

CASE REPORT

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Vitamin D - Dependent Rickets, Type II Case Report

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ABSTRACT

Aim: The aim of this work the report of one case with vitamin D-dependent rickets, type II. **Methods:** Diagnosis has been established based on anamnesis, physical examination, laboratory findings and radiological examination. **Results:** A female child (age 25 months) has been hospitalized due to bone deformity, bone pain, alopecia and walking difficulties. The laboratory findings have revealed that the calcium values was low (1.20 mmol/L), phosphates in the reference value (1.30 mmol/L) the alkaline phosphatase value was quite high (852 IU/L), high value of parathyroid hormone (9.21 pmol/L), normal value of 25- hydroxyvitamin D, whereas the values of 1,25-dihydroxyvitamin D was high (185 µmol/L). Radiographic changes were evident and typical in the distal metaphysis of radius and ulna as well as in the bones of lower limbs (distal metaphysis of femur and proximal metaphysis of tibia and fibula). After treatment with calcium and calcitriol, the above mentioned clinical manifestations, laboratory test values and the radiographic changes in bones withdrew. **Conclusions:** Vitamin D-dependent rickets, type II is a rare genetic recessive disease, and its treatment includes a constant use of calcium and calcitriol.

Key words: Vitamin D receptor, 1,25- dihydroxyvitamin D, Bone, Alopecia, Calcium intravenous.

1. INTRODUCTION

Active vitamin D, 1,25-dihydroxyvitamin D [calcitriol or 1,25(OH)₂D], is crucial for normal calcium homeostasis. The vitamin D receptor facilitates the downstream biological action of 1,25-dihydroxyvitamin D₃ at target tissues.

Vitamin D receptor is a member of the steroid-thyroid-retinoid receptor gene super family of nuclear transcription factors. In humans, heterogeneous mutations in the vitamin D receptor gene cause the rare autosomal recessive genetic disease known as vitamin D-dependent rickets type II, also known as hereditary vitamin D resistant rickets (1-3). Patients with vitamin D-dependent rickets type II develop early onset rickets and have hypocalcemia, elevated serum 1,25-dihydroxyvitamin D and secondary hyperparathyroidism (4). Some patients with vitamin D-dependent rickets type II have total or partial alopecia and may develop skin lesions or dermal cysts (5).

2. AIM

The aim of the work was presentation of one case with vitamin D-dependent rickets type II, treated at the Pediatric Clinic.

3. METHODS

For the diagnose the following examinations were used: anamnesis, physical examination, concentration in serum of

calcium, phosphates, alkaline phosphatase (using a photometric method I Lab-650), parathyroid hormone (using radioimmuno-metric assay), 25-hydroxyvitamin D and 1,25- dihydroxyvitamin D was measured by HPLC (High Performance Liquid Chromatography) which test were done in Tirana Lab- Albania, radiographic examination of the bones, pedigree and karyotype which was done from the peripheral lymphocytes.

4. CASE REPORT

A female child (Z.H.), age 25 months, with the body weight 12 kg (25-50 percentile), height 84 cm (10-25 percentile), head circumference 48 cm (50 percentile) was admitted to hospital in April 2012 due to perspiration, constipation, deformed extremities, walking difficulties, partial alopecia and early convulsions. She was a third child from the fourth pregnancy; a mother had an abortion during the second month of pregnancy, the parents and other children were healthy and they deny the

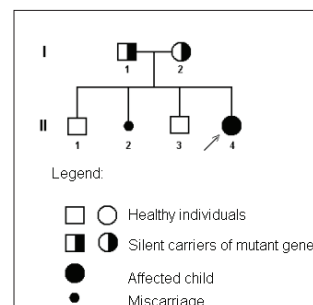


Figure 1. Pedigree of the family of a child with vitamin D dependent rickets, type II



Figure 2. A. Partial alopecia before treatment. B. During the treatment new hair started to grow

existence of any hereditary disease (Figure 1). Rickets prevention with vitamin D daily dosage 500 IU was done on a regular basis during the first year, whereas during the second year of life patient was not given vitamin D. As an outpatient and in a regional hospital child was treated with ergocalciferol once with attacking doses (600.000 IU) intramuscularly, but without positive results. In physical examination, anterior fontanel was open (1x1 cm), the posterior fontanel was closed, the cranial suture were normal and there was mild frontal bossing. The distribution of hair was abnormal. She had patches of scalp that were devoid of hair (partial alopecia), while other regions had sparse hair and still other areas had full hair (Figure 2 A), during the treatment these changes started to disappear (Figure 2 B). The widening of the distal metaphysis of the radius and ulna (so-called double joints) was evident (Figure 3) also in distal metaphysis of fibula, two maleoli can be seen, so-called Marfan's tubercule (Figure 4). The lower extremities looked like the letter X- crura valga rachitica (Figure 5).

