CASE REPORT

The Unseen Fragility: Challenges in Diagnosing Osteogenesis Imperfecta in Neonates

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SUMMARY

Unexplained multiple bone fractures in infant can indicate non-accidental injury, however metabolic bone disease or skeletal dysplasia should always be considered as a differential diagnosis. We report a case of a term baby delivered via spontaneous vertex delivery following induction of labour for intrauterine growth restriction. Third trimester sonography revealed multiple congenital anomalies namely Dandy-Walker variant, hypomineralization and short limbs. At birth he showed relative macrocephaly, a long trunk and rhizomelia. In the absence of bony fractures and blue sclerae, he was diagnosed with skeletal dysplasia and discharged home on day five of life. On day thirty of life, he returned with a closed fracture of right femur prompting further evaluation. Blue sclerae, and a skeletal survey indicated of multiple old fractures with Wormian bones, suggesting Osteogenesis Imperfecta Type III. In conclusion, suspecting and evaluating Osteogenesis Imperfecta in infant with skeletal anomalies in the absence of initial overt symptoms is challenging. Early recognition and management are crucial for optimizing outcomes and preventing long term complications.

INTRODUCTION

Unexplained multiple bone fractures in infants often raise suspicion of non-accidental injury, but metabolic bone diseases or skeletal dysplasia should also be considered. Conditions associated with increased bone fragility, such as osteogenesis imperfecta (OI), can be subtle and challenging to diagnose, especially in the absence of obvious fractures. A high index of suspicion is critical when clinical features of bone fragility are present, though the correct subtype diagnosis can be difficult to determine.

This case highlights the challenges in early recognition and diagnosis of bone fragility disorders, particularly when clinical signs may not fully manifest at birth.

CASE PRESENTATION

A term infant was delivered via spontaneous vertex delivery following induction of labour for intrauterine growth restriction. Third-trimester sonography identified multiple congenital anomalies, including a Dandy-Walker variant, skeletal hypomineralization, and limb shortening. Amniocentesis revealed a normal karyotype (46, XY). The mother's antenatal course was unremarkable, with no significant complications or medical history. There was also no family history of bone-related problems. The infant had good Apgar scores and did not require resuscitation at birth. His birth weight was 2.97kg (between the 10th to 50th centile), with a length of 47cm (at the 10th centile), and a head circumference of 34.5cm (at the 50th centile).

Clinically, the infant exhibited relative macrocephaly, a long trunk, and rhizomelia, with no other significant dysmorphic features. A chest radiograph performed at birth was reported to show normal bone density with no evidence of fracture. Formal brain ultrasonography on day four of life revealed bilateral choroid plexus cyst and prominent cisterna magna. In the absence of bony fractures or blue sclerae, further investigations for bone hypomineralization and a skeletal survey were not pursued, and a clinical diagnosis of skeletal dysplasia was made. The infant was discharged on the fifth day of life with a scheduled follow-up plan.

On the day thirty of life, the infant was re-admitted with swelling and pain in the right thigh, without any preceding trauma. Re-evaluation revealed blue sclerae, though no other obvious bony deformities were noted. A skeletal survey demonstrated generalized osteopenia, old rib fracture (Figure 1), bowing of both femora with a fracture of the right femur (Figure 2), bowing of both humeri a distal right radius fracture with callus formation, and the presence of Wormian bones (Figure 3). Blood investigation showed a normal bone profile (calcium 2.7mmol/L, phosphate 2.12mmol/L and alkaline phosphatase 319IU) and a normal parathyroid hormone level of 3.31pmol/L (normal range: 1.59 – 7.24pmol/L), but a deficiency in Vitamin D at 20.8nmol/L (normal range: 75 – 100nmol/L). Based on clinical and radiographic findings, a diagnosis of osteogenesis imperfecta type III was established. The Orthopaedics team initiated non-surgical management, and the infant was supplemented with multivitamins. A repeat Vitamin D assessment at the age of 2 months showed normalisation of levels. He was also referred for genetic evaluation.

DISCUSSION

Osteogenesis imperfecta (OI) is a genetic disorder resulting from mutations affecting type I collagen synthesis, presenting as a rare skeletal dysplasia. It is characterized by decreased bone density, increased fragility, and a heightened risk of

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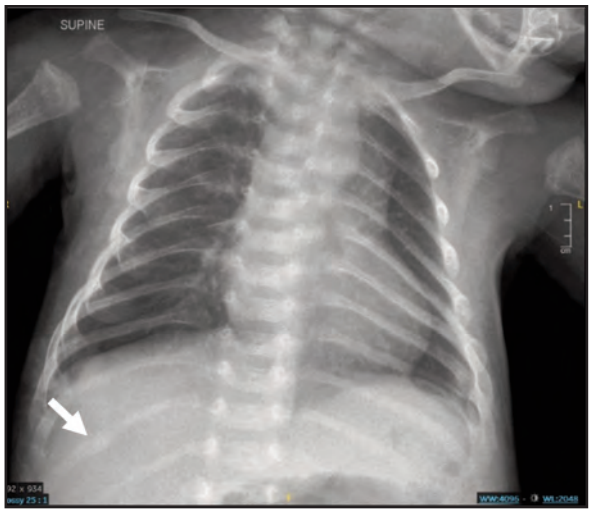

