Pathological Processes in Oral Cavity at Vitamin D-Resistant Rickets (Family Case Reports)

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Abstract: Vitamin D-resistant rickets of X-linked dominant transmission type is caused by pathology of renal tubular apparatus resulting in impaired absorption of calcium and phosphorus in the small intestine; it proceeds with the injuries of varying severity to skeletal system as well as dental and periodontal complex. The purpose of the study is to describe a family case of vitamin D-resistant rickets.

Family Case Report: Mother – K. S. X-linked hypophosphatemic vitamin D-resistant rickets, 35 years old, height-143 cm; as for the skeletal system – osteoporosis and tandem disorder were revealed. The patient underwent 3 surgical interventions for the treatment of lower limbs. Dental status - delayed teeth eruption, gothic arch, saddle-like shape of the upper dental arch, trapezoidal shape of the lower dental arch, hypoplasia, hyperesthesia, change in tooth color, extrinsic dental stains; presence of dental stones and plaque in the oral cavity, a decompensated forms of caries. Chronic apical periodontitis - 1, apical granuloma - 2, periapical abscess with sinus - 1, periapical abscess without sinus - 4, root cyst - 1. Generalized periodontitis of medium severity.

Son, Patient A. O., 3 years old, Male: Characteristic systemic anomalies observed: Inadequate physical development, related to the musculoskeletal system - scoliosis; 0-shaped legs, joint hypermobility. Marked decrease in muscle tone. Delayed teeth eruption, low gate of the oral cavity, chattering in upper and lower dentitions, anomalies in tooth position. Change in tooth color, stained caries-5, enamel caries-2, dentin caries-3, extracted tooth-1 were observed. Biochemical indicators: total serum calcium and serum phosphate are within the norm; Parathyroid hormone, 24 hr urine phosphate (mmol/l 24h), renal phospat cliearanse (ml/min), D1 25 (nG/ml); serum alkaline phosphatase level - increased; Decreased urine calcium concentration, phosphate tubular reabsorption (ptr) (%), creatinine levels in blood and urine.

Conclusions: In case of familial vitamin D-resistant rickets, the identification of genetically determined phosphate diabetes in children is of great importance. Detecting the manifestations of vitamin D-resistant rickets in the oral cavity at an early stage of child development would be desirable to ensure early prevention of complications.

Key words: Vitamin D-resistant rickets, family case, pathological processes in the oral cavity.

Introduction

Vitamin D regulates blood calcium and phosphate concentrations, playing a key role in bone growth and remodeling. The circulating active form of vitamin D, 1,25-dihydroxyvitamin D, binds vitamin D receptor (VDR), which heterodimerizes with retinoid X receptor to regulate the expression of target genes [5]. Vitamin D-resistant rickets of X-linked dominant transmission type is caused by pathology of renal tubular apparatus [14], resulting in impaired absorption of calcium and phosphorus in the small intestine; it belongs to the group of hereditary tubulopathies, clinical picture of which mimics rickets at early stage of the disease, but it is not associated with vitamin D deficiency; it belongs to rare metabolic bone diseases, the pathologies with bone metabolism disorders, majority of which combines various degrees of damage to the skeletal system, teeth and periodontium in general [19]. The disease is characterized by complete penetrance. A woman has a 50% chance of transmitting pathological trait to daughters and sons, and men to their daughters - 100%, respectively. In boys, the course of the disease is more severe compared to women. Incidence rate – 1 : 20,000–25,000. Frequency - 1 : 12,000-20,000 [4, 6]. Patients showed: low concentration of phosphorus, normal parathyroid hormone level, blood calcium level within the normal range or below the norm [11]. Clinical polymorphism, especially in terms of pathogenesis and metabolic disorders, and wide range of response to vitamin D indicate to genetic heterogeneity of vitamin D-resistant rickets [10].

A large number of candidate genes and the lack of specific clinical and laboratory criteria to differentiate diseases might be considered as the main difficulty in diagnosing this disease. According to the results of the studies, in children carrying the "slow" allelic type of the CYP2C9 gene, a decrease in the concentration of 25(OH)D3 was revealed. Patients with rickets and rickets-like diseases have a genotype, representing a "slow" allelic type heterozygote of CYP2C9*3 and CYP2C9*2 genes [12]. Therefore, the low serum 25(OH)D3 concentration can be explained by a genetically determined disorder of vitamin D metabolism, and in particular, vitamin D3 – 25(OH)D3 [3].

