

Dental manifestations of the hypophosphatemic rickets – a case report

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SUMMARY

Rickets is a disorder of bone mineralization in children's skeleton. It is most often associated with vitamin D deficiency, however, it can also occur due to a decrease in serum phosphate levels, which leads to inadequate tissue mineralization, with consequent skeletal deformity and growth disorders. Patients with hypophosphatemic rickets show teeth changes at the morphological and histological level, as well as on radiological images.

The aim of this study was to perform clinical and radiological evaluation of dental manifestations of hypophosphatemic rickets in a four-year-old boy, as well as to point out the necessity of including a dentist in the treatment of this disease in order to prevent oral complications.

Keywords: hypophosphatemia; rickets; dentin; periapical abscess

INTRODUCTION

Hypophosphatemic rickets, also known as vitamin D resistant rickets, or X-linked rickets, is an inherited syndrome characterized by inadequate cartilage and bone mineralization leading to skeletal deformities and growth disorders. It is caused by a mutation in the PHEX gene (endopeptidase responsible for the regulation of phosphate encoded by the X chromosome), leading to an increase in fibroblast growth factor 23 (FGF23), which is a regulator of renal phosphate reabsorption [1, 2]. The pathophysiological mechanism is reflected in the reduction of phosphate reabsorption by renal tubules, which leads to hyperphosphaturia and hypophosphatemia, causing rickets [3]. The prevalence of the disease is 1:20,000 [4, 5]. Standard treatment of these patients include the administration of oral phosphate supplements and active vitamin D [1, 3]. Recently, attempts have been made to use anti-FGF23 antibodies that act on the primary disease by blocking FGF23 and thus regulating phosphate homeostasis [1, 2]. Hypophosphatemia is the cause of dentin dysplasia due to disorders in the mineralization of the dentinal matrix when the globular dentin is clearly observed. Tubular defects are also present, which can extend to the dentin-enamel junction. In addition to disturbances in mineralization, thin enamel, dentinal clefts, especially large pulp chambers, as well as prominent pulp horns that extend to the dentin-enamel junction could be clearly observed on radiological images [4]. There are indications in the literature that patients with hypophosphatemic rickets are characterized by the appearance of multiple spontaneous periapical abscess-

es [5, 6, 7]. Among dental characteristics, taurodontism, poorly defined lamina dura and hypoplasia of the alveolar ridges could be also present [6, 8].

CASE REPORT

A four-year-old boy was referred from the Clinic of Pediatrics, Clinical Center Niš, due to oral complications related to hypophosphatemic rickets. The treatment of the rickets included treatment with phosphate supplements and active form of vitamin D, which led to the correction of clinical and laboratory findings.

General examination revealed a patient with clinical characteristics of the rickets: deformity of the lower extremities, changes in gait and short stature. No extraoral changes were observed. Intraoral examination revealed that all teeth of deciduous dentition were erupted. In the upper jaw, all anterior teeth were completely destroyed by decay and residual roots were present. According to the father, there was swelling in the area of the anterior teeth previously, and a dentist provided first aid but further cooperation with the child was not established. Circular decay was observed on the upper canines, large carious lesions with open pulp chamber and necrotic pulp were observed on the upper first molars, while superficial caries in occlusal fissures was observed on the upper second molars. In the lower jaw, anterior teeth were heavily destroyed, large class V caries on the canines, large carious lesions with open pulp chamber, necrotic pulp and class V cavities on the first molars, and class I cavities on the



Figure 1. Carious lesions on mandibular deciduous teeth
Slika 1. Karijesne lezije na mlečnim zubima donje vilice



Figure 2. Large carious lesions on anterior deciduous teeth
Slika 2. Velike karijesne lezije na mlečnim prednjim zubima

