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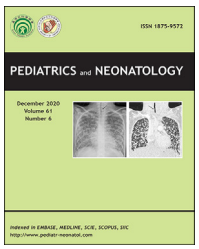

Letter to the Editor

Aggressive posterior retinopathy of prematurity in a preterm infant with congenital hyperinsulinemia without persistent hyperglycemia

Dear Editor,

Retinopathy of prematurity (ROP) is characterized by abnormal blood vessel growth in the retina of preterm infants.[1] Aggressive ROP (APROP) is the most severe form of ROP, which is predominantly found among the smallest neonates.[2] Prematurity and oxygen exposure are two major risk factors for ROP. Several studies have also reported hyperglycemia as a risk factor, but this was not confirmed in a recent meta-analysis.[3]

ROP has pathophysiological similarities to diabetic retinopathy. Hyperinsulinemia and hyperglycemia are reportedly involved in the development of diabetic retinopathy.[4] However, whether insulin independently affects ROP progression is unclear since insulin therapy is usually performed for preterm infants with persistent hyperglycemia. Herein, we report a case of transient congenital hyperinsulinemia and development of APROP within 1 month in a 27-week-old preterm infant.

A 34-year-old woman was referred to our institute at 27 weeks 4 days of gestation because of premature rupture of membranes. Subsequently, an emergency Cesarean section was performed at 27 weeks 5 days.

A female infant (birthweight 1155 g) was born not breathing. She was intubated 3 min after birth and treated with artificial pulmonary surfactant for respiratory distress syndrome. After admission, her cardiopulmonary status was stabilized by routine management.

To maintain blood glucose (BG) levels, intravenous glucose infusion was started with a 5 mg/kg/min of glucose infusion ratio (GIR). However, hypoglycemia had been prolonged; eventually, multiple doses of intravenous hydrocortisone in addition to GIR (12 mg/kg/min) were needed to maintain BG levels over 60 mg/dL. Finally, we diagnosed her with hyperinsulinemic hypoglycemia based on an elevated plasma insulin concentration (>1 μU/mL), which is inappropriate in the presence of hypoglycemia in infants receiving GIR of >8 mg/kg/min. Enteral feeding was started on day 4, her plasma insulin concentration decreased, and GIR was gradually reduced. She was extubated on day 14, and her respiratory condition was stable under continuous positive airway pressure. Her intravenous glucose infusion was discontinued on day 30.

On day 32, APROP was diagnosed at her first ophthalmological examination, and an intravitreal bevacizumab injection was administered on day 33. The posttreatment course was favorable, and no additional APROP treatment was required.

Hyperinsulinemic hypoglycemia was observed up to day 51, after which no hypoglycemic episodes were observed. Moreover, no persistent hyperglycemia ($\geq$150 mg/dL) was observed during treatment (Fig. 1).

Although insufficient evidence showed a relationship between ROP and insulin alone, a relationship between ROP and hyperglycemia has been discussed broadly. Intriguingly, Lee et al. retrospectively assessed extremely low birth weight infants and reported that while hyperglycemia alone was not associated with ROP, hyperglycemia requiring insulin treatment was significantly associated with the development of severe ROP.[5] This suggests that insulin therapy itself during hyperglycemia might be associated with the exacerbation of ROP. In our case, APROP was developed with hyperinsulinemia alone and without a hyperglycemic episode, supporting the premise of insulin's effect on ROP.

In conclusion, hyperinsulinemia may be a risk factor for the development of severe ROP, independent of the presence of hyperglycemia.

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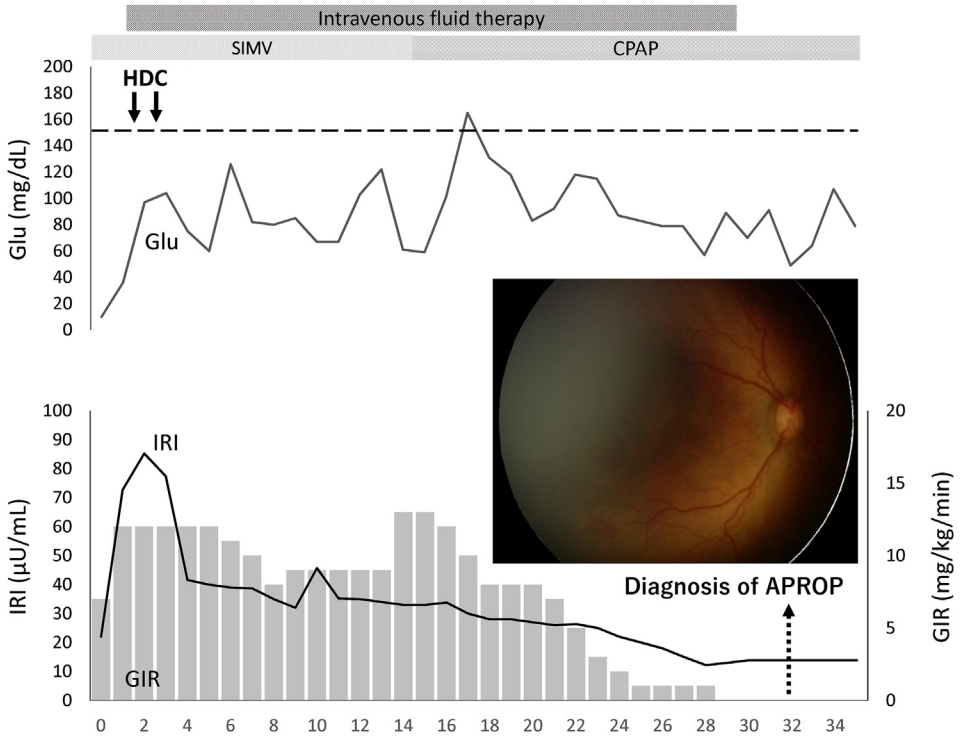

Figure 1 Clinical course and changes in glycemic control. Retinal images of the patient showing intensive shunt vessels with plus disease (day 32, postconceptional 32 weeks 2 days). AP-ROP, aggressive posterior retinopathy of prematurity; CPAP, continuous positive airway pressure; GIR, glucose infusion ratio; Glu, glucose; HDC, hydrocortisone; IRI, immunoreactive insulin; SIMV, synchronized intermittent mandatory ventilation.

Declaration of Competing Interest

None.

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