

Osteogenesis imperfecta type II: case report, Ecuador

Summary

Osteogenesis imperfecta (OI) is a rarely sporadic genetic disease. The prevalence of this disease affects only 1/60,000 newborn with familiar antecedents of this disease or not. It is characterized by extreme bone fragility, delayed cranial ossification and long bones fractures, leading to perinatal death or during lactation. The case we will present it's about a 37 week newborn diagnosed with (OI) before he was born. Son of a 33 year-old woman without relevant medical history related to his son. Physical examination shows multiple malformations in the skull, face, upper extremities and lower extremities. The patient ended with death after 70 hours after he was born.

Keywords: osteogenesis imperfecta type II, multiple fractures, blue sclera, crystal bones

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Introduction

Osteogenesis imperfecta (OI), is defined as a genetic mutation on the COL1A1 and COL1A2 genes which act at the level of the connective tissue.¹ This leads to alterations in the sequence and variants in the carboxyl terminal of the coding domain of type I procollagen, causing its abnormal synthesis.² OI was described for the first time by Remigio PA. in 1970 and McKusick in 1972,³ and its characterized by: Multiple fractures, skull with poor bone mineralization, broad and communicating fontanelles, shallow orbits, blue sclera, shortened and widened bones and bone calluses especially in the lower extremities.⁴ Type II Osteogenesis Imperfecta is the most lethal variant divided into three subgroups depending on the radiographic findings.⁵

- Presents shortened and wide long bones, accordion tibia and rosary ribs.
- Short, wide and wrinkled long bones, but rosary bead rib appearance is not observed.
- Fine and fractured long bones are observed, elongated, thin and rosary bead appearing ribs.

Death usually happen within the first days of life secondary to respiratory distress due to the absence of adequate movements of the thoracic cage because of the multiple costo-sternal malformations.⁶ The Prenatal diagnosis was made at 17 weeks of gestational age with obstetrical ultrasound which demonstrated a little ossified cranial vault, small rib cage and shortened extremities.⁷ However, prior to the suspicion of this entity, the synthesis of procollagen in cells of the amniotic liquid was analysed; if there is any doubt, the diagnosis of type II Osteogenesis Imperfecta can be confirmed by examination of the collagen fibers synthesized by fibroblasts grown in one or more tissues.⁸

Clinical case

24 hour-old male patient, born to a 33 year-old female, was the product of a third poorly controlled pregnancy. During gestation, folic acid intake started on the sixth month but was poorly compliant.

The patient had a DT vaccination and was diagnosed with bacterial vaginosis by gardenerella at seventh and eighth month of gestation for which she received treatment with metronidazole ovules every day for seven days. The birth was by emergency cesarean section due to fetal distress. Through the Capurro test, a gestational age of 37 weeks is estimated, APGAR was 7 and 8 at one and five minutes respectively. Downes score was 4/10, weight: 1930 gr, height: 35 cm, head circumference was 32 cm and, thoracic perimeter was 26 cm. Was admitted to the neonatal intensive care unit due to respiratory distress and hypotonic cyanosis. Genetic interconsultation is performed at 24 hours of life of the newborn where clinical assessment is evidenced, skull with lack of ossification (figure 1), hypertelorism, exophthalmus, blue scleras (figure 2), mezomelic shortening of the four limbs and internal curvature of the lower extremities (Figure 3), which is why a transfontanellar ultrasound is requested, showing grade one hemorrhage at the germinal matrix level, and x-rays of the skull, thorax and lower extremities; observing the typical radiological characteristics of multiple fractures with ossification centers (Figure 4). Newborn remains in neonatal intensive care with ventilatory support, where death occurs at 70 hour of life.



Figure 1 Skull with lack of ossification.



Figure 2 Hypertelorism, exophthalmos, blue sclera.



Figure 3 Mesomelic shortening of the four limbs and converging lower extremities.

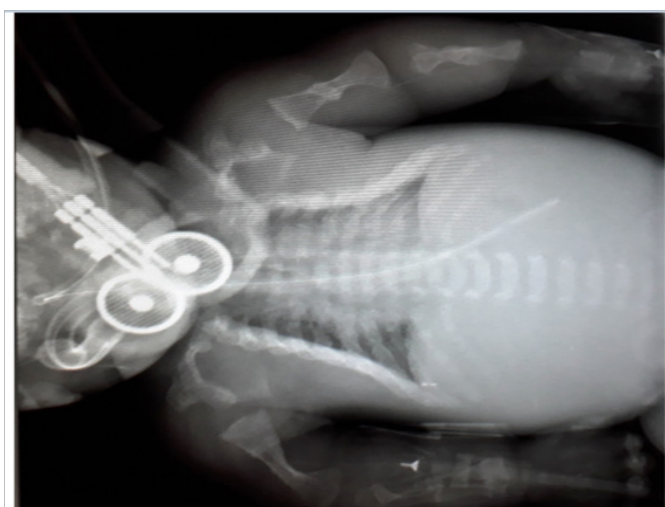


Figure 4 Multiple fractures with ossification centers.

