

Brittle teeth with brittle bone in a family for four generations: Case report and literature review

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Abstract

Dentinogenesis imperfect (DI) is a hereditary dentine disorder affecting both deciduous and permanent teeth. DI is caused by mutations in genes encoding for type I collagen leading to discoloration of teeth. Shield around 30 years ago classified DI into 3 types (type I, II, and III). DI type I is associated with osteogenesis imperfect (OI), which is an inheritable disorder of connective tissue. Bone fragility and fracture of bone with minor trauma are hallmarks of this disorder. The objective of this article is to report and review a rare case of DI with OI affecting 4 generations of the family. Through this article, we intend to highlight genetic influence that affected a family for many generations, discuss the oral manifestations that can lead to the diagnosis of OI, and the importance of early diagnosis of OI.

Keywords: Dentinogenesis imperfecta, opalescent teeth, osteogenesis imperfecta

Introduction

Dentinogenesis imperfect (DI) is inherited as an autosomal dominant trait, and is characterized by an opalescent discoloration, with brittleness affecting both deciduous and permanent teeth. It was probably first recognized by Barret in 1882, and the term “hereditary opalescent dentin” was first used by Skillen, Finn, and Hodges. The incidence of DI is estimated to be 1 in 6000 to 8000 live births. It occurs with equal frequency in both sexes and usually affects whites. There are three types of DI, as classified by Shield *et al*. Type I occurs in association with osteogenesis imperfecta; in type II there is no associated osteogenesis imperfecta; and when the condition is associated with the Brandywine triracial isolate and large pulp chambers, it is classified as type III. Clinically, the teeth with DI show amber-like translucency, the color ranges from yellow to blue-gray. The affected teeth have a marked cervical constriction with a broad crown giving

tooth a tulip-like shape. The enamel is found to fracture easily leading to exposure of the dentin. Teeth appear worn out, most often up to the gingival level and become sensitive while some patients demonstrate an anterior open bite.^[1-3]

OI, also known as brittle bone disease or glass bone disease, is a clinically and genetically heterogenous group of disorders transmitted as an autosomal dominant trait. The basic defects lie in the mutation of the gene encoding for type I collagen (COL1A1 and COL1A2), which is the major protein of bone, teeth, sclera, and ligaments.^[4] This leads to the production of defective and imperfect collagens, leading to defects in tissues containing type I collagen fibres.^[5] The phenotypic presentation varies from mild to lethal. Silence *et al* classified OI into 4 types based on clinical, genetic, and radiographic criteria (mild, perinatal lethal, progressive deforming, and moderately severe). Each of the 4 types of OI is further subdivided on the basis of the absence or presence of DI. Although widely accepted, many patients with OI still do not readily fall into the 4 classes of Silence’s classification due to the broad spectrum of molecular abnormalities resulting in OI. This has prompted some investigators to propose existence of other subtypes of OI, namely, type V, VI, and VII [Table 1]. The incidence ranges from 1:5000 to 1:20,000 live births with no racial or ethnic predilections. OI is characterized by bone fragility and fractures, blue sclera, ligament fragility, long bone deformity, decrease in hearing capacity, growth deficiency, and DI [Table 2].^[6,7]

Some patients with OI display no abnormalities in the dentition, whereas others manifest significant dentinal involvement. Although mild cases of OI are difficult to diagnose, presence of tooth abnormalities may serve as a diagnostic indicator in such cases. The objective of this article is to report and review a rare case of DI with OI affecting 4 generations of the family. Through this article, we intend to highlight genetic influence that affected the family for many generations, discuss the oral

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Table 1: Classification of osteogenesis imperfecta by Silence et al.

Type	Mode of inheritance	Stature	Fracture	Deformity level	Sclera	Dentinogenesis imperfecta	Lethality
I	AD	Normal stature	Most of the fractures occur during the preschool years and are less common after puberty	Moderate	Blue sclera	Absent or present	Nonlethal
II	AD parental mosaicism	—	Exhibits extreme bone fragility and frequent fractures, which may occur during delivery	Severe	Blue sclera	Present	Many patients are still born and 90% of patients die before 4 weeks of age
III	AD	Short	Fractures may be present at birth	Progressively deforming	Normal or pale blue at birth; fades with age	Present	The majority of affected individuals die during childhood, usually from cardiopulmonary complications caused by kyphoscoliosis
IV	AD	Short	Fractures present during childhood and decreases after puberty	Mild to moderate	Normal or pale blue at birth; fades with age	Present or absent	Nonlethal

AD: Autosomal dominant

Table 2: Clinical features of osteogenesis imperfecta

Race	OI does not seem to have a predilection for any particular race
Gender	OI does not seem to have a predilection for any particular race
Age	For type I, the age of onset is variable. This form most commonly appears during the preschool years when the child is starting to stand. Type II occurs in utero. In type III, abnormalities are present at birth (i.e., abnormalities develop in utero) in more than 50% of patients. Fractures are frequent during the first 2 years of life. Type IV abnormalities are present at birth in approximately 50% of patients. The onset of this form is during infancy or the preschool years
Clinical features	Bone fragility, blue sclera, altered appearance of teeth, hypoacusis (hearing loss), long bone and spine deformities, joint hyperextensibility
Oral manifestations	Large head size, frontal and temporal bossing, exaggerated occiput, Class III malocclusion, anterior and posterior crossbites and open bites, and DI

DI: Dentinogenesis imperfect; OI: Osteogenesis imperfecta

manifestations that can lead to the diagnosis of OI, and the importance of early diagnosis of OI.

