Osteogenesis Imperfecta

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Summary

OSTEOGENESIS IMPERFECTA (O.I.), also known as Maladie de Lobstein, is a group of inheritable, generalized disorders of connective tissue with clinical manifestations in the skeleton, ears, joints, ligaments, teeth, sclerae and skin.

Biochemical studies suggest that the defect involves collagen material. The frequency of O.I. has been estimated at more than one in twenty thousand births.

Case Presentation

The patient, a 25-year-old married lady, presented with the complaints of blue discoloration of the sclerae, slight impairment of hearing, weakness, difficulty in walking and a limp. The patient's complaints had begun in childhood when she had just started walking. She sustained fractures after minor trauma, like bumping into an object or tripping. These fractures healed poorly and the patient had reduction done several times. These mal-unions resulted in deformities of the left arm (Photo No. I) and shortness of the left leg with a resultant limp. The patient has had no fractures since she was 12–13 years old.

She gives no history of blue sclerae or multiple fractures amongst her siblings (4 brothers and 2 sisters), parents or other ancestral or blood relations. But out of the four children she has born (3 sons and 1 daughter), three were affected (2 sons and 1 daughter) having blue sclerae and being born with bent bones (not broken). Out of these, one male infant died in a hospital nursery (cause unknown) and the second son died at the age of 6 months due to a chest infection. The affected daughter, $3\frac{1}{2}$ years old, also has had multiple fractures (Photo No. 2) and blue sclerae (Photo No. 3). The unaffected son had neither blue sclerae nor any fractures (he was $2\frac{1}{2}$ years old); unfortunately he died of an opium overdose given by an ignorant grandparent during his mother's hospitalization.

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Photo No. 1 — Patient showing deformity and shortening of left arm.

