Dental and Histologic Findings of X-linked Hypophosphataemic Vitamin D-resistant Rickets: A Case Report.

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Abstract

The aim of this case report is to present X-linked vitamin D resistant hypophosphataemia with clinical features, the dental findings and treatment. Also, X-linked vitamin D resistant hypophosphataemia in a 5-year-old Turkish girl, as well as the histologic findings of her extracted mandibular primary left second molar is showed.

The pathophysiology of the disease is thought to be impaired phosphate transport, especially decreased phosphate resorption in the renal proximal tubule, as well as in the intestine.

X-linked vitamin D resistant hypophosphataemia is identified by clinical symptoms, such as deformities in the limbs, gait disturbance, dwarfism, familial occurrence, bowlegs, and knock-knees, as well as by laboratory findings. Furthermore in patients with Rickets, the dentition is highly susceptible to dental caries or attrition, and bacteria can invade easily from the oral cavity to dental pulp by menas of structural defects in enamel and dentin, resulting in pulpitis.

The dentist as well as the pediatrician should be made aware of the features of this disorder so that early intervention can prevent subsequent serious and more invasive dental procedures.

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Introduction

A disease that occurs during childhood, rickets is the failure of growing bone to mineralize. Proper bone formation requires a complex interplay of several organs and chemicals, and vitamin D deserves special mention because any disturbance in its production, absorption, or metabolism is paramount in the development of rickets[1].

X-linked vitamin D resistant hypophosphataemia (XLH), first reported by Albright et al[2], is a syndrome showing marked hypophosphatemia, short stature, and rickets. In general, the main abnormality is considered to be a congenital impairment of phosphate transport and hypophosphatemia, resulting from decreased phosphate reabsorption in the brush border membrane on the luminal side of the proximal renal tubule and impaired phosphate reabsorption in the intestine.

X-linked hypophosphataemia (XLH) is also characterized by growth retardation, osteomalacic bone disease and hypophosphataemia[3,4]. Sporadic cases are often initially detected by limb deformity or gait abnormality. The systemic findings of XLH include bowed legs because of a body load showing immature skeletal bone calcification, spinal curvature deformities and beading of the ribs called rachitic rosary[5-7].

The vitamin D–resistant types are familial hypophosphatemic rickets and hereditary hypophosphatemic rickets with hypercalciuria. Rickets refractory to vitamin D treatment may be caused by the most common heritable form, known as vitamin D–resistant rickets or familial hypophosphatemic rickets[8,9].

This phenomenon is associated with well documented oral and dental findings[7,10-13].

Hypophosphataemic vitamin D-resistant rickets have been attiributed to the enlarged coronal pulp spaces and to the grossly defective dentine allowing ingress of micro-organism to the dental pulp once attrition has removed the overlying protective enamel14. The enamel in some affected individuals

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has been described variously as relatively thin, hypocalsified or hypoplastic, although it is not always obvious from the text which dentition is affected by these changes[14]. In general, both primary and permanent teeth have dentinal dysplasia[13]. The teeth usually show taurodontism, poorly defined lamina dura and a hypoplastic alveolar ridge[14,15].

Spontaneous periapical abscess formation is also often observed in patients with XLH without dental caries or traumatic injury[10,16]. Because the teeth of patients with XLH are often associated with high pulp horns, large pulp chambers, and dentinal clefts, it is believed that the abscesses are caused by pulpal infection that was caused by bacterial invasion through enamel cracks and dentinal microcleavage of the teeth[13]. Dentists have diagnosed a few cases in which the systemic features were mild and dental abscesses were the first presenting sign[11].

The aim of this case report is to present X-linked vitamin D resistant hypophosphataemia with clinical features, the dental findings and treatment. Also, X-linked vitamin D resistant hypophosphataemia in a 5-year-old Turkish girl, as well as the histologic findings of her extracted mandibular primary left second molar is showed.

