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| RESEARCH ARTICLE

Vitamin D-dependent Rickets Type II

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| ABSTRACT

The work aimed to present one case with vitamin D-dependent rickets type II, treated at Nasser Hospital – in the Gaza Strip. The patient was 3 years old with a body weight of 8.5 kg and a height of 90 CM. Skin color was cyanotic, but skin moisture was dry. Body temperature was 39 C from axillary; Turgor was warm and rough. The texture of vascularity was ecchymosis. The patient was on NGT and ETT and had alopecia in their hair. His Nails color was pale but was clubbing in shape. Deformity in the head and face; his eyes are symmetrical, but he is blind with corneal opacities bilateral, about ears are symmetrical auricles and gross hearing acuity. Mouth mucous membrane was moist but had ulcers and infection; teeth were missing, and tongues cyanotic and cracked. He has dysphagia, dyspepsia and hoarseness of voice. Full range of motion of the neck. Carotid pulsation rate 160 b/min symmetrical and bounding, cervical lymph nodes are enlarged and tender. Respiratory rate 40 b/min, barrel chest and abnormal breathing pattern. The patient complained of productive cough, on percussion, lung sound was dullness, but in auscultation, bilateral wheezy; apical heart rate was 140 b/min regular and strong. His blood pressure was 130/83 mm Hg. Capillary refill was 3 seconds. Normal heart sounds. The abdomen was soft and relaxed but distended. A genitalia was normal, About range of motion was limited and flaccid motor response.M. Aker 3 years old of cons. marriage 1st cousin, the second order of birth; the chief complaint was Rickets Type 2, which is badly responding to vit D. The Personal history of this disease was discovered when he was two months old with a history of sibling died at the age of 4 years (his sister), at birth. The patient was normal without any symptoms, and at the age of two months, he started the symptoms; 1st one was hair loss with fragile bone. With investigation, there is Vit D deficiency, so calcium supplement and Vit D were given; at the age of one year, the condition worsened, and bones were more fragile with bowing of legs, so doctors advised increasing the dose of Vit D and calcium with calciless treatment, but the immune system suppressed, and he got a lot of chest infections, so hospital admission many times with intravenous antibiotics, sometimes he was intubated on Mechanical ventilation in pediatric (I c u), on 2 years, he was Oxygen-dependent then later he developed Respiratory Failure, at 3 year pt. was complaining severe chest infection and was intubated on Mechanical ventilation; unfortunately the child died at the age of 3 years.

| KEYWORDS

Vitamin D, dependent rickets type II, Nasser Hospital, Gaza Strip

| ARTICLE INFORMATION

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1. Introduction

Type II vitamin D-dependent rickets is an uncommon genetic condition. The gene chr. 12q12-q14, which codes for the vitamin D receptor, is mutated, and this results in the condition. The distinctive symptoms include end-organ resistance to 1,25-(OH)2vitamin D3 and, in severe cases, baldness (Schlingmann, 2011).

An inherited autosomal recessive condition, vitamin D-dependent rickets (VDDR) type II is also referred to as hereditary vitamin D-resistant rickets type II. The gene chr. 12q12-q14, which codes for the vitamin D receptor (VDR), is mutated, and this results in the disease. End-organ resistance to 1,25-(OH)2 vitamin D3 and severe alopecia are distinguishing characteristics. The rachitic alterations brought on by VDDR type II are not sensitive to vitamin D therapy. In severe situations, alopecia and VDDR type II are both present (Cheng, 2004).