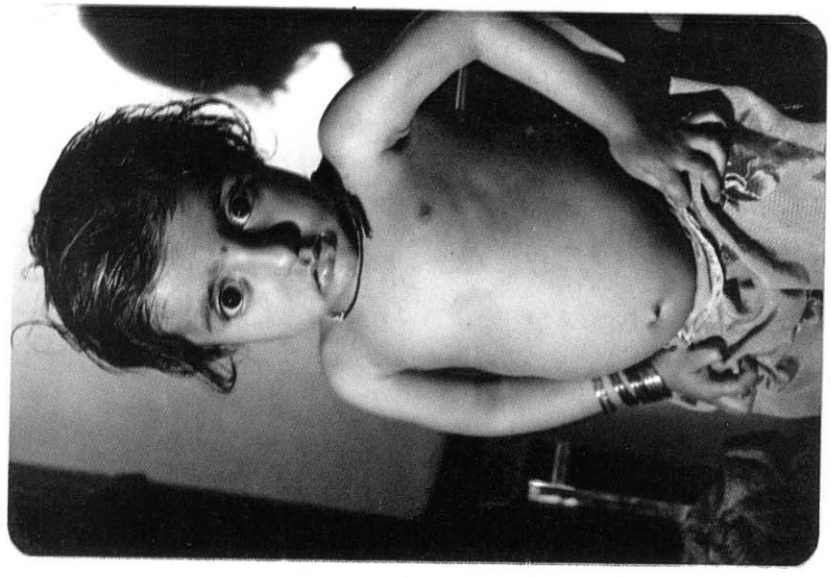


Photo No. 2 — Daughter showing deformity and shortening of left arm

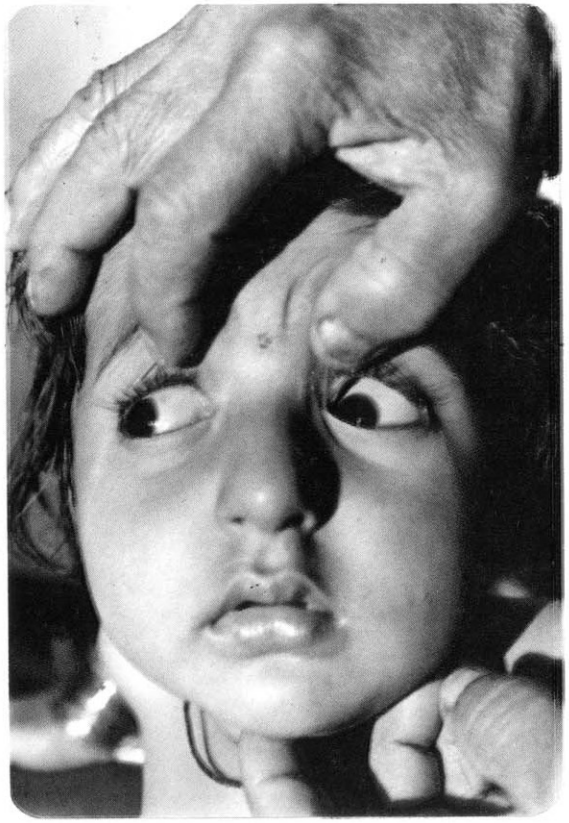


Photo No. 3 — Daughter showing blue sclerae.

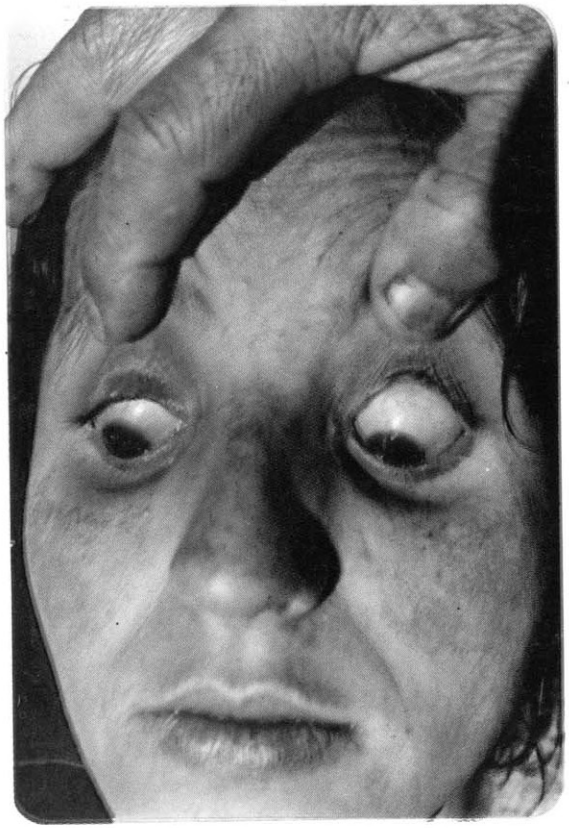
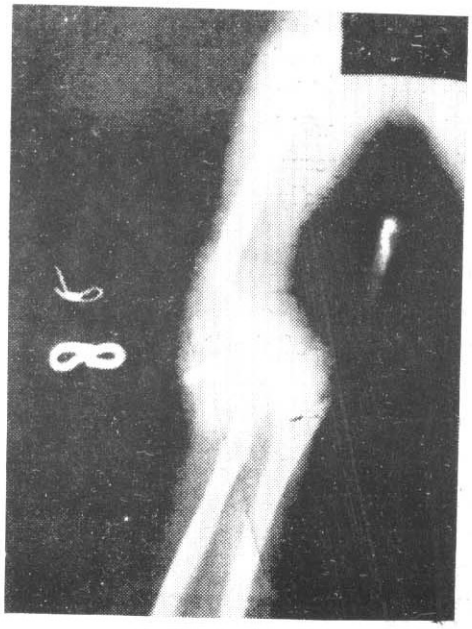


Photo No. 4 — Patient showing blue sclerae

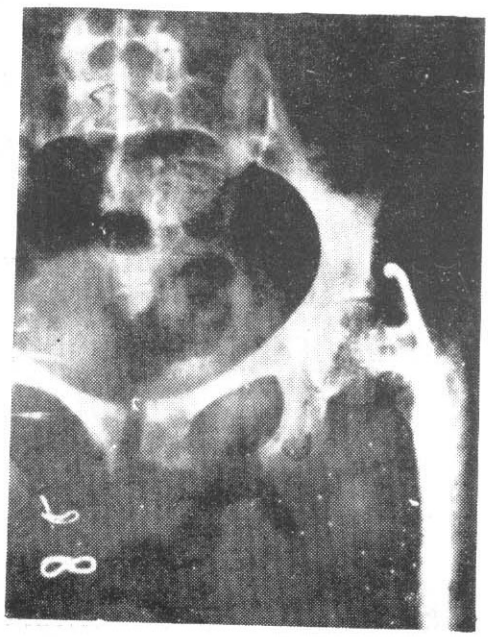
CLINICAL EXAMINATION : On general physical examination, the patient is a short statured lady of light built, walking with a limp. She has pale mucous membranes suggestive of anaemia; blue sclerae (Photo No. 4); difficulty in hearing beyond 6 years; head comparatively large; features small and pinched; and misshapen, discoloured yellowish-bluish grey teeth. No other positive findings.

