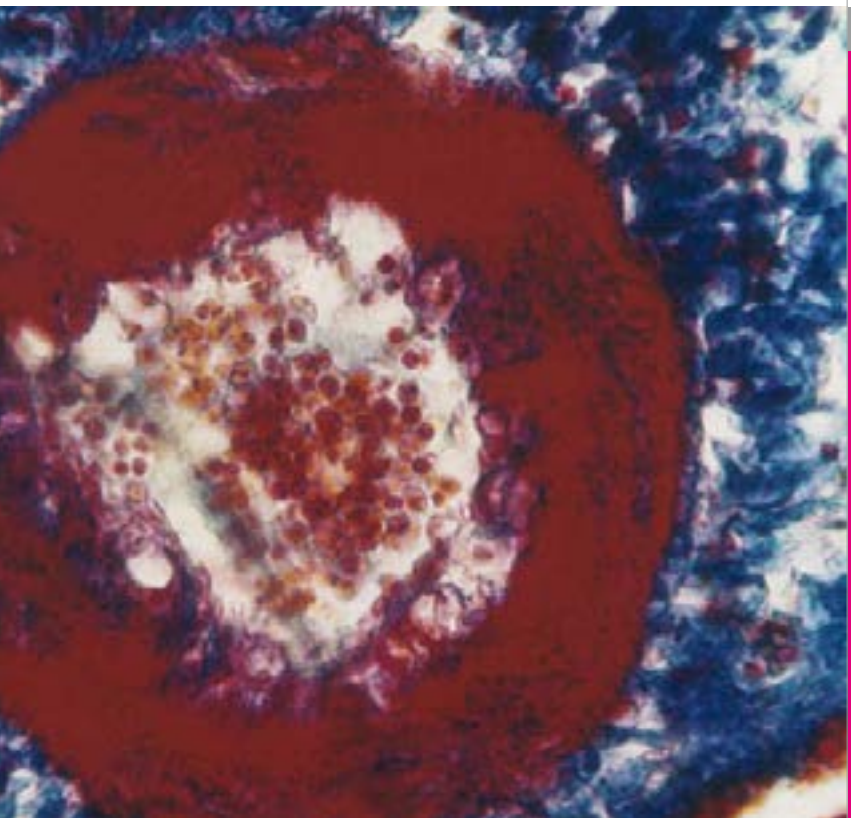
SWISS SOCIETY OF NEONATOLOGY

Preterm infant with pulmonary hypertension and hypopituitarism



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A female preterm infant was delivered at 31 1/7 weeks of gestation by cesarean section secondary to intrauterine growth restriction with oligohydramnion of unknown origin. Birth weigth was 1100 g (P3-10), length 38 cm (P10) and head circumference 26 cm (P<3).

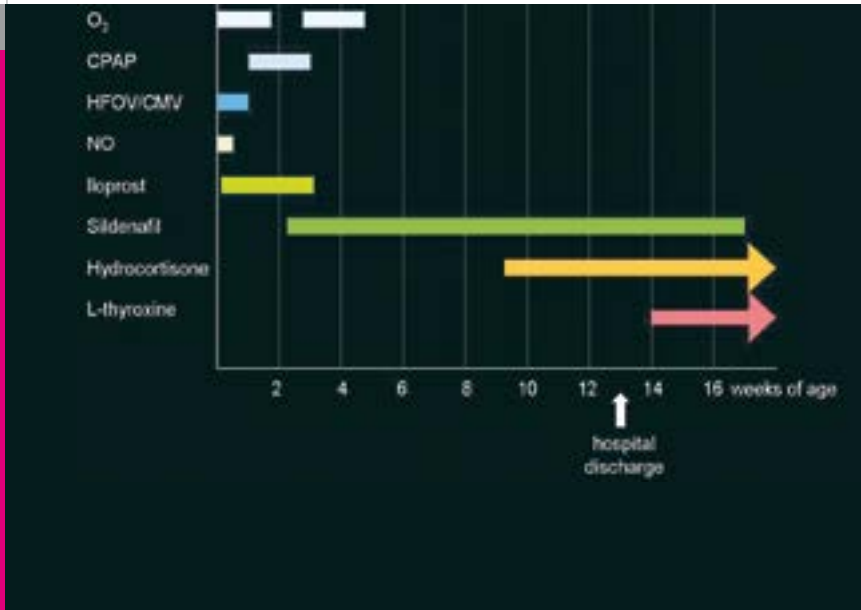
Because of severe respiratory distress she was intubated and surfactant was administered in the delivery room. Nevertheless, arterial oxygen levels remained low, and HFOV was started (FiO2 1.0, MAP 12.5 cmH2O, pO2 4.6 kPa, oxygenation-index (OI) = 36). When echocardiography confirmed severe pulmonary hypertension with suprasystemic pressures, inhaled nitric oxide (iNO) was started. Despite HFOV, iNO (maximal dose 40 ppm) and high doses of cardiovascular pressors (dopamine, dobutamine, epinephrine), oxygenation remained poor (at 24 hours of age: FiO2 1.0, MAP 8.6 cmH2O, pO2 5.4 kPa, OI = 22). At this point, iloprost (Ilomedin®) was added at a maximal dose of 16 nanogram/kg/min. This resulted in an immediate and sustained improvement of arterial oxygenation (at 36 hours of age: FiO2 0.4, MAP 7.0 cmH2O, pO2 7.6 kPa, OI = 5). Inhaled NO could be stopped on the 4th day of life and HFOV was changed to conventional mechanical ventilation. On the 8th day of life, extubation to NCPAP was possible. When dose reduction of iloprost resulted in a exacerbation of pulmonary hypertension, enteral sildenafil (up to 2 mg/kg/dose 6hrly) was started.