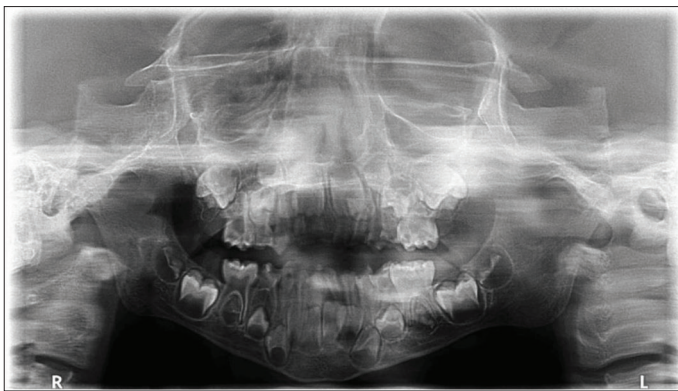


Figure 3. Panoramic radiograph shows large pulp chambers of deciduous molars, large carious destructions of deciduous teeth and unerrupted permanent teeth.

Slika 3. Panoramski snimak pokazuje uvećane komore pulpe na mlečnim molarima, velike karijesne destrukcije na mlečnim zubima i zemetke stalnih zuba.

second molars were observed. According to the father, there was no swelling in the lower jaw (Figure 1 and 2).

The analysis of the panoramic radiograph showed the presence of unerrupted permanent teeth, unerrupted first and second mandibular molars and first maxillary molars. On the deciduous molars, large pulp chambers with prominent horns were clearly visible. The chambers of the other deciduous teeth could not be examined due to large carious destructions (Figure 3).

The recommended treatment included conservative restoration of all four deciduous second molars, which was postponed due to lack of child cooperation. Since extractions of necrotic teeth would lead to even more intensive odontophobia, frequent controls were recommended. Parents were instructed on the need to maintain good oral hygiene.

DISCUSSION

Hypophosphatemic rickets is a skeletal disorder that is characterized by hypophosphatemia. As phosphate is essential for mineralization, this condition affects the tissues in which mineralization takes place physiologically

- bones, teeth and the growth plate cartilage [1]. The presence of dental malformations in patients with hypophosphatemic rickets has been reported in numerous studies [7, 9, 10]. Teeth in patients with hypophosphatemic rickets show enlarged pulp chambers, a wide zone of predentin, visible globular dentin, and defects in tubular dentin that extend from the pulp to enamel. Enamel is thin, usually normal structure, but sometimes can be hypoplastic [6, 7]. Histological sections can also show extensive enamel cracking and fissuring, as well as defects in dentin mineralization. Unmerged dentin calcospherites are observed and separated by large non-mineralized interglobular spaces [10].

Although odontoblast function is normal, hypophosphatemia leads to poor mineralization which causes dentin dysplasia with clearly visible globular dentin. Due to the period of formation and mineralization of dentin in deciduous teeth in the period from 4 months in utero to 11 months of age of the child, defects in deciduous dentition usually cannot be prevented [6, 7]. If the treatment of the rickets starts as soon as possible after birth, it could be expected to have a positive effect on the formation and development of permanent teeth [6]. However, despite treatment, abnormalities in tooth development and dentin formation in permanent dentition could be observed [7]. Radiological findings in such patients most often show thin enamel, decreased radiological density of dentin, enlarged pulp chambers, prominent pulp horns, taurodontism and anodontia [8, 10].

The dominant feature of this disease is the appearance of multiple spontaneous periapical abscesses [4, 5, 7, 10]. These abscesses can also occur on teeth that show no signs of caries or trauma. Clinically, the patient's teeth may look normal and healthy, which complicates proving the endodontic origin of the infection and makes it difficult to identify causing teeth. This specificity can be explained by defects in dentin mineralization. Initial caries or even initial attrition can remove a thin layer of enamel, which facilitates the access of microorganisms to the pulp chamber through the exposed horn of the pulp or through poorly mineralized dentin. Thus, a seemingly non-carious or minimally carious tooth could be subject to infection

of the pulp tissue and formation of periapical abscess [4]. Light microscopic examinations showed penetration of microorganisms through enamel microcracks and their further spread along the dentin-enamel junction [5].

Data on the association of hypophosphatemic rickets with the occurrence of malocclusions were not frequently reported. In a study by Souza et al. (2010) that included 20 patients, it was reported that open bite was the most frequent anomaly that can be explained by delayed maxillary growth in relation to the growth of mandible. Although reported as a common occurrence in the literature, none of their patients showed taurodontism [6].

