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CASE REPORT

# Amelogenesis imperfecta with renal disease – a report of two cases

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**Amelogenesis imperfecta (AI) is a collective term for a number of developmental conditions characterized by abnormal enamel formation. AI is usually not associated with generalized findings; however, a few cases of AI associated with syndromes and metabolic disorders have been reported in the literature. We report two cases of AI presenting with renal disease and thereby highlight the importance of recognizing this possible association at an early stage, as AI in some cases, may be a marker of renal disease.**
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## Introduction

Amelogenesis imperfecta (AI) is a diverse group of hereditary disorders that affects the quality and quantity of dental enamel. Most of the cases are inherited, either as an X-linked, autosomal dominant or autosomal recessive trait, and there is a possibility that this condition can occur spontaneously in one or more members of the same family. The sporadic cases may represent examples of autosomal recessive AI, or may be due to new mutations, or may be because of variable expression with or without incomplete penetrance of a dominant gene. Although the terminology AI refers to inherited enamel defects unassociated with generalized findings, many authors have included syndromes and metabolic disorders as cases of AI (1). AI occurs in association with multiorgan syndromes such as, cone rod dystrophy, platyspondyly, nephrocalcinosis, hypothalamo–hypophyseal insufficiency and Kohlschutter syndrome. AI is now considered as a group of conditions genomic in origin, which affect the structure and clinical appearance of the enamel of all or nearly all the teeth, and which may be associated with morphological or biochemical changes elsewhere in the body (2).

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## Case report 1

A 23-year-old female patient reported to the outpatient department of Ragas Dental College and Hospital, Chennai, seeking cosmetic correction of discoloured teeth. Family history revealed that the patient's parents were not related and neither of them had history of any developmental dental abnormality. The patient's siblings (16-year-old sister and 15-year-old brother) also presented with a similar discolouration. Medical history was non-contributory at the time of presentation. On intraoral examination, all the teeth were yellowish brown and severely attrited with large interproximal spaces (Fig. 1A). Panaromic radiograph revealed the presence of second and third molars, which were clinically absent in all four quadrants and there was thin radio-opaque enamel in all the teeth. A provisional diagnosis of AI, hypoplastic type was made, based on the history, clinical and radiographic presentation. Endodontic management was carried out, followed by complete rehabilitation with ceramic crowns (Fig. 1B). The patient was asked to report for a follow-up every month, and the follow-up was uneventful for a period of 3 months, after which the patient did not report back.

One year later, the patient reported back to the hospital with a localized swelling in the left anterior maxilla of 2 months duration. Interestingly, she had been diagnosed with chronic renal failure (CRF) 6 months back. Laboratory findings at the time of diagnosis of renal failure were a raised blood pressure of 200/130 mmHg and increased serum levels of urea and creatinine, 126 mg/dl (normal: 10–50) and 10.1 mg/dl (normal: 0.5–1.3), respectively. Alkaline phosphatase and parathormone levels were also raised, 415 units/l (normal: 40–125) and 806 pg/ml (normal: 10–65), respectively. Serum levels of potassium and calcium were 7.8 meq/l (normal: 3.5–5.5) and 9.3 mg/dl (normal: 9–11), respectively, and abdominal ultrasound