Case Report

A 30-year-old male patient reported to the Department of Oral Medicine and Radiology with the chief complaint of discoloration of his upper and lower teeth, which he had observed since childhood. The patient's history revealed that his milk teeth were also discolored, small, and worn out. He reported with occasional sensitivity to cold water. His medical history revealed frequent fractures since he was 5–6 years of age and bone pain during childhood. He also underwent multiple surgical treatments, which were unsatisfactory, leading to bowing of his left and right leg. A picture of patient when he was 3 years old, before the fracture and bowing of legs. Eight members in the family, including present and previous generations, had a similar problem of frequent bone fractures and discolored teeth. The patient is married and has 2 children, who are unaffected.

On general examination, he was poorly built and nourished with short stature, bowing of tibia and fibula, altered gait, and erect posture was observed. There was no evidence of blue sclera or altered joint mobility, and flexibility was within normal limits. Intraoral examination revealed generalized brownish blue opalescence of the teeth with loss of enamel, and generalized attrition of teeth [Figure 1]. Based on history and clinical findings, provisional diagnosis of DI associated with OI (type I DI) was given. Further investigation such as full mouth intraoral periapical radiographs (IOPA), panoramic radiograph, lateral cephalometric radiography, and posterior–anterior (PA) and lateral leg radiographs were advised. IOPA and panoramic radiographs showed



Figure 1: Brownish blue opalescence of teeth



Figure 3: Panoramic radiographs showed obliterated pulp chambers, thin slender roots, and marked cervical constrictions

obliterated pulp chambers, thin slender roots, and marked cervical constrictions [Figures 2 and 3]. PA and lateral leg radiographs showed bowing of tibia and fibula [Figure 4]. A lateral cephalogram revealed class I maxilla–mandibular relationship, with average vertical height. Radiographic features were characteristic and confirmed the clinical diagnosis of DI associated with OI.

Discussion

OI is a heritable disorder of collagen I metabolism, which results from mutations in the genes (COL1A1 and COL1A2). These genes encode the pro-alpha 1 and pro-alpha 2 polypeptide chains of type I collagen. There are more than 150 mutations of the COL1A1 (17q21.3-q22) and COL1A2 (7q22.1) genes, which have been identified for the development of OI.

DI and OI are inherited as an autosomal dominant trait. The illustration Figure 5 shows the pedigree of this family, which extends back 4 generations. History to elicit frequent fractures and stained or discolored teeth in the family was elicited. Table 3 summarizes number of affected and unaffected males and females in the family for 4 generations. These data show that there are 8 affected and 10 unaffected offspring making roughly, a 1:1 ratio. The table also shows an excess of affected males compared with affected females (6 to 2). This result is different from the expected 1:1 sex ratio. Pedigree chart reveals that in each instance an affected



Figure 2: Intraoral periapical radiograph reveals obliterated pulp chambers, thin slender roots, and marked cervical constrictions

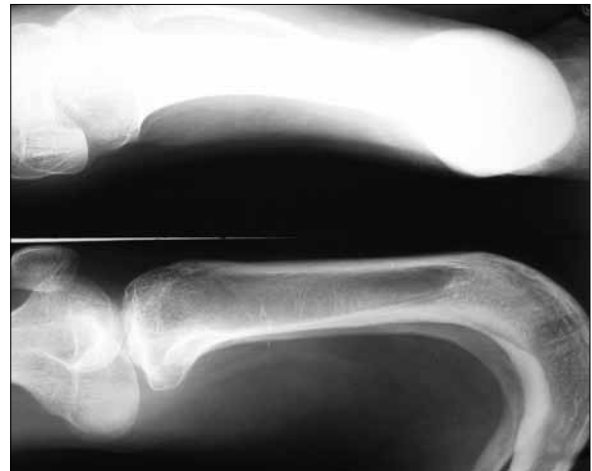


Figure 4: Posterior–anterior and lateral leg showed bowing of tibia and fibula

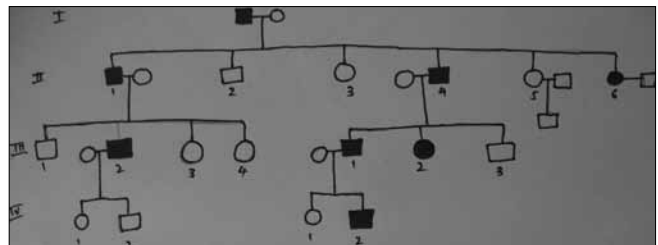


Figure 5: Pedigree chart of the affected family

child had an affected parent, indicating an autosomal dominant mode of inheritance, which has previously been reported. As OI and DI are inherited in an autosomal dominant fashion, there is a 50% chance that a child born to an affected parent will themselves be affected. Although history, clinical examination, and radiographs are sufficient for the diagnosis of OI and DI, molecular genetic diagnosis may prove to be a useful adjunct to clinical analysis, particularly where the precise diagnosis is in doubt. But since molecular genetic diagnosis is not a readily available

