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CASE REPORT

Late Onset of Vitamin D-Dependent Rickets Presenting with 8 Years of Low Back Pain: A Case Report

Ehsan Arjmandzadeh[1], Azam Ghanei[2]*, Mohammad Bagher Owlia[3], Sara Talebi[4]
[1,4]*Department of Medicine, International campus, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*
[2,3]*Department of Internal Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*
Corresponding Author: Azam Ghanei, E-mail: a.ghanei@ssu.ac.ir

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ABSTRACT

Vitamin D (Vit D) is a prohormone that can be activated during a sequential hydroxylation done by two major mitochondrial cytochrome P450 liver and renal enzymes. Vit D-dependent rickets type 1 (VDDR1) is a rare autosomal recessive hereditary disorder resulting from defective renal 1α-OHase presenting with severe rickets, hypocalcemia, and secondary hyperparathyroidism. Although homozygous Vit D hydroxylation deficient patients develop severe rickets symptom and signs before the age of 12 months, heterozygous types have minor symptoms and are extremely rare presenting as late as 14 years after birthday. Here we present a suspicious case of VDDR1 at 21 years old of age with mild symptoms and signs.

INTRODUCTION

Active vitamin D (Vit D) is one of the most important regulatory hormones playing a critical role in blood minerals homeostasis, especially calcium. There are two forms of Vit D, Ergocalciferol (Vit D_2) produced by plants and cholecalciferol (Vit D_3) which is generated by animal tissues and in humans, synthesized by the skin from 7-dehydrocholestrol under the action of ultraviolet light (1). Whether it is digested or synthesized in the skin, Vit D is a prohormone or inactive hormone that can be activated during a sequential hydroxylation done by two major mitochondrial cytochrome P450 liver, and renal enzymes which named Vit D 25-hydroxylase and 25-hydroxy Vit D-1α-hydroxylase (1α-OHase), respectively (1-3). When the blood levels of calcium or $1,25(OH)_2D$ decreases and phosphate increases, parathyroid hormone (PTH) is released (3). Rickets defined as defective mineralization of skeleton before epiphyseal closure, is one of the most common pediatric diseases (4). Rickets affects an estimated 1 in 200,000 children, however, hereditary types, especially Vit D-dependent rickets type 1 (VDDR1), is much less common and its prevalence is unknown (5). Typical rickets symptoms include growth retardation, joint widening (such as ankles, wrists and costochondral), seizure episodes, frontal bossing, and proximal muscle weakness (6). The VDDR1 also as know Vit D hydroxylation deficient rickets type 1 or pseudo-Vit D deficiency rickets type 1, is a rare autosomal recessive hereditary disorder resulting from defective renal 1α-OHase presenting with severe rickets, hypocalcemia, and secondary hyperparathyroidism (7). Although homozygous Vit D hydroxylation deficient patients develop severe rickets symptom and signs before the age of 12 months, heterozygous types have minor symptoms and are exceedingly rare (8). Up to now, about 68 mutations in 1α-OHase have been reported worldwide (7, 9). Here we report a case suspicious for a kind of Vit D hydroxylation deficient rickets with late onset and presenting with only chronic low back pain and proximal myopathy.

CASE PRESENTATION

A 21-year old girl admitted to the endocrinology ward due to proximal muscle weakness, chronic low back pain, and occasional tetany from 8 years ago. Her low back pain was the prominent location of pain, and she was complaining of

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a whole body pain and weakness that the pain was persistent and aggravated by normal daily activity. She reported difficulty to stand up without the assistant of hands due to muscle weakness especially from 4 years ago. She was also complaining of loss of appetite and myalgia especially for shoulder and pelvic girdle muscles. Her past medical history was normal, and there was no history of thyroid, parathyroid, and kidney diseases. On physical examination, she was lethargic but co-operative, she was not febrile, there was no tachycardia or tachypnea and her blood pressure was 130/70 mmHg within the normal range. Her chest expansion was normal, and no kyphosis or scoliosis was seen. She exhibited carpopedal spasm when taking her pressure that occurred at 50 mmHg (Figure 1), but her Chvostek's sign was negative. There was no clinical evidence of rickets including enamel hypoplasia and genu varum except muscle hypotonia specially proximal lower limb weakness (with a muscle strength of 3/5). Also, there was no radiological findings mainly widening of the wrists or Looser's line in her pelvic and wrist x-rays graph. However, lowered bone density was seen in her pelvic x-ray graph. When she was asked to walk for assessing her gait the patient used circumduction for compensating her weakness and her gait was waddling. No other abnormality could be detected, and further investigations showed no biochemical evidence for malabsorption, renal, and hepatic disease. Echocardiography showed prolonged QT interval (Figure 2). The biochemical analysis of the blood sample are presented in the Table 1. Regarding the Table 1, serum calcium and phosphorous levels were 7.4 mg/dl and 2.6 mg/dl that indicated the hypocalcemia and hypophosphatemia, respectively. The blood alkaline phosphatase level was 1222 U/L (normal range less than 280 U/L) and the PTH level was 189 ng/L (normal range less than 65 ng/L). X-rays imaging of her hand, legs and chest did not show any signs of rickets.