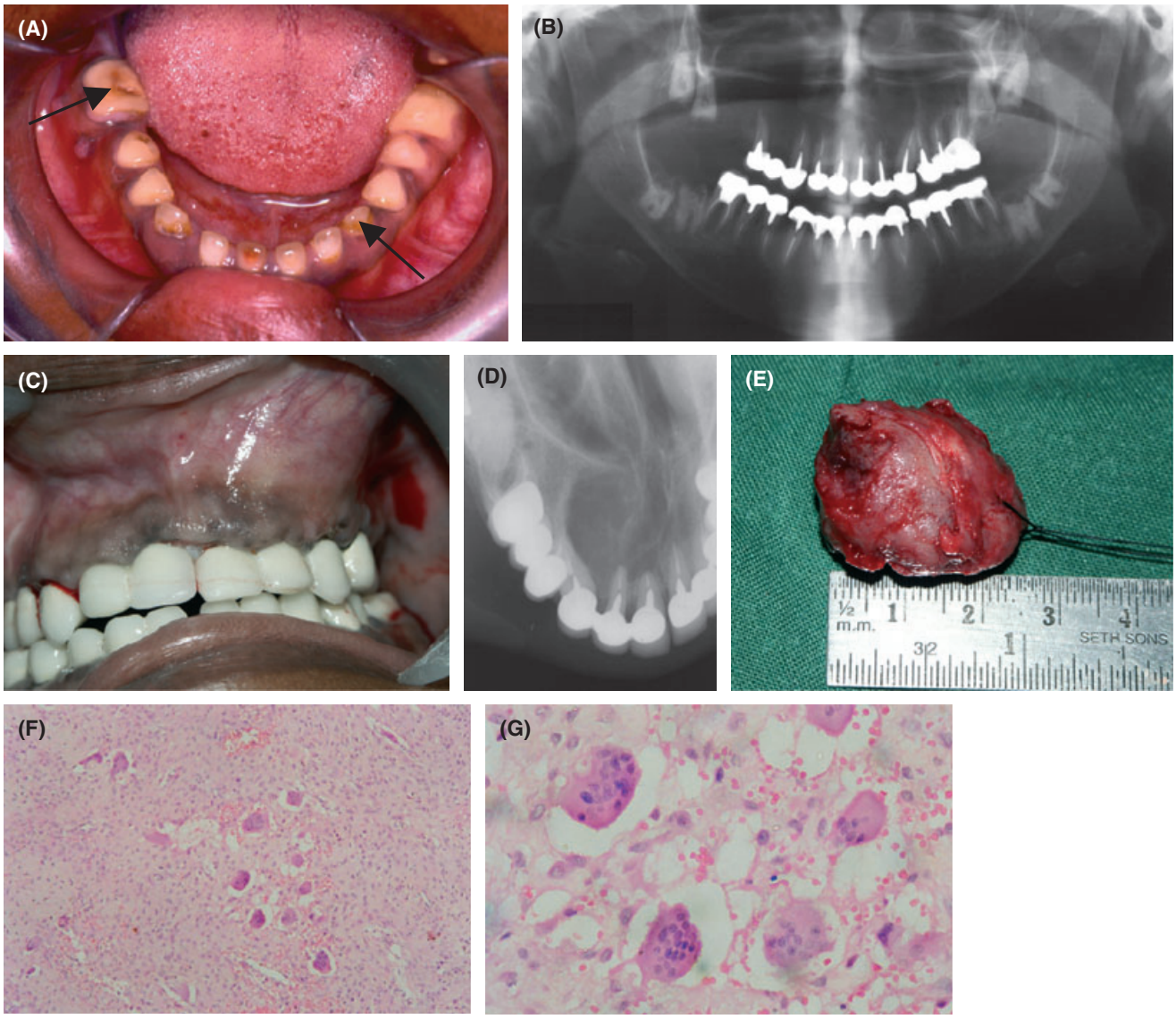


**Figure 1** Case report 1: (A) Hypoplastic dentition with large interproximal spaces and severe attrition. (arrows indicating extensive attrition). (B) Orthopantogram showing impacted second, third molars and endodontically managed teeth in all quadrants. (C) Obliteration of left upper vestibule. (D) Occlusal radiograph revealing a well-circumscribed radiolucency in the anterior maxilla. (E) The gross specimen measuring 2.5 × 2.5 × 2 cm. (F) A cellular fibrous connective tissue showing numerous mulinucleated giant cells [haematoxylin and eosin (H&E) ×10]. (G) High power view of the multinucleated giant cells H&E×40.

revealed bilateral medullary nephrocalcinosis. She was stabilized with dialysis twice a week. None of the family members have a history of renal disease.

On extraoral examination a swelling in the size of 3 × 2 cm was observed close to the alae of the nose .The swelling was obliterating the left upper vestibule, in relation to 23, 24 25, 26 and a well-circumscribed radiolucency was observed in the occlusal radiograph (Fig. 1C,D). Surgical excision was performed and histopathological examination revealed a cellular fibrous connective tissue with numerous multinucleated giant cells and spicules of bony trabeculae with osteoblastic rimming (Fig. 1E–G). Based on the clinical, radiographic and histopathological features and an increased serum parathormone level, a diagnosis of osteitis fibrosa (a form of renal osteodystrophy) with secondary hyperparathyroidism was made.

## Case report 2

A 20-year-old girl reported to the outpatient department of Ragas Dental College and Hospital, with the complaint of discolouration of all her teeth and dislodgement of veneers in the upper and lower anterior teeth, which had been restored with composite veneers 5 years earlier for aesthetic purpose. History revealed that her deciduous teeth were also discoloured. She was admitted in a hospital at 8 years of age with the complaint of weakness of lower extremities, inability to walk and nocturnal enueresis, at which time a diagnosis of renal

tubular acidosis (RTA) was made. The laboratory findings included, low serum potassium, calcium, phosphorus and bicarbonate levels, 2.1 meq/l, 7.6 mg/dl, 2.4 mg/dl and 10 mM (normal: 3.5–5.5, 9–11, 3.0–4.5 and 20), respectively, a positive oral ammonium chloride test and the presence of bilateral medullary nephrocalcinosis in the ultrasound. The patient had no contributory family history.

