

# Osteogenesis Imperfecta in neonatal period in Cameroon: A case report

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## Abstract

Osteogenesis Imperfecta is a genetic disorder of connective tissue leading to bone fragility. Diagnosis of this condition can be considered during pregnancy, at birth or during childhood. Early onset forms are severe with high mortality rate. We report two cases during neonatal period in Cameroon.

## Key clinical message

Early forms of Osteogenesis Imperfecta should be considered as main etiology of bone deformities in newborns. Prenatal diagnosis and genetic counselling should be improved in Africa. Management of these children remain difficult in low income countries.

## INTRODUCTION:

Osteogenesis Imperfecta (OI) is a group of inherited disorders of connective tissue due to mutations in one of the two genes encoding for type 1 collagen [1]. Clinical features include bone fragility and low bone mass resulting in bone fractures, bone deformity and growth impairment. This disorder affects approximately 0.3-0.7/10.000 births[2]. Age at diagnosis varies depending on the OI type. The *Sillence* classification reported four types depending on clinical, radiological and genetic features [3]. This classification was extended by some authors to include new genetic forms of OI due to recessive inherited mutations [4]. Type II and III are the most severe forms with high mortality rate during antenatal and neonatal period. In sub-Saharan Africa, few cases of neonatal diagnosis have been described [5]. We report two cases of neonatal diagnosis of this rare condition in Cameroon.

## CASE HISTORY

### Case 1:

We received a 26 days male newborn who was referred from a regional hospital for multiple fractures and limb deformities discovered at birth. He was born at 39 weeks through vaginal route with breech presentation and a birth weight of 2700g. It was an uneventful twin pregnancy. Antenatal laboratory tests were normal. Three ultrasounds were done during prenatal period with no reported abnormalities. There was no consanguinity, no family history of short stature but limb deformity from a 6 year old cousin. The twin sister was in good health at birth.

At clinical presentation, anthropometric parameters included a weight of 3200 g (-1 SDS), height 47 cm (-2 SDS) and head circumference of 35 cm (+ 0.5 SDS). The child presented with reduced mobility, frontal bossing, white sclerae, moderate respiratory distress, bowed legs and shortened limbs (**Figure 1**). Limbs X-rays showed multiple diaphyseal fractures of long bones, demineralization and curved bones (**Figure 2**). Transfontanelar brain ultrasound and cardiac ultrasound were normal. Laboratory findings included normal calcium (97.2 mg/l) and increased alkaline phosphatases (374.68 IU/L). Genetic tests are not yet available in our country. According to clinical and radiographic findings, Osteogenesis Imperfecta was the more likely diagnosis of this bone fragility. We suggested OI type III as diagnosis due to early presentation. For management of this condition, the child performed orthopedic treatment for recent fractures and oral Vitamin D supplements. The child is actually 9 months old with a weight of 7750 g (-1 SDS), a height of 57 cm (- 3.5 SDS) and a head circumference of 44 cm. He recently received the first dose of bisphosphonates. He performed a lumbar spine X-ray which revealed tiered vertebral collapse from T12 to L3 with no spinal deformities (**Figure 3**). The physiotherapist tried to maintain a semi-sitting position to avoid spinal deformities.

### Case 2:

We received a 37 days male baby who was referred by a surgeon for medical management of multiple fractures and limb deformities discovered at birth. It was an eventful pregnancy with normal prenatal tests. An ultrasound done at 3 rd trimester revealed femoral bowing and shortening. He was delivered through cesarean section at 37 weeks due to uterine scar from a 32-years-old mother. He had a birth weight of 3000g and a height of 40 cm. At birth, he presented with limb deformities and painful mobility of lower limbs. He was admitted for an early neonatal sepsis at day 2 of life with good improvement. He is the second child of the family with no family history of consanguinity nor limb deformities.

At clinical presentation, anthropometric measures included a weight of 4000 g (-1 SDS), height of 45 cm (-2 SDS) and head circumference of 35 cm (+ 0.5 SDS). The child presented with reduced mobility, frontal bossing, blue sclerae, bowed legs and shortened limbs. Limbs X-rays showed multiple incomplete diaphyseal fractures of long bones and curved bones (**Figure 4**). The patient also presented an undisplaced sternal fracture. Genetic tests are not yet available in our country. According to clinical and radiographic findings, Osteogenesis Imperfecta was the more likely diagnosis of this bone fragility. We suggested OI type II or III as diagnosis due to antenatal deformities and multiple fractures at birth. For management of this condition, the child performed orthopedic treatment with many casts for recent fractures. Bone callous was obtained after 8 weeks with pain improvement. He also received oral Vitamin D supplements. Bisphosphonates are planned but not yet available for this child.

### DISCUSSION:

Osteogenesis Imperfecta is a common cause of bone fragility in children. Clinical diagnosis is usually based on skeletal signs as in our patient. This genetic disorder can also present with extraskeletal signs such as respiratory distress, cardiovascular abnormalities, dentinogenesis Imperfecta, blue sclerae, hearing impairment and vascular fragility[6][7]. Genetic tests can confirm the diagnosis but molecular abnormalities of type 1 collagen (*COL1A1* and *COL1A2*) are only reported in 85% of patients[2]. Antenatal or neonatal onset of this condition as in our patient suggests a severe form with high mortality rate. These forms can be suspected on antenatal ultrasound (bone deformity, fracture, bone shortening)[6]. These features were reported during antenatal ultrasound of our second patient. This highlights importance of ultrasound for antenatal diagnosis of this condition.

*Sillence* classification distinguishes four types of OI based on clinical phenotypes and disease severity[3]. Recently, *Glorieux* et al. added three types with the same phenotype of OI previously described but not related to type 1 collagen mutations [4]. Types II and III are the most severe forms with antenatal or neonatal onset. Our patients probably had Type III OI due to early onset of bone fractures and deformities. The prognosis is reserved in neonatal forms due to intracranial hemorrhage or respiratory insufficiency following chest deformity[6]. Respiratory distress of the first patient at admission caused fear of respiratory insufficiency or

associated cardiovascular malformation. A normal cardiac ultrasound ruled out these comorbidities that are life-threatening in severe forms. In addition, transfontanellar ultrasound eliminated intracranial hemorrhage.

The management of OI is multidisciplinary including surgical and medical treatment of bone fragility [8]. Orthopedic management or surgical treatment of fractures and bone deformities is essential during follow-up [6]. Physiotherapy helps to maintain mobility, maintain muscle mass and improve motor skills. Bisphosphonates are considered as first line medical treatment for OI [9]. Benefits of this treatment include reduced pain, increased bone mass density and reduced incidence of fractures[10]. The psychosocial support of families is necessary. In our country, management of these patients remain difficult due to low socio-economic level.

#### CONCLUSION:

Osteogenesis Imperfecta is a rare inherited disease leading to abnormal bone fragility. Early forms are reported to be severe. Therefore, caregivers should be aware of this condition when bone deformities and fractures are observed in a neonate. Genetic counselling and prenatal diagnosis should be considered in these families.

**Authorship:** All the authors managed these patients, searched literature and revised the manuscript. MBRC and MANNY designed the manuscript.

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