A case report of vitamin D dependent rickets in identical twins

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Introduction

Rickets is a common disorder of childhood in which mineralization of the organic matrix of the growing skeleton is defective. This leads to a widening of the epiphyseal plates of long bones due to a disorganization of otherwise highly ordered columns of hypertrophied cartilage cells. In addition, the poorly mineralized long bones are incapable of withstanding mechanical stress and tend to undergo bowing deformities. Growth of the epiphyseal plate is diminished, stunting the growth of long bones¹. Most patients with rickets have nutritional deficiency of vitamin D that responds to conventional doses of Vitamin D₃. Rickets secondary to hypophosphataemia, Vitamin D dependency, renal tubular acidosis and renal failure are refractory to treatment with vitamin D₃.

Case report

Two-year old twin sisters, born after full term normal hospital delivery to parents of non-consanguineous marriage, came to hospital with complaints of difficulty in walking and keeping limbs apart for last 1 year. Their birth weights were 2 kg and 2.25 kg respectively and milestones of psychomotor development were appropriate for age. Their weights were 8.0 kg and 8.5 kg (70% and 75% of expected weight as per CDC 2000 standards), heights 70 cm and 69 cm (81% and 82% of expected height as per CDC 2000 standards), and head circumferences 48.5 cm each. Their three year old elder brother was apparently normal. There was no history of repeated respiratory illness or features suggestive of malabsorption syndrome.

On examination, they had mild pallor and just palpable liver (span- normal for age). They had classical features of rickets – palpable round rachiticrosary, widening of wrists, forward projected sternum, frontal and parietal bossing, and delayed dentition. The twins had normal hair growth. Both had bowlegs. Distances between the knees, with the child standing and heels touching, were 6.5 cm and 7 cm respectively. Both were normotensive (Figure 1).

Their haemoglobin levels were 12 g/dl and 11.2 g/dl with normal haemograms. Both had hypocalcaemia (serum calcium 7.7 mg/dl with ionized calcium 3.4 mg/dl and serum calcium 7.4 mg/dl with ionized calcium 3.2 mg/dl respectively) and hypophosphataemia (serum inorganic phosphate 2.5 mg/dl and 2.4 mg/dl). Renal function tests were normal and liver function tests revealed elevated alkaline phosphatase level (840 IU/L and 800 IU/L respectively). Urine analysis revealed no glycosuria or proteinuria with normal urinary calcium level. Stool microscopy and estimation of stool fat were normal. Radiological evaluation revealed typical changes of rickets in wrists, knees and pelves in both patients (Figure 2). Arterial blood gas analysis revealed normal values with no acidosis. Serum parathormone levels were high in both cases (112 IU and 120 IU respectively).

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Suspecting Vitamin D dependent rickets, these twins were treated with physiological doses of 1 hydroxyvitamin D₃ (60 ng/kg/d) along with calcium supplementation, which resulted in healing of the rickets and its clinical features. On follow up after 8 weeks, both twins showed general improvement along with healing of the radiological features.

**Figure 2**: X-ray of wrists

**Discussion**

Vitamin D dependent rickets, one of the refractory rickets, is mainly of two types. Vitamin D-dependent rickets type I (VDDR-I), also known as pseudo vitamin D deficiency rickets (PDDR), is characterized by decreased conversion of 25-hydroxyvitamin D₃ to 1,25 dihydroxyvitamin D₃. Genetic linkage studies indicate that the mutation causing 1 alpha-hydroxylase deficiency is linked to chromosome 12 at 12q14. Vitamin D-dependent rickets type II (VDDR-II) is characterized by mutations in the vitamin D receptor which impairs its function by altering the binding of the receptor heterodimer complex to DNA. Individuals with this disorder have high circulating level of 1,25 dihydroxyvitamin D₃, but the hormone is ineffective because of the impaired responsiveness of target organs to 1,25 dihydroxyvitamin D₃. To date, a total of 13 mutations causing vitamin D-dependent rickets type II have been characterized. Both these disorders have autosomal recessive modes of transmission.

These twins presented with clinical features and bony deformities resembling rickets. X-rays of wrists and knees were obtained. On finding the radiological features of rickets, in the form of cupping, fraying and osteopenia, they were treated with Vitamin D₃ 600,000 IU over 10 days. X rays were repeated after 4 weeks. When evidence of healing was not found, a repeat course of Vitamin D₃ 600,000 IU was given. On follow up x-rays after another 4 weeks, when the line of healing was not seen, the cases were classified as refractory rickets and further biochemical evaluation was undertaken.

On biochemical evaluation, we found low calcium, low phosphorus and high alkaline phosphatase levels. Arterial blood gas analysis was normal and urine analysis revealed no abnormality. Urinary calcium was normal. Serum parathormone levels were high in both cases differentiating them from hypophosphataemic rickets. This finding confirmed the diagnosis of vitamin D dependent rickets. Definitive diagnosis of VDDR-I and VDDR-II requires estimation of 1,25 dihydroxyvitamin D₃ with low levels in VDDR-I and elevated levels in VDDR-II. This could not be done due to lack of availability and affordability. Absence of alopecia pointed towards the diagnosis of VDDR-I, as this is a common finding in VDDR-II. As management of the two is different only in that higher doses of vitamin D metabolites are required in cases of VDDR-II, a trial of vitamin D metabolites can be more practical than this test which is costly and not easily available.

These twins were treated with physiological doses of 1 hydroxyvitamin D₃ (60 ng/kg/d) along with calcium supplementation. After administration of these doses for eight weeks, improved clinical and radiological features were noted. VDDR-I is an autosomal recessive disorder and presence of this disorder in identical twins has not been reported so far to the best of our knowledge and despite extensive literary search.

**References**