Dental examination revealed that anterior open bite was not associated with any adverse oral habits. The entire permanent dentition revealed hypoplasia and yellowish brown discolouration (Fig. 2A). The lower second molars exhibited hypoplasia characterized by pitting on the occlusal surfaces, and the partially erupted third molars were also hypoplastic (Fig. 2B). Although the radiographic density of dentin appeared to be normal and the pulp chambers were of normal size, enamel was thin and radio-opaque in all the teeth and the left upper permanent canine was impacted (Fig. 2C). The clinical and radiographic features led to the diagnosis of AI, hypoplastic-pitted type and appropriate cosmetic rehabilitation was carried out.

## Comments

Amelogenesis imperfecta is a group of inherited anomalies of dental enamel. Since its first classification as hypoplastic and hypocalcified type in 1945, several classifications have evolved. Four major types were recognized based on phenotype (hypoplastic, hypocalcified, hypomaturation and hypomaturation–hypoplastic) and then subdivided into 15 subtypes based primarily on phenotype and secondarily on mode of inheritance. This classification based primarily on phenotype was considered unsatisfactory as variable phenotypes of AI are found within families and within different teeth of the same person. Hence, the recent workable classification proposes that the mode of inheritance be considered as the primary factor in the diagnosis of AI, followed by the gene mutation, the biochemical outcome if known and finally the phenotype (1). To date, mutations in four genes (AMELX, ENAM, KLK4 and MMP20) have been reported to cause AI (2), but the molecular defects of all forms of AI have not yet been established. So, the clinicians should rely on the clinical and radiographic findings when diagnosing and planning treatment for patients with AI. Till date, only a few cases associating AI and renal diseases have been reported (3).

The present report of two cases describes the occurrence of AI in association with two different types of renal diseases. Both the cases presented with bilateral medullary nephrocalcinosis where case 1 progressed to renal failure, with an associated secondary hyperparathyroidism and case 2 had RTA, but did not present with renal failure. Nephrocalcinosis, which is precipitation of calcium salts in the renal tissue, is frequently associated with CRF and RTA. In the first patient nephrocalcinosis, secondary hyperparathyroidism and increased alkaline phosphatase levels were present at the time when CRF was diagnosed (6 months after the diagnosis of AI). Subsequently, she presented with osteitis fibrosa, which is the most common form of renal osteodystrophy. Kalyvas et al. in their review of literature, listed 16 cases of jaw enlargements in dialysis patients, of which 14 patients presented with diffuse swelling of both the jaws and three patients had localized swelling of the mandible (4). Our case had