Clinical manifestations related to X chromosome-linked hypophosphatemia include: O-shaped deformation of the legs, stunted growth, hypocalcemia, osteoid tissue hypoplasia, no myopathy, calcium serum level - in norm or slightly decreased (2.25-2.37 mmol/l). Patients have great muscle strength. Bone deformities are less pronounced in girls, sagittal craniosynostosis, tooth deformation/injuries and interglobular dentin are not rare manifestations as well.

Normally, dental enamel hypoplasia was not observed. No glucosuria, potassiumuria, aminoaciduria were revealed. Parathyroid hormone is normal, alkaline phosphatase is moderately elevated [1]. Dental disorders observed during the vitamin D-resistant rickets: hypocalcification of teeth enamel and jaws, hypomineralization, enamel hypoplasia,

hypophosphatemia leading to interglobular dentin distribution inside the tooth [8, 11], which significantly worsens tooth tissue calcification and causes the appearance of enamel microscopic cracks. Hypomineralization of tooth surface (enamel and dentin) increases the dentin permeability and bacterial penetration into the tooth, thereby contributing to the formation of an abscess in the oral cavity. Late and irregular eruption of primary teeth was observed; enamel defects as well as caries of primary and later, permanent teeth are very common. The reason causing teeth damage might be explained on the one hand by the fact that, teeth are formed in the first months of life i.e. at active phase of rickets, and on the other hand, by malocclusion caused by jawbone deformity (taking trapezoid shape instead of parabolic). High- arched palate is a common clinical finding for the patients with this pathology [7]. Spontaneous infection of the dental pulp tissue resulting in the development of tooth abscess is considered as an essential sign indicating to the severe dental status [15].

Unlike endodontic infection, abscess occurs in the intact tooth area, without any trauma, both in primary and permanent teeth. Clinically, teeth normal appearance complicates the identification of endodontic origin of the infection. Radiologically, the enamel layer is thinned, pulp cavity is enlarged, pulp horns reach the dentin-enamel junction. Histologically, enamel cracks, dentin mineralization defects [16] and non-mineralized interglobular space [18] were observed in the examined area.

Family Case Description /Report:

Patient A.O., 3 years old, male, X-linked hypophosphatemic vitamin D-resistant rickets, mother K.S. - suffering from the same disease.

Mother – K.S., 35 years old, height-143 cm; as for the skeletal system – osteoporosis and tandem disorder were revealed. The patient underwent 3 surgical interventions for the treatment of lower limbs. Dental status - delayed teeth eruption, gothic arch, saddle-like shape of the upper dental arch, trapezoidal shape of the lower dental arch, hypoplasia, hyperesthesia, change in tooth color, dental stains (Fig. 1A); presence of dental stones and plaque, decompensated caries;

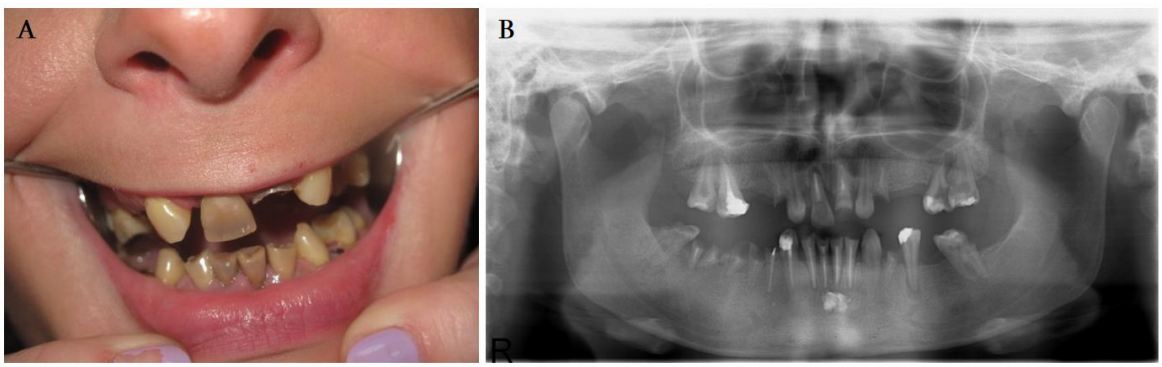

Fig. 1. Patient K.S., A.O.'s mother (A). Patient K.S. Orthopantomography (B)

dentin and cementum caries; number of carious teeth - 3, number of tooth filling - 11, number

of extracted teeth - 6, root - 7. Chronic apical periodontitis - 9, periapical abscess with sinus - 2, root cyst - 1. Generalized periodontitis of medium severity (Fig.1B).