For healthy calcium homeostasis, 1,25-dihydroxyvitamin D, also known as calcitriol or 1,25(OH)2D, is essential. The 1,25-dihydroxy vitamin D3's biological effect in target tissues is facilitated by the vitamin D receptor. Rich clinical and biochemical research that revealed the crucial function that vitamin D played in ensuring adequate bone and mineral metabolism led to the realization that genetic abnormalities in vitamin D activation or responsiveness might result in rickets (Takeyama, 1997; Quesada-Gomez, 2018)

The nuclear transcription factor super family of steroid-thyroidretinoid receptor genes includes the vitamin D receptor. Vitamin D-dependent rickets type II, also known as hereditary vitamin D resistant rickets, is a rare autosomal recessive genetic disorder that affects humans and is brought on by diverse mutations in the vitamin D receptor gene. Patients with vitamin D-dependent rickets type II exhibit hypocalcemia, increased serum 1,25-dihydroxyvitamin D levels, and secondary hyperparathyroidism in addition to early-onset rickets. In addition to skin lesions or dermal cysts, some patients with vitamin D-dependent rickets type II experience total or partial alopecia (Luxwolda, 2013; DeLuca, 1976).

1.1 Main Objective:

To present case with vitamin D-dependent rickets type II as a rare case

2. Methods:

For the diagnosis, the following examinations were used: anamnesis, physical examination, concentration in serum of calcium, phosphates, alkaline phosphatase, and radiographic examination of the bones.

3. Discussion

This is one of the rare cases of Vitamin D-dependent rickets type II diagnosed in Gaza. Different forms of rickets used to exist even before, but it is evident that a priority in preventive pediatrics in our country was vitamin D deficiency rickets. In spite of continuous prevention of rickets with vitamin D, the signs of rickets were present during the physical examination in our case.

Vitamin D is essential for bone growth, mineralization, and absorption of calcium and phosphate, which is deficient in rickets. Vitamin D is obtained by dietary intestinal absorption and through the skin and is available as vitamin D2 and vitamin D3. Initially, in the liver, vitamin D is hydroxylated to 25-hydroxyvitamin D3 (25-OHD3). Later, 25-OHD3 bound to the vitamin-binding protein is transported to the kidney, where it undergoes hydroxylation to form the hormonally active metabolite, dihydroxy vitamin-1,25 D3 (1,25-OH_2D3). The tissue receptors for vitamin D metabolites are localized in various organs, including the kidney, intestine, pancreas, parathyroid gland, muscle, pituitary, skin, and bones, and 1,25-OH_2D3 binds specifically to a receptor in the nuclei to stimulate calcium transport and also controls the expression of target genes mediated through the nuclear VDR. Mutations of the VDR gene lead to VDDR type II (McSheehy, 1987; Maierhofer, 1983).

The patient was treated in the Nasser hospital with the attacking doses of high dose 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 (Scarpelli, 1960; Nesterova, 2013).

The identical changes in bones also appear in cases with vitamin D deficiency rickets, but they do disappear with the giving the therapeutic dosage of vitamin D_3 (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. The slow disappearance of radiological changes in bones in line with thenormalization of other laboratory findings is in favor of thediagnosis of vitamin D –dependent rickets type II (Shafeghati, 2008; Sahay, 2012; Azemi, 2014).

The initial laboratory findings were suggestive of Vitamin D-dependent rickets type II, but the elevated 1, dihydroxy vitamin-25 D levels and the severity of rickets both clinically had raised the possibility of a diagnosis of nonvitamin D deficiency rickets. Values of calcium, alkaline phosphatase, parathyroid hormone, and 1, 25–dihydroxy vitamin 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 (Sahay, 2012).

The patient was initially treated with 50 mg/kg/day elemental calcium orally; Administration of oral calcium suppresses parathyroid hormone is again elevated prior to the next oral calcium. The dose has to be titrated based on serum calcium, phosphates, parathyroid hormone, and urine calcium and phosphates excreted. During that time, his alkaline phosphatase levels decreased, his bone pain resolved, and he started to demonstrate improved musculoskeletal strength (Azemi, 2004).

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 transport through the intestinal wall to achieve serum calcium levels ≥8mg/dL.

Treatment Optimal therapy consists of oral calcitriol (0.5-1.5 mcg/day). Calcitriol prevents increases in parathyroid hormone caused by phosphate therapy. Minor changes in calcitriol dose may produce hypercalcemia and renal damage. The calcium-creatinine (mg/mg) ratio in urine must be closely monitored at first and then every 3-6 months (Feldman, 2014; Christakos, 2012; Malla, 2011).

