A CASE OF VITAMIN D DEPENDENT RICKETS TYPE 1 WITH A NOVEL MUTATION IN CYP27B1 (25-OH VITAMIN D-1-A-HYDROXYLASE) GENE

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BACKGROUND

Vitamin D dependent type 1 rickets is a rare, autosomal-recessively inherited disorder due to an inactivating mutation in CYP27B1 (25-OH Vitamin D-1-α-hydroxylase) gene. It is characterized by early onset of rickets with hypocalcemia and low 1,25-$(OH)_2$ vitamin D level in spite of normal or increased 25-OH vitamin D level. We report a boy admitted with symptoms of hypocalcemia and who carried a novel mutation in CYP27B1 gene.

CASE

The patient was admitted from Turkmenistan with tetany at the age of 12 months. When he had his first tetany or seizure, he was 9 months old. He never had prophylaxis of vitamin D until detection of hypocalcemia in his country. Vitamin D was administered orally; carbamazepine was added for the treatment of seizures and pancrelipase for the treatment of repeated diarrhea episodes. He was born at term from a consanguineous marriage. He teethed first at the age of 10 months. He had one healthy sister and one brother died at the age of 12 months because of hypocalcemia and pneumonia. At physical examination, he had carpopedal spasm and overactive tendon reflexes. Height, weight and head circumference SDS's were -1.83, -1.02, 1.64 respectively. He had caput quadratum and enlargement of wrist. He had two central incisors. At the neurological examination, he had carpopedal spasm. His serum calcium, phosphorus, alkaline phosphatase levels were 5,9 mg/dL, 3.5 mg/dL and 987 IU/L respectively. No abnormalities of acid-base metabolism or renal function were detected. Radiological findings included metaphyseal fraying and cupping in wrists. Serum levels of parathormone (182,8 pg/ml) and 25-OH vitamin D levels (125 mcgr/L) were high; 1, 25 $(OH)_2$ vitamin D level (8,5 pg/ml) was low; urine calcium/creatinine ratio was 0,006. Renal ultrasound revealed nephrocalcinosis grade 1. The patient was diagnosed clinically vitamin D dependent rickets type 1. Calcium carbonate (elementary calcium 75 mEQ/kg/d) and calcitriol (110 ng/kg/d) were administered orally. In follow-up, his liver enzyme levels (SGOT: 68 IU/L, SGPT: 123 IU/L) increased, that was related to Cytomegalovirus (CMV) infection (CMV IGM positive, CMV DNA 5640 copies). With normal electroencephalography findings and stool, treatments of carbamazepine and pancrelipase were withdrawn. Serum levels of calcium were normal under treatment with calcitriol and calcium-carbonate. DNA sequencing revealed a novel homozygous mutation ofp.Q135X (c.403 C>T) in CYP27B1 gene. Genetical analysis could not be performed to other family members.

Patient (boy) at the age of 12 months

Complaints: Tetany
Age of onset: 9 months
Family history: Consanguineous family
One brother died because of pneumonia and hypocalcemia at the age of 12 months

Physical Examination
Caput quadratum and enlargement of wrist carpopedal spazm, overactive tendon reflexes

Ca ↓, P↓, ALP↑↑, PTH ↑
Metaphyseal fraying and cupping in wrists

↓

25-OH Vitamin D level ↑

↓

1, 25 $(OH)_2$ Vitamin D level ↓

↓

Vitamin D dependent rickets type 1
(inactivation in 1-α hydroxylase enzyme)

Figure 1: Homozygous mutation c.403C>T (p.Q135X) in CYP27B1 gene

CONCLUSION

Vitamin D dependent rickets tip 1 is a rare disorder but must be considered even in countries where vitamin D deficiency is still common.