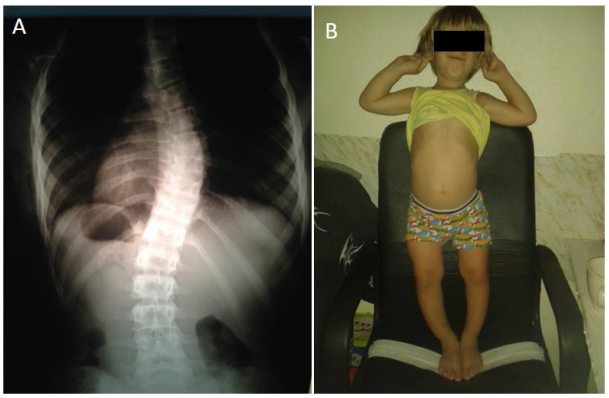

Fig. 2. Patient A.O. (A), Spinal (vertebras) X-Ray (B)

Patient A.O. 3 years of age. He was born from the first pregnancy, via C- section, mother suffered from toxicosis during pregnancy. Characteristic systemic anomalies observed:

Inadequate physical development, related to the musculoskeletal system - scoliosis (Fig. 2A); 0-shaped legs (Fig. 2B), joint hypermobility. Marked decrease in muscle tone.

Patient A.O. Dental status: Delayed teeth eruption, low gate of the oral cavity, chattering in upper and lower dentitions, anomalies in tooth position. Change in tooth color, stained caries-5, enamel caries-2, dentin caries-3, extracted tooth-1 were observed. Periapical abscess with sinus - 2 (Fig.3).

