CASE REPORT

Hypopituitarism in A Neonate with Hyperbilirubinemia and Decreased Level of Consciousness: A Case Report Study

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Abstract- Decreased level of consciousness in neonates may result from different etiologies, including rare metabolic and hormonal disorder due to anterior pituitary insufficiency. In this case report, a five-day-old newborn boy was referred to the neonatal intensive care unit of Mustafa Khomeini hospital of Ilam, Iran. He had an open anterior fontanel with no history of prenatal and familial diseases. Clinical examination showed decreased level of consciousness so that this patient responded only to painful stimuli. Furthermore, unconsciousness, hyperbilirubinemia, and hypotonia were fully evident. Given the clinical findings and decreased level of consciousness, hormonal diagnostic tests and brain CT scan were performed for any evidence of hypopituitarism. Clinical and experimental findings were consistent with the generalized edema and pituitary insufficiency secondary to central hypothyroidism and cortisol deficiency. Based on the findings, the neonate was put on the hormonal replacement therapy and, as the result, all of the abnormal clinical symptoms disappeared. In conclusion, fatal neonatal diseases may be mistaken with unimportant clinical findings at the first examination. Therefore, comprehensive attention to all potential causes of such symptoms in the neonates should be given for early diagnosis and treatment, and to prevent any fatal and irreversible complications.

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Introduction

Neonatal jaundice may result from a variety of causes, including hemolytic anemia, intestinal obstruction diseases, and decreased clearance of bilirubin, inborn errors of metabolism, and hormonal disorders such as hypopituitarism (1). Neonatal hypopituitarism is a very rare condition that is not generally diagnosed in the early neonatal period because it has no specific physical manifestations. The clinical features of the disease are diverse and may include a broad spectrum of manifestation from discrete brain syndromes without apparent structural lesions to gross abnormality such as anencephaly, holoprosencephaly, etc. Neonatal hypopituitarism may cause hypoglycemia that appears as drowsiness, apnea, hypotonia, convulsion, and cardiovascular collapse in the first few hours and days of life. The afflicted infants have normal weight and stature and are usually born at term; however the male patients may show microphallus (micropenis). Other clinical manifestations that may occur along with neonatal hypopituitarism include less differentiated scrotum, cryptorchidism, cleft lip and palate, and undeveloped nasal septum. The patients often have severe growth hormone deficiency and do not respond to glucose infusion. The decreased levels of cortisol especially in the setting of hypoglycemia and hyponatremia may be evident, however hypothyroidism is more common (2).

Case Report

A five-day-old boy with decreased level of consciousness, hyperbilirubinemia, and conspicuous hypotonia was admitted to the neonatal intensive care units (NICU) department at the Mustafa Khomeini hospital in Ilam, Iran. He was born at 39 weeks of gestation to a 31 years old mother following an uneventful cesarean delivery. The mother also had a previous cesarean delivery. The patient had a birth weight 3.4 kg, head circumference 34 cm, length 50.5

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cm, and the Apgar scores were 8.1 and 9.1 after 1 and 5 min, respectively. Laboratory findings were negative for hepatitis B, cytomegalovirus, rubella, toxoplasmosis, coxsackievirus, and syphilis. The only prominent laboratory findings on blood were glucose 45 mg/dl and bilirubin 15 mg/dl.

The newborn was highly icteric and unconscious and only responded to painful stimuli through puckered his face. Head CT scan demonstrated a generalized edema of the brain. Other clinical findings were as follows: highly attenuated infantile reflexes, normocephalous cranium without protruded superficial vessels or opened sutures, opened frontal fontanel, pupils sensitive to light with normal size and red reflex, normal brain stem reflexes, positive bilateral Babinski reflex along with decreased deep tendon reflexes, and normal male genital organ.

On admission, the vital signs of the newborn were as follows: Blood pressure 75/45 mmHg, pulse rate 132/min, breath 41/min, temperature 37.3°C. Results of the initial laboratory experiments are shown in table 1.

The results of the chest examination were normal and the brain CT scan reflected a generalized brain edema with no evidence of bleeding or structural abnormality (Figure 1).

Analysis of pituitary hormones (Table 2) indicated the diagnosis of anterior pituitary gland insufficiency; therefore, hormone replacement therapy was instituted. 24 hours after hormone therapy, the newborn regained his normal consciousness and muscle tone. On the day-11 of therapy, the icterus condition was disappeared without phototherapy. The newborn was eventually discharged from the hospital with a satisfactory recovery and was further looked after as an outpatient.

Table 1. Results of the initial laboratory experiments on admission.