CASE

A case of X-linked hypophosphataemia (XLH) or familial hypophosphatemic vitamin D-resistant rickets accompanied by specific systemic and dental and histologic findings is reported. A 5-year-old girl with X-linked vitamin D resistant hypophosphataemia complaining of a toothache in the left mandibular primary second molar was referred to the Department of Pediatric Dentistry, Dicle University, Diyarbakir, Turkey. A detailed medical, dental, and social history was obtained for examination, dental evaluation and treatment (Figs 1,2). Three other family members of the patient, her older brother and younger sisters, also had XLH, whereas the other 2 members, her mother and father, are healthy. Those with XLH show systemic signs of the disease, such as growth retardation, limb deformity, beading of the ribs and spinal curvature disorders; however, these symptoms are more severe in the patient than in the others (Figs 3,4).

The patient was the first offspring of the parents after a full term gestation and measured 3230 g in weight and 43 cm in length at birth. Because she had not yet walked by the age of 1 year, 6 months, she was referred to the pediatric clinic of a medical school, where a diagnosis of skeletal hypoplasia was made. At the age of 2 years and 3 months, skeletal abnormalities and bowed legs were noted at the public health examination for infants. The patient was admitted to the same pediatric clinic as before for a thorough examination.

The patient had typical features of XLH: severe bowing of the legs, marked genu valgum and rachitic rosary, growth retardation, radiographic signs of rickets, low serum phosphate concentration, tubular phosphate reabsorption, low urinary calcium excretion, elevated serum alkaline phosphatase activity, and normal serum parathyroid hormone, and 1,25-(OH) vitamin D3 levels.

Laboratory examinations showed an elevated alkaline phosphate level at 1634 mU/mL (normal range, 30 - 85 mU/mL) and hypophosphataemia at 2.5 to 2.8 mg/dL (normal range in children, 4.5 - 6.5 mg/dL). Measurement of urinary phosphate excretion also showed an abnormal phosphate reabsorption rate of 69.4% (normal range, 84.7% - 97.9%). From these clinical, radiographic, and laboratory findings, the patient was diagnosed with vitamin D resistant hypophosphatemic rickets and was administered active vitamin D (calcitriol) and neutral phosphate. She had been treated with 125 mg of sodium acid phosphate and 40 mg/kg of 1,25-dihydroxy vitamin D daily.

Radiographic findings

Radiographic findings include widening of the distal physis, fraying and widening of the metaphysis, and angular deformities of the arm bones. Rachitic changes at epiphyses of the radius, ulna, were showed by radiographic examination (Fig 5).

Intra oral radiographic findings

Radiological findings noted in the primary dentition included generalized enlargement of the pulp spaces, large mesial pulp horns and similar to the taurodontic aspects in all primary first and second molars. Periapical radiolucencies were found on the mandibular primary left second molar (Fig 6).

Oral findings

As a result of the anamnesis, her early primary teeth, which were primary molars were beginning to erupt at tha age of 1 year 7 months. In intra oral examination the absence of maxillary and mandibular primary centrals and mandibular laterals, which were determined to be lost soon after having erupted, were detected. The patient had also two dental caries, periodontal abscess on the one of

corresponding tooth at the time of her oral examination. The abscess was thought to be caused by pulpal infection, which came from bacterial invasion through enamel cracks and dentinal microcleavage of the teeth. An abscess was found at the labial periapical region of the mandibular primary left second molar, along with a negative response to pulp vitality testing; clinically detectable changes such as caries that induce pulp necrosis were found and that tooth was extracted. The mandibular primary left second molar separated to the two parts, and examined histologically. The mandibular primary right second molar was restored with compomer restorative materials (Fig 7).

Histologic examination

The tooth which is extracted left mandibular primary second molar from the patient was bisected and examined histologically. One half was decalcified and stained with hematoxylin and eosin. A histologic examination of an extracted the mandibular primary left second molar showed marked globular dentin and an increased predentin width (Fig 8).