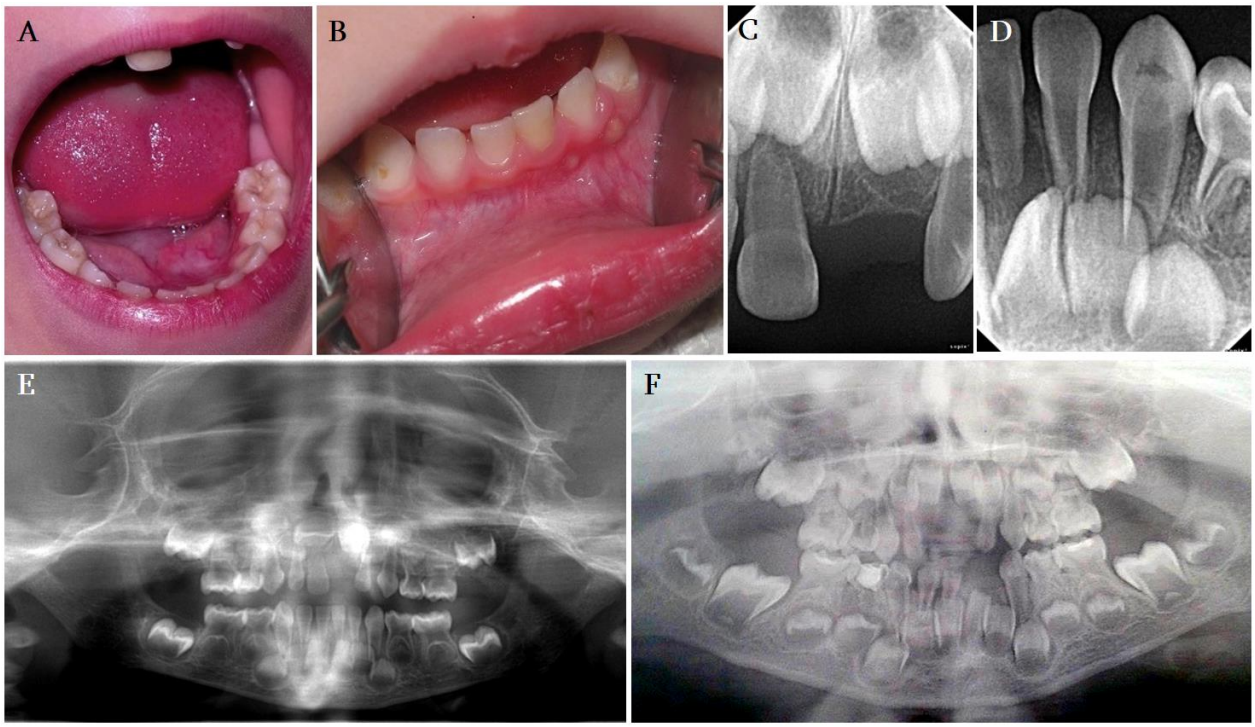

Fig. 3. Periapical abscess with sinus: carious teeth (A), sinus in area of 7.1 and 7.2- Change in tooth color (B), A.O. 51 Visiodentogram (C), A.O. 71,81 Visiodentogram (D), Patient A.O. - Orthopantomography (E), Orthopantomography after 1 year and 9 months (F)

Biochemical indicators of patient A.O. are given in Table 1.

Total serum calcium and serum phosphate are within the normal range; Parathyroid hormone, 24 hr urine phosphate(mmol/l 24h), renal phospat cliearanse(ml/min), D1 25(nG/ml); serum

alkaline phosphatase level - increased; decreased urine calcium concentration, phosphate tubular reabsorption (ptr) (%), creatinine in blood and urine.

Table 1. Patient A.O. - Biochemical indicators

Biochemical indicators	Normal range	Patient's indicators
Serum Ca mmol/l	2.2-2.7	2.31
Serum phospate(mmol/l)	1.05-1.8	0.87
Serum alkaline phosphate(U/l)	55-380	620
Serum PTH (ng/ml)	16-62	61
24hr urine Ca (mmol/l 24h)	2.5-7.5	0.1
24 hr urine phosphate (mmol/l 24h)	15-35	22.6
Renal phospat cliearanse (ml/min)	<10	7.21
Phosphat tubular reabsorbtion (ptr) (%)	>80	10
Kreatinine bl (mmol/l)	35.36-53.04	24.752
Kreatinine urine (24) (mmoli/l)	300.56-2024.36	192
D1 25 (nG/ml)	20-70	23.1

Thus, the patient showed a pronounced biochemical and clinical picture of vitamin D-resistant rickets, reflecting on dental status - the patient was presented with tooth discoloration, dental stains, carious teeth and apical abscesses.

Premature loss of primary teeth was observed; according to the mineralization degree the follicles of permanent teeth were below the age norm.

Discussion:

X-linked hypophosphatemic rickets is a hereditary disease caused by impaired tubular reabsorption of phosphate in renal tubules characterized by rickets-like changes in the skeletal system.

The disease progress is associated with decreased phosphate and calcium reabsorption, as well as hyperfunction of the thyroid gland [10,17].

In the case discussed, serum alkaline phosphatase level was increased; concentration of calcium in urine was decreased, phosphate tubular reabsorption (ptr)(%), creatinine in blood serum and urine.

X-linked hypophosphatemic rickets is associated with sharp structural changes of hard dental tissues and the development of multiple abscesses and perforations/orifices [13].

In the cases reviewed above, the patients were presented with delayed teeth eruption, anomalies of occlusal development and teeth position. Hypomineralization of enamel and dentine, change in tooth color, enamel, dentine and cementum caries; Pulp horns often reached the enamel-dentine junction; Periapical abscesses with sinus.

Enamel abnormalities, such as microscopic cracks in the enamel and dentin, enlarged pulp cavities, may represent a route of entry of microorganisms to the pulp, causing periapical infections without signs of dental caries or trauma [2].

Conclusions: In case of family history of vitamin D-resistant rickets, the identification of genetically determined phosphate diabetes in children is of great importance.

Detecting the manifestations of vitamin D-resistant rickets in the oral cavity at an early stage of child development would be desirable to ensure early prevention of various complications and deformations of the jaw-dental system.

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პირის ღრუში მიმდინარე პათოლოგიური პროცესები D ვიტამინ რეზისტენტული რაქიტის დროს (ოჯახური შემთხვევის აღწერა)

ნინო ჯაფარიძე

ივანე ჯავახიშვილის სახელობის თბილისის სახელმწიფო უნივერსიტეტი, თბილისი, 0179.

