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# ENAMEL HYPOPLASIA ASSOCIATED TO PROXIMAL RENAL TUBULAR ACIDOSIS: A CASE REPORT

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Proximal renal tubular acidosis (pRTA) is a syndrome caused by abnormal proximal tubule reabsorption of bicarbonate that yields disturbs in some mineralized tissues as dental enamel. We reported a case of an 8-year-old girl diagnosed with proximal renal tubular acidosis who presented all her teeth with a yellowish color and apparently with absence of enamel. Two shed primary teeth have been examined under scanning electron microscopy to analyze the enamel areas and their relationship with dentin, which structure has been also examined. The present findings showed that pRTA affects amelogenesis as severely as the metabolic acidosis affects the patient. Disturbed amelogenesis may result in hypoplastic enamel with the consequent exposition of dentin in the affected teeth.

**Key words**: enamel hypoplasia, amelogenesis, renal tubular acidosis, electron microscopy

Proximal renal tubular acidosis (pRTA) is a syndrome caused by abnormal proximal tubule reabsorption of bicarbonate that yields a decreased renal bicarbonate threshold resulting in metabolic acidosis. Acid-base disorders and electrolyte abnormalities interfere with normal functioning of many processes in the body, especially with development of mineralized tissues in which calcification requires specific pH conditions. The mainstay of treatment of RTA remains alkali replacement in which sodium bicarbonate is usually systemically administered Alper 2010; Hague et al, 201.

Enamel is the highest mineralized tissue that covers the crown of teeth. It is formed by ameloblasts, epithelial cells derived from the embryonic oral ectoderm, through a conspicuous developmental process referred to amelogenesis. Once ameloblasts are fully differentiated, they form enamel by two successive stages, secretion and maturation. The first mineral crystals start to immediately nucleate while ameloblasts secreting a pool of amelogenin and nonamelogenin matrix proteins. Simultaneously, ameloblasts release some proteases, in special matrix metalloproteinase-20 (MMP-20 or enamelysin), which create the necessary space for nucleating the nascent crystals Habelitz et al, 2005. When the bulk of enamel reaches its definitive thickness, it contains only 15% of mineral: thin hydroxyapatite crystallites appear among a protein-rich matrix Bechtle et al, 2010. Then, ameloblasts embark into the maturation stage in which a high influx of calcium and phosphate ions is responsible for the growth of mineral crystals, while enamel proteins are degraded by proteases, mainly kallikrein-related peptidase-4 (KLK-4) Simmer et al, 2012. Although several mechanisms in amelogenesis remain unclear, both crystal growth and protease activity are believed to be pH-dependent (Lacruz et al, 2010a). Enamel defects include several alterations, mainly related to hereditary/genetic disorders (amelogenesis imperfect) and to fluorosis.

Ameloblasts are believed to regulate the extracellular pH for supporting crystal growth (Smith, 1998). Since transcellular bicarbonate transport is suspected to be an important pathway in enamel mineralization (Lacruz et al, 2010a), pRTA may be responsible for defects during amelogenesis. Koppang et al (1984) described altered tooth eruption and shedding patterns as well as severe enamel hypoplasia in a patient with congenital pRTA, while. Elizabeth et al (2007) reported two cases of patients with renal disease that presented enamel characteristics of amelogenesis imperfecta. Although some recent experimental studies have focused on the role of mutations to the *SLC4A4* gene that codes for the sodium

bicarbonate cotransporter NBCe1, especially in mouse and rat amelogenesis (Lacruz et al, 2010b), few human cases have been reported in the literature.

This article described the case of an 8-year-old girl diagnosed with proximal renal tubular acidosis who presented all her primary teeth with a yellowish color and apparently with absence of enamel. Shed primary teeth have been examined under scanning electron microscopy to analyze the enamel areas and their relationship with dentin.

**CASE REPORT**

An 8-year-old girl diagnosed with proximal renal tubular acidosis was referred by her general dental practitioner to the Center for the Study and Care of Handicapped Patients. The patient was fully informed about the procedures and her parents' written consent was obtained. The study was authorized by the Ethical Committee for Human Experimentation of the Paulista University.