Laboratory data: RBCc 33.82, Hb 10.9, Ht 33.1, NEUT 22.7, LYMP 69.4, PLT 76.00, Glucose 43, alkaline phosphatase 309.

Discussion

There are currently 7 OI classifications, three more than those originally proposed by Sillence (Table 1). However, at present, the difficulty persists in the correct diagnosis of the different variants of OI, particularly in cases where intermediate phenotypes are observed. The main clinical characteristics of these patients are bone fragility, short stature, multiple fractures, lack of ossification of the skull and blue scleras.⁹ The diagnosis is usually simple as long as most of the clinical characteristics mentioned are present; in the same way, since the aforementioned clinical characteristics do not exist, a differential diagnosis must be made with the metabolic causes of osteoporosis, child maltreatment, rickets and osteomalacia¹⁰.

Table 1 Classification of Sillence for OI

Type	Clinical Severity	Typical Features	Heritage
I	Mild not deforming	Bone fragility, blue sclera, presenile deafness, does not present dentinogenesis imperfecta	AD
II	Lethal perinatal	Extreme bone fragility, stillbirth or perinatal death. Fractured ribs	AD
III	Severely deforming	Extreme low size, triangular facies, severe scoliosis, Bone fragility, severe and progressive deformation of long bones, normal or gray sclera, dentinogenesis imperfecta	AD
IV	Moderately distorted	Moderate low size, mild to moderate scoliosis, white or gray sclera, dentinogenesis imperfect.	AD
V	Moderately distorted	Mild to moderate, short stature, dislocation of the head of the radius, mineralized interosseous membrane, hypertrophic callus at the fracture sites, white sclera, sindentinogenesis imperfecta	AD
VI	Moderate / severe distorted	Moderate low size, scoliosis, osteoid accumulations in bone tissue, without dentinogenesis imperfecta	UK
VII	Moderately distorted	Slight low size, short femur and humerus, coxa rod, blue sclera, dentinogenesis imperfect	AR

AD, Autosomal dominant; AR, Autosomal recessive, UK: unknown.

The biochemical parameters of bone metabolism and minerals are usually within the normal range in the OI. Some parameters within laboratory tests are usually altered, such as elevated alkaline phosphatase, and hypercalciuria.¹¹ The management of these patients must be carried out by a multidisciplinary team composed of neonatology, genetics, traumatology, physiotherapy, audiology, nutrition and psychology.¹¹ The treatment with bisphosphonates in patients with OI is to reduce the incidence of bone fractures, minimize pain, prevent long bone deformities and scoliosis and, maximize mobility.¹²

A study carried out in Argentina in 2007, in which alendronate was administered orally to patients with OI and a reduction in the pain

of the fractures was achieved, as well as the repetition of fractures in these people with OI. In addition, this medication caused few side effects in these patients¹³.

When the prenatal diagnosis of severe OI is made and, it is decided to continue with the pregnancy, all the preventive measures for the possible complications must be taken into account. Delivery should be by caesarean section, with wide incisions to prevent rubbing especially of the baby's head in the uterine cavity and abdominal wall and have the presence of neonatologists to perform management for assisted ventilation support due to multiple respiratory complications. It is also recommended to limit the manipulation and movements of the newborn, since these would increase the possibility of fractures.

Due to respiratory distress and limited mobility of the thoracic cage and diaphragm, patients with OI should be fed continuously by enteral nutrition to maintain caloric-protein intake. The few patients who manage to be discharged from the hospital require multiple special care at home, being essential to avoid fractures and continuous manipulation and similarly the use of water mattresses or soft foam (Table 1).¹⁴

Conclusion

Type II OI presents a low frequency in the population and, is frequently poorly diagnosed or not valued in abortions due to lack of knowledge of this disease by health personnel. Genetics play a fundamental role in prenatal, perinatal and postnatal assessment and genetic counseling should be offered to the parents to avoid recurrence of this disease which, in most cases, is lethal.

Bioethical aspects

The parent authorized via informed consent to this case could be made known, with the condition of protecting the patient's identity.

Acknowledgments

None.

Conflicts of interests

There is no conflict of interest present in the realization of this clinical case.

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