POSTER #

Osteogenesis Imperfecta: A Comprehensive Overview and Two Case Reports

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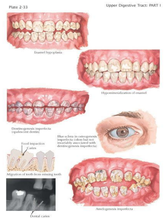
ABSTRACT

Osteogenesis Imperfecta (OI) is a rare genetic disorder characterized by bone fragility, joint hypermobility, and connective tissue abnormalities. This disorder, resulting from mutations in collagen-related genes, manifests in various types and severities. Dental implications are prominent, including dentinogenesis imperfecta, tooth abnormalities, and an increased risk of jaw fractures. Comprehensive and cautious dental care, emphasizing trauma minimization and bleeding risk reduction, is crucial. Routine dental procedures pose minimal risks, but vigilant monitoring and meticulous oral hygiene practices are essential. Ongoing research into gene therapies, stem cells, and advancements in dental materials contribute to enhancing the quality of life for individuals with OI.This case report highlights the interconnected challenges of OI and DI, emphasizing the importance of specialized dental care and ongoing research for improved patient outcomes.

BACKGROUND



Overview
- Genetic condition characterized by bones that break easily, often without apparent cause
- Involves genetic connective tissue disorders
- Primarily related to a defect in type I collagen, a key structural component in bones and teeth
- Exhibits a spectrum of clinical manifestations, from mild to severe forms
- Impacts skeletal integrity and dental health
- Important for dental professionals to understand nuances of OI
- Presents unique challenges and considerations in dental care

Etiology
- Predominantly caused by mutations in the COL1A1 and COL1A2 genes
  - Encode the alpha-1 and alpha-2 chains of type I collagen
  - Leads to either a quantitative or qualitative defect in collagen
- Prevalence of OI is estimated to be 1 in 10,000 births
- Inheritance pattern is typically autosomal dominant, but around 35% of cases arise from de novo mutations
- Genetic landscape of OI is complex, with recent studies identifying mutations in other genes such as IFITM5, CRTAP, and P3H1, contributing to the disease's heterogeneity

Diagnosis
- Cinical evaluation, family history, and radiographic analysis
- Key diagnostic features include a history of frequent fractures, bone deformity, and other connective tissue manifestations
- Advanced imaging techniques like dual-energy X-ray Absorptiometry (DXA) are used to assess bone mineral density, providing insights into the bone's strength and fracture risk
- High-resolution peripheral quantitative computed tomography (HR-pQCT) offers detailed analysis of bone microarchitecture
- Genetic testing, including next-generation sequencing, plays a crucial role in confirming the diagnosis of OI
  - Helps in identifying specific mutations, which is essential for understanding disease prognosis and guiding family planning decisions

Clinical Presentation
- Characterized by a spectrum of symptoms
  - Most prominent being bone fragility and frequent fractures
  - Other clinical features include blue sclera, short stature, hearing loss, joint hypermobility, skin hyperlaxity and dentinogenesis imperfecta
- The Sillence classification categorizes OI into four main types based on severity and symptoms, with later additions recognizing the genetic complexity of the disorder
  - Type I represents the mildest form, while Type II is the most severe, often leading to perinatal mortality

Systemic Presentation
- Neurological: hydrocephalus, macrocephalus, cerebral atrophy, Idiopathic seizures, hypoacusia
  - Typically no alteration of intellectual status
- Cardiovascular: presence of congenital cardiac malformations
- Renal: hypercalciuria
- Connective tissue: skeletal dysplasia characterized by bone fragility, high incidence of fractures, increased capillary fragility, decreased platelet retention and reduced factor VIII, reduced muscle strength, joint hyperlaxity, flat feet, hernia
- Respiratory: intrinsic lung abnormalities, pulmonary function decreases with age
- Ocular Changes: blue sclerae, corneae juvenilis, corneal thickness significantly reduced in mild OI

Treatment and Management
- Treatment of OI is primarily aimed at preventing fractures and managing symptoms
- Bisphosphonates are the cornerstone of pharmacotherapy, improving bone density and reducing fracture incidence
- Emerging therapies, such as anti-sclerostin antibodies, are under investigation for their potential to enhance bone formation
- Multidisciplinary approach involving physiotherapy, occupational therapy, and orthopedic interventions is essential for managing OI
- Rehabilitation focuses on muscle strengthening, improving mobility, and maximizing independence
- Surgical management, particularly intramedullary rodding, is often necessary to correct and prevent bone deformities
- Spinal fusion may be required for scoliosis

OI and Dental Implications
- Dental professionals play crucial role in the management of OI
- Patients with OI often present with specific dental challenges, necessitating tailored dental care strategies
- Dental manifestations of OI include Dentinogenesis Imperfecta, malocclusion, and a high risk of dental trauma
- These conditions require specialized dental interventions to preserve oral health and function
- Managing dental care in OI patients involves considerations for dental surgeries, anesthesia, and long-term oral care
- Dental professionals must be adept at handling these patients delicately to prevent fractures and provide effective pain management

