TRANSIENT HYPERINSULINISM IN AN ASPHYXIATED SMALL FOR GESTATION INFANT

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Abstract - Transient hyperinsulinism has been implicated in the prolonged hypoglycemia observed in small for gestational age or asphyxiated newborns. These infants are at high risk for severe and permanent brain damage, thus necessitating appropriate diagnosis and correct treatment.

A term male asphyxiated small for gestation 30 day infant with long-standing hypoglycemia and intractable seizures was managed successfully. The case is described with a review of the literature.

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Key Words: Hyperinsulinism, hypoglycemia, asphyxiated, glucose, diazoxide

INTRODUCTION

Hypoglycemia has been frequently reported in small for gestational age (SGA) infants, however the reported incidence has been very variable (1-3).

The primary reason for hypoglycemia in SGA and asphyxiated newborn is glycogen depletion (4), but decreased glyconeogenesis and ketogenesis, deficient provision or oxidation of fatty acids, abnormality of counter regulatory hormonal mechanisms, hyperinsulinemia or excessive sensitivity to insulin are also implicated (5,6,7).

The propensity for hypoglycemia is greatest during the first 3 days of life and in the case of hyperinsulinism it may continue until 2-4 weeks or more (7). Regarding the duration of hyperinsulinism, these infants are at high risk for neurological damage, therefore, efficient diagnosis and treatment are essential.

CASE REPORT

The patient was a 1400 g full term infant born to a gravida 2, para 1, preeclamptic mother by normal vaginal delivery with low Apgar score. At three days of life, he became hypoglycemic and with 10 mg/kg/min glucose infusion rate and 10 mg/kg/day hydrocortisone, the plasma glucose (PG) were in the range of 45-60 mg/dl. At 6th and 20th days of age he had seizures and received phenobarbital and phenytoin. Evaluation for sepsis was negative and he was managed with ampicillin, ceftizoxime and gentamicin.

When he was referred to our hospital at 30 days of age, he had another convulsion, was pale and had the wizened facies of SGA infant (Fig. 1).

The PG level was 45 mg/dl; blood count, urea nitrogen, electerolyte, amonia, CRP and ESR were normal.

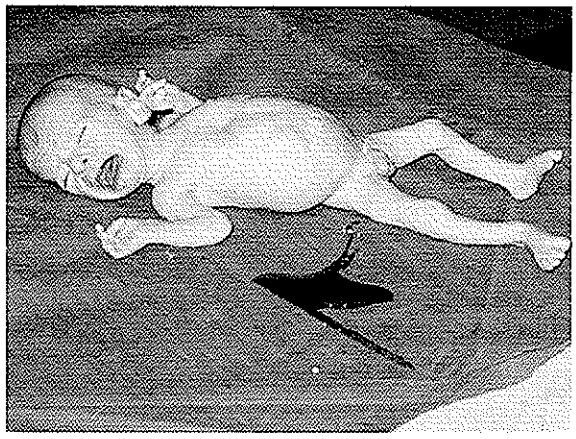

Fig. 1. Term SGA infant, demonstrating wizened facies and hanging skin at 35 days of life : weight 1650 g

Serologic evidence for STORCH and cultures were negative and serum and amino acids screening were normal. Urine was also negative for ketones and glucose reducing substances.

Brain CT scan showed cerebral cortical atrophy and ex vacuo hydrocephalus (Fig. 2)

With plasma glucose level of 37 mg/dl, the insulin level was 40 μu/ml (range. 2.1-30.8) RIA We raised glucose infusion rate from 8mg/kg/min to 10 mg/kg/min and cefotaxime and cloxacillin and phenobarbital were started by increasing the blood glucose infusion rate, the PG raised and 5 days later at 35 days old of age the insulin level did so 14.1 μu/ml (range 2.1-30.8) RIA with plasma glucose of 78 mg/dl.

The patient was seizure free with normal plasma glucose and insulin level thereafter.

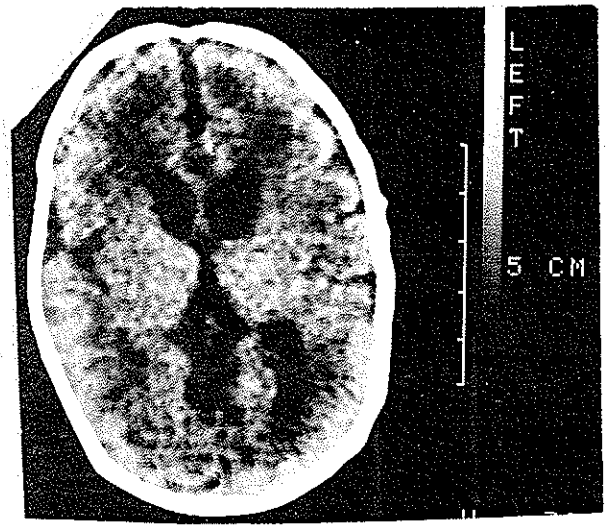

Fig. 2. CT scan of SGA asphyxiated patient with prolonged hyperglycemia shows atrophy of cerebral cortex and ex vacuo hydrocephalus

DISCUSSION

Transient hyperinsulinism is not only well recognized in infants of diabetic mothers but also has been implicated in the prolonged hypoglycemia seen in SGA or asphyxiated newborns. Persistent hypoglycemia occurs in a group of disorders of congenital hyperinsulinism that are the most common causes of hypoglycemia in early infants beyond the immediate neonatal period. Patients with any of the various forms of hyperinsulinism are at high risk for seizures and permanent brain damage. The cause of prolonged hyperinsulinism in SGA and asphyxiated newborns is unknown, although advances in understanding the regulation of insulin secretion may provide answers to this problem, in the near future. It occurs especially in infants of preeclamptic mothers, or those under other stresses at the time of delivery and may continue until 2-4 weeks of age or more but then seems to resolve completely (8).