Subsequently iloprost could be stopped without recurrence of pulmonary hypertension (Fig. 1).

During the first month of life, the infant's growth was unsatisfactory (Fig. 2), and repeated episodes of hypoglycemia as well as persistent cholestasis were noted. Hypopituitarism with partial deficiency of ACTH leading to secondary adrenal insufficiency as well as a deficiency of growth hormone were diagnosed. In addition, the infant developed euthyroid sick syndrome with a slight deficiency of TSH. The MRI of the head showed hypoplasia of the pituitary (Fig. 3). When hydrocortisone was substituted (20 mg/m2/day) hypoglycemia and cholestasis disappeared.

Fig. 1

Treatment modalities used to control pulmonary hypertension.



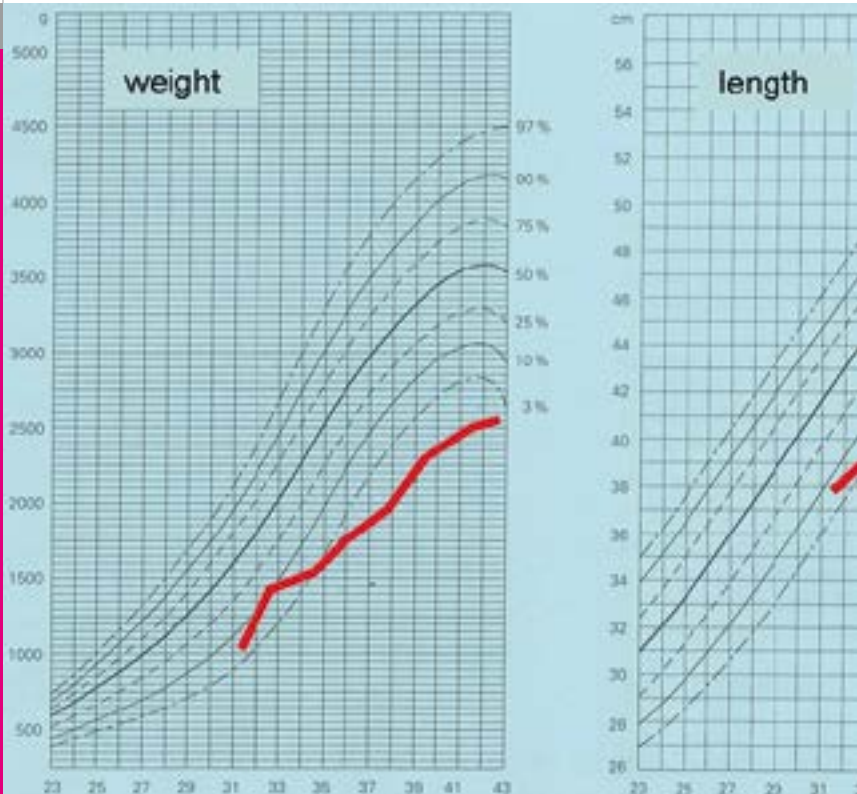
Several attempts to reduce sildenafil resulted in deterioration of pulmonary hypertension. Interestingly, when the child was started on L-thyroxine (25 mcg/day), pulmonary hypertension disappeared within 2 weeks (Fig. 1) and sildenafil could be weaned and discontinued after a total of 15 weeks of therapy. During the first year of life substitution with hydrocortisone and L-thyroxine was continued and pulmonary arterial pressures remained normal. Neuromotor development was normal at the age of 1 year.