Systemic examination showed no positive findings suggestive of cardiovascular disease; chest is slightly deformed, there being slight forward bulging of the sternum and flattening of the normal curvature of the ribs in front; no positive findings in gastro-intestinal tract and central nervous system.

Routine investigations included blood urea/sugar, complete blood and routine urine examination. Hb. was 55% or 88 gm% (normal range 12–16 gm%); other investigations were normal: Serum calcium = 8.4 mg/100 ml (normal range 8–11 mg/100 ml); Serum phosphorus (inorganic) = 4.0 mg/100 ml (normal range 2.0–4.7 mg/100 ml) and Serum alkaline phosphatase = 48 units/L. (normal range 20–48 units/L). X-ray chest: suggestive of Koch's disease. Skeletal survey showed generalized osteoporosis, pseudoarthrosis in the right humerus (X-ray No. 1) and a fractured medullary nail in the left femur (X-ray No. 2).



X-ray No. 1 — X-ray of right humerus and elbow showing pseudoarthrosis.



X-ray No. 2 — X-ray of left femur showing a fractured medullary nail.

Discussion

There are four distinct types of O.I. :

O.I. TYPE I occurs as a mutation in almost 50% cases, while it is inherited in the rest as an autosomal dominant with blue sclerae (and is almost certainly heterogenous). This is the most prevalent type of O.I. There may be 2 distinct sub-types: one with and one without distinct dental abnormalities.

The cardinal features are: blue sclerae, impaired hearing, multiple fractures after birth and abnormalities of the teeth in some families.

Bone fragility may be present at birth, but fractures do not occur until the child begins to stand or walk. Fractures may occur with minor trauma and frequently involve the long bones of the body. Most often the susceptibility to fractures decreases after puberty, but it may return later, especially with inactivity, pregnancy and menopause. Roentgenograms may show wormian bones in the skull; this can be a finding that may help establish the diagnosis. Osteoporosis is usually present; skeletal deformity is unusual and stature is generally near normal.

The sclerae appear to be translucent, thin and blue, owing to the partial visualization of the underlying choroid. This is probably the most frequent manifestation. Progressive hearing impairment due to otosclerosis may begin in childhood, but deafness usually does not develop until adulthood. Abnormalities of the ligaments and tendons lead to loose-jointedness which cause in turn the increased frequency of kyphoscoliosis, flat feet and recurrent joint dislocation. Hypoplasia of dentin and pulp causes the characteristically small and mis-shapen blue-yellow teeth.

O.I. TYPE II (LETHAL PERINATAL) is the most common type of O.I. and is uniformly lethal. Infants are either still-born or die within days to weeks after birth. Short stature and marked deformity of the limbs are present. Almost all bones break in utero.

O.I. TYPE III (PROGRESSIVELY DEFORMING) is characterized by multiple bone fractures, growth retardation and progressive skeletal deformity. Numerous fractures are often present at birth, but the bones are better developed than in type II. Almost all children surviving infancy have a very short stature. Severe kyphoscoliosis is often present by the time of puberty. Sclerae may be pale blue in infancy, but, thereafter, are white. Hearing loss is rare.

O.I. TYPE IV (DOMINANT WITH NORMAL SCLERAE). Without a clear family history, it may be difficult to distinguish O.I. early in its course from Idiopathic Osteoporosis.

Conclusion

The above is a typical illustration of a family with Osteogenesis Imperfecta type I showing an apparent mutation in one generation and autosomal dominant inheritance in the next generation.

No specific treatment is known; careful orthopaedic management and avoidance of immobilization are essential. Infants with type II are either born dead or die in infancy, while types I and IV are more benign disorders. Disability may occur from multiple fractures or skeletal deformities.

The proposed regimen for the management of progressive Osteopenia, that invariably occurs in the majority of young adults affected with this disorder, includes therapy with Sodium fluoride, Vitamin–D, Androgens and Magnesium oxide.

References

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