Table 3: Affected and unaffected males and females in the family for four generations

Generation	Affected		Affected	
	Male	Female	Male	Female
I	1	-	-	-
II	2	1	1	2
III	2	1	2	2
IV	1	0	1	2
Totals	6	2	4	6

procedure, careful family history and clinical examination will help us to arrive at a proper diagnosis and further counseling of such families.

Among the different clinical features that can be seen in OI patients [Table 2], our patient had a history of frequent fractures during childhood, short stature, altered gait, bowing of tibia and fibula, normal sclera, and presence of DI. Based on the classification by Silence *et al.* [Table 1], we grouped our case as type IV OI.

Among the 3 types of DI, type I is associated with occurrence of OI. Lund *et al* conducted a study to find the prevalence of DI and other dental anomalies in patients with OI. Twenty-eight percent of OI patients had DI.^[8] Our patient also reported with severe manifestations of DI. O'Connell *et al* reported that Class III dental malocclusion occurred in 70%–80% of types III and IV of the OI population, with a high incidence of anterior and posterior crossbites and open bites.^[9] Chang *et al* conducted a study to identify craniofacial characteristics in OI, which showed that the OI patient had a more prominent Class III occlusal relationship, prognathic mandible, larger facial divergence, shorter face heights, defective sagittal growth of the maxilla and mandible, a flattened cranial base angle, impaired cranial base growth, and more forward counter clockwise rotation in mandibular growth compared with the controls.^[10] In contrast, our patient had Class I skeletal relationship with average vertical facial height. Class III skeletal relationship was not found in our case as reported by Chang *et al* and O'Connell *et al*, because the attrition of teeth in our case was not so severe. Although attrition was present, teeth had sufficient incisocervical height to maintain facial height and normal anterior bite.

In practice, the diagnosis of OI is by exclusion along with consistent clinical presentation, family history, radiographs, and low bone mineral density scores.^[11] Radiologic findings in OI reveal evidence of new and healed fractures, osteopenia, thin cortices, wormian bones, bowing or deformation of bones, and scoliosis. The characteristic radiologic findings of DI type I are bulbous crowns, constriction of the cemento-enamel junction, pulp obliteration, slight to marked attrition of the occlusal surface, and short and slender roots.^[12-14]

Currently there is no cure for OI. All the treatment strategies are essentially palliative and designed to reduce deformity, promote normal function, and improve quality of life. Physical therapy interventions to improve gross motor development, muscle strength, and functional skills. Orthopedic interventions, such as the use of bracing, rods, and plates to prevent or correct skeletal deformities, improve mobility. Medical therapies to strengthen the bone, such as the use of calcitonin, sodium fluoride, growth hormone, cortisone, anabolic steroids, vitamins C and D, and minerals have proved ineffective. Over few decades, bisphosphonate therapy is effective in reducing fracture risk and decreasing bone pain in OI patients. Novel approaches using bone marrow-derived mesenchymal stem cells and gene therapy are currently being investigated as potential treatments for OI.^[4,15]

Depending on the severity of the tooth involvement, approach to dental management of patient with DI must be individualized. Therapeutic interventions should be aimed to improve patient's vertical height, normal growth, and improve esthetics. Full coverage restorations, over dentures, orthognathic surgeries, and orthodontic therapy can be given to preserve function and esthetics. Our patient was advised for full crown restorations to improve esthetics, and to prevent further loss of tooth structure and to maintain vertical facial height.^[7,16]

Conclusion

The high prevalence of dental aberrations in OI stresses the importance of clinical and radiographic odontologic examination as part of the clinical investigation. In patients with mild forms of the disease, and in whom the medical diagnosis is uncertain, demonstration of disturbances in dental development can be crucial for establishing the OI diagnosis. Patients with OI and opalescent teeth should be evaluated as soon as the deciduous teeth erupt, so that an attempt can be made to prevent loss of tooth structure. Since our patient was not diagnosed of OI at an early stage, treatment given was unsatisfactory and when patient reported to us, was suffering from severe skeletal deformity. Therefore, this case definitely stresses the importance of early diagnosis of OI to prevent subsequent physical and psychological damage to such patients. Hence, the dentist can play a major role in early diagnosis of OI and contribute for betterment of quality of life of OI patients.

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