Osteogenesis imperfecta (OI) is a genetic disorder commonly known as brittle bone disease. Poor quality of collagen or smaller quantity of collagen is found in affected newborn. Minimal trauma is sufficient to cause fractures. Fractures can occur with minimal trauma, even as result of lifting the infant from the crib during bath. Infant and children with OI require increased caregiver assistance and may need significant adaptations to their environment.

Medical, surgical, nursing, physiotherapy and occupational therapy assessment and directed treatment - all have a role in the management of these children. The easy way to remember is mnemonic BLOOD and 3F’s in osteogenesis imperfect. BLOOD stands for BL-Blue sclera, ostosclerosis, osteoporosis, dentinogenesis imperfecta (transparent, discoloured, and fragile teeth that fracture easily and is evident in approximately 50 percent of people with OI) and 3P’s (fragile bone, fractures - multiple and frequent, foetal variety is fatal).

Classification of OI
Different authors have given different classification:

Looser classification
Type 1 (osteogenesis imperfecta congenita): fractures occur in perinatal period.
Type 2 (osteogenesis imperfecta tarda): fractures occur after perinatal period.

Sedorff classification
The subgroup osteogenesis tarda of former classification is divided into two subtypes:
Type 2a (tarda gravis): the first fracture occur with in first year of life - so severe type.
Type 2b (tarda levis) the first fracture occur after first year of life – so less severe.

Falvo et al classification
Age may not correlate with severity so bowing of the long bones is given importance. Tarda without bowing of long bones is type I tarda with bowing of legs is type II.

Silence classification
It includes five different types (I, II, III, IV and V) based on genetic and clinical criteria. In 2004 and 2007 this classification was expanded with OI types V-VIII because of distinct clinical features and/or different causative gene mutations and some more was revised for type VII and VIII. The majority of OI cases (possibly 85 to 90%) are caused by a dominant mutation in a gene coding for type 1 collagen (Types I, II, III, and IV in the following list). Types V and VI do not have a type 1 collagen mutation, but the genes causing them have not yet been identified.

Types VII and VIII are newly discovered forms that are inherited in a recessive manner, and the genes causing these two types have been identified. The general features of each of the known types of OI, which vary in characteristics and severity, are as follows:

Type I: This is the mildest and most common autosomal dominant form of OI with absent or minimal deformity of bones. The onset of symptoms in infancy and the stature is normal / near normal. It is mainly characterised by blue sclera and triangular face. There is possibility of scoliosis / kyphosis,
brittle teeth, hearing loss.

Type II: It is autosomal dominant and lethal form with onset of symptoms in utero, most severe form of OI, often lethal at or shortly after birth, numerous fractures, severe bone deformities, small stature, underdeveloped lungs, improperly formed collagen, possible blue sclera and small nose.

Type III: Severe form with autosomal dominant or recessive transmission, half the cases show symptoms in utero, the other half in the neonatal period. Bones fracture easily, short stature, blue sclera, loose joints, poor muscle development in arms and legs, barrel-shaped rib cage, triangular face, possible respiratory problems, possible scoliosis / kyphosis, possible hearing loss, often severe bone deformity, possible brittle teeth, improperly formed collagen.

Type IV: It is intermediate form of autosomal transmission, rare, onset of symptoms usually in infancy, between Type I and Type III in severity, sclera are normal or near-normal in colour, mild to moderate bone deformity, short stature, barrel-shaped rib cage, triangular face, possible brittle teeth, possible scoliosis/kyphosis, possible hearing loss, collagen is improperly formed.

Type V: It is inherited, moderate in severity and represents 5 percent of moderate-to-severe OI cases. It is similar to OI Type IV in terms of frequency of fractures and the degree of skeletal deformity. The most conspicuous feature of this type is large, hypertrophic calluses in the largest bones at fracture or surgical procedure sites. Hypertrophic calluses can also arise spontaneously. Calcification of the interosseous membrane between the radius and ulna restricts forearm rotation and may cause dislocation of the radial head. Patients anticipating pregnancy should be screened for hypertrophic callus in the iliac bone.