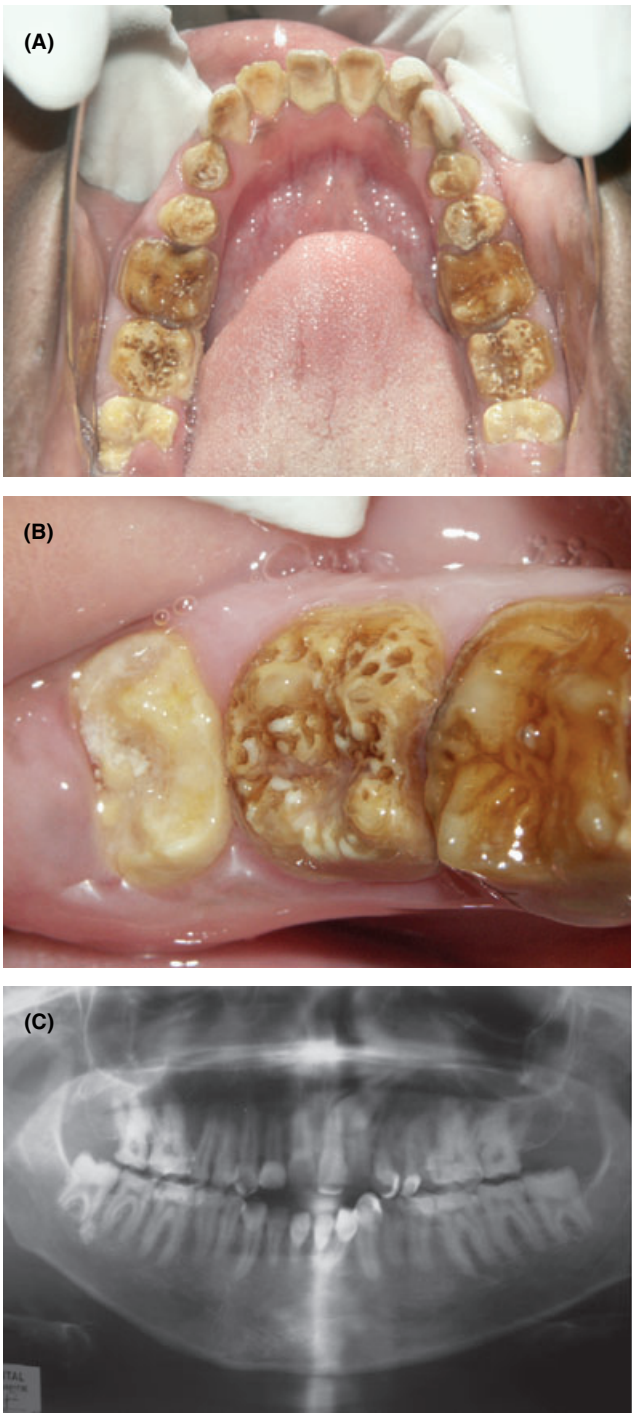


**Figure 2** Case report 2. (A) Hypoplasia and yellowish discolouration of all the mandibular teeth. (B) Pitted type of hypoplasia in 37. (C) Orthopantomogram revealing reduced thickness of enamel and impacted left upper canine.

localized involvement of the maxilla. The second patient had nephrocalcinosis and RTA diagnosed at an earlier age. RTA is a group of disorders in which renal excretion of acid is reduced out of proportion to any reduction of glomerular filtration rate, and as a result metabolic acidosis sets in. Medullary nephrocalcinosis is usually associated with RTA as either its cause or consequence (5). This treatable cause of renal damage if neglected may result in acidosis and hypokalemia that can be life-threatening. To our knowledge, only one case of AI and distal RTA has been described (6).

Amelogenesis imperfecta and nephrocalcinosis syndrome has been reported in a few families. The first sibling pair was described by Mac Gibbon in a nonconsanguineous family in 1972 (7). The following reports describe this association, in sibling pairs and in isolated cases from consanguineous as well as nonconsanguineous families (3, 8–12). The occurrence of this syndrome in consanguineous families suggests an autosomal recessive pattern of inheritance and out of the types of AI, hypoplastic AI is frequently associated with this syndrome. This syndrome of AI and nephrocalcinosis is characterized by delayed eruption, enamel agenesis, unexplained nephrocalcinosis, normal plasma calcium, vitamin D3, alkaline phosphatase levels and parathyroid function (3). Varying degrees of impairment of urinary concentrating ability and tubular acidification have also been reported. Although renal function was stable at the time of diagnosis of nephrocalcinosis in all the previous reports describing this syndrome, one of the siblings described by Mac Gibbon progressed to renal failure and died at the age of 26 (7). More recently a case of AI, cleft lip and palate and polycystic kidney disease was described by Suda et al., in a consanguineous family and in this case nephrocalcinosis was secondary to polycystic kidney disease (13). Although both the cases described here had no family history of AI or renal disease and no consanguinity was present, the siblings of the first patient presented with AI.

The combination of AI and nephrocalcinosis may suggest a contiguous gene syndrome or pleotropism. One hypothesis suggests that there is an underlying abnormality in the interstitial matrix, which leads to dystrophic calcification in the kidney and abnormal enamel production in the teeth. Involvement of two separate but closely linked genes has also been suggested (9). Another hypothesis suggests that many of the dental proteins that were thought to be tissue-specific may also be expressed in non-dental tissues and the role of these proteins in calcium and phosphate metabolism and renal function needs further research. The genetic basis of AI and nephrocalcinosis syndrome is yet to be established (12).

Our cases illustrate that AI may be associated with renal disease and hence highlight the importance of evaluating the renal function in patients with AI. As the deciduous dentition is also involved in patients with AI, an early diagnosis of the associated condition may be made. Its importance is because of the morbidity associated with unrecognized and untreated renal disease. Awareness of the possibility of such an association is very essential among dentists as they can aid in an early referral of these patients. To conclude, the present cases bring forth the necessity of a thorough medical history and systemic examination, including renal ultrasound and renal function tests in all patients with AI.

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