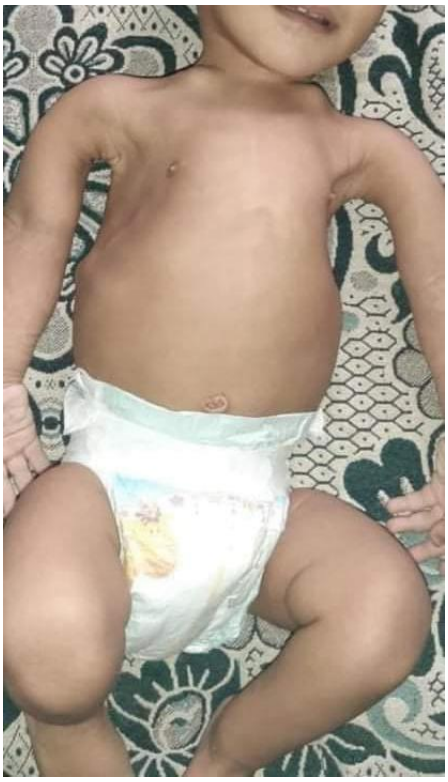


Figure 1: abdominal distention, malformed chest, Rachitic Rosary
Wide sternal angle
Wide chest in the lower part

Figure 2: Rachitic rosary

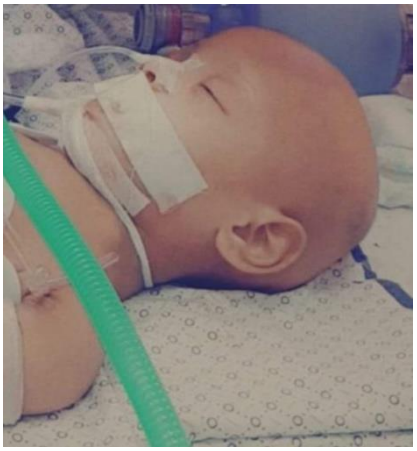


Figure 3: Alopecia and Ryle tube

Figure 4: Widened wrist

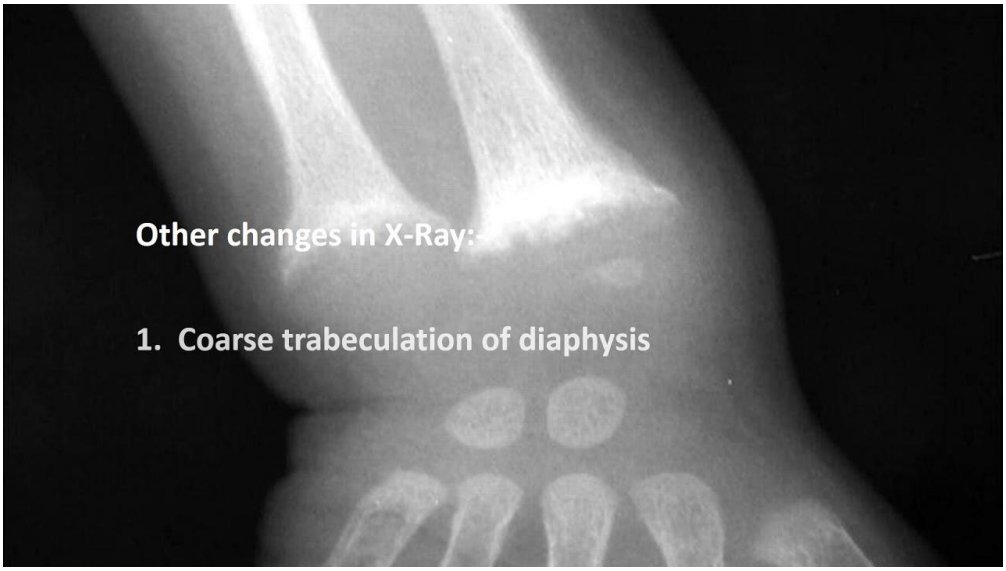


Figure 5: Radiographic changes and clinical manifestation in bones (in distal metaphysis of radius and ulna as well as distal metaphysis on tibia and fibula) were characteristic of rickets in our case.