The therapeutic approach is mainly related to the treatment of periapical abscesses. These abscesses, especially those in deciduous teeth, spread rapidly through the jawbone, which is why extraction of such teeth is necessary [6, 7]. Prevention of abscess formation should involve the application of self-etching adhesive systems and filling the tooth surfaces with light-cured flowable resin to form a barrier that would prevent the penetration of microorganisms. Deciduous teeth treated this way should be frequently checked, and, if necessary, resin barriers should be repeated until the teeth exfoliate [10]. At the same time, fluoride should be applied, and oral hygiene should be rigorously maintained. Prophylactic protection of deciduous molars with metal crowns and protection of anterior teeth with composite resins were also found in the literature [4]. However, this protection measure is often criticized because during the preparation of the teeth, the already enlarged pulp could be open, but also if multiple extractions of deciduous posterior teeth are needed it leads to the loss of the vertical dimension [7]. Preventive pulpotomy of all deciduous teeth with superficial caries is also mentioned as one of the treatment options [4, 5].

CONCLUSION

Hypophosphatemic rickets, as a rare form of rickets, present a diagnostic challenge and require extensive labora-

tory and clinical examinations. Early diagnosis is of great importance in order to prevent the occurrence of bone deformities, as well as dental complications and invasive dental procedures.

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Dentalne karakteristike hipofosfatemijskog rahitisa – prikaz bolesnika

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KRATAK SADRŽAJ

Rahitis predstavlja poremećaj mineralizacije koštanog tkiva u dečjem skeletu. Najčešće je povezan sa deficitom vitamina D; međutim, može nastati i usled pada serumskih fosfata, što dovodi do neadekvatne mineralizacije tkiva, sa posledičnim deformitetom skeleta i poremećajem rasta. Pacijenti sa hipofosfatemijским rahitisom pokazuju promene na zubima na morfološkom i histološkom nivou, kao i na radiološkim snimcima. Cilj ove studije je bio da se izvrši klinička i radiološka evaluacija dentalnih manifestacija hipofosfatemijskog rahitisa kod četvorogodišnjeg dečaka, kao i da se ukaže na neophodnost uključivanja stomatologa u tretman ovog oboljenja u cilju prevencije oralnih komplikacija.

Ključne reči: hipofosfatemija; rahitis; dentin; periapeksni apsces

UVOD

Hipofosfatemijски rahitis, takođe poznat kao rahitis rezistentan na vitamin D, ili X- vezani rahitis, nasledni je sindrom koga karakteriše neadekvatna mineralizacija hrskavice i kosti, što dovodi do deformiteta skeleta i poremećaja rasta. Uzrokovan je mutacijom gena PHEX (endopeptidaze odgovorne za regulaciju fosfata šifrovane genom na X hromozomu), dovodeći do porasta fibroblastnog faktora rasta 23 (FGF23), koji je regulator renalne reapsorpcije fosfata [1, 2]. Patofiziološki mehanizam se ogleda u smanjenju fosfatne reapsorpcije renalnih tubula, što dovodi do hiperfosfaturije i hipofosfatemije, usled čega se razvija rahitis [3]. Prevalenca pojave oboljenja je 1 : 20000 [4, 5]. Standardna terapija ovih pacijenata podrazumeva nadoknadu elementarnog fosfora i primenu aktivnih oblika vitamina D [1, 3]. U novije vreme pokušava se sa primenom anti-FGF23 antitela koja deluju na primarno oboljenje tako što blokiraju FGF23 i time regulišu homeostazu fosfata [1, 2]. Hipofosfatemija je uzrok nastanka displazije dentina zbog poremećaja u mineralizaciji dentinskog matriksa kada se jasno uočava globularni dentin. Prisutni su i tubularni defekti koji mogu da se pružaju do gleđno-dentinske granice. Pored poremećaja u mineralizaciji, uočavaju se tanka gleđ, rascepi u dentinu, naročito velike pulpne komore, kao i jako visoki rogovi pulpe koji se pružaju do gleđno-dentinske granice, što se jasno vidi na radiološkim snimcima [4]. U literaturi postoje navodi da je kod pacijenata sa hipofosfatemijским rahitisom karakteristična pojava multipnih spontanih periapeksnih apscesa [5, 6, 7]. Od dentalnih karakteristika prisutni su još i taurodontizam, loše definisana lamina dura i hipoplazija alveolarnih grebenova [6, 8].