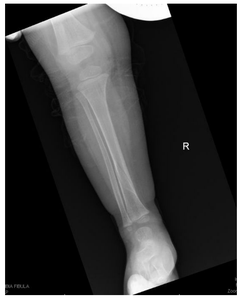
Dentinogenesis Imperfecta
- Dentinogenesis Imperfecta (DI): hereditary condition often associated with OI
  - Characterized by opalescent and brittle dentin
- Clinically, DI presents with discolored (blue-gray or yellow-brown) teeth, bulbous crowns, and obliterated pulp chambers
- Radiographically, DI is characterized by short, conical roots, early pulp obliteration, constricted CEJ
- Enamel may shear readily from dentin when subjected to occlusal stress as a result of deficient dentinal support or abnormal scalloping of DEJ
  - Due to early loss of enamel, exposed dentin can undergo rapid attrition and result in a loss of vertical dimension

Diagnosis and Treatment of DI
- DI is diagnosed through a combination of clinical examination, dental radiographs, and family history
- Genetic testing can confirm the diagnosis, especially in cases associated with OI
- Molecular genetics of DI involves mutations in the DSPP gene, which disrupt the normal formation and mineralization of dentin
  - Leads to weakened tooth structure and increased susceptibility to wear and breakage
- Classified into three types:
  - Type I: Associated with osteogenesis imperfecta and characterized by translucent or opalescent teeth.
  - Type II: Occurs as an isolated dental condition, featuring gray to brownish-blue discoloration and more severe structural abnormalities
  - Type III: Similar to Type II but often associated with short stature
- May affect both primary and permanent teeth (primary>permanent)
- Management of DI focuses on preserving tooth structure and aesthetics
  - Includes the use of crowns and other restorative materials
- Ongoing dental care and regular check-ups are essential to address potential issues and maintain oral health in individuals with Dentinogenesis Imperfecta

CASE REPORT 1

Chart Review
- 4y5m male
- Medical History: Osteogenesis Imperfecta type I (confirmed with genetic testing)
  - Blue sclerae present
- Medications: multivitamin
- Allergies: NKA
- Family History: mother and sister diagnosed with osteogenesis imperfecta
  - Both family members have had multiple breaks
- Social History: lives with mother, father and sister

Pertinent Medical History
- 20 months old: first fracture- closed nondisplaced spiral fracture of shaft of right tibia
- 2 years old- IV Zoledronate overdose
  - Developed severe hypocalcemia and hypophosphatemia
  - Received 2 hemodialysis treatments in an effort to remove the drug from the blood
  - Discharged on calcium and phosphorus supplements
  - Continues to have annual blood work and urine studies to look for evidence of kidney damage
- Has been in physical therapy since 1.5 years old
  - Goes 1x/week at this time



Impression: Acute nondisplaced spiral fracture of the distal right tibial diaphysis (bones somewhat osteopenic)

Dental History
- Patient of MCHC since 2 years old
- Medical consult sent to PCP in regards to dental treatment
  - Antibiotic prophylaxis not recommended
  - Use of restraints (papoose, mouth prop, etc.) contraindicated due to possibility of fractures
- Last Recall: 11/27/23
  - Primary dentition
  - Mesial step bilaterally
  - OHI: fair
  - Extraoral: no pathologies detected
  - Soft tissues- no pathologies detected
  - Hard tissue:
    - #D-fil enamel fracture (small-obs), no mobility
    - #F-fil enamel fracture (small-obs), no mobility
    - No caries
  - Radiographs not taken due to patient's inability to tolerate intraoral
    - Does not meet height requirements for extraoral at this time (risk of fall with stool)

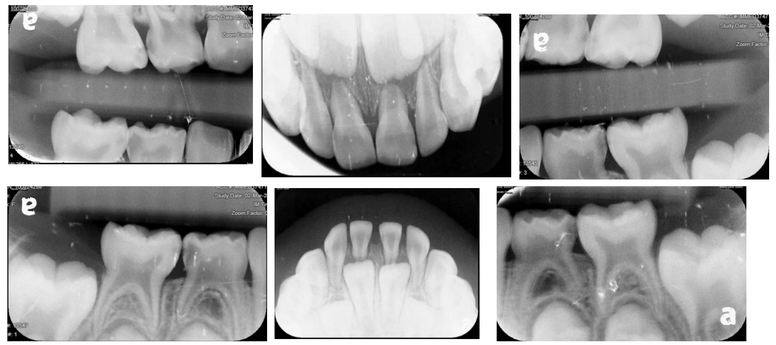
CASE REPORT 2

Chart Review
- 7y2m female
- Medical History: Osteogenesis Imperfecta OI
  - Blue sclera present
- Medications: multivitamin
- Allergies: NKA
- Family History:
  - Father: suspected to have OI, no testing done; history of fractures (about 5 total including foot), left-sided hearing loss, and gray sclerae
  - Paternal aunt: genetic test positive for OI (COL1A1 mutation)
  - Paternal cousin: genetic test positive for OI (COL1A1 mutation); history of fractures in both legs and rib cage
  - Paternal grandmother: suspected OI with history of blue sclera, no history of fractures, no testing done
- Social History: parents separated and splits time with both parents
  - Has one older brother

