Significance of Syndromic Forms of Amelogenesis Imperfecta: Illustrated by Two Cases of Tricho-Dento-Osseous Syndrome and Cone-Rod-Dystrophy

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Abstract:
Amelogenesis imperfecta (AI) is a genetic disease of the teeth which could exist in isolation or in combination with syndromes. Tricho-dento-osseous syndrome (TDO) is a disease that is inherited in an autosomal dominant manner characterized by AI with taurodontism, increased thickening and density of the skull bones and curly/kinky hair. Cone-rod-dystrophy (CRD) with AI is an extremely rare condition characterized by photophobia, horizontal nystagmus and reduced central vision which develops during the first few years of life followed by hemeralopia, namely the inability to see clearly in bright light which develops by the end of the first decade of life. The main dental sign is hypoplastic or hypomineralized type of AI.

The aim of the report is to present two patients with syndromic forms of AI namely Tricho-dento-osseous Syndrome and Cone Rod Dystrophy to create awareness among dental surgeons and pediatricians on a multidisciplinary approach being essential for the management of such patients.

Key words: Amelogenesis imperfecta, cone-rod-dystrophy and tricho-dento-osseous syndrome

Introduction:
Amelogenesis imperfecta (AI) was initially considered as purely a dental disease with a genetic basis which gives rise to specific enamel defects (1-4). However, recent findings have led AI to be considered as a genetic disease that may exist in isolation as a dental disease or in combination with syndromes (1-4). The non syndromic forms of AI are classified depending on the structural defect of enamel observed, inheritance pattern and clinical phenotype.

The syndromic forms of AI described to date includes Tricho-dento-osseous Syndrome (TDO) (5-8), Cone rod dystrophy (CRD) (5), Kohlschutter –Tonz Syndrome (5,6) and McGibbon Syndrome (AI with nephrocalcinosis) (5,6). However, these syndromic forms of AI are very rare to the extent that most dental surgeons, who treat patients suffering from AI, may not recognize the existing syndromes. In addition, pediatricians and other medical professionals should play a major role in the management as these are patients who suffer from medical problems as well.

The present report aims to describe the clinical presentations of two syndromic forms of AI namely Tricho-dento-osseous Syndrome and Cone Rod Dystrophy using AI patients who sought treatment at a Paedodontic clinic in Sri Lanka.
Lanka, in order to create awareness in the medical profession.

Case reports

1. **Tricho-dento-osseous syndrome**

   A 13 year old girl who presented with discoloured teeth was diagnosed as having AI due to the fact that this patient has had discoloured deciduous teeth as well and a positive family history with maternal grandfather, mother and uncle having similar defective teeth. In addition meticulous clinical examination, which showed pits on buccal surfaces and yellowish discoloration on other tooth surfaces, confirmed the patients’ condition as AI (Fig 1). Pedigree analysis resulted in inheritance pattern being identified as autosomal dominant as the patient had one parent with AI, in addition, transmission of disease from both genders with affected males and females showing similar clinical features. Radiological investigations using a dental panoramic radiograph (DPT) revealed taurodontic lower first molars (Fig 2). This fact led us to suspect the possibility of the patient having TDO and skull radiographs confirmed the presence of osteosclerosis (Fig 3). Further, supporting a diagnosis of TDO, patient has had extremely curly hair at the time of birth which became less curly as the patient grew older, and both, mother and daughter had obtuse mandibular angles (Fig 4).

   On examination the patient had dental caries in lower right second primary molar and lower left primary molars teeth. All carious teeth were restored with stainless steel crowns and appointments were given to place stainless steel crowns for first permanent molar teeth and composite restorations for anterior erupted permanent teeth as well. As the teeth were sensitive during restorative treatment the girl was reluctant to get the restorations done. Although the option of treatment under general anesthesia was suggested the parents and the patient did not consent.

2. **Cone – rod Dystrophy**

   A 2 year old child with small and discoloured teeth presented to a Paedodontic clinic and was suspected to have AI. With reference to pedigree analysis autosomal recessive pattern of inheritance could be confirmed as the patient was from a family exhibiting consanguinity and her parents were without any dental abnormalities. When the patient was examined, the deciduous teeth had a brown tinge similar to permanent teeth which erupted subsequently (Fig 5a, b). In addition, anterior open bite was also observed (Fig 5a).

