Case Report

A rare case of Vitamin D dependent rickets type II: a case report

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ABSTRACT

Vitamin D-dependent type II rickets (VDDR II) is a rare autosomal recessive disorder caused by mutation in the vitamin D receptor gene, leading to end-organ resistance to 1,25(OH)2 vitamin D3. It presents with refractory rickets and growth retardation presenting in the first year of life. It is frequently associated with alopecia totalis. Due to target organ-resistance, its response to vitamin D is poor. The recommended treatment is giving supra physiological dose of 1,25(OH)2 vitamin D3 and a high dose of oral or intravenous calcium. The response of alopecia to treatment is generally poor. We present a 3½ year-old male child with VDDR II whose alopecia and rickets partially responded to 1,25(OH)2 vitamin D3.

Key words: Autosomal recessive, End-organ resistance, Refractory rickets, Vitamin D, 1,25(OH)2 Vitamin D3

INTRODUCTION

Vitamin D-dependent type two rickets (VDDR II) is a rare autosomal recessive disorder caused by mutation in the vitamin D receptor gene, leading to end-organ resistance to 1,25(OH)2 vitamin D3. It presents with refractory rickets and growth retardation presenting in the first year of life.1 It is frequently associated with alopecia totalis. Its biochemical parameters are hypocalcemia, hypophosphatemia, hyperparathyroidism, and elevated circulating levels of 1,25(OH)2 vitamin D3. The significantly elevated serum levels of 1,25(OH)2 vitamin D3 distinguishes this disorder from 1-α – hydroxylase deficiency, which is associated with low levels of 1,25(OH)2 vitamin D3. Due to target organ resistance, its response to vitamin D is poor. The recommended treatment is giving supraphysiological dose of 1,25(OH)2 vitamin D3 and high dose oral or intravenous calcium. The response of alopecia to treatment is generally poor although there has been one previous report of alopecia responding to 1,25(OH)2 vitamin D 3.2 Till date, 50 unique mutations of vitamin D receptor gene have been noted.3 We present a 3-year-old male child with VDDR II whose alopecia and rickets partially responded to 1,25(OH)2 vitamin D3.

CASE REPORT

A three and half year-old male child, born out of a nonconsanguineous marriage presented with progressive loss of hair since 5 months of age over the scalp and bilateral eyebrows. History of widening of wrists since 1 year, inward curving of the right lower limb since 2 years. The mother also noticed abnormal shape of the chest.(Figure 1) The child has gross motor developmental delay. He had achieved neck-holding at 6 months, sitting without support at 1 year, able to stand with support at 2 years and not able to stand without support. His other developmental domains were normal. The child also had history of delayed dentition. He was born through normal
vaginal delivery with birth weight of 2.78kgs. No h/o polyuria, polydipsia. At admission, the child’s weight was 11.42 kg (<3rd percentile the World Health Organization (WHO) weight for age), his length was 84 cm (<3rd percentile WHO weight for age), and he had a normal head circumference of 50 cm. He had evidence of rickets in the form of wide open anterior fontanel, frontoparietal bossing, rickety rosary, Harrison’s sulcus, wrist widening, with wind swept deformity of lower limbs (genu valgum of right lower limb and genu varam of left lower limb), (Figure 2). There was no evidence of other vitamin or mineral deficiencies.

Investigations revealed hemoglobin of 9.2 gm%. His renal function tests (urea-18 mg/dL, serum creatinine - 0.5 mg/dL), sodium (139 mEq/L), potassium (3.6 mEq/L), chloride (107 mEq/L) and venous bicarbonate 18 mmol/L were in the normal range, ruling out the renal etiology of rickets. His serum calcium was low (7.2 mg/dL) serum phosphorus was 3.6 mg/dl, alkaline phosphatase (1600IU/L). The x-ray of his wrist was suggestive of rickets, which was further confirmed by raised parathormone levels of 858.1. His 25(OH)2 vitamin D3 levels indicated insufficiency (15.3) and 1,25(OH)2 vitamin D3 levels were raised, suggestive of end-organ insensitivity. Ultrasound of the abdomen was normal without any nephrocalcinosis.

The patient was given intravenous calcium gluconate for 3 days and was started on 1, 25-OH vitamin D at dose of 2 mcg/kg daily and oral calcium at 1,000 g/day. At 1-month follow-up, the patient showed an improvement in motor functions.

**DISCUSSION**

When there is a high prevalence of nutritional rickets, other etiologies of rickets are often not thought of. This results in the delayed initiation of treatment, resulting in severe growth retardation and deformities.

Estimation of vitamin D levels are costly and high doses of vitamin D is routinely given without confirming diagnosis. Such unwarranted treatment may lead tonephrocalcinosis, especially in renal tubular acidosis. Red flag signs suggesting nonnutritional etiologies are early onset of rickets, severe deformity, deformities localized to lower limbs, associated failure to thrive, acidotic breathing, and the presence of dental abscesses, cataracts, or alopecia.

Our patient had alopecia with severe deformities, aiding the diagnosis, VDDRII is an extremely rare disorder caused by target organ resistance to 1,25(OH)2 vitamin D, the biologically active form of vitamin D. There are a few isolated case reports from India earlier but the exact prevalence of the disease is not yet known.²³ It is diagnosed through the finding of normal or elevated circulating levels of 1,25(OH)2 vitamin D, which differentiate it from vitamin D-dependent rickets type I (VDDR I).

![Figure 1: Alopecia, windswept deformity of lower limbs, double malleoli.](image)

![Figure 2: Frontoparietal bossing, rickety rosary, Harrison sulcus.](image)

The latter is caused by defective1-α hydroxylation of 25(OH) vitamin D in the kidneys, resulting in low serum
levels of 1,25(OH) vitamin D3. The most common defect is undetectable binding of 1,25(OH)2 vitamin D to the receptor either because of an absent VDR or a defective steroid-binding domain of the vitamin D receptor (VDR). Patients with VDDR2 are early-onset rickets, hypocalcemia, and associated total body alopecia. The alopecia may be present at birth or within the first few months of life and progresses to alopecia totalis by childhood. Alopecia is generally not responsive to treatment. The development of alopecia is felt by some investigators to be associated with a more profound 1,25(OH)2 vitamin D3 resistance. The relationship between alopecia and resistance to 1,25(OH)2 vitamin D3 in 22 cases from 30 kindreds in whom they noticed that alopecia was associated with the severest grades of resistance to 1,25(OH)2 vitamin D3. There is one previous case report of alopecia in VDDR II responding to 1,25(OH)2 vitamin D3. Authors also found a similar improvement in alopecia. There is a report of two patients with presentation of only alopecia in the absence of rachitic changes, which might be explained by differences in sensitivity to 1,25(OH)2D3 of bone formation and hair growth. The use of intravenous high-dose calcium infusions followed by a high dose of oral calcium is an effective method of treatment of VDDRII. The treatment is more effective if started early in the course of the disease and leads to early healing and better growth with prevention of bone deformities. Early treatment may also lead to improvement in alopecia, the mechanism for which needs to be elucidated.

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