Some of these infants may have beta cell hyperplasia but there is no pathologic confirmation. The islet cells may also be abnormally sensitive to glucose, so that both synthesis and release of insulin are maximally stimulated by fairly low glucose concentration.

Cornblath and co-workers demonstrated a significantly abnormal response to leucine and tolbutamide in hypoglycemic/premature and SGA infants versus normoglycemic control group neonates. They postulated that a sensitive insulin release mechanism appears to be present in these infants. Some authors speculate that an asphyxiated hypotensive infant may share the same pathophysiologic mechanisms as an adult shock victim for whom the initial phase of hyperglycemia and hypoinsulinism is followed within a few hours by hypersecretion of insulin which may last for weeks. The exact mechanism is not well understood but may somehow be related to stress. The hyperinsulinemic phase of adult shock patients suggests an insulin resistant state, which is not the case with hyperinsulinemic SGA and asphyxiated infants. Regulatory disturbances in insulin secretion after brith may be the most likely explanation for hyperinsulinism in many of these SGA and asphyxiated infants, however the etiology of hyperinsulinism in this group of infants remains an enigma (4).

Cornblath and co-workers reported eight cases, six of whom were SGA infants with symptomatic hypoglycemia beginning on the second or third days of life, born to a mother with toxemia. The hypoglycemia was quite refractory but self-limited. Serum insulin levels were not measured, but these infants required glucose infusion of up to 12 mg/kg/min, strongly suggesting hyperinsulinemia (9).

Le Dune in a study of hypoglycemic SGA infant, found that some had high insulin levels (2).

Collins and Leonard reported 3 asphyxiated infants with persistent fetal circulation (PFC) and 3 SGA infants with hyperinsulinemia between 40 and 48 hours after birth. All SGA infants and one asphyxiated infant required diazoxide therapy for variable periods (2-6 Mon). Recovery, however was complete (10).

Bhowhick and Lewandowski reported a case of asphyxiated SGA hyperinsulinemic infant that needed diazoxide therapy for 13 months. They believed, transient islet cell dysfunction leading to hyperinsulinemic hypoglycemia was more common in SGA and asphyxiated infants than is generally recognized (4).

Collins and co-workwes measured insulin level of 27 SGA neonates during the first 48 hours, from these 10 patients were hypoglycemic, 5 of whom had hyperinsulinemia and 4 had prolonged hypoglycemia (11).

In asphyxiated SGA patients high dose glucocorticoid therapy is not very effective and should be discouraged. Diazoxide, which specifically supresses insulin release, has been reported to be effective and provides a more rational and appropriate mode of therapy than glucocorticoids (8).

Our patient was an asphyxiated, SGA infant almost at the end of the expected period of transient hyperinsulinism. During the first 30 days of his life, hypoglycemia and hyperinsulinism had persisted despite administration of steroids and glucose at a high perfusion rate.

Five days later, at. 35 days of age, insulin level decreased and PG level became normal without using high glucose infusion rate, steroid, or diazoxide.

Serial measurements of insulin level in hypoglycemic

asphyxiated SGA infants is mandatory especially when the history of toxemia of pregnancy and stressful delivery exist and also when response to high glucose infusion rate or steroid therapy is poor.

Diazoxide is an appropriate treatment and must be continued until insulin level returns to normal, Permanent complications may thus be prevented in this group of infants.

REFERENCES

1. Kliegman R M. The fetus and the neonatal infant In: Behrman R E, Kliegman R M, Arvin A M, Neslon W E(eds): Nelson textbook of pediatrics. 15 th ed. Philadelphia, WB. Saunders : 1450-1451, 1996.

2. Le Dune MA. Intravenous glucose tolerance and plasma insulin studies in small for date infants, Arch. Dis. Child 47: 111, 1972.

3. Lubchencho L O et al: Incidence of hypoglycemia in newborn infants classified by birth weight and gestational age. Pediatrics 47: 831, 1981.

4. Bhowmick S. K. and Lewandowski Ch. Prolonged hyperinsulinism and hypoglycemia in an asphyxiated small for gestation infant. Case management and literature review. Clinical. Pediatrics (Phila). 28(12): 575-8; 1989.

5. Crouse D. and Cassady G. The small for gestation infant. In: Avery Gordon B, Fletcher Marry Ann, Macdonald, Mhairig (eds) Neonatology Pathophysiology and management of the newborn, 4th ed. Philadelphia: JB Lippincot company. 381-382, 1994.

6. Kalhan S C. and Saker F. Metabolic and endocrine disorder. In: Fanaroff A, Martin R Y. (eds). Neonatal perinatal medicine. Diseases of the fetus and the infants. 6th ed. St Louis, Mosby Yearbook : 1450-1451, 1997.

7. Kliegman R M. Intrauterine growth retardation. In: Fanaroff A, M R Y. (eds) Neonatal perinatal medicine. Diseases of the fetus and the infants. 6th ed. St Louis: Mosby Yearbook : 232-235, 1997.

8. Stanely C A. Hyperinsulinism in infants and children. Pediatric Clinics of North America 44(2): 636-374, 1997.

9. Cornblath M., Odell GB. and Levin EY. Symptomatic neonatal hypoglycemia associated with toxemia of pregnancy, J. Pediatr. 55: 45-62; 1959.

10. Collins JE. and Leonard JV. Hyperinsulinism in asphyxiated and small for dates infants with hypoglycemia. Lancet. 2: 311-313; 1984.

11. Collins JE. and Leonard JV, Teal D. Hyperinsulinemic hypoglycemia in small for date babies. Arch. Dis. Child. 65: 1118-1120; 1990.