Figure 6: On Mechanical Ventilation

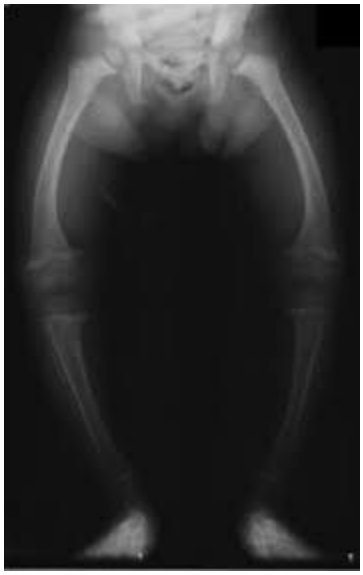
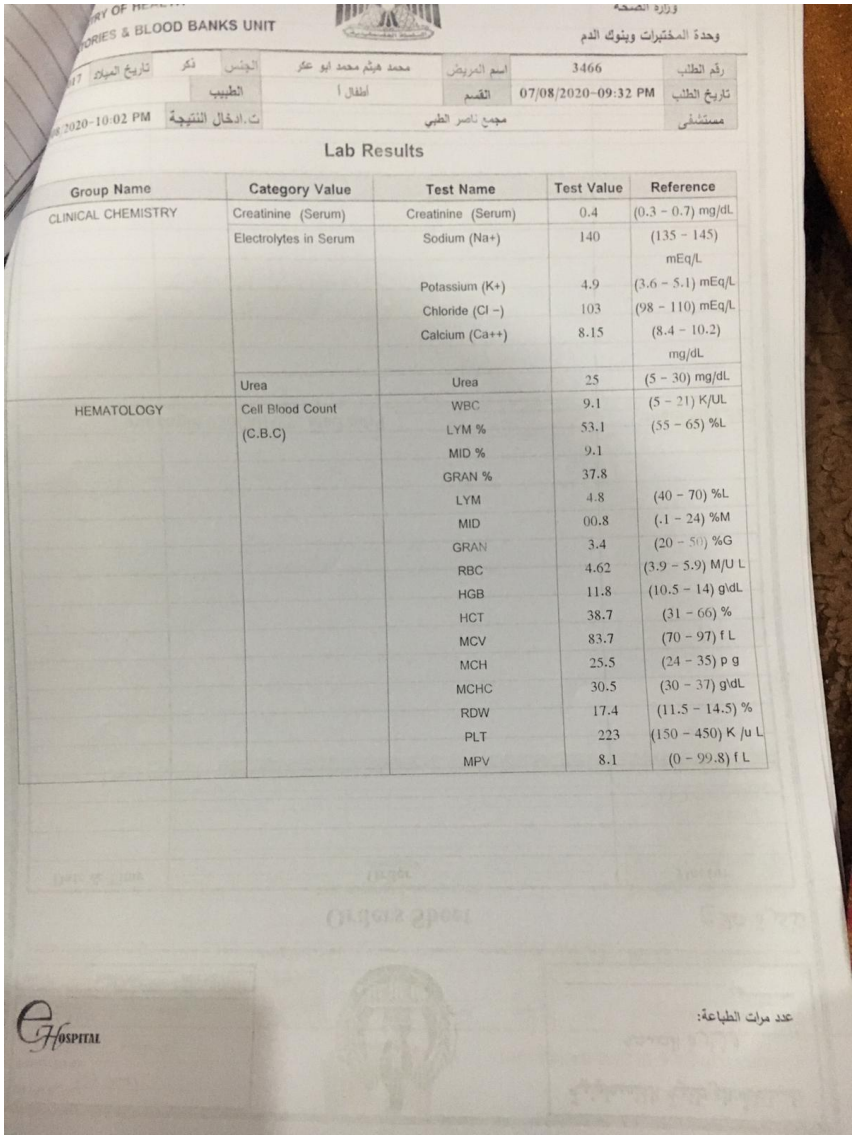