PRIKAZ BOLESNIKA

Četvorogodišnji dečak upućen je sa Klinike za dečje interne bolesti zbog oralnih komplikacija vezanih za hipofosfatemijски rahitis. Tretman osnovnog oboljenja podrazumevao je terapiju elementarnim fosforom i aktivnim oblikom vitamina D, uz čiju primenu je došlo do korekcije kliničkih i laboratorijskih nalaza.

Opšte ispitivanje ukazivalo je na pacijenta sa kliničkim karakteristikama osnovnog oboljenja: deformitet donjih ekstremiteta, promene u hodu i nizak rast. Ekstraoralne promene nisu uočene. Intraoralnim pregledom uočeno je da je kod pacijenta došlo do nicanja svih zuba mlečne denticije. U gornjoj vilici su svi frontalni zubi bili potpuno karijesno destruirani i bili su prisutni zaostali korenovi. Prema rečima oca, ranije se javljao otok u predelu prednjih zuba, kod stomatologa je pružena prva pomoć, ali dalja saradnja sa detetom nije uspostavljena. Na gornjim očnjacima uočen je cirkularni karijes, na gornjim prvim molarima su uočene uznapredovale karijesne lezije sa otvorenom komorom pulpe i gangrenom, dok je na gornjim drugim molarima uočen superficijalni karijes u okluzanim fisurama. U donjoj vilici su frontalni zubi bili potpuno karijesno destruirani, uočene su veliki karijesi V klase na očnjacima, uznapredovale karijesne lezije sa otvorenom komorom i gangrenom, karijesi V klase na prvim molarima, i karijesi I klase na drugim molarima. Prema rečima oca, u donjoj vilici nije bilo otoka (slike 1 i 2).

Analizom panoramskog snimka zapaženo je prisustvo stalnih zamenika svih mlečnih zuba, zametaka prvih i drugih donjih molara i prvih gornjih molara. Na mlečnim drugim molarima se jasno vide velike komore pulpe sa prominentnim rogovima. Komore ostalih zuba nisu mogle biti sagledane zbog uznapredovalih karijesnih destrukcija (Slika 3).

Predložena terapija je podrazumevala konzervativnu sanaciju sva četiri druga mlečna molara, koja je odložena zbog nemoćnosti saradnje sa detetom. S obzirom na to da bi ekstrakcije gangrenoznih zuba dovele do još izraženije odontofobije, preporučene su česte kontrole. Roditeljima je ukazano na neophodnost održavanja dobre oralne higijene.

DISKUSIJA

Hipofosfatemijски rahitis je skeletni poremećaj koji se u osnovi karakteriše hipofosfatemijom. Kako su fosfati od suštinske važnosti za mineralizaciju, ovo stanje dovodi do deficita u mineralizaciji, što primarno utiče na tkiva kod kojih se mineralizacija fiziološki odigrava – kosti, zubi i hrskavičavi deo metafize dugih

kostiju [1]. Prisustvo ozbiljnih dentalnih malformacija kod pacijenata sa hipofosfatemijom dokazano je u brojnim studijama [7, 9, 10].

