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Case Report PEDIATRICS

A rare cause of respiratory distress and edema in neonate: Panhypopituitarism

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ABSTRACT

Clinical presentation of hypopituitarism may be variable in the neonate. Symptoms are generally nonspecific, ranging from absent to severe, and even life-threatening, due to adrenocorticotrophic hormone deficiency. Presently described is a case of unexplained respiratory distress and edema in a neonate. Initial screening revealed panhypopituitarism. Respiratory distress improved after replacement treatment with hydrocortisone and thyroxine.

Keywords: Neonate; panhypopituitarism; respiratory distress.

Congenital hypopituitarism (CH) in the neonate, which manifests as deficiency in 1 or more pituitary hormones, can present with a highly variable phenotype, either as isolated hypopituitarism or with associated developmental defects, such as ocular, midline, and genital abnormalities [1].

Neonates may manifest with nonspecific clinical symptoms, such as poor feeding, hypoglycemia, prolonged neonatal jaundice, and lethargy, as consequence of combined pituitary hormone deficiencies, or may be initially asymptomatic, but at risk for developing pituitary hormone deficiencies over time. Adrenocorticotrophic hormone deficiency is associated with increased risk of neonatal death [1]. Early diagnosis of CH in absence of any obvious external malformations is often difficult during neonatal period as a result of nonspecific clinical presentation. In a case of clinical appearance as sepsis and circulatory disorder in neonate with negative acute phase reactants and no response to antimicrobial treatment, CH should be suspected. Presently described is a case of a newborn diagnosed as CH with severe respiratory distress and generalized edema, but no specific symptom like hypoglycemia. Significant clinical improvement was observed after initiation of hormone replacement treatment.

CASE REPORT

A male newborn was transferred to the intensive care unit due to respiratory distress. He was born at 37th gestational week by cesarean section to a 42-year-old mother who had gestational diabetes. His general appearance was poor. Tachycardia, tachypnea, respiratory distress, hypotonia, hypoactivity, and generalized edema were present. He had facial dysmorphic findings and micropenis. Clinical findings are summarized in Table 1.

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TABLE 1. Clinical features of the patient

Clinical findings	1st day	3rd day	7th day	10th day	15th day
Physical examination					
Weight (g)	3740 (>90th p.)	3750	3800	3650	3800
Height (cm)	53 (>90th p.)				
Head circumference (cm)	38 (>90th p.)				
General appearance	Poor. Generalized edema, particularly in the scalp. Anterior fontanel: 4x4 cm, sagittal suture open	Enteral feeding, no hypoglycemia, generalized edema, no weight loss	Poor feeding, vomiting, hypotonia hypoactivity, ongoing edema no weight loss	Vomiting ceased and generalized edema diminished	Edema and respiratory distress disappeared, enteral feeding
Dysmorphic features	Prominent forehead, low-set ears, flat nose, highly-arched palate				
Respiratory system	Tachypnea, retractions		Tachypnea, retractions		
Abdomen	Normal				
External genitalia	Testes: 1 mL/1 mL, Penile length: 2x1 cm				
Laboratory findings					
Blood gases	pH: 7.17 HCO_3: 21 pO_2: 64 pCO_2: 79	pH: 7.33 HCO_3 :2 pO_2: 0.79 pCO_2: 36	pH: 7.23 HCO_3: 18 pO_2: 0.60 pCO_2: 50	pH: 7.36 HCO_3: 24 pO_2: 0.79 pCO_2: 34	pH: 7.37 HCO_3: 25 pO_2: 0.78 pCO_2: 33
CRP (mg/dL)	0.3 (N <0.5)	0.4	0.5	1.3	0.3
Glucose (mg/dL)	45/50/92	94	79	70	94
Sodium (mEq/L)	135	129	135	122	139
Potassium (mEq/L)	3.5	3.9	4.9	4.1	5.2
TSH (mIU/mL)		6.15 (N: <5)	13	16	1.42
Free-T4 (ng/dL)		0.64 (N: >0.8)	0.6	0.73	1.29
Baseline cortisol (µg/dL)		0.44			
30th min. cortisol (µg/dL)		4.5			
LH (mIU/mL)					0.6
FSH (mIU/mL)					2.45
Total testosterone (ng/mL)					0.01
Treatment and progress					
Respiratory support	Intubation (mechanical ventilation, surfactant)	CPAP	Intubation (mechanical ventilation)	Intubation (mechanical ventilation)	Extubation
Medication	Ampicillin+ gentamicin	Ampicillin+ gentamicin	Hydrocortisone (10 mg/m²/day) L-thyroxine (8 mcg/kg/day) vancomysin+ meropenem	Hydrocortisone (10 mg/m²/day) L-thyroxine (8 mcg/kg/day) vancomysin+ meropenem	Hydrocortisone (10 mg/m²/day) L-thyroxine (8 mcg/kg/day)

CPAP: Continuous positive airway pressure; CRP: C-reactive protein; FSH: Follicle-stimulating hormone; L-thyroxine: Levothyroxine; LH: Luteinizing hormone; P: Percentile; N: Normal; T4: Thyroxine.