Figure 7: Bowing LEGS



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Lab Results

Group Name	Category Value	Test Name	Test Value	Reference
CLINICAL CHEMISTRY	Creatinine (Serum)	Creatinine (Serum)	0.4	(0.3 - 0.7) mg/dL
	Electrolytes in Serum	Sodium (Na+)	140	(135 - 145) mEq/L
		Potassium (K+)	4.9	(3.6 - 5.1) mEq/L
		Chloride (Cl -)	103	(98 - 110) mEq/L
		Calcium (Ca++)	8.15	(8.4 - 10.2) mg/dL
	Urea	Urea	25	(5 - 30) mg/dL
HEMATOLOGY	Cell Blood Count (C.B.C)	WBC	9.1	(5 - 21) K/UL
		LYM %	53.1	(55 - 65) %L
		MID %	9.1	
		GRAN %	37.8	
		LYM	4.8	(40 - 70) %L
		MID	00.8	(.1 - 24) %M
		GRAN	3.4	(20 - 50) %G
		RBC	4.62	(3.9 - 5.9) M/U L
		HGB	11.8	(10.5 - 14) g\dL
		HCT	38.7	(31 - 66) %
		MCV	83.7	(70 - 97) f L
		MCH	25.5	(24 - 35) p g
		MCHC	30.5	(30 - 37) g\dL
		RDW	17.4	(11.5 - 14.5) %
		PLT	223	(150 - 450) K /u L
		MPV	8.1	(0 - 99.8) f L

HOSPITAL

عدد مرات الطباعة:

Figure 8: Lab Test

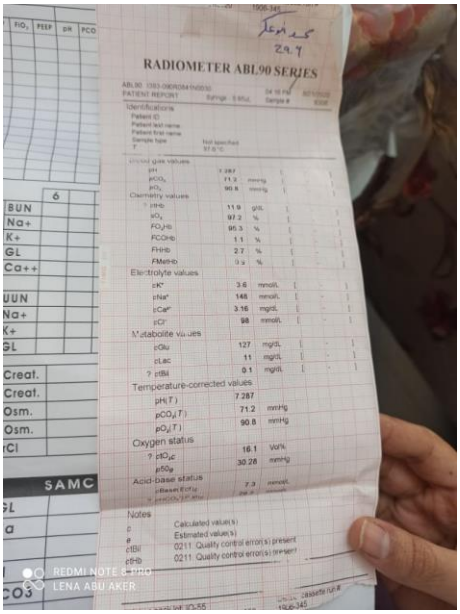

Figure 9: ABG

4. Conclusion

The current study revealed that treating Vitamin D-dependent type II combined with rickets type II with continuous large doses of vitamin D is beneficial. The patient was complaining of a severe chest infection and was intubated on Mechanical ventilation. Unfortunately, the child died at the age of 3 years. A patient with vitamin D-dependent rickets type II can provide valuable insights into the diagnosis, treatment, and management of this rare genetic disorder. By examining the symptoms, laboratory findings, and genetic mutations associated with the condition, healthcare professionals can gain a better understanding of the underlying mechanisms and pathophysiology of vitamin D-dependent rickets type II. Additionally, this case can help identify potential risk factors, such as the family history of the disease or exposure to certain medications or environmental toxins, that may contribute to the development of the disorder. This information can be used to develop targeted screening and prevention strategies for individuals at risk of developing vitamin D-dependent rickets type II. It is worth mentioning that this case typically focuses on a single patient, which limits their ability to be generalized to larger populations. Therefore, Further investigations into the genetic basis of the disorder could help to identify additional genetic mutations that contribute to the development of the disease. This could lead to improved diagnostic accuracy and targeted therapies for affected individuals. Also, studies could explore the clinical features and long-term outcomes of Vitamin D-dependent type II in larger populations.

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Conflicts of Interest: There are no conflicts of interest.

Ethical approval: Ethical approval was obtained from Helsinki Committee, approval was obtained from the Ministry of Health, and the patient's family asked for permission.

