Case Report

Osteogenesis imperfecta Type XI: A rare cause of severe infantile cervical kyphosis

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ABSTRACT
Osteogenesis imperfecta is a genetic disorder by bone fragility and decreased bone density. Ligamentous laxity is also a feature. We present a case report of a very young, nonmobile infant of 5 months who initially presented with a tibial fracture, and during a skeletal survey, was found to have other features consistent with osteogenesis imperfecta, including rib fractures of different ages, and multiple Wormian bones within the skull. The skeletal survey also revealed a severe cervical kyphosis, unusual in both osteogenesis imperfecta, and this age group. This presented a significant management challenge in such a young patient, and both computed tomography and magnetic resonance imaging were utilised to further characterise the bony anatomy, degree of kyphosis, spinal canal stenosis, and to visualise the spinal cord. The patient was treated with surgical reduction and an Aspen collar in a tertiary centre. Subsequent genetic testing was consistent with a diagnosis of compound heterozygous osteogenesis imperfecta Type XI.

Keywords:
Osteogenesis imperfecta (OI) Type XI
Cervical kyphosis
Cervical fracture

Introduction

Osteogenesis imperfecta is a rare genetic disorder of Type 1 collagen. Although rare, it is one of the more common skeletal dysplasias, and is well-known to pediatric radiologists. The incidence is approximately 1 in 10,000-20,000 births [1]. The disorder causes bone fragility and low bone density and is usually inherited in an autosomal dominant fashion, although it can be autosomal recessive or due to a spontaneous mutation [1]. Fractures in children with osteogenesis imperfecta may be caused by normal handling.

Seventeen genetic causes of OI have been identified. Approximately 90% of the mutations are found in the COL1A1 and COL1A2, which encode for the alpha-1 and alpha-2 chains of type I collagen [2].

The phenotype of the disease varies greatly, ranging from mild to severe, and may even cause death in-utero. OI type XI is an autosomal recessive form of OI [3] caused by homozygous or compound heterozygous mutations in the FKBP10 gene on chromosome 17q21, which encodes a chaperone involved in type I procollagen folding. Alanay et al determined that FKBP10 mutations affect type I procollagen secretion [3].

However, the resulting phenotype and range of severity from mutations in the same gene are wide [4], so patients may have a wide range of severity of clinical disease, and variable presence or absence of extra-skeletal manifestations.

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Fig. 1 – (a and b) AP and lateral radiographs of the right lower limb demonstrating a minimally displaced recent fracture of the midshaft of the tibia (circled), an unusual pattern of injury for a nonmobile 5-months old.

Fig. 2 – Oblique chest radiograph as part of skeletal survey demonstrating healing fractures of the right ninth and tenth lateral and posterior ribs with some periosteal reaction. More mature healing fractures of the posterior aspects of the right eleventh posterior rib and likely the right posterior twelfth rib are also present. On the left, there is a healing fracture of the posterior aspect of the fourth and the eleventh ribs with associated mature callus.
The common skeletal features of osteogenesis imperfecta in general include multiple Wormian bones, kyphoscoliosis, and vertebral compression fractures. Vertebral fractures in infants can be difficult to diagnose and characterise on plain radiograph, and even on CT, because of the lack of complete ossification of the cervical vertebrae with the presence of open synchondroses.

There are also extra-skeletal manifestations of osteogenesis imperfecta, since Type 1 collagen is also present in dental enamel, eye sclera, skin, tendons and ligaments. Patients with osteogenesis imperfecta may have blue sclerae (mainly in Type 1, the mild form), a greyish or yellowish aspect of the teeth, skin fragility, joint and ligament hyperlaxity, early hypoaacusia and cardiovascular abnormalities (particularly aortic valve disease) [9].

Case report

A 5-month-old female infant presented to the emergency department with a tender, swollen lower leg and foot. On examination, the right lower limb and foot were slightly swollen. A plain radiograph was performed in the first instance and this revealed a right diaphyseal tibial fracture. In a non-mobile infant of this age, nonaccidental injury (physical abuse) was considered as a cause for the injury. A skeletal survey was therefore performed.