Both primary upper canines were extracted and quickly placed in a fixative containing 2% glutaraldehyde buffered at pH 7.4 with 0.1M sodium cacodylate for 4 hours at room temperature and then left in the same fixative overnight at $4^{o}$C. They were then washed in 0.1 M sodium cacodylate buffer, pH 7.4 for 1 hour and subsequently fractured following its long axis in a buccolingual orientation. Then, each piece was treated with 2% sodium hypochlorite for 30 min in an ultrasonic apparatus (Branson 1210, CT, USA) to remove all the soft tissues covering teeth. The sections were then washed with distilled water, transferred to 30% ethanol and dehydrated in increasing concentrations of ethanol. To avoid shrinkage of the specimens during air-drying, the teeth were immersed in 100% hexamethyldisizilane, HMDS, for 10 minutes and left under a fume hood equipped with an exhaust system for complete evaporation of HMDS. Specimens were mounted on aluminum stubs using colloidal silver adhesive and sputter-coated with gold in a Balzers SDC-050 apparatus. Andia-Merlin et al, 2001.

. The specimens were examined with a LEO 430 scanning electron microscope, operated at 15 kV.

Clinical findings: Intraoral examination revealed poor oral hygiene with moderate gingivitis. All the permanent teeth exhibited absence of enamel and a yellowish color. No caries were detected in the present teeth. While enamel is present in the central lower incisors, it exhibits a chalky appearance. The other permanent teeth presented no enamel on their surfaces. The central upper incisors were restored with resin at their buccal surfaces,

while the primary upper canines that were the only primary teeth present were extracted and processed for scanning electron microscopy evaluation (Fig. 1).

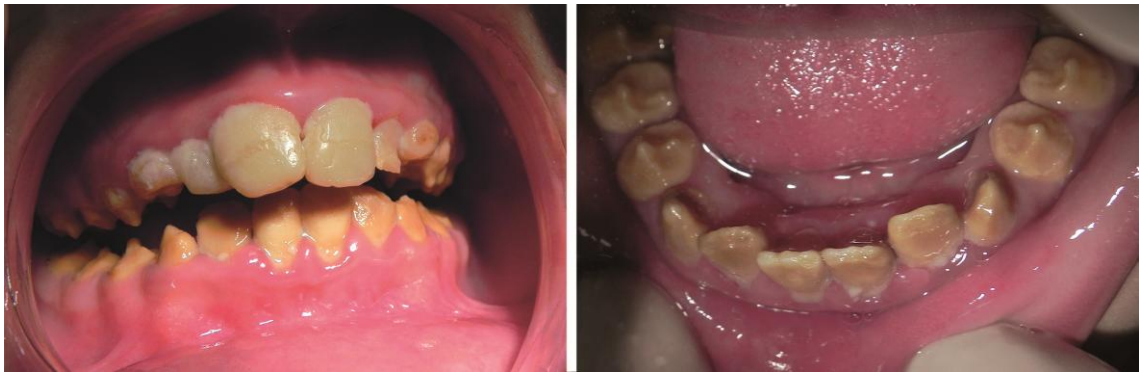

Fig. 1. Intraoral photographs showing all teeth with severe structural alterations. While enamel is present in the central lower incisors, it exhibits a chalky appearance. Apart from the lower incisors, all permanent teeth present no enamel on their surface. Note that both the central upper incisors had been restored with resin at their buccal surfaces. No caries were detected in the present teeth.

Microscopic findings: Scanning electron microscopy examination revealed the lack of a layer of enamel. Only few and very short enamel areas could be seen over the dentin. They appeared as small enamel islands that resembled string mop heads. Examination at higher magnifications revealed that the enamel islands were formed by regularly packed mineral crystals which were adhered to the dentinal surface. At the bottom of enamel islands, the enamel crystals were regularly adhered to the subjacent dentin. However, at these areas, the dentinoenamel junction appeared smooth, instead undulated. Dentin exhibited regular dentinal tubules in both longitudinal and cross sections. The dentinal tubules were surrounded by a regular wall of peritubular dentin, while intertubular dentin filled all the remaining tissue (Fig. 2).