To prevent gingival abscess as observed in our patient, both early treatment and preventive care for caries and attrition are necessary. In patients with either definite or suspected XLH, therefore professional dental care consisting of periodical examinations, compomer restoration, topical fluoride application, and the maintenance of good oral hygiene (with implication of the parents and care takers) was performed. The patient has been periodically recalled at six-months intervals.

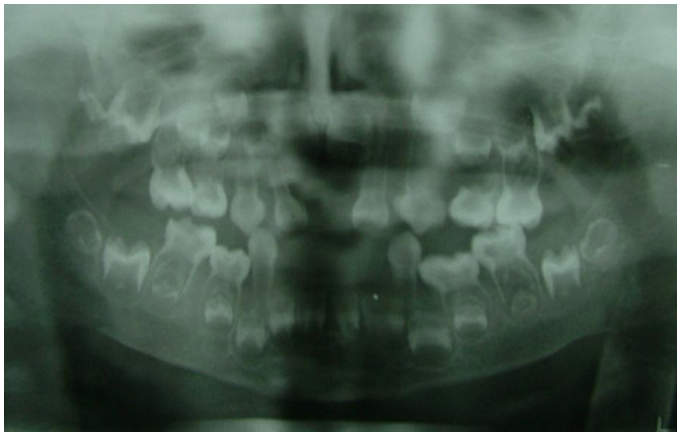

Fig. 2 Initially panoramic radiography showing primary mandibular right second molar's caries and periapical radiolucency on the mandibular primary left second molars. Also, having similar to the taurodontic aspects in all primary first and second molars.

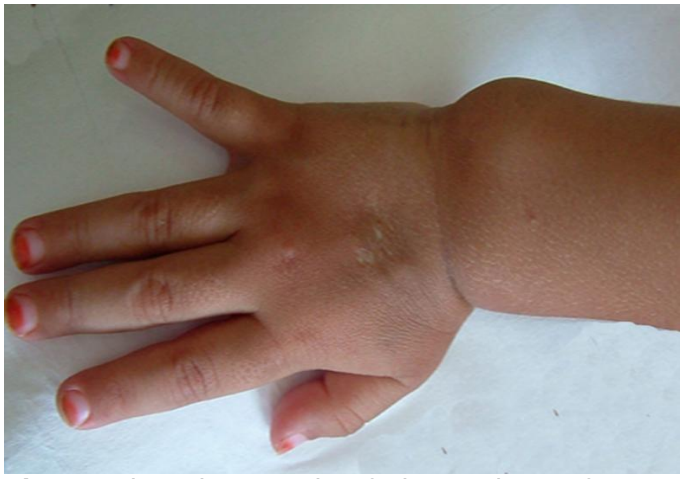

Fig. 3 The photograph of the patient's forearm showing widening of the metaphysis

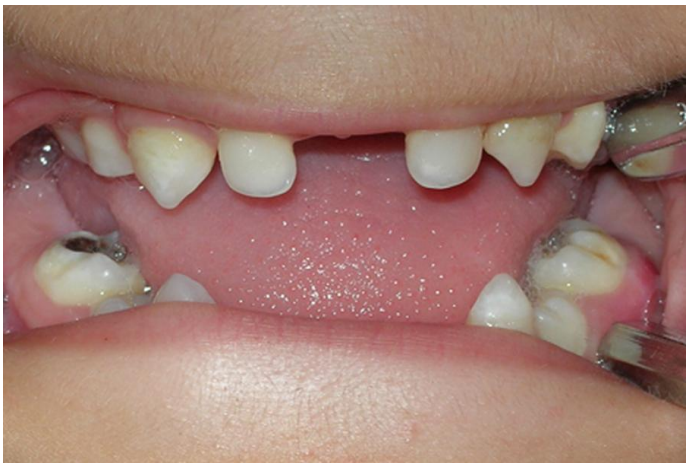

Fig.1 Maxillary and mandibular arches (anterior view). In intra oral examination revealed the absence of maxillary and mandibular primary centrals and mandibular laterals.