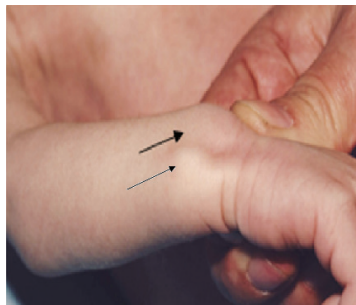


Figure 3. Widening of the distal metaphysis of radius and ulna (so-called double joints)

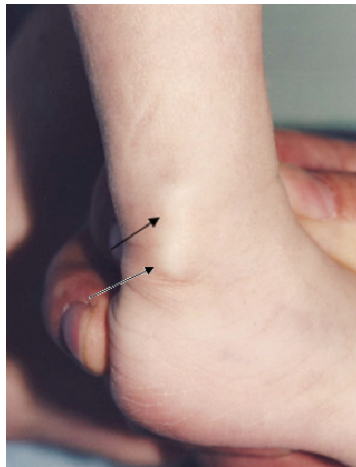


Figure 4. Widening of the distal metaphysis of fibula above fibular maleollus (so-called Marfan's tubercule)



Figure 5. Deformities of lower limbs, like the letter X- crura valga rachitica

Laboratory findings: At presentation, her serum chem-

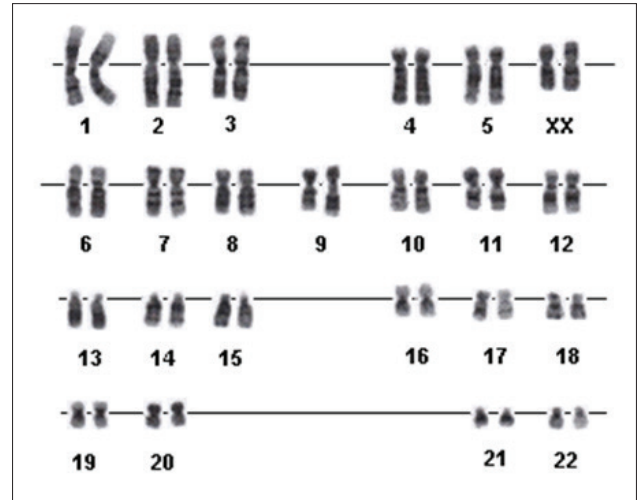


Figure 6. Karyotype (46, XX) of patient with vitamin D dependent rickets, type II

istry panel showed normal values of serum electrolytes, albumin, magnesium and renal function. The karyotype was normal 46, XX (Figure 6).

The calcium value before treatment was low 1.20 mmol/L (reference value 2.20-2.70 mmol/L), also of phosphates 1.30 mmol/L (reference value 1.4-2.1 mmol/L), the alkaline phosphatase was quite high in the beginning (852 IU/L) and during treatment it decreased to 142 IU/L (reference value 50-155 IU/L). The value of 25-hydroxyvitamin D was normal (28 µg/L), 1,25-dihydroxyvitamin D was high (185 µmol/L- reference value 60-108 µmol/L) and the value of parathyroid hormone was high 9.2 pmol/L (reference value 0.95-6.8 pmol/L), tab 1.

Parameter	Before treatment	During treatment (after 4 months)
Calcium	1.20 mmol/L	2.3 mmol/L
Phosphorus	1.30 mmol/L	1.7 mmol/L
Alkaline phosphatase	852 IU/L	142 IU/L
25-hydroxyvitamin D	28 µg/L	28 µg/L
1,25-dihydroxyvitamin D	185 µmol/L	102 µmol/L
Parathyroid hormone	9.2 pmol/L	6.1 pmol/L

Table 1. Laboratory findings in a case with vitamin D-dependent rickets type II

Radiographic changes in bone were typical in our case. The specific radiographic changes in the bones of the extremities were expressed in the distal metaphysis of the radius and ulna: the metaphysis is widened and deepened (gaining a concave shape), the line between the epiphysis and metaphysis is not clear (it appears in a shape of the brush).

After establishing a diagnosis of the disease we started the treatment with calcium and calcitriol. The patient had a prolonged hospitalization in which she was treated with large amounts of intravenous calcium 50 mg/kg/day, calcitriol 60 ng/kg/day divided into two doses orally.

