CHOLESTASIS AND HYPERCALCEMIA SECONDARY TO PANHYPOPITUITARISM IN A NEWBORN

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INTRODUCTION

The rare disorder of hypopituitarism of infancy is clinically characterized by failure to thrive, recurrent hypoglycemia, and prolonged jaundice caused by cholestatic hepatitis. The endocrinological diagnosis is frequently delayed and the majority of infants with hypopituitarism and neonatal cholestasis undergo liver biopsy .

It is unclear which hormone causes cholestasis in patients with congenital panhypopituitarism. Some authors suggested that growth hormone deficiency is the major cause of cholestasis . But there is now good evidence that central adrenal insufficiency is the main cause of cholestatic hepatitis in hypopituitarism.

Hypercalcemia was reported in 5.5 % of primary adrenocortical insufficiency in adults. Although the mechanism of hypercalcemia in adrenocortical insufficiency is unknown, lack of serum cortisol is considered to be related increased calcium reabsorbtion from renal tubules and release from bone .

Herein, we report a newborn that was investigated for cortisol deficiency and other pituitary hormone deficiencies and diagnosed with panhypopituitarism upon detection of cholestasis after referral to the endocrinology department for hypercalcemia, a very rare sign of cortisol deficiency.

CASE REPORT

A male infant with a birth weight of 3900 gr born via caesarean section at full term to non-consanguineous parents was referred to our newborn intensive care unit from an outside center for further work-up of hypoglycemia and newborn convulsion 12 hours after birth. On physical examination his body weight was 3740 gr; he had a poor general status and was tachypneic. His anterior fontanel was measured 2x1.5 cm. No cardiac murmur was auscultated, and there was no hepatosplenomegaly, abdominal tenderness, or dysmorphic features; testes were bilaterally in scrotum, and extended penis length was 2 cm. He was intubated due to respiratory difficulty. He was extubated 2 days later. Hypoglycemia did not recur. An EEG and metabolic screens performed to search for an etiology for convulsions were all normal. His jaundice was intensified on the third day after birth and therefore he was begun on phototherapy. Since he could not tolerate enteral feeding. Having also hypercalcemia and hyperphosphatemia, the patient was referred to pediatric endocrinology division at 15th day. Cortisol deficiency was considered due to cholestasis and hypercalcemia. Low dose ACTH test was done with 1 mcg ACTH. Since he had cortisol levels of less than 1 mg/dl at 0th and 30th minutes, the patient was evaluated for panhypopituitarism (Table). Thyroid function test was normal at seventh day but central hypothyroidism was detected at 18th day (Table). The patient was first put on hydrocortisone 10 mg/m²/day followed by L-thyroxine 5 days later. The patient could now tolerate oral feeding after hydrocortisone therapy. Hypercalcemia was also improved. In addition to an extended penis length of 2 cm, the patient's hypogonadotropic hypogonadism was also confirmed by laboratory examinations(Table). A hypophysis MRI revealed a hypophyseal height of 1.5 mm and an ectopic neurohypophysis. Diagnosed with panhypopituitarism clinically and biochemically, the patient's cholestasis recovered at 45th day. Now 20-month-old, he does not take growth hormone yet since his height and growth rate remained normal. PROP- 1 mutation analysis studied for the genetic etiology of panhypopituitarism was normal. This case was reported to stress that newborns with cholestasis and hypercalcemia should definitely be investigated for cortisol deficiency and panhypopituitarism.

Table: Laboratory Findings of the Patient

Laboratory Findings	1st day	7 th day	15th day	18th day	33thday	45thday
CRP (mg/dl)(N<0. 6)	0.2	0.2	0.2		0.2	
ALT(IU/L)	15	81	22	15	68	24
AST(IU/L)	61	43	41	42	102	36
GGT (IU/L)	NA	603	213	154	94	43
ALP(IU/L)		110	144	218	588	123
Total bilurubin	6.3	17.2	10.7	7.8	7.7	0.6
Direct bilirubin	1.07	1.53	3.03	3.8	5.7	0.5
Glucose (mg/dl)	80	70	72	73	67	80
Sodium (mEq/L)	137		139			140
Potassium(mEq/L)	4.5		4.6			4
Calcium (mg/dl)	9.8	10.6	12.4	9.1	10.3	10
Phosphate(mg/dl)	5.1	7.8	7.9	4.9	5.8	5.8
TSH (mIU/mL)		2.2		6.9	2.8	0.05
Free-T4 (ng/dl) (N: 0. 8- 2. 4)		0.95		0.61	0.85	1.2
Baseline Cortisole (µg/dl)				<1		
30th minute Cortisole (µg/dl)(N>18)				<1		
ACTH (pg/ml)(N<60)				13.7		
PTH(pg/mL) (N:15- 60)				15.6		
25OHD3 (ng/ml) (N>20)				27.7		
IGF- 1 (ng/ml)(N25-200))					<25	
LH(mIU/mL) (N:0.05- 7)					<0.05	
FSH (mIU/mL) (N:0.16- 4.1)					<0.05	
Total Testosterone (ng/ml)(N: 0.6- 4)					<0.13	
Respiratory Support	Intubation (mechanical ventilation)	Spontaneous respiration	Spontaneous respiration	Spontaneous respiration	Spontaneous respiration	Spontaneous respiration

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