Type VI: The mode of inheritance is probably recessive, but it has not yet been identified; it is extremely rare and moderate in severity and similar in appearance and symptoms to OI Type IV. This type is distinguished by a characteristic mineralisation defect seen in biopsied bone.

Recessively Inherited Types of OI (Types VII and VIII): Two recessive types of OI, Types VII and VIII, were recently identified. Unlike the dominantly inherited types, the recessive types of OI do not involve mutations in the type 1 collagen genes. These recessive types of OI result from mutations in two genes that affect collagen posttranslational modification:

* Cartilage-associated protein gene (CRTAP)
* Prolyl 3-hydroxylase 1 gene (LEPRE1).

Recessively inherited OI has been discovered in people with lethal, severe, and moderate OI. There is no evidence of a recessive form of mild OI. Recessive inheritance probably accounts for fewer than 10 percent of OI cases. Parents of a child who has a recessive type of OI have a 25 percent chance per pregnancy of having another child with OI. Unaffected siblings of a person with a recessive type have a 2 in 3 chance of being a carrier of the recessive gene.

Type VII: Some cases of OI Type VII resemble OI Type IV in many aspects of appearance and symptoms. Other cases resemble OI Type II, except that infants have white sclerae, small heads and round faces. Short humeri and femora are common. Short stature is common. Coxa vara is common. OI Type VII results from recessive inheritance of a mutation in the CRTAP gene. Partial (10%) expression of CRTAP leads to moderate bone dysplasia. Total absence of the cartilage-associated protein has been lethal in all identified cases.

Type VIII: Cases of OI Type VIII are similar to OI Types II or III in appearance and symptoms except for white sclerae. OI Type VIII is characterised by severe growth deficiency and extreme under mineralisation of the skeleton. It is caused by absence or severe deficiency of prolyl 3-hydroxylase activity due to mutations in the LEPRE1 gene.

Management

Diagnosis

In most cases the diagnosis is based on the clinical manifestations, genetic history, and radiographs. When the diagnosis is not clear, a skin biopsy, may be done for collagen testing, X-rays, bone biopsy, collagen molecular testing, collagen biochemical testing. Dual Energy X-ray Absorptiometry (DXA) bone mineral density test provides information about bone quantity, not quality. Prenatal determination on the foetus can be achieved by amniocentesis and estimation of elevation of inorganic pyrophosphate 3 to 4 times than normal value. There are no specific lab tests for this disease.

Treatment

Prevention and cure of symptoms, surgery, healthy diet, avoiding excessive smoking and alcohol are beneficial. The fractures unite readily, but in more severe cases marked deformity often
develops, either from malunion or from bending of the soft bone and such patients may be badly crippled. In milder cases there is a tendency for fracture to occur less frequently in later life. Fractures are generally treated in ordinary way, but in a severe case intramedullary nailing of affected long bones should be considered as a means of preventing crippling deformity and permitting earlier presumption of activity. Newer techniques have been developed with telescoping rods, to obviate the need of multiple operations. Protective appliances, such as walking calipers, may be required in older children and adults. The increased remodelling activity suggests a basis for the efficacy of pamidronate and other bisphophonates in the treatment of OI. The benefits of bisphophonates as reported in the medical literature include fewer fractures, improved bone density, normalisation of diaphoresis, and pain reduction. The combination of bisphophonates and physical therapy has been reported to increase mobility in people with OI. Researchers at many medical centers are studying further effects of bisphophonates and growth hormone treatment for OI e.g teriparatide (synthetic parathyroid hormone), effect of bone and vibration treatment, evaluating the effect of diet on growth rates and bone mass in children.

**Nursing Considerations**

Medical staff that is new to child’s medical history that has not been diagnosed with a mild form of OI while working in paediatric set up especially in immunisation centres may lead to false accusations of fracture. Fractures in multiple stages of healing – rib fractures, spiral fractures, fractures with no adequate explanation of trauma. Explanation of injury doesn’t appear to match the injury found by the medical staff. In such situation a picture of OI should come into mind if child does not present with any of the other classical sign mentioned earlier.

