GENETIC ASPECTS OF DENTINOGENESIS IMPERFECTA

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Abstract

Dentinogenesis Imperfecta (DI) is a hereditary, simple autosomal dominant disorder showing abnormalities in the dentin of the developing teeth and occurring at a rate of about 1 in 8000 births. The expression of DI shows a high penetrance and a low mutation rate.

Two main types of DI appear to exist: type I which is the defect associated with osteogenesis imperfecta, and type II which is the classical hereditary opalescent dentin. The formerly proposed DI type III appears to be only a modified expression of the same gene as in the classical DI type II.

Any gene therapy type of treatment is unrealistic for adolescent patients who already exhibit the symptoms. However, there is a good prospect for early screening since DI is inherited as a dominant disorder, and known trait from parents or siblings is a strong indication for later exposure to DI. At present there are no practical means to correct the genetic defect or to avoid the symptoms. Nevertheless, screening provides an early warning and helps to guide protective and restorative treatment so early that maximum amount of the natural dentition can be retained.

1. Introduction: Characteristics of Dentinogenesis Imperfecta

Dentinogenesis imperfecta (DI) is a hereditary disorder that is manifested during the developmental period of dental histodifferentiation. DI is characterised by anomalous dentin, easy fracturing of the enamel away from the underlying dentin and subsequent chipping and rapid attrition of the exposed weak dentin. Teeth colours vary from brown to translucent gray or even blue, with an opalescent sheen and darkening with age. The permanent teeth often seem to be of better quality and suffer less destruction than the primary teeth. The teeth have bulbous crowns with a cervical constriction and short pointed roots, often with periapical areas present. The pulp chambers and canals become progressively obliterated after eruption, mostly in the coronal segment. The relatively easy
fracturing of the enamel, particularly at the incisal edges of the anterior teeth and the occlusal surfaces of the posterior teeth, is due to lack of scalloping of the dentinoenamel junction and weak anomalous dentin base\(^1\). Enamel and cement appear normal, but dentin exhibits extensive variation in the microscopic structure\(^2\). The circumpulpal dentin is characterised by dysplastic appearance with amorphous areas, high organic content and interglobular calcification, while the mantle dentin appears normal. At least locally poorly mineralised regions occur eg adjacent to the mantle dentin. Although mostly orientated in the pulpal direction, the dentinal tubules are short, varied in width and branched \(^3,\)\(^4,\)\(^5\). When associated with more general osteogenesis imperfecta, additional systemic disorder such as blue sclera, flaccid ligament and brittle bones also occur\(^4,\)\(^5\).

According to expression, DI has been classified into two main categories. Of these type I represent the defect associated with osteogenesis imperfecta and type II is the isolated classical hereditary opalescent dentin (with no osteogenesis imperfecta). The oral manifestations are similar, whether DI occurs as isolated type II trait or as in type I in combination with systemic disease\(^1,\)\(^3,\)\(^9\). A rare type III has also been described, in which the teeth have a shell-like appearance with multiple pulp exposures\(^5\) but which is otherwise fairly similar to type II.

Interestingly, with DI a marked coincidental reduction of caries and sensitivity has been reported\(^9\).

Treatment of DI has three main objectives\(^2,\)\(^6,\)\(^7\): to provide the patient with an esthetic appearance as early as possible to avoid psychological problems; to recover the lost vertical dimension of occlusion caused by severe attrition; and to avoid interfering with the eruption of the remaining permanent teeth. Presently the main routes for treatment of DI include eg multiple crowns, overlays for primary and crowns for permanent teeth, and programs using overdenture\(^1,\)\(^2\). Here the genetic aspects and implications of DI are reviewed, with the aim of exploring the prospects for possible new routes to treatment.

2. Genetic Aspects of Dentinogenesis Imperfecta

Dentinogenesis imperfecta is inherited as a simple autosomal dominant (Mendelian) disorder with high penetrance and a low mutation rate. It occurs at a rate of about 1 in 8000 births, and mainly in families with known trait to express DI\(^1,\)\(^3,\)\(^5\). However, also sporadic rare mutations occur with no similar cases in siblings or parents\(^1,\)\(^2\). A typical family pedigree with DI over three generations is shown in Fig 1.

