

**CASE REPORT**

Vitamin D Dependent Rickets Type II : Late Onset Disease associated with Double Inlet Left Ventricle and Facial Dysmorphism

Rekha Harish , Ashu Jamwal , Deepak Kumar

Abstract

Vitamin D dependent rickets type II is a rare autosomal recessive disorder. It is characterised by end organ resistance to 1,25 dihydroxy cholecalciferol. Patients present with early onset rickets, alopecia, severe hypocalcemia and secondary hyperparathyroidism. We report a 7 year old girl who presented with this disorder in association with congenital cyanotic heart disease and dysmorphic facies. Such an association has not been reported in literature.

Key Words

VDDR type II, Hypocalcemia, Calcitriol

Introduction

Vitamin D dependent rickets type II is a rare genetic disorder resulting from a recessively inherited aberration in calcitriol receptor causing end organ resistance to vitamin D. The clinical and biochemical profile usually consists of early onset rickets with or without alopecia, severe hypocalcemia and secondary hyperparathyroidism. Serum levels of 1,25 dihydroxy vitamin D3 are typically elevated (1). Treatment consists of high dose of vitamin D3 or its analogue along with calcium supplements. We report a case of Vitamin D dependent rickets Type II in association with dysmorphic facies and cyanotic congenital heart disease presenting as symptomatic hypocalcemia at the age of seven years. There is no such report available in literature.

Case Report

A seven year old female child, presented to us with carpopedal spasms of few hours duration. She had been diagnosed as a case of double inlet left ventricle in early infancy and had undergone Fontan's operation. Anthropometry revealed weight 19kg (10th centile),

height 110cm (<3rd centile), US:LS ratio of 1.2:1, body mass index of 15.7(50th centile) and head circumference of 48cm(<3rd centile). Eye examination revealed a convergent squint left eye with coloboma of both iris. Left ear was dysplastic with a preauricular pit. There was no evidence of alopecia, dental anomalies or bony deformities . Investigations revealed severe hypocalcemia (S.calcium 4.7mg/dl, Ionized Calcium 0.48mmol/l), hypophosphatemia (S.phosphorus 2.32mg/dl), raised alkaline phosphatase (228.6u/l) and markedly elevated parathyroid hormone levels (238.3 pg/ml). Liver function tests, kidney function tests and serum magnesium were within normal limits. Skeletal survey did not reveal any features of rickets. She was treated with intravenous calcium gluconate which relieved the carpopedal spasms, however serum calcium did not improve. Further evaluation of vitamin D metabolites disclosed normal 25-hydroxyvitamin D3 (29.2ng/ml) with markedly increased 1,25 dihydroxy vitamin D3 (181.2 pg/ml). The patient was initiated on calcitriol 1microgram / day along with

From the Department of Pediatrics, SMGS Hospital, Jammu J&K-India

Correspondence to : Dr Rekha Harish, Professor & Head Department of Pediatrics, SMGS Hospital, Jammu J&K- India



Fig. 1 A 7 yr old with VDDR Type II



Fig. 1 A 7 yr old with VDDR Type II - Pre Auricular Pit

calcium supplements and calcium levels returned to normal. The onset of the disease at 7 years, absence of response to routine dose of calcium supplements and the characteristic laboratory abnormalities were compatible with the diagnosis of Vitamin D Dependent Rickets type IIb in this patient.

Discussion

Vitamin D Dependent Rickets type II (VDDR II), also known as Pseudovitamin D Deficiency Type II or Hypocalcemic Vitamin D Resistant Rickets is characterised by end organ resistance to physiological dose of 1,25 dihydroxy cholecalciferol. Depending on the



Fig.2 A 7 yr old girl with VDDR Type II& Coloboma Both Irises

presence or absence of alopecia, it is further classified as Vitamin D Dependent Rickets Type IIa or IIb respectively (1). Patients may display rachitic bone changes, hypocalcemia and secondary hyperparathyroidism with elevated levels of serum 1,25 dihydroxy vitamin D₃. The basic defect involves the unresponsiveness of vitamin D receptors to 1,25 dihydroxy vitamin D (2). Eil *et al* (3) demonstrated defective nuclear uptake of 1,25-dihydroxyvitamin D in cultured fibroblasts from these patients. Laboratory clue to diagnosis of VDDR II is high level of 1,25-dihydroxyvitamin D in a patient with hypocalcemia and hypophosphatemia as observed in this case.

VDDR type II is a rare genetic disorder. It was first reported by Brooks *et al* in 1978 in a 22 year old African American woman with hypocalcemia, secondary hyperparathyroidism, osteomalacia and osteitis fibrosa in association with normal serum 25-hydroxy vitamin D and markedly raised serum 1,25- dihydroxy vitamin D. They proposed that the entity be called Vitamin D Dependent Rickets Type II and suggested that the disorder results from impaired end organ response to 1,25- dihydroxy vitamin D (1).

Many publications followed reporting similar clinical observations but most of the cases reported had early onset disease with or without alopecia. Marx *et al* reported vitamin D dependent rickets type II in a brother



and sister beginning at the ages 20 and 5 months respectively (4). Rosen *et al* (5) described two sisters aged 3 and 7 years, who had onset of rickets and alopecia in the first year of life (5). Khan *et al* (6) described five siblings from a Bahraini family who presented with vitamin D dependent rickets and alopecia. Liberman *et al* (7) reported a 13 year old girl with total alopecia who had profound hypocalcemia and rickets since infancy. Her sister who died at the age of 6 months also had total alopecia, rickets and hypocalcemia (7). Arita *et al* reported a 6 year old who had rickets and alopecia in infancy and was diagnosed with sensorineural hearing loss at one year of age. He also had papular eruptions of face and scalp from age of two years along with mild facial dysmorphism (frontal bossing, wide and flat nasal bridge and epicanthal folds (8)).

Late presentation of the disease has also been reported. The patient described by Brook was a 22 year old female (1). Kudoh *et al* (10) described a girl with end organ unresponsiveness to vitamin D without alopecia. She suffered from bone pains beginning at the age 12 years and was found at the age of 14 to have hypocalcemia, secondary hyperthyroidism and osteomalacia (9). Sachin *et al* (10) reported a case of VDDR type II with onset of rickets at the age of thirteen years without alopecia progressing to marked disability by twenty three years of age (10).

Conclusion

Our patient had late onset disease in association with congenital cyanotic heart disease, eye and ear anomalies. Though congenital heart disease and facial anomalies are commonly seen in association with hypocalcemia in Di George syndrome, till date there is no report of any such association with hypocalcemia due to VDDR type II.

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