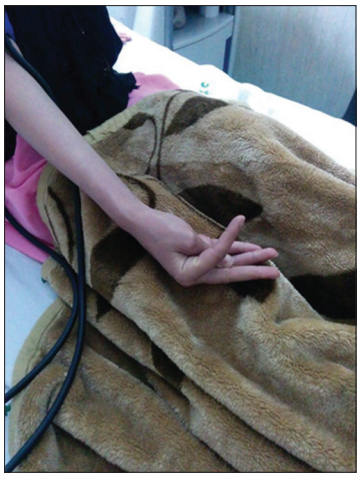

Figure 1: The patient carpal spasm during taking her blood pressure

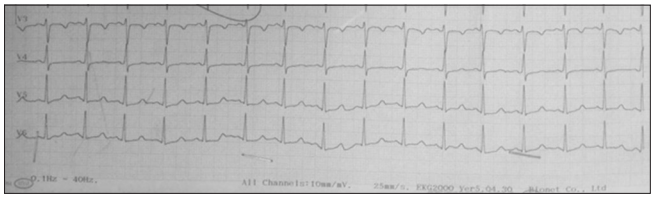

Figure 2: Electrocardiograph of the patient. Note the location of T wave between R to R interval and prolonged QT

DISCUSSION

According to the history, lab data, and clinical course of our patient, her condition, and the laboratory rickets was not just due to Vit D deficiency, malabsorption, and chronic renal or hepatic disease. Although some disease like celiac and other malabsorption diseases cannot be ruled out without further investigations like small intestine biopsy, generally it is felt that the tests were not indicated in such patient with the obvious wellbeing developmental and growth pattern regarding that her tissue transglutaminase antibody (anti- tTG) was negative. Also considering the child's good response to the physiological dose of active Vit D, it is strong evidence against these conditions. Keeping the facts above in mind, and due to the hallmark biochemical findings in VDDR1 that are hypocalcemia, hypophosphatemia and raised serum level of PTH, the most likely diagnosis is a mild (heterozygous) variant of Vit D-dependent rickets. Although due to low level of 25OHD (less than 3 ng/ml), measuring $1,25(OH)_2D$ was not valuable, but as mentioned before, not persistent Vit D deficiency and dairy-poor diet nor typical homozygous VDDR1 can describe the late onset of symptoms and

Table 1. Patient biochemical markers on admission

Marker	Amount	Normal range	Units
WBC	5,400	4,500-11,000	µL
RBC	3,900,000	4.2-5.4	µL
Hb	12.1	12±2	gr/dL
MCV	91.8	80-96	fL
Plt	178,000	150-450×10^3	µL
ALT	7	Up to 50	U/L
AST	19	Up to 40	U/L
Alk-P	1137	44-147	IU/L
CPK	95	22-198	IU/L
ESR	10	Up to 29	mm/h
TSH	2.3	0.5-5	mIU/L
T3	1.38	0.5-1.5	ng/dL
T4	8.3	5-12	µg/dL
Urea	18	7-20	mg/dL
Cr	0.7	0.5-1.1 in females	mg/dL
Ca	7.4	8-10	mg/dL
P	2.6	2.5-5.5	mg/dL
Na	138	135-145	mEq/L
K	3.6	3-5	mEq/L
Alb	4.1	3.5-5.5	g/dL
PTH	341	10-55	pg/mL
Vit D3 (25OH)	<3	20-50	ng/mL
24h urine Ca	19	100-250	mg/d
24h urine P	240	170-1200	mg/d

signs of the patient (7, 10). On the other hand, her phosphorus level was always around the lower limit of normal range while we expect lower levels in case of isolated Vit D deficiency. Currently, some studies have shown these patients do not necessarily have the same autosomal recessive trait and therefore the phenotype is variable, and it is believed that if the defect was less severe, the presentation of the affected patients would be later (11, 12). The patient was treated by both Vit D3 and calcitriol, her symptoms was controlled, and on discharge, serum calcium level was 8.8 mg/dl and serum phosphorus level was 3.6 mg/dl with a high level of well- being. Finally, although the patient does need more follow-up and investigations, it seems that patient has a mild form of VDDR1 and needs daily active Vit D for preventing the progression of symptoms and signs.

CONCLUSION

Considering the essential roles of Vit D in major body minerals homeostasis mainly calcium and phosphorus, and plenty of other important functions like cell differentiation and immune system modification and due to the high prevalence of Vit D deficiency, we should always think about it especially in those patients with musculoskeletal symptoms.

ETHICAL APPROVAL

This article did not need any ethical approval.

CONSENT

In this case report, patient feel the agreement to publish his disease.

AUTHOR CONTRIBUTION

All the authors contributed in this study equally.

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