CASE REPORT

Amelogenesis imperfecta with bilateral nephrocalcinosis

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SUMMARY

A 12-year-old patient presented with a severe delay of eruption in permanent maxillary and mandibular incisors. On examination, there was over-retained primary teeth and delayed eruption of permanent teeth. Retained primary teeth showed light yellow discolouration whereas permanent teeth were distinct yellow with thin or little enamel. Subsequent imaging revealed all the premolars except maxillary left first premolar showed signs of intra-alveolar coronal resorption, nephrocalcinosis with bilateral multiple calculi and small papillary tip calcifications, marked increase in alkaline phosphatase. Subsequent dental treatment for restoring the functional and aesthetic requirement followed by appropriate treatment for renal problem was undertaken.

BACKGROUND

The rarity of this syndrome makes diagnosis difficult. The relationship between the enamel defect and nephrocalcinosis is still unknown. The hypothesis has been made of an underlying abnormality in the interstitial matrix leading to dystrophic calcification in the kidney, and abnormal enamel production in teeth.¹ Though very few cases were reported in the past, cases reported in this paper have had some typical metabolic abnormalities which were found to be normal in the previously reported cases.

CASE PRESENTATION

A 12-year-old patient reported with a severe delay of eruption in permanent maxillary and mandibular incisors. Apart from consanguineous marriage, medical history was non-contributory. There was no family history of either amelogenesis imperfecta (AI) or failure of eruption of permanent teeth. His general, physical and clinical findings were normal.

Intraoral examination showed partially erupted permanent maxillary right and left central incisors, left lateral incisor, left first premolar and mandibular first molar. Over-retained primary maxillary right and left lateral incisor and canine, mandibular right and left canine which were well widely placed and associated with generalised gingival hyperplasia. Moderate dental caries was seen in relation to primary maxillary right first and second molars as well as left first molar and mandibular left and right first and second molars. The primary teeth exhibited advanced wear. Retained primary teeth showed light yellow discolouration, whereas permanent teeth were distinct yellow with thin or little enamel. Maxillary left first premolar showed complete lack of enamel, anterior open bite and

posterior open bite on right side were present (figure 1A). A structural abnormality in enamel and delayed eruption were diagnosed, which confirmed hypoplastic variety of AI.

INVESTIGATIONS

Panoramic radiograph (figure 2A) showed that a significant amount of bone covering was present over permanent mandibular right central, lateral incisors, first molar and left central and lateral incisors even after complete root formation but there had been little or no axial movement of the above teeth through bone. Radiograph also revealed absence of periodontal ligament (PDL) space and lamina dura in primary and erupted permanent teeth. The density of enamel appearing was very similar to that of dentin. Pulp chamber and root canal of permanent teeth were calcified. All the premolars except maxillary left first premolar showed signs of intra-alveolar coronal resorption. Interestingly mandibular second molars showed abnormal shortening of roots.

Ultrasound (figure 2B) and x-ray of kidney, ureter, bladder (figure 2C) showed nephrocalcinosis with bilateral multiple calculi and small papillary tip calcifications. Nephrocalcinosis (NC) was confirmed with renal CT (figure 2D).

Biochemical and haematological investigation revealed marked increase in alkaline phosphatase to 728 IU/l (N=100–290 IU/l) which is consistent with reduced 25-hydroxy cholecalciferol vitamin D to 18.9 ng/ml (less than 20 ng/ml considered as deficient), raised bicarbonate to 29.1 mmol/l (N=20–22 mmol/l), while serum creatine, calcium and phosphorus were within normal limits. A 24 h urine

Figure 1 (A) Pretreatment and (B) post-treatment intraoral photographs.

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Figure 2 (A) Panoramic radiograph, (B) renal USG, (C) x-ray kidney-ureter-bladder, (D) renal CT scan and (E) karyotyping.

examination revealed reduced calcium (13.2 mg/day) and phosphorous (196 mg/day) excretion with normal creatine excretion. Based on the systemic investigation patient has been diagnosed to have bilateral medullary calcinosis and a vitamin D deficiency state with hypocalcemia and hypophosphatemia with metabolic alkalosis.

Karyotyping revealed no numerical or structural chromosomal anomalies at the GTG banding at the 450–550 resolution (figure 2E).

DIFFERENTIAL DIAGNOSIS

AI is a feature of several multiorgan syndromes, but pathognomonic of only few syndromes namely: amelo-onychohypohidrotic syndrome, Morquio syndrome, Kohlschütter syndrome (AI, progressive neurological deterioration and epilepsy), AI and nephrocalcinosis syndrome (McGibbon-Lubinsky syndrome), Trichodonto-osseous syndrome, AI with taurodontism, oculodonto-osseous dysplasia, epidermolysis bullosa hereditaria.² AI and nephrocalcinosis syndrome was confirmed by

1. Clinical findings such as yellow discolouration of retained primary and erupted permanent teeth, delayed eruption of permanent teeth, absence of enamel on partially erupted teeth indicative of intra-alveolar coronal resorption, roughened enamel all these features are suggestive of hypoplastic AI.
2. Radiographic findings such as multiple unerupted permanent teeth associated with intra-alveolar resorption, obliteration of pulp chamber and root canal, uniform radiodensity of enamel and dentin are suggestive of hypoplastic AI.
3. Ultrasonography examination of kidneys showed bilateral multiple renal calculi indicative nephrocalcinosis.
4. Patient was the first born child and the only affected sibling is suggestive of autosomal recessive inheritance in both the cases.