On further questioning, the parents reported that there was also a background of possible developmental delay and hypotonia, but this had not yet been investigated. On examination by the pediatric team, the infant was also noted to be holding her neck in flexion, and her sclerae were thought to be slightly blue. This raised the possibility of an underlying skeletal dysplasia as an alternative explanation for the tibial fracture.

The initial plain radiograph of the lower limb revealed a mildly displaced and angulated fracture of the tibial diaphysis which appeared recent, as there was no evidence of healing (Fig. 1a and b).

The subsequent skeletal survey revealed multiple bilateral rib fractures, with imaging appearances making them highly likely of to be of different ages, (Fig. 2) and also multiple Wormian bones within the lambdoid and sagittal sutures of the skull (Fig 3a and b). Along with the clinical presentation, these findings raised the suspicion of osteogenesis imperfecta as an underlying cause, and the most likely diagnosis.

However, of particular concern on the skeletal survey, there was also a marked angulation in the mid-cervical spine with apparent joint space widening and anterior subluxation in the region of C2–3. (Fig 4a and b). Of note, there was no appreciable wedging of the cervical vertebrae or loss of vertebral height within the cervical spine. The alignment and vertebral height within the thoracic and lumbar spine were normal.

Because of concerns about cervical spine instability, a non-contrast CT of the cervical spine was performed immediately, whilst the infant was in the department. A small soft collar was sought by the spinal team, to give some support to the cervical spine during imaging.

A non-contrast CT head was also performed, to complete the skeletal survey, as per protocol and national guidance for infants under one year of age. The CT head revealed normal intracranial appearances with no intra- or extra-axial hemorrhage, and bony reconstructions of the skull were also performed, which better demonstrated the multiple Wormian bones.
The CT cervical spine confirmed a significant abnormality of alignment (Fig. 5). The C1 vertebra appeared normally aligned and intact for age, but there was a significant anterior subluxation of C2 on C3 with disc space widening. There was also angulation of the body of C2 with respect to the posterior elements, with apparent widening of the lateral synchondroses, greater on the right, and subtle widening of the right C2-3 facet joint, raising the possibility of a fracture dislocation at C2-3. (This was subsequently confirmed as a C2 fracture on follow-up imaging). Extreme ligamentous laxity was also a possibility, given the likely underlying diagnosis of osteogenesis imperfecta. At the C3 level, there was a linear lucency within the left pedicle which could reflect a fracture or delayed fusion of the synchondrosis. At the C4 level, there was significant canal narrowing with approximately two-thirds reduction in AP canal width, and potential for cord compression.
Due to concerns regarding potential spinal cord compression, an magnetic resonance imaging scan was also performed (Fig. 6). This revealed a marked cervical kyphosis centered upon C3/4 with loss of height of anterior vertebral bodies at these levels. There was no bony oedema to suggest acute injury and appearances were presumed long-standing and related to the underlying bone disorder. The sagittal calibre of the spinal canal was markedly narrowed at this point due to a combination of canal distortion secondary to the kyphosis and prominence of the anterior lip of the foramen magnum. Linear increased cord signal suggested underlying cervical myelomalacia. Subsequent axial images confirmed cord compression at these levels with diffuse increased signal within the cord.

The patient was referred to a specialist pediatric neurosurgical centre and underwent surgical reduction of the acute C3/4 kyphosis and treatment in an Aspen collar. The patient was referred for genetic evaluation and a subsequent diagnosis of compound heterozygous osteogenesis imperfecta Type XI was made. In this patient, there was no family history of OI.

Postoperatively, the hypotonia resolved, and there was no discernible persistent neurology. The child continues to be followed up at regular intervals by the spinal and pediatric teams. There are currently no further plans for intervention, and no developmental concerns.

A follow-up radiograph at 6 weeks demonstrated less marked cervical kyphosis, and a healing fracture through the posterior elements of C2 (Fig. 7). This was thought to be due to underlying osteogenesis imperfecta, possibly exacerbated by the ligamentous laxity common in this condition. The residual cervical kyphosis and this fracture will be followed up with serial radiographs, along with clinical assessment by the tertiary centre spinal team.