Parameter	Result	Parameter	Result
WBC	10300 (poly: 68%, lymph: 29%)	AST	73 IU/l
Hb	17.1 g/dl	ALT	20 IU/l
PLT	242000	Blood culture	Negative
BG	O^+	CRP	Negative
BUN	14 mg/dl	Urine glucose	1+
Cr	0.5 mg/dl	CSF culture	Negative
Glucose	45 mg/dl	Calcium	10 mg/dl
Total bilirubin	15.1 mg/dl	Direct bilirubin	3.0 mg/dl
CSF protein	65 mg/dl	PH	7.34*
CSF glucose	48 mg/dl	PCO_2	43 mmHg*
CSF_{WBC}	0	PO_2	80 mmHg*
CSF_{RBC}	0	Bicarbonate	23.3mmol/l

Abbreviations: WBC, white blood cell; poly, polymorphonuclear cells; lymph, lymphocytes; Hb, hemoglobin; PLT, platelets; BG, blood group; BUN, blood urine nitrogen; Cr, chromium; CSF, cerebrospinal fluid; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CRP, C-reactive protein. *Arterial blood

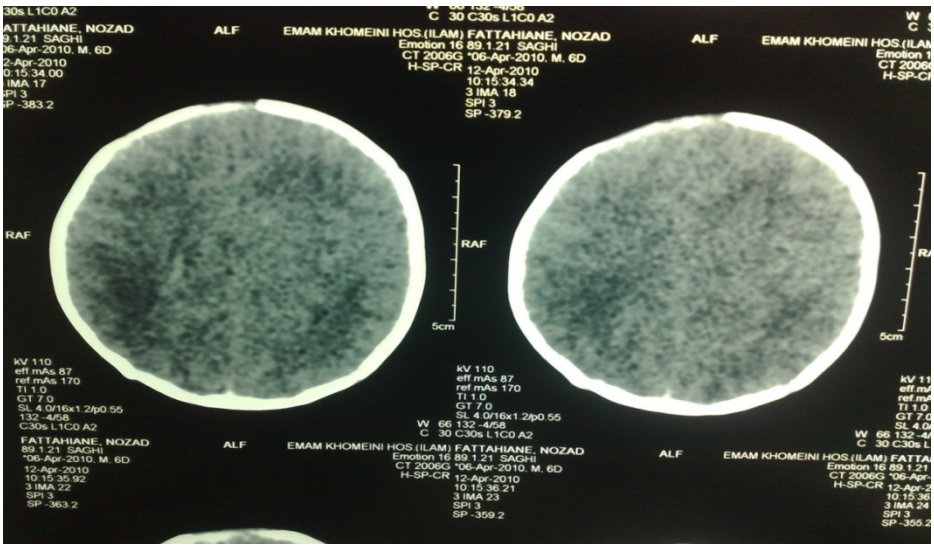

Figure 1. CT scan examination reflected a generalized brain edema.

Table 2. Results of hormonal analysis

Hormone	Result
TSH	0.2 μIU/ml
FT_4	1.02 ng/dl
Cortisol	2.5 μg/dl
GH	0.57 ng/ml

Abbreviations: TSH, thyroid stimulating hormone; FT_4, free thyroxine; GH, growth hormone.

Discussion

Regarding the clinical clues and the decreased levels of consciousness, the diagnosis of premature sepsis and meningitis was first suspected for the newborn. Premature sepsis is more associated with pneumonia or meningitis and is usually occurring in the second week of birth. According to the results of the blood and cerebrospinal fluid culture, the bacterial meningitis no longer was taken into account, but the existence of encephalitis due to *Mycoplasma hominis* and viruses such as enteroviruses and Epstein-Barr virus must be evaluated through culture analyses and polymerase chain reaction that unfortunately these techniques were not available. The second cause that may create this condition is prenatal asphyxia. The normal Apgar scores at the delivery, the absence of asphyxia risk factors in the mother, and the absence of any related symptoms in the newborn for two days, all refused the asphyxia problems. Structural disorder, trauma, hemorrhage, and thrombosis in brain tissues also could lead to hypotony and decreased levels of consciousness. In these cases, the disorders are associated with convulsion and other abnormal findings on brain examination. Furthermore, head CT scan results were inconsistent with structural disorder, trauma, hemorrhage, and thrombosis involvements. Secondary hypothyroidism due to anterior pituitary hormone deficiency is rarely determined in neonatal period and is clarified by the decreased levels of free thyroxin (FT_4) and thyroid stimulating hormone (TSH). Other cases of this disease are usually associated with the brain structural abnormality or the anoxia in uterus or around the delivery (3-5).

In a reported case, two newborns with pituitary insufficiency along with hepatomegaly, elevated liver enzymes and hypoglycemia were reported that their growth hormone and liver enzymes had been returned to normal during 5 months after birth (6).

In another study, 4 newborns with pituitary insufficiency and microphallus were reported that had no apparent brain structural lesion or birth weight and length abnormality. However, all pituitary hormones were reduced in the patients (7).

In another report, a female newborn with hypoglycemic attacks and conjugated hyperbilirubinemia was reported that had no infectious or metabolic disorders in her liver or biliary ducts, while had pituitary hormones deficiencies (8). Also, another female newborn with anorexia and attenuated hypoglycemic attacks along with conjugated hyperbilirubinemia and pituitary insufficiency were reported (9).

Altogether, the present symptoms and the clinical and experimental findings were suggestive of hypothyroidism and cortisol deficiency secondary to hypopituitarism. Although the incidence of neonatal hypopituitarism is very rare and is difficult to be determined, the early diagnosis and treatment of the present case prevented severe complications of pituitary insufficiency.

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