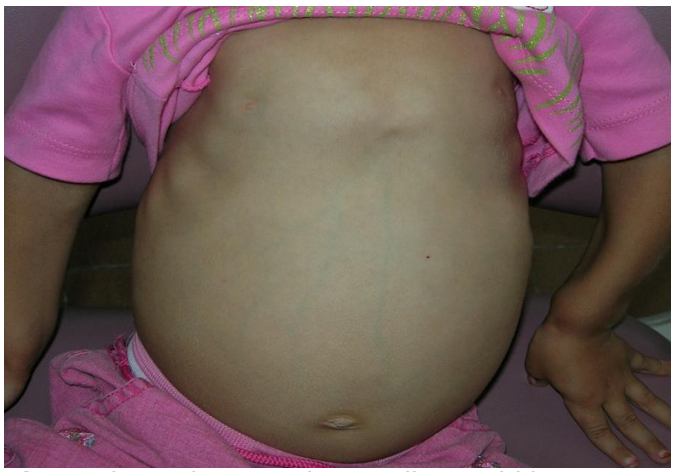

Fig. 4 Chest photograph revealing rachitic rosary.

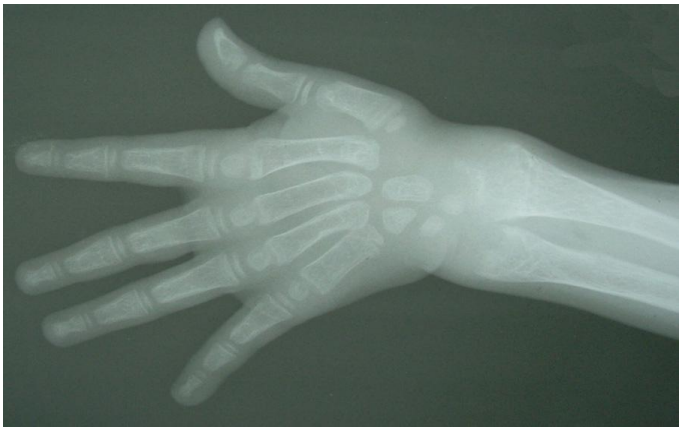

Fig. 5 Radiographic image showing typical changes of rickets at the wrist. The distal ends of the radius and ulna display extensive cupping, fraying, and splaying of the diaphysis, with widening of the metaphysis.

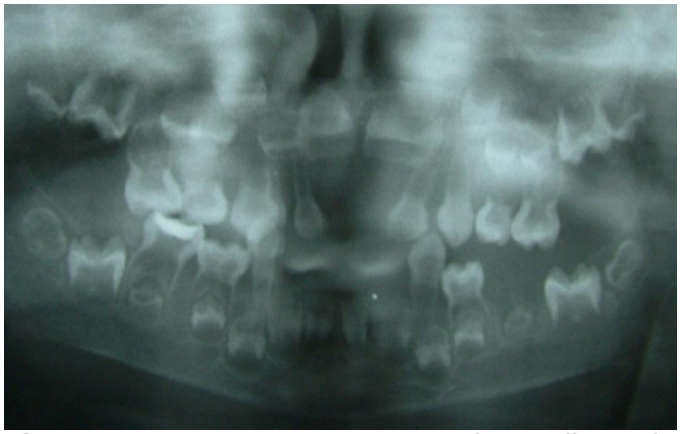

Fig. 7 Posttreatment panoramic radiography showing the right mandibular primary second molar restoration and the left mandibular primary second molar extraction.