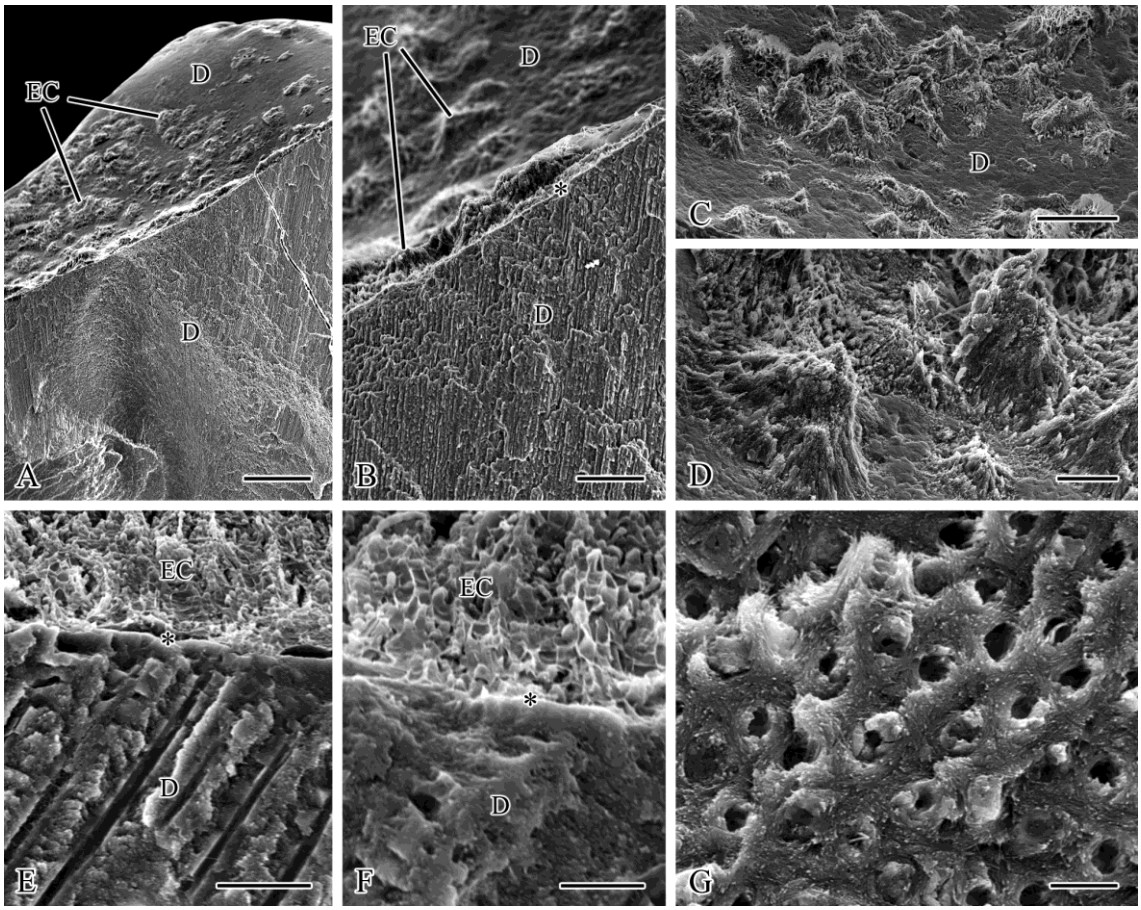


Fig. 2. Scanning electron micrographs illustrating several regions of the extracted teeth. In A, a low magnification view of a tooth that has been fractured following the longitudinal axis. Observe only few enamel areas resembling small islands over the dentin. B shows the enamel islands resembling string mop heads. In C, it could be seen that groups of enamel crystals constitute the string mop heads adhered to the dentinal surface. D shows the dentinoenamel junction that appears smooth, whereas the fractured dentin exhibits regular dentinal tubules. In E, cross sectioned dentinal tubules show a regular wall of peritubular dentin, while intertubular dentin fills all the tissue with a regular aspect. Bars: A = 200 µm; B = 100 µm; C = 25 µm; D = 10 µm; E = 5 µm.

## DISCUSSION

The findings of the present study in primary teeth from a patient with pRTA suggest that enamel develops hypoplastic, a condition that ultimately yields to the lost of the enamel bulk after tooth eruption, when teeth are exposed to the oral environment and function.

