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Osteogenesis Imperfecta

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Osteogenesis Imperfecta

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"Fragile bones" have been described in medical literature for centuries. Cases dating from antiquity include dental and skeletal details eerily similar to those found among modern patients whose bones fracture easily and whose bodies show signs of muscular and other weakness. Osteogenesis imperfecta — whose name implies "imperfect birth of bone" — is one of these inherited fragile bone syndromes. A generalized disorder of the body's connective tissues, it is most obvious in its effect on bone, but also involves the body's ligaments, tendons, fascia, eyes, skin, teeth and ears. Radiographs, bone scans and other imaging tools are essential in the initial diagnosis, assessment of fracture risk, and planning and tracking of treatment.

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After completing this article, readers should be able to:

- *Recognize the major clinical signs of osteogenesis imperfecta.*
- *Explain the condition's most common genetic origin.*
- *Discuss the major types of osteogenesis imperfecta.*
- *Describe the role imaging professionals play in diagnosis and treatment.*
- *Summarize strategies for dealing with common obstacles in imaging patients with osteogenesis imperfecta.*

Osteogenesis imperfecta (OI), also called "brittle bone disease," is a congenital disorder of connective tissue. It originates from a genetic mutation and results in unusually fragile bones. Although it is present from birth, clinical evidence of the disorder may not surface for years, depending on the disease type and degree of severity. Fragility of bone, laxity of ligaments and unusually thin skin are among the most common signs of the disorder. Others include poorly formed teeth, hearing loss due to weaknesses in the bone structure of the inner ear and blue-tinted sclerae, or whites of the eyes.[1]

OI was recognized as an inheritable disorder in 1972, but recent advances in protein chemistry and molecular biology have allowed for a broader understanding of its genetic basis. Its prevalence is approximately 1 case in every 20 000 people, including those diagnosed in childhood and as young adults. Newborns afflicted with a usually lethal form of OI typically die within days or weeks of birth. Including these newborns in prevalence figures increases prevalence to 1 case in every 15 000 to 18 000 births.[2] Life expectancy varies with the severity of the condition. OI occurs with equal frequency in both sexes and among all racial and ethnic groups. Nothing inherent in the disorder affects intellectual development or cognitive ability. As diagnostic methods improve and previously undiagnosed cases are uncovered, OI may move from being considered a rare genetic disorder to one that is more commonly encountered among the general population.[3] Medical imaging already plays a key role in the diagnosis and evaluation of OI. As it continues to do so, radiologic science professionals undoubtedly will encounter increasing numbers of adult and pediatric patients suspected or known to be living with the symptoms and implications of OI.

Genetic Origins of OI

OI usually is transmitted as an autosomal dominant genetic trait, meaning its expression requires a mutated gene from only 1 parent. Spontaneous mutation, or mutation that does not appear to be inherited, also is known to occur. Some rarer types of OI appear to be transmitted as autosomal recessive traits, meaning their expression requires a mutated gene from each parent. Most types of OI originate from mutations in the 2 genes (*COL1A1* and *COL1A2* [collagen, type I, alpha 1 and 2]) that encode for the α^1 and α^2 peptides of type 1 collagen.

Collagen is a fibrous protein and a principal component of the extracellular matrix, which is the structural framework that supports bone, tendon and skin. OI mutations result in the production of too little type 1 collagen or of poor-quality collagen.

Clinical Signs of OI

Clinical signs of OI vary greatly. Even among affected family members, differences in severity and types of symptoms can be significant.[4] The severity of OI ranges from cases serious enough to cause prenatal death to those that offer a nearly symptom-free adulthood. Box 1 lists the signs of OI. Patients might exhibit some or all of these signs to varying degrees, depending on the severity of their underlying condition.

General Radiographic Appearance of OI

Radiography is used to help diagnose OI, either at birth or when symptoms first appear. On radiographs, OI is identified by observing the patterns of bone deposition and destruction throughout the entire skeleton. Other bone disorders may present similar patterns of growth and destruction, sometimes making positive diagnosis difficult.[6] Diagnostic radiography typically reveals osteopenia (low bone density) and recent fractures or fractures in various stages of healing. Compressed vertebrae are common. The long bones, such as the femur, may be markedly bowed. Bones affected by OI may be abnormally thin and flat and may appear wider in diameter on radiographs than they actually are. Some patients exhibit wormian bones in the skull; these are small, irregular plates of bone interposed along sutures on the occipital, parietal and temporal bones. Throughout the body, the outer layer of the bone (ie, the cortex) may appear thin and porous. The trabeculae, the branching latticework of bone strands that shore up the spongy or cancellous portion of the bone and are located near the internal surface of the cortex, appear thin, delicate and widely separated.[1] In radiographs of patients with milder forms of OI, these skeletal alterations can be difficult to detect.

Original Types of OI

Most cases of OI fall into 1 of 4 main categories of phenotype, the name given to physical manifestations of a genotype or a genetically determined condition such as OI. These 4 classifications of OI were identified by Sillence and others in 1979, and are based on age of onset, clinical and radiographic features and disease severity.[7] Although some overlap occurs between types, the 4 main classifications provide relatively straightforward and clinically useful distinctions in most cases.[8] Subsequent research has revealed that as many as 12 forms of OI could exist. Not all of these rare additional forms are caused by collagen-related genetic mutations. The type of OI, however, is less important to imaging professionals than the patient's individual abilities, strengths and weaknesses.[9]

Box 1
Signs of Osteogenesis Imperfecta[2,5]

Muscular/Skeletal Features

- Skeletal malformations, such as markedly bowed extremities.
- Short stature due to growth impairment.
- Overall or particular muscle weakness (secondary to anomalies of the tendons and joints and to general debility associated with reduced physical activity in the wake of frequent fractures).
- Disproportionately short limbs relative to body size.
- Need for assistive gait devices, such as crutches and canes, or wheelchairs.

Other Prominent Clinical Signs

- Noticeable laxity in ligaments.
- Unusual joint flexibility.
- Particularly thin skin that is noticeably soft and smooth and may resemble the atrophic skin of older people.
- Healing of wounds and surgical incisions that results in wider than normal scars.
- Triangular face shape.
- Noticeably brown, purple or opalescent teeth.
- Blue tint to the sclerae.
- Hearing loss.
- Increased perspiration.
- Late fontanel closure, with fontanels remaining open until 3 or 4 years of age in some patients.

Mild OI

The first phenotype, Type I OI, also known as mild OI, accounts for 45% to 50% of OI cases and presents clinical signs of mild-to-moderate severity. Type I results from the production of lower than normal quantities of collagen, while the other 3 main phenotypes of OI