Fig. 1: Chest radiograph showing osteopenia and old rib fracture

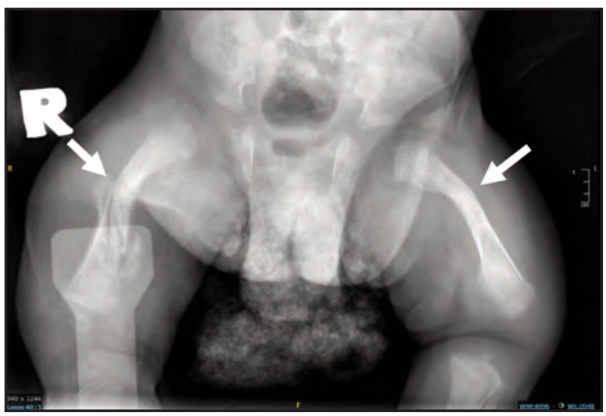

Fig. 2: Pelvic radiograph showing bowing of bilateral femur and fracture of right femur

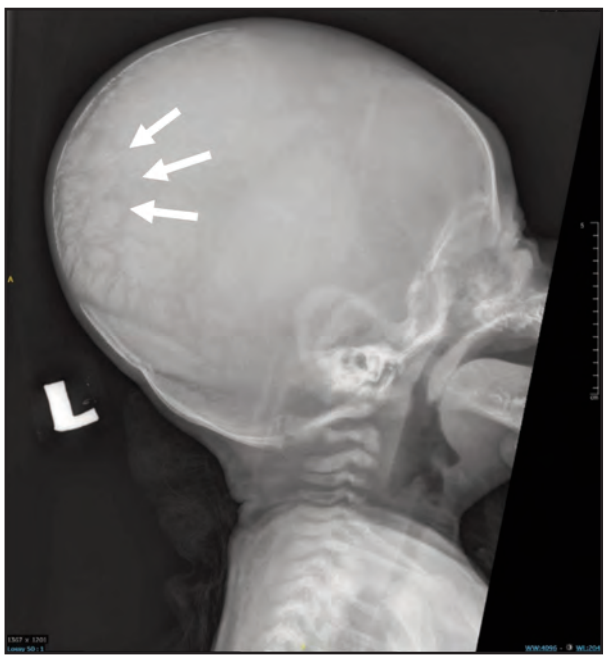

Fig. 3: Skull radiograph showing presence of Wormian bones

fractures.[1] The clinical spectrum of OI is highly variable, ranging from perinatal lethal forms marked by crumpled ribs, a fragile cranium, and multiple long bones fractures at birth, to milder forms that are either asymptomatic or present with subtle osteopenia and no skeletal deformities.[2]

Diagnosis of OI is primarily based on clinical and radiographic findings; however, on general examination, the absence of fractures and blue sclerae at birth makes recognising non-lethal forms of OI particularly challenging. Prenatal ultrasound can therefore be especially valuable in identifying non-lethal forms of OI, providing early insight into potential skeletal abnormalities, particularly when skeletal hypomineralization or limb shortening is detected.[3] In this case, however, these ultrasonographic findings, along with other suggestive features of OI were overlooked, resulting in a delay in diagnosis and management until the patient presented again one month later. This underscores the importance of not neglecting antenatal findings, even when classic features like fractures or blue sclerae are absent. Bone hypomineralization and limb shortening may be the earliest indicators of OI and ensuring close postnatal follow-up and early imaging in such cases can significantly improve patient outcomes by enabling timely diagnosis and intervention.[4]

Since the diagnosis of OI was not initially established, the patient was at risk of being misidentified as a victim of child abuse when presenting with multiple fractures. Differentiating OI from nonaccidental injury can be challenging, as OI is rare while child abuse is more common.[5] Features that helped to distinguish OI in our case include the presence of blue sclerae, Wormian bones on skull X-ray, and bone deformities. However, milder forms of OI, may not have these typical features, making diagnosis more difficult. Additionally, blue sclerae can be a normal finding in infants up to four months old, further complicating the distinction. While OI should always be considered in cases of unexplained fractures, it is also important to recognize that children with OI can still be victims of abuse. A careful and thorough assessment is essential to ensure the correct diagnosis and appropriate management.

The management of OI requires a multidisciplinary approach focused on fracture prevention, bone density improvement, and orthopaedic complications.[6] Bisphosphonates are commonly used to enhance bone strength and reduce fracture risk, while surgical interventions may be necessary to correct deformities and improve mobility.[7] In this case, the infant was managed conservatively, highlighting the importance of ongoing monitoring and early intervention to optimize long-term outcomes. Additionally, the patient had a low vitamin D level, a common finding in OI.[8] Vitamin D deficiency can worsen bone fragility and influence disease severity. Therefore, supplementation along with drug therapy and adequate calcium intake, is essential to support bone health and mitigate disease progression.

The discussion has emphasized the critical role of early detection and intervention in improving outcomes for neonates with OI. Through heightened awareness, serial imaging, and genetic testing, healthcare providers can identify the condition early, enabling timely management.

CONCLUSION

In conclusion, the early identification of OI is essential for optimizing outcomes. By recognizing prenatal signs, performing comprehensive post-natal assessments, and conducting serial imaging, healthcare providers can ensure timely diagnosis. Genetic testing further confirms the condition, allowing for early intervention that significantly reduces complications and improves long-term prognosis for affected infants.

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DECLARATIONS

The authors have no conflicts of interest to disclose.

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