Although the teeth examined suffered physiological wearing for a few years into the oral cavity, it is conceivable to suppose that enamel was formed hypoplasic rather than hypocalcified. The presence of small groups of enamel crystals resembling string mop heads

adhered to the dentinal surface allow us to suppose that enamel failed to reach a significant thickness during the secretion stage of amelogenesis. Whereas secreting ameloblasts lay down a viscous gel rich in enamel proteins, fine and highly organized mineral crystallites are immediately nucleated. As the highly precise control of pH that takes place through mechanisms of H/base transport is prevented in pRTA (Lacruz et al, 2010b), most of early nucleated enamel crystals could have subsequently dissolved. Indeed, the pH conditions in the matrix play a key role for deposition and maintenance of mineral crystals (Lacruz et al, 2010a) (Fang et al, 2011). Crystal nucleation and growth result in releasing of numerous hydrogen ions, which decrease the pH to very acidic levels that could yield to the crystal dissolution Habelitz et al (2005)

In addition, the few string mop heads of enamel crystals suggest that it was no hypocalcified but hypoplasic, i.e., it is possible that the synthesis and/or secretion of enamel proteins could be also affected in the patient with pRTA.

Different from enamel, the dentinal structure was no affected by pRTA. Dentinal tubules were regularly surrounded by a homogeneous wall of peritubular dentin and then by an intertubular dentin that showed its classic granular aspect when examined under scanning electron microscopy. This was noted in rats with pRTA in which the dentin hardness was much less affected than enamel (Lacruz et al 2010b). However, although the dentinal structure was structurally normal, the dentinoenamel junction in the examined primary teeth was smooth, different from that present in regular teeth in which this junction is undulated and scalloped (Bechtle et al, 2010). This finding suggests that the pRTA interference on amelogenesis from its early stages, when the dentinoenamel junction is established.

In summary, the microscopical findings obtained in this case offered important suggestions regarding the pathogenesis of enamel hypoplasia in patients with pRTA.

## CONCLUSIONS

The present findings showed that pRTA affects amelogenesis as severely as the metabolic acidosis is leave to be present in the patient. Disturbed amelogenesis may result in hypoplastic enamel with the consequent exposition of dentin in the affected teeth.

## REFERENCES


- Alper SL. Familiar renal tubular acidosis. J Nephrol 2010;16:S57-76.
- Andia-Merlin RY, Garone-Netto N, Arana-Chavez VE. SEM evaluation of the interaction between a three-step adhesive and dentin. Oper Dent 2001;26:440-4.

- Bechtle S, Fett T, Rizzi G, Habelitz S, Klocke A, Schneider GA. Crack arrest within teeth at the dentinoenamel junction caused by elastic modulus mismatch. Biomaterials 2010;31:4238-47.
- Elizabeth J, Lakshmi E, Umadevi KMR, Ranganathan K. Amelogenesis imperfecta with renal disease – a report of two cases. J Oral Pathol Med 2007;36:625-28.
- Fang PA, Margolis HC, Conway JF, Simmer JP, Dickinson GH, Beniash E. Cryogenic transmission electron microscopy study of amelogenin self-assembly at different pH. Cells Tissues Organs 2011;194:166–70.
- Habelitz S, DenBesten PK, Marshall SJ, Marshall GW, Li W. Amelogenin control over apatite crystal growth is affected by the pH and degree of ionic saturation. Orthod Craniofacial Res 2005;8:232–8.
- Hague SK, Ariceta G, Batle D. Proximal renal tubular acidosis: a not so rare disorder of multiple etiologies. Nephrol Dial Transplant 2012;27:4272-87.
- Koppang HS, Stene T, Solheim T, Larheim TA, Winsnes A, Monn E, Stokke O. Dental features in congenital persistent renal tubular acidosis of proximal type. Scand J Dent Res 1984;92:489-95.
- Lacruz RS, Nanci A, Kurtz I, Wright JT, Paine ML. Regulation of pH during amelogenesis. Calcif Tissue Int 2010;86:91-103.
- Lacruz RS, Nanci A, White SN, Wen X, Wang HJ, Zalzal SF, Luong VQ, Schuetter VL, Conti PS, Kurtz I, Paine ML. The sodium bicarbonate cotransporter (NBCe1) is essential for normal development of mouse dentition. J Biol Chem 2010;285:24432-38.
- Simmer JP, Richardson AS, Hu YY, Smith CE, Ching-Chun Hu J. A post-classical theory of enamel biomineralization and why we need one. Int J Oral Sci 2012;4: 129-34.
- Smith CE. Cellular and chemical events during enamel maturation. Crit Rev Oral Biol Med 1998;9:128-61.