5. DISCUSSION

This is the first case with Vitamin D-dependent rickets type II diagnosed in Kosovo. Two decades ago vitamin D deficiency rickets used to be quite frequent (30%) and it was a public issue, whereas now days thanks to the continuous prevention with vitamin D it decreased considerably to 0.8%. Different forms of rickets used to exist even before, but it is evident that a priority in preventive paediatrics in our country was vitamin D defi-

ciency rickets. In spite of continuous prevention of rickets with vitamin D, the signs of rickets were present during the physical examination in our case. The patient was treated in the regional hospital with the attacking doses of vitamin D (ergocalciferol), but without any clinical improvements, and that, together with the laboratory results, made us believe that we were dealing with vitamin D-dependent rickets type II. Alopecia is a very common clinical characteristic in cases with Vitamin D-dependent rickets type II. It can be areata and totalis (in our case it was partial, and after treatment it started to disappear. The authors (6-9) registered in their cases the existence of partial alopecia, whereas the author Stojanov presented one case suffering from total alopecia (10). Radiographic changes and clinical manifestation in bones (in distal metaphysis of radius and ulna as well as distal metaphysis on tibia and fibula) were characteristic of rickets in our case. The identical changes in bones appear also in case with vitamin D deficiency rickets, but they do disappear with the giving the therapeutic dosage of vitamin D₃ (5000 IU/per day) during the time period of 3-5 weeks, whereas in our case the changes started to disappear after three and half months (after the values of calcium and alkaline phosphatase were brought to normal) after giving the high dosages of calcitriol and calcium. Slow disappearance of radiological changes in bones in line with normalization of other laboratory findings is in favour of diagnosis of vitamin D-dependent rickets type II. The other authors (11, 12) stated that the changes in bones were not that much visible in cases with this form of rickets (because the cases were diagnosed earlier) and these changes started to disappear faster (after the second month) after use of the corresponding therapy.

The initial laboratory findings was suggestive of Vitamin D-dependent rickets type II, but the elevated 1, 25-dihydroxyvitamin D levels and the severity of rickets both clinically had raised the possibility of a diagnosis of non vitamin D deficiency rickets. Values of calcium, alkaline phosphatase, parathyroid hormone and 1, 25-dihydroxyvitamin D in our case started to normalize after the fourth month of treatment. The treatment of with vitamin D dependent rickets type II is not standardized. Several reports describe intravenous calcium therapy to achieve normal calcium levels and healing of rickets. In our case we describe the successful transition from intravenous to oral calcium therapy. Patient was initially treated with 50 mg/kg/day elemental calcium intravenous in time period of 18 hours, to allow at least few hours in the day for child activities. Administration of intravenous calcium suppresses parathyroid hormone is again elevated prior to the next infusion. The calcium dose has to be titrated based on serum calcium, phosphates, parathyroid hormone and urine calcium and phosphates excreted. During that time, her alkaline phosphatase levels decreased, her bone pain resolved and she started to demonstrate improved musculoskeletal strength.

Levels of parathyroid hormone decreased after 120 days of treatment in our patient is more convincing of a dose-related response. Large amounts of calcium are necessary to suppress parathyroid hormone secretion in children with Vitamin D-dependent rickets type II. Phosphorus supplementation was not necessary and phosphates were normalized along with suppression of hyperparathyroidism with calcium supplementation. Our patient successfully reacted to oral calcium therapy after treatment with intravenous calcium for 3,5 months and demonstrated radiographic signs of healing. Currently, frequent administration of oral calcium allows sufficient passive trans-

port through the intestinal wall to achieve serum calcium levels $\geq 8\text{mg/dL}$. Other authors (13-15) treated the patients with Vitamin D-dependent rickets type II with high dosage of calcium that was administered orally. Only after the vitamin D status was improved with high-dose calcitriol (1,25-dihydroxyvitamin D) 60 ng/kg/day divided into two doses) did the patients, 1,25-dihydroxyvitamin D level increased to concentrations more typically seen in patients with Vitamin D-dependent rickets type II. This helped to elucidate the patients resistance to active vitamin D and sustained requirement for calcium therapy.

6. CONCLUSION

Vitamin D-dependent rickets type II, is a rare hereditary autosomal recessive disease due to heterogenous mutations in the vitamin D receptors. Clinical manifestations are quite identical with Vitamin D-deficiency rickets (except alopecia and convulsions), whereas hypocalcemia and high values of 1,25-dihydroxyvitamin D in serum were characteristic in laboratory findings regarding the Vitamin D-dependent rickets type II. Treatment is long lasting followed with giving high doses of calcium and constant dosage of calcitriol.

CONFLICT OF INTEREST: NONE DECLARED.

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