Zubi kod pacijenata sa hipofosfatemijom pokazuju uvećane komore pulpe, široku zonu predentina, jasan globularni dentin i defekte u tubularnom dentinu koji se pružaju od pulpe do gleđi. Gleđ je tanka, najčešće normalne građe, ali nekad može biti i hipoplastična [6, 7]. Na histološkim preseccima mogu se videti i široki rascepi u gleđi i defekti u mineralizaciji dentina. Uočavaju se brojni kalcosferiti između kojih su prisutni široki nemineralizovani interglobularni prostori [10]. Iako je funkcija odontoblasta normalna, hipofosfatemija dovodi do loše mineralizacije, što uzrokuje pojavu displazije dentina sa jasno vidljivim globularnim dentinom. Zbog perioda formiranja i mineralizacije dentina mlečnih zuba u periodu od četiri meseca fetalnog života do 11 meseci starosti deteta, defekti u mlečnoj denticiji najčešće ne mogu biti sprečeni [6, 7]. Ukoliko se sa lečenjem osnovnog oboljenja krene što pre po rođenju, može se očekivati da dođe do pozitivnog uticaja na formiranje i razvoj stalnih zuba [6]. Međutim, uprkos terapiji, nekad se mogu uočiti abnormalnosti u razvoju zuba i formiranju dentina u stalnoj denticiji [7].

Radiološki nalaz kod ovakvih pacijenata najčešće pokazuje tanku gleđ, smanjenje radiološke gustine dentina, uvećane komore pulpe, prominentne robove pulpe, taurodontizam i anodontije [8, 10].

Dominantna osobenost ovog oboljenja je pojava multipnih spontanih periapeksnih apscesa [4, 5, 7, 10]. Ovi apscesi se javljaju i na zubima na kojima nema znakova karijesa ili traume. Klinički, zubi pacijenta mogu izgledati normalno i zdravo, što komplikuje dokazivanje endodontskog porekla infekcije i otežava identifikaciju zuba uzročnika. Ova specifičnost se može objasniti defektima u mineralizaciji dentina. Početni karijes ili čak i početna atricija mogu ukloniti tanak sloj gleđi, što olakšava pristup mikroorganizama tkivu pulpe preko eksponiranog roga pulpe ili kroz loše mineralizovani dentin. Tako naizgled nekariozan

ili minimalno kariozan zub podleže infekciji pulpnog tkiva i stvaranju periapeksnog apscesa [4]. Svetlosno mikroskopska ispitivanja su pokazala penetraciju mikroorganizama i kroz mikropukotine na gleđi i njihovo dalje širenje duž gleđno-dentinske granice [5].

U literaturi se ne sreću često podaci o vezi hipofosfatemijom rahitisa sa pojavom malokluzija. U studiji Souza i saradnika [2010], koja je obuhvatala čak 20 pacijenata, objavljeno je da je otvoreni zagrižaj bio najčešća anomalija, koja se može objasniti zakasnelim rastom maksile u odnosu na rast mandibule. Iako se u literaturi navodi kao česta pojava, nijedan od njihovih pacijenata nije pokazao taurodontizam [6].

Terapijski pristup se uglavnom odnosi na tretman periapeksnih apscesa. Ovi apscesi, posebno oni kod mlečnih zuba, brzo se šire kroz viličnu kost; zbog toga je ekstrakcija takvih zuba neophodna [6, 7]. Prevencija stvaranja apscesa podrazumevala bi primenu samonagrizujućih adhezivnih sistema i zalivanje površina zuba tečnom smolom da bi se formirala barijera koja bi sprečila penetraciju mikroorganizama. Ovako tretirane mlečne zube treba često kontrolisati i po potrebi ponavljati barijere od smole sve dok ne dođe do smene zuba [10]. Uporedo sa time, treba primenjivati fluore i rigorozno održavati oralnu higijenu. U literaturi se sreće i profilaktična zaštita mlečnih molara metalnim krunama i zaštita prednjih zuba kompozitnim smolama [4]. Međutim, ova mera zaštite je često kritikovana jer u toku brušenja zuba lako može da dođe do otvaranja već uvećane pulpe, ali i zbog gubljenja vertikalne dimenzije, naročito ukoliko treba izvršiti multipne ekstrakcije mlečnih bočnih zuba [7]. Kao jedna od procedura navodi se i preventivna pulpotomija svih mlečnih zuba sa početnim karijesima [4, 5].

Hipofosfatemijom rahitis, kao retka forma rahitisa, predstavlja dijagnostički izazov i zahteva obimna laboratorijska i klinička ispitivanja. Rana dijagnoza je od velikog značaja da bi se sprečila pojava deformiteta kostiju, kao i većina dentalnih komplikacija i invazivnih dentalnih procedura.