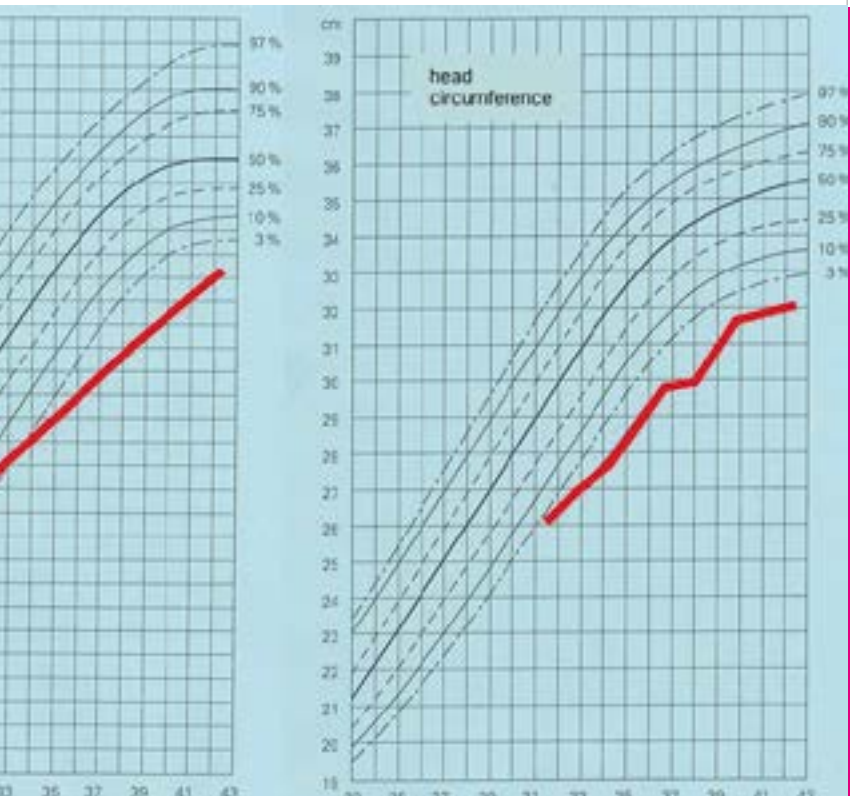
DISCUSSION

Persistent pulmonary hypertension of the newborn (PPHN) is characterized by severe hypoxemia shortly after birth, absence of cyanotic heart disease, and right-to-left shunting of blood across the ductus arteriosus and the foramen ovale. Management of pulmonary hypertension includes maintenance of adequate systemic blood pressure, sedation and analgesia, as well as ventilator and pharmacologic measures to optimize pulmonary vasodilatation. The first line therapy for pulmonary hypertension is inhaled nitric oxide (1). Sildenafil and prostacyclin (iloprost) are alternatives, but their safety and efficacy in the treatment of PPHN has not yet been established (2, 3). A potential synergistic effect on pulmonary vascular tone using these drugs in combination has been described (3). Inhaled NO promotes the conversion of GTP to cGMP. Sildenafil causes vasodilation by inhibition of phosphodiesterase which is the enzyme that breaks down cGMP. Prostacyclin (iloprost being a synthetic analogue) increases the level of cAMP.

Growth curves.

Fig. 2

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Congenital hypopituitarism is an uncommon cause of neonatal hypoglycemia and cholestasis, but deficiencies of cortisol and thyroid hormones may play a significant role in the developement of cholestasis (4). The combination of endocrinological abnormalities and PPHN is uncommon in the neonatal literature. In a case report, Oden described a newborn infant with neonatal thyrotoxicosis and PPHN (5). On the other hand, the prevalence of hypothyroidism in adult patients with primary pulmonary hypertension is high (6). The interaction of hormonal disturbances and pulmonary vascular pressure are not well understood. In an animal model, thyroid function has been shown to affect tissue levels of endothelin-1, a potent vasoconstrictor peptide, and Diekman and colleagues demonstrated increased peripheral vascular resistance in patients with hypothyroidism with normalization after restoration of an euthyroid state (7). In our case, pulmonary hypertension persisted for 3 months and disappeared within 2 weeks after substitution of L-thyroxine.