Tracheal intubation was performed soon after hospitalization. Intratracheal surfactant was administered, since severe respiratory acidosis, clinical and radiological findings, and being the infant of diabetic mother suggested diagnosis of respiratory distress syndrome. Broad-spectrum antibiotics were prescribed. Umbilical catheterization was required, since peripheral venous puncture was prohibited by severe edema. Respiratory functions began to improve on third day, and continuous positive airway pressure was well tolerated at end of 72nd hour after surfactant treatment. Enteral feeding was also well tolerated, and no hypoglycemic attack was detected during follow-up. However, generalized edema did not diminish, expected weight loss was not observed, poor feeding, vomiting, hypoactivity, and hypotonia became apparent, and mechanical ventilation was again necessary on 7th day. Metabolic screening was normal. Portal, splenic, renal Doppler investigations, and echocardiography were normal. Laboratory analyses revealed central hypothyroidism with low free-thyroxine (T4) and slightly elevated thyroid-stimulating hormone (TSH) level. Hyponatremia was present, while potassium levels were all normal (Table 1). Baseline cortisol level was 0.44 μg/dL. Low-dose adrenocorticotropic hormone test (with 1 μg intravenous Synacthen; Mallinckrodt Specialty Pharmaceuticals Ireland Ltd., Dublin, Ireland) was performed and 30th minute cortisol level was 4.5 μg/dL, supporting diagnosis of secondary adrenal insufficiency. Glucocorticoid replacement with hydrocortisone and thyroid hormone replacement with levothyroxine were initiated. Vomiting and hyponatremia receded, and edema was significantly improved on the third day of treatment. He was extubated on the 15th day, and there was no need for supplemental oxygen on 23rd day. Gonadotrophic hormone levels were below levels expected in mini-puberty stage.

DISCUSSION

Clinical presentation of hypopituitarism in the neonate varies, ranging from absent to severe, nonspecific symptoms. Pituitary hormone deficiencies, especially adrenocorticotropic hormone deficiency, may be life-threatening in severely ill patients [1–3].

Diagnosis of hypopituitarism must be based on clinical grounds, especially when hypoglycemia, prolonged jaundice, micropenis, or midline alterations are found in neonatal period. Neonatal presentation may be mistaken for sepsis, which can present with similar clinical features of hypothermia, hypoglycemia, lethargy, and poor feeding [4]. Hypoglycemia, which is most common finding of CH, was not present in our patient, suggesting that it is not essential. Whenever central hypothyroidism is detected in a patient, accompanying anterior pituitary hormone deficiencies should be considered, since 78% of patients with central hypothyroidism have been found to have another pituitary hormone deficiency. Central hypothyroidism is characterized by low free-T4 level with discordantly normal or mildly elevated TSH level [5].

Hyponatremia may be present even if mineralocorticoid synthesis is adequate, since cortisol is needed for free-water excretion action of anti-diuretic hormone. Due to its effect on the stabilization of blood pressure, cortisol deficiency also may lead to hemodynamic instability and even shock [6]. Micropenis, which may arise from gonadotropin deficiency or growth hormone deficiency, might be another important finding of hypopituitarism in male infants [7].

The underlying cause of hemodynamic instability in the present patient was CH. Severe edema and respiratory distress did not improve with conventional therapies. Dramatic clinical response to hormone replacement treatment was observed. Unexplained edema and respiratory distress in a neonate and associated with dysmorphic findings suggesting midline defect and hypogenitalia should bring CH to mind.

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REFERENCES

1. Filges I, Bischof-Renner A, Röthlisberger B, Potthoff C, Glanzmann R, Günthard J, et al. Panhypopituitarism presenting as life-threatening heart failure caused by an inherited microdeletion in 1q25 including LHX4. Pediatrics 2012;129:529–34.

2. Scommegna S, Galeazzi D, Picone S, Farinelli E, Agostino R, Bozzao A, et al. Neonatal identification of pituitary aplasia: a life-saving diagnosis. Review of five cases. Horm Res 2004;62:10–6.
3. Vallette-Kasic S, Brue T, Pulichino AM, Gueydan M, Barlier A, David M, et al. Congenital isolated adrenocorticotropin deficiency: an underestimated cause of neonatal death, explained by TPIT gene mutations. J Clin Endocrinol Metab 2005;90:1323–31.
4. Lammoglia JJ, Eyzaguirre F, Unanue N, Román R, Codner E, Cassorla F, et al. Congenital hypopituitarism: report of 23 cases. Rev Med Chil 2008;136:996–1006.
5. van Tijn DA, de Vijlder JJ, Verbeeten B Jr, Verkerk PH, Vulsma T. Neonatal detection of congenital hypothyroidism of central origin. J Clin Endocrinol Metab 2005;90:3350–9.
6. Geffner ME. Hypopituitarism in childhood. Cancer Control 2002;9:212–22.
7. Grumbach MM. A window of opportunity: the diagnosis of gonadotropin deficiency in the male infant. J Clin Endocrinol Metab 2005;90:3122–7.