Hypocalcemic seizure due to congenital rickets in the first day of life

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SUMMARY: Erdeve Ö, Atasay B, Arsan S, Şıklar Z, Öcal G, Berberoğlu M. Hypocalcemic seizure due to congenital rickets in the first day of life. Turk J Pediatr 2007; 49: 301-303.

Congenital rickets is considered a rare disease entity in the newborn period. Hypocalcemic seizure due to congenital rickets has been reported, but this symptom generally appears at the earliest at the end of the first month of life.

A congenital rickets case presented unusually with seizure on the first day of life is reported, and the continuing occurrence of the disease with serious consequences even at the beginning of life is emphasized.

Despite improved prenatal care offered today, congenital rickets still occurs. It seems that vitamin D deficiency in the neonate secondary to maternal deficiency should be a consideration for the pediatrician or neonatologist caring for newborns. Physicians should be aware of risk factors that can trigger the development of this condition and should be alert to the signs of congenital rickets in order to commence appropriate treatment and prevent complications such as seizure occurring as early as shortly after birth.

Key words: congenital rickets, hypocalcemia, newborn, seizure, vitamin D.

Vitamin D is the essential precursor of 1-25-dihydroxyvitamin D_3, which is required for calcium absorption, bone development and growth. In full-term infants, serum 1-25-dihydroxyvitamin D_3 concentration is low at birth, but increases to normal ranges within 24 hours of life. Vitamin D disturbance does not appear to have a role in early neonatal hypocalcemia. Congenital rickets is considered a rare disease entity in early infancy and only a few case reports and series have been described in the recent pediatric literature. Most reported cases have been secondary to prolonged maternal disturbance of vitamin D, calcium phosphate and parathyroid homeostasis[1-3]. Seizure due to hypocalcemia has been reported, but this symptom generally appears at the earliest at the end of the first month of life[2-4].

We report a congenital rickets case presented unusually with seizure on the first day of life and emphasize the continuing occurrence of the disease with serious consequences even in the beginning of life.

Case Report

A full-term male baby weighing 2750 g was admitted to our neonatal intensive care unit due to clonic seizure on the second day of life. The newborn had developed the first clonic seizure through the end of the first day of life, which was a generalized type and had lasted for 30 seconds. He was referred to our hospital because of the second seizure recorded on the second day. It was the mother's first pregnancy, and she was from Central Anatolia, where women are veiled according to religious belief. Her dietary intake of vitamin D during pregnancy was estimated as approximately 200 IU, which was lower than the recommended daily intake during pregnancy[5]. Moreover, the mother was not exposed to sun light during her pregnancy because of her gowning habits and the winter season.

On physical examination, the infant was found to be term and appropriate for gestational age, and examination was recorded as normal except pes equinovarus of left foot and pectus excavatum. Neurological examination revealed normal tonus and newborn reflexes.

Serum total and ionized calcium levels collected before the infusion of calcium gluconate for the management of neonatal convulsion were reported as 4.4 mg/dl and 0.75 mmol/L, respectively. The biochemical study revealed phosphorus, magnesium and serum alkaline phosphatase levels as 2.8 mg/dl, 2.2 mg/dl and 614 U/L, respectively (Table I). Roentgenogram of the wrist revealed rarefaction with a little cupping (Fig. 1). All evaluations for the etiology of the seizure, including cranial tomography and electroencephalography, were normal. Hence, hypocalcemia was considered the cause of the seizure according to these laboratory findings, and investigation for the etiology of hypocalcemia determined vitamin D deficiency (serum 25-OH D_3: 5.9 nmol/L) in the child with increased parathormone level (81.2 pg/ml) (Table I). Serum 25-OH D_3 level of the mother was studied and reported as 6.5 nmol/L (N: >25 nmol/L) with normal calcium level (8.6 mg/dl).

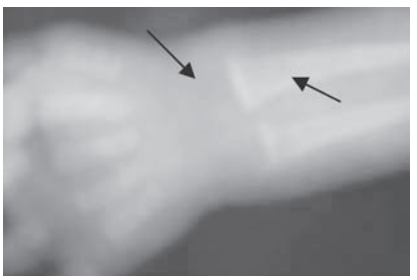

Fig. 1. Wrist roentgenogram of the congenital rickets case presenting rarefaction with a little cupping.

