explain this rapidly reversible pulmonary edema [1, 2]. In this case, hemodynamic data with WP values in the "upper normal", despite normal left cardiac function at echography and rapid clinical improvement in parallel with increased diuresis and a decrease in pulmonary wedge pressure (WP), suggest volume overload. The drop in hemoglobin without evidence of significant blood loss and the decrease in plasma proteins also suggest abrupt hemodilution, probably caused by fluid retention. The reduced colloid oncotic pressure we observed could also have contributed to the pulmonary edema. Biologic data support the hypothesis of hypotonic fluid retention.

The infusion of large volumes of isotonic saline in healthy young women should not lead to pulmonary edema. In pregnant women, however, aldosterone secretion is increased and can cause greater retention of sodium, especially in the 32nd week [3]. Moreover, tocolytic treatment results in further activation of an already activated renin-angiotensin system in pregnancy, as demonstrated by measurements of plasma renin activity, active renin concentration, and total renin concentration in these patients [4]. Finally, sympathomimetic agents increase the secretion of antidiuretic hormone, leading to water retention and hypotonicity [5]. These mechanisms, associated with decreased colloid oncotic pressure and fluid overload, may lead to pulmonary edema due to increased hydrostatic pressure.

In conclusion, β_2 -sympathomimetic treatment may cause pulmonary edema in pregnant women. Because this syndrome is likely due to increased pulmonary vascular hydrostatic pressure, we recommend close surveillance of the hydromineral balance in patients receiving this treatment. Early recognition of the syndrome and treatment consisting of withdrawal of tocolytics and forced diuresis assure a rapid recovery in the majority of cases.

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NO treatment in a patient with severe right-to-left shunt due to an intrapulmonary av-fistula

Received: 4 September 1995

Accepted: 21 May 1996

Sir: After minor dental surgery, a 36-year-old female developed a splenic abscess (*Streptococcus milleri*). She was treated in a primary care hospital by percutaneous drainage and broad-spectrum antibiotic therapy. Because of persistent sepsis (without signs of peritonitis) and progressive respiratory failure, the patient was transferred to our hospital and underwent splenectomy.

At postoperative admission to the ICU, we noted a systolic murmur in the right chest, turtleback-like fingernails and severe hypoxemia indicated by fractional inspired oxygen (FIO_2) 1.0, arterial oxygen saturation (SAO_2) 82%, partial pressure of oxygen in arterial blood (PaO_2) 47 mmHg, partial pressure of carbon dioxide in arterial blood ($PaCO_2$) 41 mmHg, base excess 0.3, bicarbonate 24.4 mmol/l, pH 7.39, volume controlled mechanical

ventilation, tidal volume 550 ml, frequency 15/min, positive end-expiratory pressure (PEEP) 5 cmH₂O, peak inspiratory pressure (PIP) 27 cmH₂O, plateau pressure 21 cmH₂O, fraction of end-tidal carbon dioxide ($F_{et}CO_2$) 4.2%. Despite the lack of a history of clinical symptoms like cyanosis, polycythemia, hemoptysis, and cardiac hypertrophy, the above findings and echocardiography (no patent foramen ovale was found) strongly suggested a pulmonary arteriovenous fistula. This was confirmed by X-ray computed tomography and angiography of the pulmonary arteries. The presumed shunt was found to be caused by an extensive arteriovenous fistula of the right lung (Fig. 1).

The hemodynamic profile, available during angiography and subsequent right heart catheterization, revealed the following (already under nitric oxide inhalation therapy (6 ppm), see below): FIO_2 1.0, SAO_2 87.7%, PaO_2 54.3 mmHg, $PaCO_2$ 36.5 mmHg, base excess -0.1, bicarbonate 24.2 mmol/l, pH 7.42, volume controlled mechanical ventilation, PEEP 5 cmH₂O, PIP 32 cmH₂O, plateau pressure 22 cmH₂O, pulmonary artery pressure 31/26 mmHg, left ventricular end-diastolic pressure 21 mmHg, mean arterial pressure 71 mmHg, cardiac output 5.64 l/min, mixed venous oxygen saturation 67%; the calculated shunt fraction was 48% of cardiac output.

Oxygenation was substantially improved by treatment with inhaled nitric oxide (NO, 1–6 ppm). Thus, SAO_2 immediately increased (from 76–87% to 95–97%), allowing for a gradual reduction in FIO_2 , as shown in Fig. 2. Owing to the improvement in oxygenation, NO was continually reduced and stopped on day 6 (oxygenation index 92 mmHg, FIO_2 0.6, SAO_2

Fig. 1 Contrast-enhanced scan of the lungs by computed tomography. Note the arteriovenous malformation in the right middle lobe (arrow) and small basal pleural effusions and atelectasis on both sides

Fig. 2 Oxygenation index ($\text{PaO}_2/\text{FiO}_2$, mmHg) versus time after the patient was admitted to the ICU

87%, PaO_2 56 mmHg, PaCO_2 38 mmHg, base excess 1.8, bicarbonate 25.8 mmol/l, pH 7.43, pressure assisted ventilation, tidal volume 580 ml, frequency 14/min, PEEP 5 cmH_2O , F_{etCO_2} 4.0%). The patient was then successfully weaned from the ventilator. Six months later, after the patient had fully recovered, her condition was treated by embolization of the malformation.

Delivery of NO was through a custom-built device placed in the inspiratory limb of a Bennett 7200 respirator. Inspiratory NO_2 and methemoglobin concentration were monitored and never exceeded 0.1 ppm and 1.5%, respectively. Inhaled NO has been reported to dilate selectively pulmonary vessels [1]. In addition to a reduction in pulmonary arterial pressure, a decrease in venous admixture, and thereby an increase in PaO_2 , has been reported [2]. Inhaled NO has also been reported to have beneficial effects in the adult respiratory distress syndrome (ARDS) [2]. The time course and dose-response curves of NO inhalation in rela-

tion to pulmonary hypertension in patients with ARDS were established by Gerlach et al. [3]. The concentration of inspiratory NO required for an improvement in oxygenation was in the range 0.1–10 ppm, similar to the concentrations used in our case. Inhaled NO has also been used to limit right-to-left shunt in a case of patent foramen ovale [4].

Our report demonstrates a beneficial effect of this therapy in a case where the underlying shunt is, at least in part, due to an arteriovenous malformation of the lung. Our patient was obviously well adapted to her presumably congenital fistula. She had led a normal life, participating in sports and giving birth to two children without ever experiencing any respiratory problems. The life-threatening hypoxemia in the course of her septic disease may have been due to either a systemic or a local inflammatory response, which impeded the adaptive hypoxic pulmonary vasoconstriction in the malformation or caused pulmonary vasoconstriction of previously healthy areas of lung (hypoxic vasoconstriction, disseminated occlusion of pulmonary microvasculature, increased release of vasoconstrictors or decreased release of vasodilators) together with an increase in oxygen consumption. Acting as a selective pulmonary vasodilator, NO improved oxygenation, possibly by diverting blood flow away from lung areas with shunt to normally ventilated lung [5].

In summary, we propose that inhalation of NO should be considered in patients with worsening oxygenation and a strong suspicion of a pulmonary shunt.

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