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CASE REPORT

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A case of osteogenesis imperfecta type II, a diagnosis made almost too late in a resource poor setting

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Abstract *Background:* Osteogenesis imperfecta (OI) is a rare autosomal dominant disorder of type I collagen (COL I), characterised by excessive bone fragility with low bone mineral density (BMD). Type II is associated with extreme bone fragility leading to intrauterine or early infant death.
Objective: To highlight a case of OI type II and the need for an early detection of this rare bone disorder through non invasive prenatal diagnosis.
Case Report: We report a case of a full term male neonate with progressive respiratory distress from birth. He was seen in children's emergency room two hours after vaginal delivery in a peripheral clinic. Pregnancy and delivery were uneventful and the baby was born to non-consanguineous, monogamous parents. On examination he was dyspnoeic, cyanosed with malformed and fractured upper and lower limbs. A working diagnosis of osteogenesis imperfecta type II was made and baby was placed on oxygen via face mask. However respiratory distress worsened and baby died at 6 days of life.
Conclusion: Antenatal ultrasonography might have led to diagnosis in utero. If detected prenatally a more appropriate management can be instituted to reduce morbidity and mortality.

Introduction

Osteogenesis imperfecta (OI) is a rare genetic disorder caused by mutation of the gene that encodes the peptide chains that constitute type I collagen (COL1A1 and COL1A2).[1,2] This is the major collagen of the skeleton. [2] It is characterised by excessive bone fragility with low bone mineral density (BMD). There are eight different types of OI as classified by Sillence.[2] Types I ,II,III,IV and V are inherited as an autosomal dominant conditions while the other forms are inherited in an autosomal recessive manner. Type I is a mild form and the most common type accounting for 50% of the total OI in the population[2]. Type II presents with severe bone fragility and is associated with intrauterine fractures and perinatal lethality. The incidence of OI is estimated to be 1 per 20,000 live births; 6-7 per 100,000 people are affected worldwide and there are no gender, racial or ethnic differences.[3] We highlight a case of OI type II and the need for an early detection of this rare bone disorder through non invasive prenatal diagnosis.

Case report

We report a case of a full term male neonate with progressive respiratory distress from birth. He was seen in the children's emergency room two hours after vaginal delivery in a peripheral clinic with difficult breathing and lower limb deformity. Pregnancy was booked at six months in a peripheral clinic and was uneventful. Pregnancy was carried to term and delivery was vaginal. Baby was the youngest of three children born to a non-consanguineous, monogamous parents. Other siblings are alive and well. Neither parent has a limb deformity. However, a maternal aunt does have a deformity of unknown cause. Both parents are primary school teachers. On examination he was dyspnoeic, cyanosed with a respiratory rate of 80 cycles per minute. He weighed 3 kg**;** body temperature was 37^{o}C. Pulse rate was 164 beats per minute and was regular. Baby had blue sclera and was lying in a frog-like position. There was bilateral shortening and deformity of the lower limbs below the knee joints.

Fig1: Lower limb deformity of baby with OI

It was associated with hypotonia and multiple fractures of the upper and lower limbs Baby was also severely pale with a PCV of 12%. A working diagnosis of osteogenesis imperfecta type II was made. Plain radiography of baby revealed multiple fractures involving the ribs and the long bones (fig2). Respiratory assistance was given to baby by placing on oxygen via face mask, and was in addition transfused with blood. However respiratory distress worsened and baby died at six days of life.

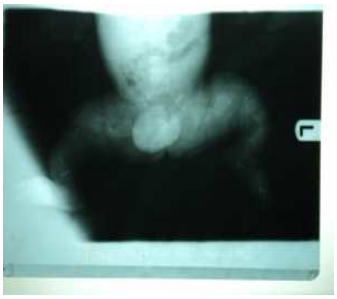

Fig 2: Radiograph showing multiple fractures of long bones

Discussion

The patient presented with severe respiratory distress due to multiple rib fractures**.** He also had severe bone deformities and suffered early infant death. These are classical features of osteogenesis inperfecta (OI) of the Sillence type II [1,2] . This is a severe form of OI inherited as autosomal dominant form. Apart from the maternal aunt who has a leg deformity both parents are said to be essentially normal. Most infants with more severe forms of osteogenesis imperfecta (such as type II and type III) have no history of the condition in their family. In these infants, the condition is caused by new (sporadic) mutations in the COL1A1 or COL1A2 gene. This diagnosis was completely missed during gestation and hence the late presentation. The mother could have benefited from non invasive prenatal diagnosis such as routine ultrasound. Routine ultrasound done as early as 20 weeks gestation can detect the lethal forms of OI and early diagnosis allows for the most appropriate method of delivery to be planned.[4] For instance, caesarean section is usually avoided if the fetus is shown to have the lethal forms with minimal chances of survival. Also, the parents can benefit from genetic counselling.[4]

Many peripheral clinics in Nigeria do not have facilities to offer routine ultrasound services during antenatal care. However, patients should be referred to hospitals where such services are available. This pregnancy was uneventful and therefore appeared to have no cause for further investigation beyond the limit and capacity of a local clinic. This underlines the need for at least one routine antenatal ultrasound scan even in apparently normal pregnancies.

As OI is usually inherited in an autosomal manner [1,2], genetic counselling is strongly recommended in this family as this will benefit them if they plan for future pregnancy. Chorionic villus sampling (CVS) done at about ten to 12 weeks gestation will be helpful to exclude OI in future pregnancy[5]. The baby died within the first week of life preceded by a worsening severe respiratory distress. This is characteristic of OI type II where 80% of affected babies die within the first week of life and survival beyond one year is rare[1,2,5,7] . Death usually results from pulmonary insufficiency related to the small thorax, rib fractures, or flail chest[1,2,3,5,6,7]

Conclusion

Routine ultrasonography should be offered even in apparently normal pregnancies. In the index case, early detection of OI would have been enhanced. Parents of probands with OI will benefit from genetic counselling to discuss future pregnancies.

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