Table I. Serum Biochemical and Hormonal Levels of the Newborn Before and After a Six-Week Treatment

Parameters (normal ranges)	Before treatment	After treatment
Calcium (8.4-11.6 mg/dl)	4.4	9.8
Phosphorus (4.5-6.5 mg/dl)	2.8	6.2
Alkaline phosphatase (98-232 U/L)	614	417
25-OH D_3 (>25 nmol/L)	5.9	39.6
Parathormone (9-65 pg/ml)	81.2	22

Intravenous calcium gluconate was started for hypocalcemia during the seizure, which could be controlled by a dose of 500 mg/kg/day. Calcium and vitamin D supplementation as 1600 IU/day for the newborn and 400 IU/day for the mother were discontinued six weeks after the initial diagnosis. The newborn developed well, and the normal serum calcium and phosphorus levels were maintained at the end of the treatment (Table I).

Discussion

Congenital rickets is recognized as a rare but serious problem in newborns. Vitamin D deficiency plays the major role in pathogenesis of the disease. Most of the vitamin D in a neonate is acquired from maternal transfer, so vitamin D deficiency in mothers is likely to have adverse consequences for their infants[6-8]. The supply of vitamin D in utero, rather than from milk, is the major determinant of vitamin D status in early neonatal life in mammals[9].

Women who are veiled are susceptible to vitamin D deficiency because clothing absorbs ultraviolet B irradiation and reduces the cutaneous production of vitamin D[7]. The amount of high energy ultraviolet B light reaching the skin depends on factors such as altitude, season, smog, and the actual amount of direct sun exposure, which is further modified by clothing and the use of sun protection agents[7,8]. Grover and Morley[7] reported that 80% of dark-skinned or veiled women attending an antenatal clinic in Australia had biochemical evidence of vitamin D deficiency. Nozza and Rodda[1] reported a group of 55 children presenting with rickets, and showed that none of the mothers who had volunteered had symptoms of vitamin D deficiency, but 81% had 25-OH D_3 concentrations below the reference range. The mother of our case was also asymptomatic but had 25-OH D_3 concentrations lower than the normal ranges. The concentration of vitamin D in neonates correlates with maternal intake and absorption of vitamin D increases in an age-dependent manner. The maternal calcium concentration and vitamin D status during pregnancy influence parathyroid function in the developing fetus, so a thorough evaluation of the newborn with hypocalcemia must include an analysis of mineral metabolism in the infant's mother[1,6-8]. A serum level of 25-OH D_3 below 40 nmol/L is indicative of vitamin

D deficiency, and a level below 25 nmol/L corresponds to osteomalacia or rickets. A study concerning maternal vitamin D deficiency in Turkey was conducted and the ratios of mothers with 25-OH D_3 below 40 nmol/L and 25 nmol/L were reported as 94.8% and 79.5%, respectively[10]. The recommended daily intake, if there is inadequate sun exposure, is 400 IU/day in children and 200 IU/day in adults. Pregnancy increases the recommended daily intake for vitamin D to 500-700 IU[5].

Rickets presenting at birth is rare, though congenital rickets due to maternal malnutrition has been reported from some countries[1,4,6]. Thompson et al.[8] reported that most mothers who had been vitamin D-deficient during pregnancy were also deficient postnatally, indicating that treatment offered, counselling and/or treatment compliance were inadequate. Congenital rickets is due to a low exchangeable pool in the mother, so both mother and baby should be treated together, as in our case.

Seizure due to congenital rickets is an unusual symptom during the first month of life. Hatun et al.[4] analyzed a total of 42 infants with vitamin D deficiency in the first three months of life and reported seizure as the major presentation. Oki et al.[2] reported a hypocalcemic focal seizure in a one-month-old infant of a mother with a low circulating level of vitamin D. They concluded that hypocalcemia in infancy may be an important factor in the cause of focal seizures that start even after the age of one month. Maiyegun et al.[6] reported a severe case of congenital rickets who presented at birth. This patient did not present with seizures, but the diagnosis was made shortly after birth. Likewise, Mohapatra et al.[11] described tetany in a congenital rickets case on the third day of life and this was the earliest reported sign of hypocalcemia due to rickets in the neonatal period. Thus, our patient is the first case reported of a newborn with serious seizure recorded soon after birth and related to congenital rickets.

Despite the improved prenatal care offered today, congenital rickets still occurs. It seems that vitamin D deficiency in the neonate secondary to maternal deficiency should be a consideration for the pediatrician or neonatologist caring for newborns. Physicians should be aware of risk factors that can trigger the development of this condition and should be alert to the signs of congenital rickets in order to commence appropriate treatment and prevent complications such as seizure occurring as early as shortly after birth.

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