The health care personnel themselves should handle the child very gently. The nursing procedure should be done in presence of family preferably in lap of mother and instruction should be given not to restrain the child forcefully. Special care should be taken during IM injection. On the other hand the family must be encouraged to provide the child with every opportunity for normal growth and development. Infants and children require careful handling when they are moved to prevent fractures e.g. repositioning car seat and stroller with additional padding, lifting baby from behind head and buttocks with fingers spread.

Teach the family how to bathe, dress, diaper, and reposition the child i.e. when diapering a severely affected infant, the parent should lift at the buttocks rather than ankles, keep baby’s fingers and toes free from catching onto clothing dress child in lightweight, cotton clothing, use molded sponge bathing aid with infants and a safety bath ring with sitting children during bath time, bathe baby with sling on and change when finished with bath; sponge bathe baby with a cast.

Teach carrying a letter certifying the child’s condition to prevent accusations of abuse. Involvement in support group is useful (the nurse can refer the family to the osteogenesis imperfect foundation at www.oif.org). Long-term goals should include genetic counselling and career planning. Remember: doctors, teachers, and social service workers are mandated to report suspected child abuse – they are concerned for the child, too. Tell parents not to change the hospital or physician treating their child without consulting.

**Case Study**

Two children of same family 6 years old male and 8 years old female reported to a genetic clinic of AIIMS hospital with complaint of repeated fractures. The boy was apparently well till one year of age. He got first fracture on left upper arm while playing bat ball. Child was taken to some government hospital for the same, where Plaster of Paris (POP) cast was applied after closed reduction. Child again had repeated fractures (6 times) at the same site without having any history of trauma or injury at the site. The child was suspected to be suffering from OI. Somewhat similar history was given for the second child. She had her first fracture at 2 months of age while she was being massaged with oil by her mother. Since then she had recurrent fracture at the site. All fractures were managed conservatively using POP cast. Both were diagnosed with type I/III osteogenesis.

There was no significant history of any other medical problem. In relation to birth history, mother had paid 6-7 antenatal visits in a maternity home near her house in both the pregnancies and both children were delivered pre-term at approximately 8 months of gestation by normal vaginal delivery. No problem was found in immediate post-natal period. In the family father, grandmother, paternal uncle and paternal aunt (Bua) have the same problem. The children had average built. Weight and height of boy and girl at the time of interview were
12 kg, 120 cm and 15 kg, 143 cm respectively. On assessment both were haemodynamically stable, both had temporal bulging, blue sclera, opalescent teeth, mild kyphoscoliosis, angular deformity at the site of fracture and there was no gross hearing impairment.

As per the diagnostic evaluation X-ray findings indicated generalised oestopenia, and evidence of previous fracture and callus formation at the site of recent fracture. Dexascan z score - 3.8 (osteopenia) for boy and -3.6 (osteopenia) for girl. Laboratory reports of boy showed Urea 29 mg/dl, creatinine 0.4 mg%, calcium 11.3 mg %, phosphorus 6.9 mg %, total proteins 8.2 gm %, albumin 5.8 gm %, globulin 2.4 gm %, SGOT 40IU, SGPT16 IU, Serum alkaline phosphate 499 IU and of girl showed Urea 25 mg/dl, creatinine 0.6 mg %, calcium 10.3 mg %, phosphorus 5.9 mg %, total proteins 8.0 gm %, albumin 5.6 gm %, globulin 2.4 gm %, SGOT 38 IU, SGPT 12 IU, serum alkaline phosphate 599 IU.

Treatment given to the children was Tab Shelcal 250 mg, twice daily tab Osteoplus 1 tab at sleep with a glass of water. Parents were advised to protect their children from any kind of vigorous activities like aerobics, jumping, running etc, and injuries. They were also advised to attend genetic clinic every 4 weeks or whenever required (SOS).

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