A Pediatric PERSPECTIVE

Gillette Children's Specialty Healthcare

VOLUME 23, NUMBER 2 2014

Understanding and Treating Osteogenesis Imperfecta

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Osteogenesis imperfecta (OI), or "brittle bone" disease as it is sometimes called, is a hereditary condition that is best known for causing bones to be fragile and subject to frequent fractures. It affects six to seven people in 100,000, and an estimated 20,000 to 50,000 people in the U.S. have the condition.

The most common forms of OI result from a defect in the formation of Type I collagen (the building block of bones, ligaments, teeth, sclera and middle ear bones). Children with OI may experience multiple fractures that cause limb bowing or scoliosis. These bowed bones are then more likely to fracture again. Fracture of middle ear bones can cause hearing loss as well.

At least eight different types of OI have been identified. Some of the newly described types do not have the classic collagen defect that is seen in the more common types of OI. Our discussion will concentrate on the classic Types I-IV, as described by Sillence[1].

Type I – Mild: This is the most common form of OI. Children with this mild form of OI suffer fractures more frequently than normal, and patients may demonstrate dentinogenesis imperfecta—an abnormality of tooth dentin. These children do not typically develop long-bone bowing deformities and their height is usually normal.
Type II – Extremely severe/lethal: Children affected with Type II OI have severe skull, spine, chest wall and long bone deformities due to intrauterine fractures. Survival past infancy is rare.
Type III – Severe, progressive deformity: These children are born with fractures resulting in moderately severe deformities at birth. With growth, further deformity develops, leading to limb shortening and marked angulation. These deformities impair upper extremity motion and are often severe enough that children are unable to stand. Short stature and a triangular-shaped face are characteristic.
Type IV – Moderate to severe: Although fractures are common with Type IV OI, typically bone deformities are not as severe. These children are more severely involved than those with Type I, but less than those with Type III.

KEY INSIGHTS

- Osteogenesis imperfecta (OI) affects six to seven people in 100,000, and at least eight different types of OI have been identified.
- OI management centers on increasing bone density and muscle mass, minimizing fractures, maintaining or restoring bone alignment, maximizing musculoskeletal function, and maintaining optimal growth and well-being.
- Intravenous bisphosphonates help inhibit bone resorption and reduce the frequency of fractures in children who have OI.
- When a child who has OI sustains a fracture, a lightweight cast or splint supports the limb while it heals. The period of immobilization is brief—often two to four weeks.
- To stabilize fractures and realign deformed arm or leg bones, we use telescoping or solid rods within the canal of the bone.
- Rehabilitation supports ongoing development, mobility and function.

Diagnosing OI

Findings from the physical exam and radiographs may initially suggest OI, but further testing is often required. Biochemical and genetic studies are used to identify OI. Some of these tests help to rule out other conditions such as hypophosphatasia, nutritional rickets, Cushing's disease, calcium deficiency/malabsorption or nonaccidental injury. DNA analysis of COL1A/COL1A2 genes and protein-based analysis of collagen gathered through a skin biopsy may also be required. LEPRE1 and cartilage-associated protein (CRTAP) tests may suggest unusual recessive forms of OI. However, negative DNA or collagen tests do not rule out OI. A dual-energy X-ray absorptiometry (DXA) scan might also be ordered to quantify bone mass. On rare occasion a bone biopsy may be needed.

Treatment

Gillette Children's Specialty Healthcare uses an interdisciplinary approach to managing OI. We focus on increasing bone density and muscle mass, minimizing fractures, maintaining or restoring bone alignment, maximizing musculoskeletal function, and maintaining optimal growth and well-being. No current treatment cures OI, but the goal of treatment is to minimize the effects of the disorder.

