Osteogenesis imperfecta

Objectives

1. Describe the basic connective tissue fault of bone in individuals with osteogenesis imperfecta
2. Describe the spectrum of severity of the clinical spectrum of osteogenesis imperfecta
3. Describe the natural history -both in regard to function and survival - of patients with osteogenesis imperfecta
4. Discuss the orthopaedic problems associated with osteogenesis imperfecta and present approaches to these problems
5. Describe present pharmacologic systemic approaches undergoing evaluation for osteogenesis imperfecta
6. Describe the genetic pattern of osteogenesis imperfecta

Discussion

Osteogenesis imperfecta (OI) as a diagnosis encompasses a variety of clinical severity, all related to the basic defect in synthesis of collagen I. The same genetic focus of mutation is shared with some forms of Ehlers-Danlos syndrome. Clinical manifestations include blue sclerae, macrocephaly, hearing loss, defective dentition, kyphoscoliosis, limb deformity, fracture, joint laxity, and growth retardation. There are several classification systems, the Sillence classification continues to have the most widespread usage. Type I is the mildest form, affected patients generally have prepubertal fractures, osteopenia, and slight growth retardation. Type II is the lethal perinatal form. Type III is characterized by progressive limb deformity and spinal deformity. Survival into adult life is expected, but early mortality can occur secondary to respiratory illness, injury with intracranial hemorrhage, or basilar invagination. Type IV is subdivided according to whether dentinogenesis imperfecta is present; it is essentially an intermediate type between I and III. A large percentage of this group function independently into adult life. Patients with Type I disease produce reduced amounts of normal collagen I; in the other types there are both quantitative and qualitative defects in collagen synthesis.

Children with type III and IV comprise the majority of problems seen by the orthopaedic surgeon. The various combinations of recurrent fracture, limb deformity, spinal deformity, and growth retardation result in wheelchair ambulation for a large number of these patients. In general, if sitting balance is not achieved by 10-12 months, meaningful ambulation doesn't follow. Treatment consists of the orthopaedic measures of intramedullary fixation of long bones, primarily of the lower extremities; and medical management, which to the recent past has not been encouraging. Studies have concluded that the basic defect is in the osteoblast, producing defective collagen; but osteoclastic activity is impaired as well. Recent studies conclude that the biphosphonate,
pamidronate, which is a potent inhibitor of bone resorption can be effective in reducing fracture rate and increasing bone mineral density. Another recent preliminary study of growth hormone administration was encouraging. Possible applications of gene therapy are presently being investigated, an obviously very complex undertaking.

Standard orthopaedic management involves multiple osteotomies to achieve reduction of deformity with intramedullary fixation. Ingenious telescoping rods have been devised to reduce the frequency of the necessity to replace the rods secondary to growth. The telescoping rods have their own set of complications, particularly in the younger tibia; successful orthopaedic management of these children is demanding. Successful management of spinal deformity is elusive secondary to problems at the bone-instrumentation interface.

References


