary perfusion and maybe by inhibiting hypoxic vasoconstriction [16]. In ventilation-perfusion studies with inert gas techniques, no true shunt has been demonstrated [15]. However in these studies, asthma was not severe and the number of patients was small. During asthma, few hemodynamic studies have been performed showing that transmural right atrial pressure could be higher than left atrial pressure during inspiration [17]. This can explain a right-to-left shunting via a communication between the two atria. In our two cases, high levels of oxygen administration and fluid administration did not improve hypoxemia and therefore true shunt was suspected. In patient 1, in the absence of right atrial pressure measurement, we cannot explain why hypoxemia occurred whereas peak airway pressures had decreased probably leading to a decrease of transmural right atrial pressure. However, several cases of hypoxemia as a result of right-to-left shunt across a patent FO in the presence of normal right heart pressures have been reported [18, 19]. Inter-atrial shunt was evidenced: in the first case from easily crossing through the patent FO of the balloon catheter; in the second case from contrast echography and Doppler analysis. In this latter case, left-to-right shunt due to a minor inter-atrial communication was probably reversed to a right-to-left shunt during acute asthma. However since contrast echography or Doppler were not performed during the hypoxemic period, right-to-left shunt could not be demonstrated.

In conclusion, during asthma, right-to-left shunt must be suspected if hypoxemia persists during high FIO_2 inhalation test whereas clinical situation has improved. This can be easily confirmed by contrast echography or Doppler. In view of the incidence of about

20–30% of patent FO found in general population, this complication might not be infrequent during acute asthma. It should be of interest to recognize this cause of hypoxemia in asthmatic patients to avoid invasive procedures which could be considered in such situation.

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