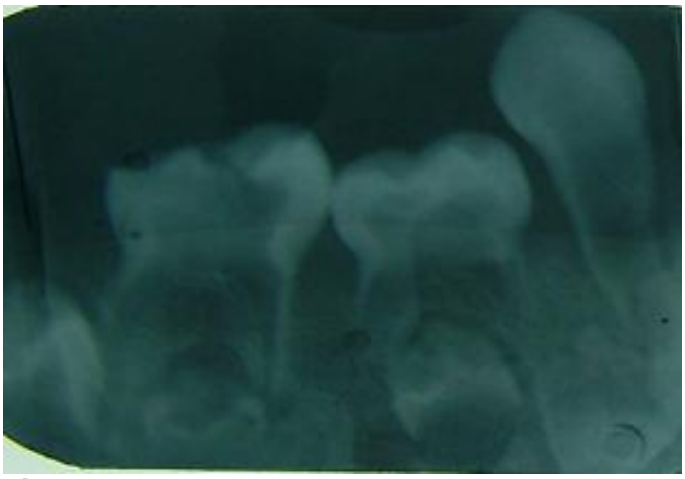

Fig. 6a

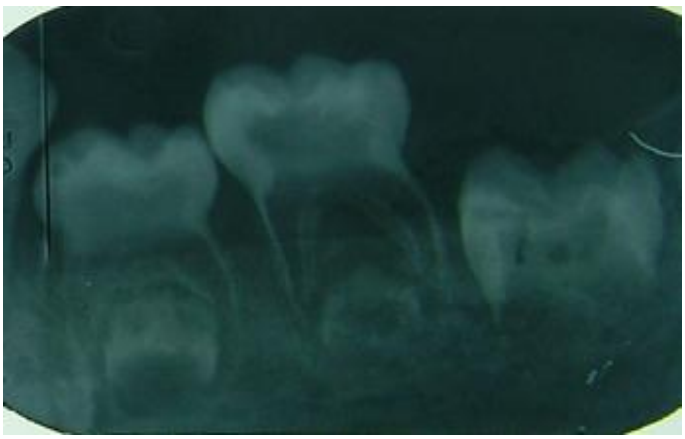

Fig. 6b At the figure **a** and **b** diagnostic periapical radiographs showing generalized enlargement of the pulp spaces and large mesial pulp horns.

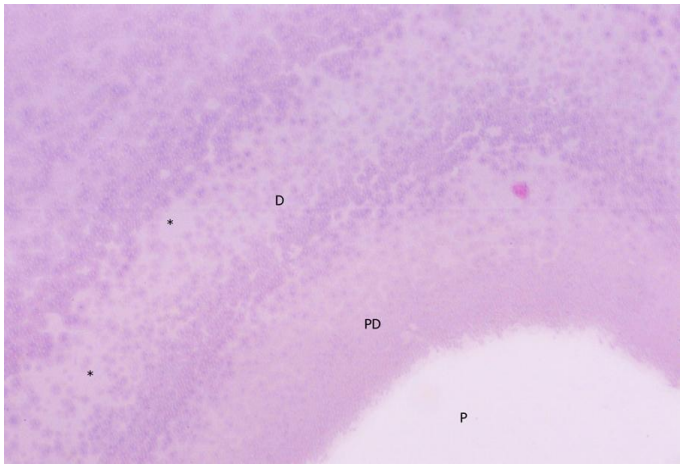

Fig. 8 Histopathology of the left mandibular primary second molar (decalcified section, hematoxylin-eosin stain). Wide globular dentin was characteristic. Predentin was also wide (D, dentin; PD, predentin; P, pulp). *Showing hypomineralized regions. (H-E Original magnification, x 41)

Discussion

Hypophosphatemic vitamin D-resistant rickets or X linked hypophosphataemia (XLH) is a hereditary disease manifesting marked hypophosphataemia caused by renal tubular loss of phosphate into urine and an associated decrease in the calcium and potassium ion product. Normal levels of calcitriol are found in this disorder[17,18].

Familial hypophosphataemic rickets, the most common form of rickets, is in most cases transmitted as an X-linked dominant trait and results from mutation of the PHEX gene located in Xp22.1.