Informed consent: Provided informed consent was obtained from the patient's family and whether the consent was written or verbal.

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References

[1] Azemi M, Berisha M, Ismaili-Jaha V, Kolgeci S, Hoxha R, Grajcevci-Uka V (2014). Vitamin D – Dependent rickets, type II case report. Mater Sociomed 26:68-70

[2] Azemi M, Berisha M, Ismaili-Jaha V, Kolgeci S, Hoxha R, Grajçevci-Uka V (2014). Vitamin D – Dependent rickets, type II case report. Mater Sociomed. 26:68–70.

[3] Christakos S, Ajibade DV, Dhawan P, Fechner AJ and Mady LJ (2012). Vitamin D: Metabolism. Rheum Dis Clin North Am. 38:1–11, vii.

[4] Cheng JB, Levine MA, Bell NH, Mangelsdorf DJ and Russell DW (2004). Genetic evidence that the human CYP2R1 enzyme is a key vitamin D 25-hydroxylase. Proc Natl Acad Sci USA. 101(20): 7711–5.

[5] DeLuca HF (1976). Metabolism of vitamin D: current status. Am J Clin Nutr; 29(11): 1258–70.

[6] Feldman D and Malloy PJ (2014). Mutations in the Vitamin D receptor and hereditary Vitamin D-resistant rickets. Bone Key Reports. 3

[7] Luxwolda MF, Kuipers RS, Kema IP, van der Veer E, Dijck-Brouwer DA and Muskiet FA (2013). Vitamin D status indicators in indigenous populations in East Africa. Eur J Nutr. 52(3): 1115–25

[8] Malla KK, Malla T, Shaw C and Thapalial A (2011). Type II Vitamin D dependent rickets: A case report. J Nepal Paediatr Soc. 30:46–9.

[9] McSheehy PM and Chambers TJ. (1987). 1,25-Dihydroxyvitamin D3 stimulates rat osteoblastic cells to release a soluble factor that increases osteoclastic bone resorption. J Clin Invest. 80(2): 425–9.

[10] Maierhofer WJ, Gray RW, Cheung HS, Lemann J Jr, Maierhofer WJ (1983). Bone resorption stimulated by elevated serum 1,25-(OH)2-vitamin D concentrations in healthy men. Kidney Int. 24(4): 555–60.

[11] Nesterova G, Malicdan MC, Yasuda K, Sakaki T, Vilboux T, Ciccone C (2013). 1,25-(OH)2D-24 hydroxylase (CYP24A1) deficiency as a cause of nephrolithiasis. Clin J Am Soc Nephrol. 8(4): 649–57.

[12] Quesada-Gomez JM and Bouillon R (2018). Is calcifediol better than cholecalciferol for vitamin D supplementation? Osteoporos Int; 29(8): 1697–711.

[13] Shafeghati Y, Momenin N, Esfahani T, Reyniers E, Wuyts W (2008). Vitamin D-dependent rickets type II: Report of a novel mutation in the Vitamin D receptor gene. Arch Iran Med11:330-4.

[14] Sahay M and Sahay R (2012). Rickets-Vitamin D deficiency and dependency. Indian J Endocrinol Metab. 2012;16:164–76.

[15] Scarpelli DG, Tremblay G and Pearse AG (1960). A comparative cytochemical and cytologic study of vitamin D induced nephrocalcinosis. Am J Pathol. 36: 331–53.

[16] Sahay M and Sahay R (2012). Rickets-Vitamin D deficiency and dependency. Indian J Endocrinol Metab 16:164-76.

[17] Schlingmann KP, Kaufmann M, Weber S, Irwin A, Goos C and John U (2011). Mutations in CYP24A1 and idiopathic infantile hypercalcemia. N Engl J Med. 65(5): 410–21.

[18] Takeyama K, Kitanaka S, Sato T, Kobori M, Yanagisawa J and Kato S (1997). 25-Hydroxyvitamin D3 1alpha-hydroxylase and vitamin D synthesis. Science. 277(5333): 1827–30.