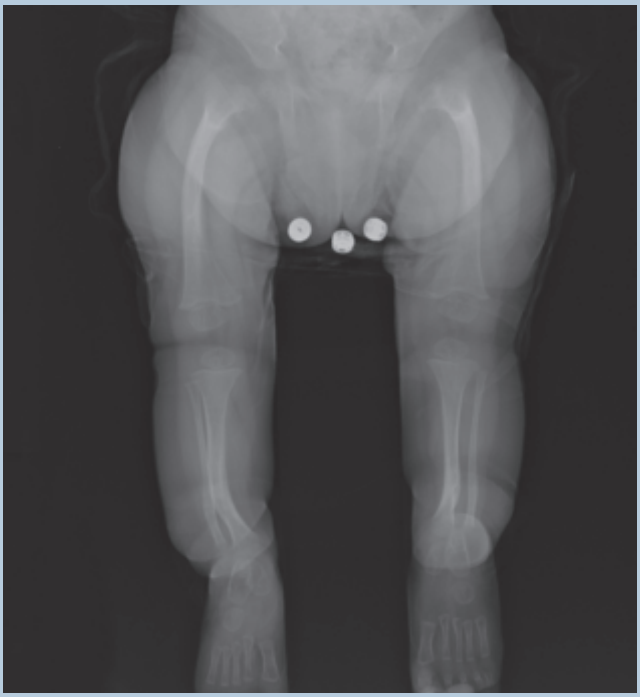
Medical Regimen

Oral and intravenous bisphosphonates, such as alendronate, pamidronate and zolendronate, are potent inhibitors of bone resorption that have been shown to reduce the frequency of fractures in children who have OI. Although oral bisphos-phonates have been used, they are poorly absorbed. Additionally, they are difficult for children and families to administer, because patients must take the medication on an empty stomach and remain upright for 30 minutes before eating a meal. Therefore, many institutions use only intravenous bisphosphonates. Typically, the intravenous medications are administered over two to four hours for three days in a row. The regimen takes place every three to four months for a few years. The length of treatment is individualized but may continue for years.

Bisphosphonates may be indicated in a patient with Type III or Type IV OI who has experienced three to four major fractures within two years. Prior to instituting such treatment, families have an extensive discussion with an endocrinologist to ensure that they understand the role the medications play in the management of OI, the course of treatment and the potential side effects.

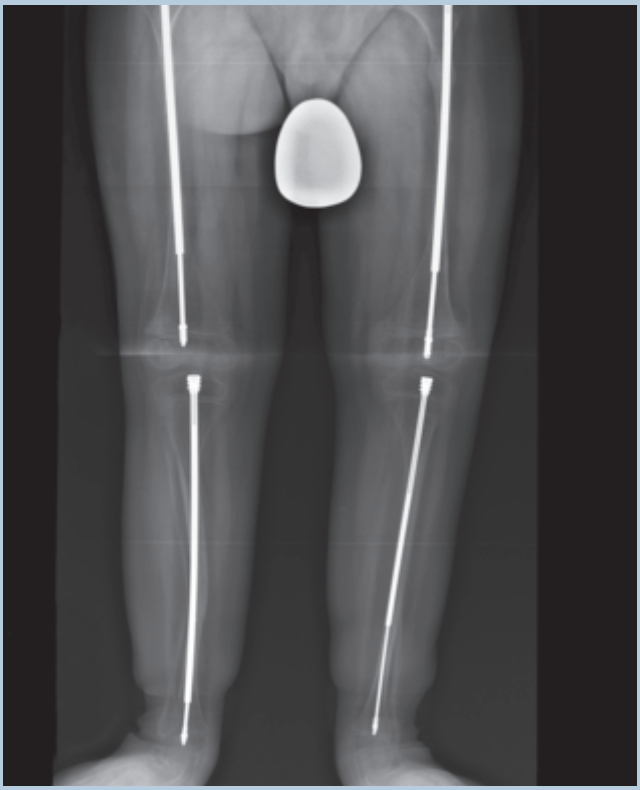
Pre-op

Prior to surgery, this boy with Type III osteogenesis imperfecta had severe leg bowing.



Post-op

The patient's bones have been straightened after he underwent expandable rod placement with realignment osteotomies.



After treatment with bisphosphonate therapy, some patients experience a reduction in bone pain within weeks. The use of bisphosphonates has also been shown to:
- Improve ambulation scores
- Decrease fracture incidence
- Maintain a more normal vertebral height
- Increase cortical bone thickness

Other treatment modalities such as growth hormone, denosumab (a bone resorption inhibitor) and teripeptide (a bone anabolic medication) may provide alternatives to bisphosphonate treatment in the future. They are not yet widely used.

Orthopedic Management

Preventing and/or correcting bone deformities and treating fractures are the mainstays of orthopedic management in OI.

Braces, splints and orthotics may be used to help prevent fractures and to offer support while patients bear weight. When a child with OI sustains a fracture, a lightweight cast or splint supports the limb while it heals. Because many of these injuries occur from minor trauma, the period of immobilization is brief—often two to four weeks—in an attempt to reduce further bone loss that could occur with prolonged immobilization.