PHEX, a phosphate-regulating gene, encodes a Zn metalloendopeptidase predominantly expressed in osteoblast and odontoblast[3,4].

In most patients, XLH appears in a familial line of X-linked, dominant inheritance with the same prevalence in both sexes; however, it may also occur sporadically. In general, more severe symptoms are noted in males[19]. Hypophosphataemic rickets will usually manifest in 50% of the male children of a woman who is a carrier. It is inherited by a female when the disease manifests in the father and the mother is the carrier of the trait[20].

XLH is identified by clinical symptoms, such as deformities in the limbs, gait disturbance, dwarfism, familial occurrence, bowlegs, and knock-knees, as well as by laboratory findings. Since the early case reports of XLH, a specific dental finding of abscess formation in clinically normal teeth has been described in most cases[10,16]. Furthermore, a case of XLH was detected based on gingival abscess formation in clinically normal teeth[11].

A family history of short stature, orthopedic abnormalities, poor dentition, alopecia, and parental consanguinity may signify inherited rickets[1]. All of these findings were seen at the our case, her brother and sisters.

Familial hypophosphatemic rickets is treated with phosphorus and vitamin D, whereas hereditary hypophosphatemic rickets with hypercalciuria is treated with phosphorus alone[1].

Case studies of children and adolescents with hypophosphataemic rickets have shown that dental problems are more commonly associated with the primary than the permanent dentition[21,22]. Our case presented similar aspects.

With regard to tooth enamel in XLH, one study showed an absence of enamel hypoplasia in most patients[6], whereas another showed enamel defects including hypoplasia in one third of the patients[7,12]. In this report, we did not observe specific enamel defects or hypoplasia in the case, but enamel and dentin layer were quite thin according to the radiographic and clinical evaluation.

Dental care of these patients should consist of periodic examinations, topical fluoride applications, pit and fissure sealants and maintenance of good oral hygiene. Some authors advocate extraction of teeth that present periradicular abscesses and eventual restoration with implants; however, endodontic and restorative treatment may not be able to maintain asepsis. The incompletely mineralized dentin exists in the form of calcospherites, which trap microorganisms and also impede mechanical endodontic cleaning[23,24]. The practitioner must conclude that the occurrence of spontaneous abscesses following a shallow cavity preparation necessitates aggressive preventive dental procedures.

In all previous known reports with a histologic examination, dentinal hypoplasia showing marked globular dentin is a common finding in XLH[5,6,16]. As to the cause of the globular dentin in XLH, some authors have suggested an impaired dentinogenesis of odontoblasts[25,26]. On the other hand, Abe et al[6], noting restorative dentin formation in XLH, suggested that the odontoblast function was not aberrant, but that the calcification process of the dentin was impaired because of hypophosphataemia. Also, in bone, an impaired osteoblast function has been suggested[27,28].

Histopathological examinations have also revealed evidence of hypo-mineralization in dentin, such as interglobular dentin, widened predentin and irregular dentinal tubules6,[29]. In this case, clinical findings such as dental caries, enlarged pulp chambers, wide predentin, marked globular dentin, and tubular dentinal defects extending from the pulp to the enamel were detected.

Conclusion

In patients with XLH, the dentition is highly susceptible to dental caries or attrition, and bacteria can invade easily from the oral cavity to dental pulp by menas of structural defects in enamel and dentin, resulting in pulpitis. Therefore, pit and fissure sealants are useful when the teeth are erupting as they prevent ingress of bacteria into the enamel microfractures as well as initiation of caries in the deep pits and fissures. Also, in patients with this disorder, professional dental care consisting of periodic examinations, topical fluoride applications and maintenance of good oral hygiene is imperative. The dentist as well as the pediatrician should be made aware of the features of this disorder so that early intervention can prevent subsequent serious and more invasive dental procedures.

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