A full risk assessment was also performed by the community pediatric and social teams, and the conclusion was that there were no concerns regarding possible nonaccidental injury (physical abuse). The fractures at presentation were attributed to normal handling of a child with an underlying skeletal dysplasia. The infant and her family continue to be followed up, with the full co-operation of her parents.
Discussion

An underlying skeletal dysplasia is part of the differential diagnosis for multiple or unexplained fractures in non-mobile infants, and these fractures may occur with normal handling. A skeletal dysplasia should be considered along with nonaccidental injury (physical abuse), particularly if the skeletal survey reveals features in keeping with this diagnosis. Of course, children with an underlying skeletal dysplasia may also be subjected to nonaccidental injury (physical abuse), so a full risk assessment involving the pediatric and social care teams is still recommended in all cases.

The diagnosis in this case was mainly based on the genetic analysis. It is unknown whether the diagnosis of OI Type XI, an unusual type, is relevant to the unique findings and presentation in this case, particularly the severity of the cervical kyphosis.

This patient did not have obvious vertebral compression fractures as a cause for the severe cervical kyphosis, but follow-up radiographs did reveal a healing fracture through the posterior elements of C2.

Spondylosis and spondylolisthesis are recognised complications of osteogenesis imperfecta [5], mainly described in the lumbar spine in the literature, and vertebral kyphosis is commonly reported in the thoracic spine [6]. However, kyphosis and malalignment of the cervical spine is less well recognised [7] and the management, particularly the surgical management, is less well established.

This patient presented at a very young age, and the management of the cervical kyphosis and impending cord compression was therefore particularly challenging.

The effect of underlying osteogenesis imperfecta on the cervical spine includes basilar invagination, atlantoaxial instability, and fractures of the cervical spine [8]. However, cervical spine fractures are rare [8], and although dens, C2 pars, hangman and subaxial compression fractures have been reported during growth periods [8], to the authors’ knowledge, there are no cases in the literature of such a severe cervical kyphosis at such a young age. This patient had a fracture through the posterior elements of C2 which was difficult to diagnose definitively on the initial imaging, but was easier to visualise on follow-up radiographs, once there was some evidence of healing.

It was hypothesised that this fracture, possibly combined with ligamentous laxity, was the underlying cause of the severe cervical kyphosis and spinal cord stenosis. Since there was no bony oedema, it was hypothesised that this fracture had occurred sometime before presentation, perhaps even at birth, or in-utero. No cervical spine abnormality was identified at birth or at the routine baby check appointments, but the cervical spine in neonates is very difficult to examine, so the exact timing of the fracture was unable to be ascertained. It was thought best management to reduce the fracture and improve alignment, before stabilising in an Aspen collar. The follow-up radiographs did show evidence of fracture healing and the beginnings of bony union. The infant continues to be managed in the collar, pending further follow-up. The literature suggests that most cervical spine fractures in children with osteogenesis imperfecta heal well with external support, such as a rigid cervical collar or Halo body jacket [8].

In this case, the severe kyphosis revealed on the skeletal survey was an unexpected finding. Infants can be difficult to examine clinically due to large head size in relation to neck length, but as with any severe vertebral malalignment, the finding should prompt neurological examination and consideration of magnetic resonance imaging to image the spinal cord. In this case, there was some high signal abnormality within the spinal cord, and when combined with the clinical finding of some upper limb hypotonia, this influenced the decision for surgical management.

This patient did have slightly blue sclerae, but was too young to assess for dentogenesis imperfecta. An audiology referral was made, and no discernible hearing impairment has yet been identified. An echocardiogram was normal.

A skeletal survey with features in keeping with osteogenesis imperfecta should prompt clinical examination for any associated clinical features, and appropriate referral for investigation. These investigations may be normal, due to the variable phenotype of the disease. As with any skeletal dysplasia, specialist referral and multi-disciplinary input is required.

Declaration of Competing Interest

None.

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