Pertinent Medical History
- 7 months old: genetic testing recommended
  - Results positive for COL1A1 mutation c.295_298+4dup8
  - Clear autosomal-dominant mode of inheritance of OI in the paternal side of the family
  - Blue sclera observed at this time
- 9 months old: closed nondisplaced spiral fracture of shaft of right humerus
  - Long arm splint placed for a week
- Continuously observed by pediatric rehabilitation, orthopedics, endocrinology, ophthalmology, and audiology

COL1A1 EXON 2 SEQUENCING ANALYSIS REPORT

DATE RECEIVED: 6/21/2017	DATE REPORTED: 7/14/2017	DATE COLLECTED: 6/20/2017
Patient Name [redacted]	DOB [redacted]	Patient ID # [redacted]
Test Request	Specimen Type	Your Code
COL1A1 Exon 2 Sequencing	Peripheral Blood	542004357 / 100724289
RESULTS:		
Alteration:	Nucleotide: c.295_298+4dup8	Consistent with the clinical diagnosis of:
COL1A1 IVS2	Amino Acid: NA	*See results below*



Radiographs taken March 2023

Dental History
- First seen at HDC at Mott Children's Hospital 3/2023
- Findings:
  - No extraoral pathologies
  - Soft tissue exam- no pathology detected
  - Hard tissue exam:
    - Primary Dentition
    - Molar classification: mesial step (bilateral)
    - OB: 10%; OJ: 1 mm
    - OHI: poor
    - Clinical caries: #C-F, #D-M, #E-D, #F-MD, #G-M, #H-F, #J-O, #K-O, #L-O, #S-O. #T-O
    - Other findings: #D-F hypocalcified enamel, #M-F decalcification, #Q-incisal fracture limited to enamel
- Radiographs: 2 occlusals, 2 BWs, 2PAs (LR and LL)
  - Radiographic caries#A-M, #B-D, #I-D, #J-M, #K-M, #L-D (approaching pulp), #S-D (approaching pulp), #T-M
- First restorative treatment completed 3 weeks after initial exam (3/2023)
  - #S- IPT/SSC and #T- mo composite restoration with N2O/O2
  - Behavior: cooperative- did well with N2O/O2
  - Recommendation: completion of treatment at University of Michigan graduate pediatric dental clinic

DISCUSSION

The multifaceted impact of OI necessitates a careful and comprehensive approach to dental treatment. Trauma minimization strategies are paramount, emphasizing the use of protective measures during dental procedures and the avoidance of excessive force during manipulations. Contrary to common misconceptions, routine dental care, including extractions, poses minimal risk of jaw fracture in individuals with OI when appropriate precautions are taken.

Dentinogenesis imperfecta, characterized by defective dentin formation, contributes to enamel defects and increased susceptibility to caries. Management of individuals with OI requires a tailored approach considering their medical and dental history, as well as potential complications such as fractures and sensitivity to dental procedures.

The presented cases illustrate the multifaceted impact of OI on dental health and treatment. Despite the challenges posed by OI, routine dental care, including restorative treatments and extractions, can be safely performed with appropriate precautions. Collaboration between dental professionals and other healthcare providers is essential for optimizing patient outcomes and ensuring holistic care.

Factors to consider during general anesthesia and surgery for OI patients encompass an elevated risk of bleeding, heightened potential for malignant hyperthermia, compromised healing, and challenges associated with intubation. Additional consideration should also be taken for patients taking bisphosphonates. Bisphosphonates can contribute to improved oral health by increasing bone density, particularly in the jawbone. However, dentists need to be aware of the patient's bisphosphonate use, especially in the context of invasive dental procedures. Bisphosphonates have been linked to a small risk of osteonecrosis of the jaw (ONJ), particularly in cases of prolonged use or high doses. The risk of ONJ is relatively low, particularly in patients taking oral bisphosphonates, but higher in individuals receiving higher doses of intravenous bisphosphonates.

Recent advances in OI research include promising developments in gene therapy, which aim to correct the genetic defects causing OI. Stem cell therapy is another area of active research, focusing on enhancing bone strength and reducing fracture risk. In the realm of pharmacology, novel agents are being explored to improve bone density and reduce fracture risk. These advancements hold significant potential for improving the quality of life for OI patients. In dentistry, advancements in materials and techniques specifically for managing dentinogenesis are noteworthy. These include improved dental crowns and bonding agents that cater to the unique needs of OI patients. Resin composites and glass ionomer cements may offer better aesthetic and functional outcomes for restorations in individuals with DI.

Ongoing research in gene therapy, stem cell technologies, and advancements in dental materials hold promise in improving treatment modalities and outcomes for individuals with OI. Continued vigilance in monitoring oral health, reinforcing oral hygiene practices, and implementing preventive measures are crucial in mitigating dental complications and enhancing the quality of life for patients with OI.

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