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აბსტრაქტი: D ვიტამინრეზისტენტული რაქიტი, X-თან შეჭიდული დომინანტური გადაცემის ტიპით, განპირობებულია თირკმლის ტუბულარული აპარატის პათოლოგიით, წვრილ ნაწლავში კალციუმის და ფოსფორის აბსორბციის დარღვევით; მიმდინარეობს როგორც ჩონჩხოვანი სისტემის, ასევე,ზოგადად, კბილებისა და პაროდონტის კომპლექსის სხავადასხვა ხარისხის დაზიანებით. ნაშრომის მიზანს წარმოადგენს D ვიტამინრეზისტენტული რაქიტის ოჯახური შემთხვევის აღწერა.

ოჯახური შემთხვევის აღწერა: დედა - ქ. ს. X-შეჭიდული ჰიპოფოსფატემიური D ვიტამინრეზისტენტული რაქიტით, 35 წლის, სიმაღლე - 143 სმ; ძვალსახროვანი სისტემის მხრივ აღენიშნება ოსტეოპოროზი, ტანდეგობის დარღვევა. პაციენტს ქვედა კიდურებზე ჩატარებული აქვს 3 ოპერაცია. სტომატოლოგიური სტატუსი - კბილების დაგვიანებული ამოჭრა, გოთიური თაღი, ზედა ყბის კბილთა რკალის უნაგირისებური ფორმა, ქვედა ყბის კბილთა რკალის ტრაპეციისმაგვარი ფორმა, ჰიპოპლაზია, ჰიპერესთეზია, კბილების ფერის ცვლილება,ლაქები კბილის ზედაპირზე; ქვების და ნადების არსებობა პირის ღრუში, კარიესის დეკომპენსირებული ფორმა. ქრონიკული აპიკალური პერიოდონტიტი - 1, აპიკალური გრანულომა - 2, პერიაპიკალური აბსცესი ხვრელარხით - 1, პერიაპიკ.აბსცესი ხვრელარხის გარეშე - 4, ფესვის კისტა - 1. საშუალო სიმძიმის გენერალიზებული პაროდონტიტი. შვილი, **პაციენტი ა. ო., 3 წლის.** მამრობითი სქესის, აღენიშნება დამახასიათებელი სისტემური ანომალიები: არადამაკმაყოფილებელი ფიზიკური განვითარება, ძვალსახსროვანი სისტემის მხრივ - სკოლიოზი; 0-ს მაგვარი ფეხები, სახსრების ჰიპერმობილურობა. კუნთთა ტონუსის გამოხატული დაქვეითება. კბილების დაგვიანებული ამოჭრა, პირის ღრუს დაბალი კარიბჭე, ზედა და ქვედა ყბის კბილთა განლაგებაში აღინიშნება ტრემები, კბილების დგომის ანომალიები. აღენიშნება კბილების ფერის ცვლილება, ლაქოვანი კარიესი-5, მინანქრის კარიესი-2, დენტინის კარიესი-3, ექსტრარგირებული კბილი-1. ბიოქიმიური მახასიათებლები: საერთო კალციუმი შრატში და შრატის ფოსფატი-ნორმის ფარგლებშია; პარატჰორმონი, 24 hr urine phosphate(mmol/l 24h), renal phospat cliearanse(ml/min), D1 25(nG/ml); ტუტე ფოსფატაზა შრატში მომატებულია; შემცირებულია კალციუმის კონცენტრაცია შარდში, phosphat tubular reabsorbtion(ptr)(%), კრეატინინი სისხლის შრატსა და შარდში.

დასკვნები: ოჯახში დ ვიტამინ რეზისტენტული რაქიტის არსებობისას აუცილებელია ბავშვების გამოკვლევა გენეტიკურად დეტერმინირებული ფოსფატდიაბეტის გამოსავლენად. D ვიტამინ რეზისტენტული რაქიტის გამოვლინებები პირის ღრუში სასურველია დადგინდეს ბავშვის განვითარების ადრეულ ეტაპზე, რაც საშუალებას მოგვცემს დროულად ავიცილოთ თავიდან გართულებები

საკვანძო სიტყვები: D ვიტამინ რეზისტენტული რაქიტი, ოჯახური შემთხვევა, პირის ღრუში მიმდინარე პათოლოგიური პროცესები.