With OI, typical orthopedic fracture fixation implants (plates/screws) are not used to stabilize fractures, nor are they used in the correction of arm or leg bowing deformities, because the bone can break above or below the stiff metal plate that is placed on the bone at the time of surgery. Instead, we place telescoping or solid rods within the canal of the bone. This allows us to stabilize fractures and realign deformed arm or leg bones. Prior to 2005, nonexpandable rods were in widespread use, but they required replacement approximately every two years. Telescoping rods have been used more frequently in the past decade. Those rods elongate within the bone as a child grows and require replacement less often—every five years is typical. Surgical deformity correction is required more commonly in the lower extremities than in the upper extremities.

The Role of Rehabilitation Medicine

The rehabilitation team (physicians, and physical and occupa-tional therapists) work toward the common goal of supporting ongoing development, mobility and function in a safe way throughout the years.

Children who have OI commonly have delays in gross motor development. Interventions begin by educating the family and other caregivers about how to safely lift and position the child to help facilitate normal development. As patients grow, we routinely evaluate their strength and developmental abilities; when needed, we recommend adaptive equipment to assist them with sitting, standing or mobility. The equipment will vary with the type and severity of OI and the age of the child, but the goal is always to support children in achieving the highest level of independence and function possible.

Another important part of care is helping the child maintain strength and endurance through a carefully designed therapy program, particularly after periods of immobilization. To achieve those goals, pool therapies are often combined with therapies in the gym.

Conclusion

Although OI cannot be cured, multidisciplinary care can mitigate its effects. Treatment helps minimize the pain and deformity that can occur in children with OI and helps to maximize that child's abilities. Gillette's interdisciplinary OI team welcomes your questions. We look forward to the opportunity to become involved with your patient's care.

[1] Sillence D, Senn A, Danks D. Genetic heterogeneity in osteogenesis imperfecta. J. Med. Genet. 16 (1979) 101-116.

Author PROFILES

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Stephen Sundberg, M.D., is a pediatric orthopedic surgeon and program medical director of the Center for Pediatric Orthopedics at Gillette Children's Specialty Healthcare. He graduated from the University of Minnesota Medical School and completed an orthopedic residency at Mayo Clinic in Rochester, Minnesota. He then completed a pediatric orthopedic fellowship at Adelaide Children's Hospital in Adelaide, Australia. He is certified by the American Board of Orthopaedics.

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Nanette Aldahondo, M.D., is board-certified in pediatric rehabilitation medicine and physical medicine and rehab-il-itation. She cares for patients who have cerebral palsy, acquired brain injury, spina bifida or other chronic disabling conditions. After receiving her medical degree from the University of Puerto Rico School of Medicine in Rio Piedras, Puerto Rico, she completed a residency at Tufts Medical Center in Boston and a fellowship in pediatric rehab-il-itation medicine at Gillette Children's Specialty Healthcare.

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Specialty Healthcare
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St. Paul, MN 55101

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Editor-in-Chief – Steven Koop, M.D.
Editor – Ellen Shriner
Designers – Becky Wright, Kim Goodness
Photographers – Anna Bittner,
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NEWS & NOTES

Gillette Mankato Clinic to Open Sept. 15

This fall, Gillette will open a multidisciplinary clinic in Mankato, Minnesota. Patients in southern Minnesota and northern Iowa will have convenient access to care from our pediatric orthopedic surgeons, pediatric neurosurgeons, pediatric neurologists, craniofacial and plastic surgeons, pediatric rehabilitation medicine specialists, sleep medicine specialists, and specialty pediatricians. Nurse practitioners, orthotists and seating specialists will also be on staff at our new Gillette Mankato Clinic.

Gillette Offers Interdisciplinary OI Clinic

Gillette provides an interdisciplinary OI Clinic on one Friday every other month at our St. Paul Clinic. Our team (orthopedic surgeons, endocrinologists, geneticists and pediatric rehabil-itation medicine specialists) evaluates and treats newly diagnosed patients in one location. Individual specialists collaborate as needed for follow-up care and ongoing management.

Cardiology Clinic Opens

In June, physicians from The Children's Heart Clinic began offering a cardiology clinic every week at Gillette's St. Paul Clinic.

New Videos and Brochures Explain Treatment Options for Cerebral Palsy

Gillette recently completed three videos about cerebral palsy: "Caring for a Child Who has Cerebral Palsy," "Spasticity Treatment Options for Cerebral Palsy," and "Orthopedic Care for Children Who Have Cerebral Palsy." You and your patients can view them at gillettechildrens.org/CPVideo. We also have recently produced two brochures: *About Cerebral Palsy* and *Managing Spasticity*. Email **Publications@gillettechildrens.com** to request brochures.