Hence diagnosis of autosomal recessive hypoplastic AI and nephrocalcinosis syndrome was confirmed.

TREATMENT

Stainless steel crown were placed for primary mandibular right and left first and second molars, all the permanent first molars except mandibular right first molar and maxillary left first premolar to prevent further loss of enamel, restore the vertical height and to maintain masticatory function. Extraction of over-retained primary was done to facilitate the eruption of successors. Gingivectomy was carried out with the intention of

uncovering the crown of the maxillary central incisors and to restore aesthetic appearance composite restoration was performed. Partial denture replacing the mandibular incisors restoring the functional and aesthetic requirement as it is well known fact that functional space maintainers stimulate the eruption of underlying teeth (figure 1B). The patient was referred to nephrologists for treatment of systemic problem.

OUTCOME AND FOLLOW-UP

The patient is under regular dental follow-up, every 3 months since 12 months, to monitor the eruption status and necessary treatment apart from nephrologist consultation. The patient was asymptomatic with no complaint of urinary tract infection, macroscopic haematuria, renal calculi, childhood enuresis or polyuria and dental restorations are found to be intact.

DISCUSSION

The first report of this syndrome, occurring in a sibling pair, appeared in 1972.³ One sibling died at the age of 26 years, having suffered severe renal failure as a complication of nephrocalcinosis; the other developed multiple urinary infections, hypertension and renal failure. Both had the same enamel defect. This syndrome has been previously described in 15 cases^{1–11} from consanguineous as well as non-consanguineous families. All cases had thin or absent enamel and bilateral nephrocalcinosis. While some cases progressed to renal insufficiency,^{1 3 5 8} others featured certain renal tubular disorders.^{1 4 7 8 10} Some cases reported association of this syndrome with other renal disorders such as polycystic kidney disease and distal renal tubular acidosis.⁷

Subsequently reported cases^{1 2 8} share the following common features: failure of eruption, enamel agenesis, unexplained nephrocalcinosis, and normal plasma calcium, 25-OH vitamin D₃, alkaline phosphatase and parathyroid functions, in contrast with previously mentioned studies, case reported in this article had reduced 25-OH vitamin D₃, raised alkaline phosphatase and reduced urinary excretion of calcium and phosphorous.

The rarity of this syndrome makes diagnosis difficult. The relationship between the enamel defect and nephrocalcinosis is still unknown. The hypothesis has been made of an underlying abnormality in the interstitial matrix leading to dystrophic calcification in the kidney, and abnormal enamel production in the teeth.¹ Two separate, but closely linked genes could also be involved. Finally, some authors have suggested that albumin and osteopontin could be involved in renal and dental defect, since they both occur in the renal and dental calcium metabolism.⁵ Most of all, the genes responsible for the synthesis of these two proteins are carried on the same chromosome.

Concerning the dental pathology, following aspects seems to be particularly interesting:

1. The delay of eruption could be explained by the pathology of dental follicle, as already been demonstrated.^{12 13} The dental follicle might be unable to synthesise the factors that initiate the eruption. It could also obstruct the eruption by a mechanical retention due to cystic or fibrous transformation. Recent experiments by the same author have shown some calcification in the dental follicle that could indirectly explain the delay of eruption.
2. AI, in both dentitions, was studied by Phakey¹⁴ and Hall.¹⁵ They found that hypoplasia of enamel matrix and the hypocalcification with hypomaturation of the enamel crystals were present on the same tooth. Nephrocalcinosis was diagnosed by radiographic examination of abdomen, intravenous

pyelography, ultrasonography and CT scan. AI was diagnosed from clinical and histological examinations.

3. Absence of PDL space and lamina dura in both primary as well as erupted permanent teeth. This finding has not been reported in any of the previously reported cases available in literature.

Renal function seems stable in our patient, who is now 12-years old, worsening of renal function or other complications can ensue, as reported by Mc Gibbon.³ Ignoring the renal involvement can lead to serious consequences. In any case, since the pathogenesis remains unknown until now, therapy consists above all in surveillance and palliative treatment of these renal complications.

Learning points

- ▶ As very few cases have been reported till date, the prognosis associated with this syndrome has not been established, though unrecognised and untreated nephrocalcinosis is known to be associated with significant morbidity.
- ▶ Children with apparently autosomal recessive amelogenesis imperfecta (AI) should, at least, have a renal ultrasound examination done to exclude such pathology.
- ▶ Going a stage further, Paula —*et al.*⁹ have advocated that all patients with AI should undergo such an examination.

Contributors All authors have made substantive contribution to this manuscript, and all have reviewed the final paper prior to its submission.

Competing interests None.

Patient consent Obtained.

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