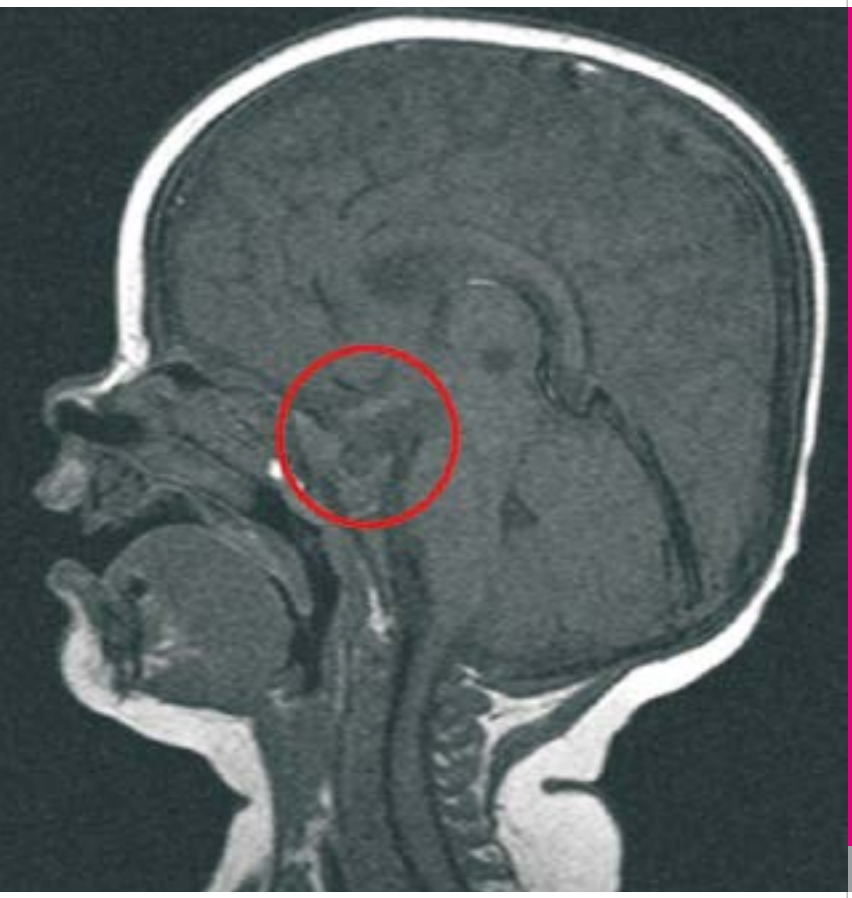

Fig. 3

MRI: Hypoplasia of the pituitary.

CONCLUSIONS

In the management of PPHN, there are potential synergistic effects with the combined use of nitric oxide and iloprost or sildenafil. Newborns with PPHN and recurrent episodes of hypoglycemia and persistent cholestasis should have an endocrinological work-up. We hypothesize that hypothyroidism may be a potentially treatable cause of or contributor to persistent pulmonary hypertension in the newborn and should be ruled out if conventional therapies fail.

1. Finer NN, Barrington KJ. Nitric oxide for respiratory failure in infants born at or near term. Cochrane Database Syst Rev 2006;(4):CD000399

2. Shah P, Ohlsson A. Sildenafil for pulmonary hypertension in neonates. Cochrane Database Syst Rev 2007;(3):CD005494

3. Konduri GG. New approaches for persistent pulmonary hypertension of newborn. Clin Perinatol 2004;3:591-611

4. Karnsakul W, Sawathiparnich P, Nimkarn S, Likitmaskul S, Santiprabhob J, Aanpreung P. Anterior pituitary hormone effects on hepatic functions in infants with congenital hypopituitarism. Ann Hepatol 2007;6:97-103

5. Oden J, Cheifetz IM. Neonatal thyreotoxicosis and persistent pulmonary hypertension necessitating extracorporal life support. Pediatrics 2005;115:e105-108

6. Curnock AL, Dweik RA, Higgins BH, Saadi HF, Arroliga AC. High prevalence of hypothyroidism in patients with primary pulmonary hypertension. Am J Med Sci 1999;318:282-292

7. Diekman MJ, Harms M, Endert E, Wieling W, Wiersinga WM. Endocrine factors related to changes in total peripheral vascular resistance after treatment of thyreotoxic and hypothyroid patients. Eur J Endocrin 2001;144:339-34615

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