   Therefore, depending on the clinical/radiological presentation and pedigree analysis the patient was diagnosed as having hypoplastic type of AI. When the patient was receiving treatment at the age of 2 years, the Consultant, Pedodontist noticed abnormal eye movement, namely horizontal nystagmus, which resulted in the patient being referred to an Ophthalmologist. The Ophthalmologist found the patient to be suffering from photophobia, reduced visual acuity, reduced central vision due to macular atrophy, reduced night vision, nystagmus, strabismus, and astigmatism. These findings together with the dental signs resulted in confirmation of the diagnosis as autosomal recessive cone rod dystrophy associated with Amelogenesis Imperfecta.

   During the primary dentition stage meticulous preventive measures were introduced to prevent development of dental caries (Fig 5a). At the age of six, patient presented with pulp exposed in all permanent first molar teeth. As the patient was anxious, the treatments were done under general anesthesia. According to the treatment plan, grossly carious upper first molar teeth were extracted and lower permanent first molar teeth were treated with indirect pulp capping and restored with stainless steel crowns. Permanent upper anterior teeth were restored in the clinic once they fully erupted (Fig 5b). Direct composite veering was done for all upper and lower permanent veneering incisors, canines and premolars (Fig 6a). Root canal treatment was also
performed in relation to non-vital upper central incisors and stainless steel crowns were placed in relation to both upper second and third molars and lower left second molar (Fig 6b). It is planned to restore untreated permanent molars and molars treated with stainless steel crowns with porcelain fused metal crowns as a definitive management.

Discussion
AI represents a group of developmental conditions, resulting in structural abnormalities of enamel. The frequency of Amelogenesis Imperfecta in the population varies from 1:700-1:14000 depending on the population studied (4). Clustering of patients in certain geographical locations, may give rise to increase prevalence in these locations. To the best of our knowledge prevalence of AI in the Sri Lankan population has not been assessed to date. It could occur either alone or in combination with other birth defects (1-4). Although, several such multiple congenital anomaly syndromes have been described in relation to AI, most dental surgeons who treat patients with AI may not be aware of these syndromes due to their rarity (5). However, dental surgeons could play a major role in the diagnosis of multiple congenital anomaly syndromes related to teeth as, identification of the dental defect usually lead to the diagnosis of the overall disease. Although, dental surgeons are knowledgeable and could easily diagnose the dental defect per se, this paper is written with the aim of educating dental and medical professionals so that they will be able to identify these rare AI associated multiple congenital anomaly syndromes as well.

As mentioned before, AI related multiple congenital anomaly syndromes, seem to be a very rare occurrence and only a few cases have been published for each disease to date (5-9). However, with the exception of Tricho-dento-ossseous syndrome (TDO) (5-8) all other diseases such as Cone-rod-dystrophy, Kohlschutter –Tonz syndrome and McGibbon syndrome (AI with nephrocalcinosis) show an autosomal recessive inheritance pattern (5). In South Asia including Sri Lanka, some individuals may still practice consanguinity and as this practice results in multiple developmental anomalies, syndromic forms of AI may not be as rare as previously thought.

The clinical presentations of TDO include enamel hypoplasia, taurodontism, kinky/curly hair and increased thickness and density of osseous structures (5-8). The patient described in this case report showed enamel hypoplasia and taurodontism, which are considered as complete penetrant features as well as sclerosis of bone.

CRDs are inherited retinal dystrophies characterized by decreased visual acuity, colour vision defects, followed by progressive loss in peripheral vision and colour blindness. CRD with AI is an extremely rare condition that is given the name Jalili syndrome (9). Two phenotypes have been described, namely patients with phenotype A, presenting with photophobia, nystagmus and visual impairment as well as AI while phenotype B presenting with visual impairment and AI. In addition, phenotype A occurs in early infancy while phenotype B occurs in early childhood (3-6 yrs) (9). Our patient may have Phenotype A as by the time those visual disturbances were observed by the clinician when she was 2 years of age.

Conclusion
This report is presented to highlight rare syndromic forms of AI, in order to educate health professionals so that they are able to identify and manage these rare entities accurately.

References


Figure legends
1. Fig 1– Clinical presentation of hypoplastic AI

2. Fig 2- Radiograph of the patient. Note: Taurodntic lower 1st molars

3. Fig 3-Skull radiograph showing osteosclerosis

4. Fig 4-Note: Obtuse mandibular angle

5. Fig 5a- Clinical presentation of AI in child with CRD in early mixed dentition

6. Fig 5b Initial treatment stage

7. Fig 6a- Post-operative photograph of AI and CRD (19 years old)

8. Fig 6b Post-operative radiograph of AI and CRD (19 years old)
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