Since the trait is autosomal dominant, the recurrence risk is high, approximately 50% \(^6,\)\(^7,\)\(^8\). Both males and females are affected in each generation, giving the typical vertical pedigree pattern for inheritance. Males can transmit DI to either males or females, and vice versa, but unaffected persons do not transmit DI. As in all autosomal dominant traits, the disease is expressed only in heterozygote, and some variation in expression can be expected\(^7,\)\(^8\). Although unaffected parents do not transmit DI, as mentioned above in very rare cases new mutations may occur\(^1,\)\(^2,\)\(^9,\)\(^10\). In such cases recurrence for same parents is no more negligible, because high-penetration mutations confined to the gonad carry a recurrence risk of up to 50%. The risk for a new mutation may increase with the paternal age\(^7\).
Fig. 1. A Family pedigree with DI affecting three generations. Open symbols mean unaffected and closed symbols affected individuals; circles stand for females and squares for males.

Of the two main types of DI type I is the defect associated with osteogenesis imperfecta, and type II is the isolated classical hereditary opalescent dentin. It is clear that these types also reflect different genetic defects, apparently involving mutations in a different locus. Family studies have shown that both conditions do not occur within same kindred, and are therefore not variations in the expression of the same gene(s). For both DI types I and II, the genetic abnormality is however expressed in defective biosynthesis of type I collagen. As is seen for type II from Fig 1, DI is clearly nonsex linked, but there are reports suggesting that girls can be more severely affected than boys. Reasons for this apparent sexual dimorphism are unclear, but may have something to do with the observation that when (in boys) less affected teeth are found, they tend to concentrate to the maxillary incisors, ie regions which is the only one where the teeth develop in the median nasal process.

DI Type III has been described from the Brandywine isolate of Maryland, USA. However, this proposed DI type III appears to be only a modified expression of the same gene as in the classical DI type II, and should probably hence be disregarded as an independent DI type.

3. Prospects for Treatment

Most patient who suffer from DI and seek treatment are motivated by both psychological and functional concerns. Therefore, treatment of DI has multiple objectives:

0# to provide an esthetic appearance for the patient to alleviate psychological problems;
0# to recover the dentition lost by severe attrition; and
0# to avoid interfering with the eruption of the remaining permanent teeth.

The rehabilitation of DI is complex and hence proper diagnosis must be ensured. Removal of some indicated teeth is usually
necessary, which provides material for histological confirmation of DI diagnosis. Normally pulpectomy and restoration are needed to save as much of the remaining teeth as possible. These teeth form the basis for further prosthodontic treatment: Since practically all patients are either children or adolescents with still developing denture, long-term treatment programes cannot be avoided. Also for the same reason, it is useful to consider removable restoration methods until definitive restoration when the full denture has appeared. This could mean using overlays for primary teeth and multiple individual crowns for permanent teeth instead of overdentures, also to avoid dangering the interproximal periodontal tissue particularly at the incisors. To further limit the risk of fractures and to obtain an adequate masticatory pattern, removable skeletal partial prostheses with cast occlusal surfaces have been used. For later treatment, overdentures have been widely applied. With such restoration programs, reasonably satisfactory results have been achieved

Regarding preventive dental maintenance, proper oral hygiene is seen important, since there is little reason to compound the risks to denture with additional complications. Since the disease is of hereditary (genetic) origin, one could in principle speculate with gene therapy. This is unrealistic for adolescent patients who already exhibit the symptoms, because the dentin development is already determined at this stage. In theory there is a good prospect for early screening since DI is inherited as a dominant disease; hence known trait from parents or siblings is a strong indication for later exposure to DI. At present there are no practical means to correct the genetic defect or to totally avoid the symptoms. However, screening provides an essential early warning and helps to guide protective and restorative treatments so that a maximum amount of the natural dentition can be retained, with minimum discomfort to the patient. Since early diagnosis is essential, the treatment programs long-term in character and the probability high of family members being affected, genetic screening provides a relatively easy and cost-effective tool for reducing the impact of DI.

4. Conclusion

Dentinogenesis Imperfecta (DI) is a hereditary, simple autosomal dominant disorder showing abnormalities mainly in the dentin of the developing teeth and occurring at a rate of about 1 in 8000 births. The expression of inherited DI shows a high penetrance and a low mutation rate.

Two main types of DI appear to exist: type I which is the defect associated with osteogenesis imperfecta, and type II which is the classical hereditary opalescent dentin. The formerly proposed DI type III appears to be only a modified expression of the same gene as in the classical DI type II.

Since the disease is of hereditary (genetic) origin, one could in principle speculate with gene therapy. This is unrealistic for typical young patients who already exhibit the symptoms, because the dentin development is already determined at this stage. In theory there is a good prospect for early screening since DI is inherited as a dominant disease; hence known trait from parents or siblings is a strong indication for later exposure to DI. However, at present there are no practical means to correct the genetic defect or avoid the symptoms. Screening can provide an early warning and helps to guide cost-effective protective and restorative treatment, so that maximum amount of the natural dentition can be retained and the discomfort to the DI patient is minimized.

Literature


