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Review

The genetic basis of inherited anomalies of the teeth. Part 2: Syndromes with significant dental involvement

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Abstract

Teeth are specialized structural components of the craniofacial skeleton. Developmental defects occur either alone or in combination with other birth defects. In this paper, we review the dental anomalies in several multiple congenital anomaly (MCA) syndromes, in which the dental component is pivotal in the recognition of the phenotype and/or the molecular basis of the disorder is known. We will consider successively syndromic forms of amelogenesis imperfecta or enamel defects, dentinogenesis imperfecta (i.e. osteogenesis imperfecta) and other dentine anomalies. Focusing on dental aspects, we will review a selection of MCA syndromes associated with teeth number and/or shape anomalies. A better knowledge of the dental phenotype may contribute to an earlier diagnosis of some MCA syndromes involving teeth anomalies. They may serve as a diagnostic indicator or help confirm a syndrome diagnosis.

Keywords: Syndromic amelogenesis imperfecta; Syndromic enamel defects; Syndromic dentinogenesis imperfecta; Osteogenesis imperfecta; Syndromic hypodontia; Ectodermal dysplasia; Axenfeld–Rieger malformation

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1. Introduction

Dental anomalies, even when minor, have been reported as significant components of many syndromes. Their presence may be a valuable diagnostic clue in the identification of specific patterns of developmental disturbance. Teeth abnormalities may serve as a diagnostic indicator or help confirm a syndromic diagnosis. The Winter–Baraitser Database v 1.0.12 (previously: London Dysmorphology Database – LDDB) references 793 entities with abnormal teeth, among which 147 have abnormally shaped teeth, 219 oligodontia, 28 dentin and 128 enamel anomalies. A closer look at the relevant entries demonstrates that, in most situations, the exact dental anomalies are poorly or even inadequately described, or concern a minority of cases.

For didactic reasons, isolated abnormalities of the shape and/or structure of the teeth were distinguished from the abnormalities of number associated with multiple congenital anomalies (MCAs). This oversimplification should not hide the fact that, in some instances, a mutation in a gene involved in MCA can also be reported as an isolated dental symptom.

In this paper, we will focus on the most important and most characteristic disorders. The reader will find additional data on other syndromes in Tables I–X (Supplementary Material 1). All the loci of the syndromes presented in these reviews are summarized in appendix 1 (Supplementary Material 1).

2. Syndromes associated with amelogenesis imperfecta (AI) and enamel hypoplasia

Although usually isolated, AI is a component of several MCAs (Supplementary Material 1, Table I). Constitutional enamel anomalies must be considered cautiously as they can easily be misdiagnosed, when they are secondary to metabolic or environmental factors (including extensive decay…), as shown in a review of oro-dental defects in the Prader–Willi syndrome [5].

2.1. Tricho-dento-osseous syndrome

The tricho-dento-osseous syndrome (TDO, OMIM 190320) is characterized by kinky, coarse and/or curly, fair coloured hair, present at birth in 80% of cases. Half of the patients retain this phenotype beyond infancy. More than 90% of individuals with TDO have an increased cranial thickness, obliterated diploë and absence of mastoid pneumatization [156]. Teeth show uniformly thin or pitted hard enamel, enlarged pulp chambers, and taurodontism. The degree of taurodontism and the distribution of affected teeth are highly variable. In some individuals there is severe taurodontism of all the posterior teeth while the anterior teeth show only enlarged pulp chambers. Both primary and permanent teeth are typically affected [61]. Dental anomalies in TDO are similar to those observed in AI hypomaturation–hypoplasia type with taurodontism (AIHHT, OMIM 104510), which is inherited as a highly penetrant autosomal dominant trait. AIHHT shows no alterations in hair or bone.

A common four base pair deletion in exon 3 of the human *DLX3* gene located on human chromosome 17q21.3–q22 [132] has been identified in TDO families [121]. Although the dental findings of the AIHHT are similar to those of TDO, AIHHT is a distinct condition, usually not linked to *DLX3* [122]. Nevertheless, Dong et al. [35] identified a deletion of two nucleotides in the homeodomain of the *DLX3* gene in a large AIHHT pedigree, suggesting that some forms of AIHHT are allelic to TDO. The clinical pattern of expression of *DLX3* mutations depends on the altered functional domain of the DLX3 protein: AI and taurodontism are a constant feature but hair and bone anomalies are observed with mutations outside the homeodomain [121].