Clinical History:

Female neonate delivered with elective Cesarean section at 38 weeks of gestation, because of suspicion of severe skeletal dysplasia based on prenatal ultrasound. After delivery, the neonate deceased within four hours due to respiratory failure.

Imaging Findings:

Prenatal ultrasound performed at 27 weeks of gestation showed severe skeletal dysplasia with a relatively small chest and multiple intrauterine fractures (Fig. 1 a-e). After interdisciplinary discussion and genetic counselling, elective Cesarean section was performed.

Post-mortem radiographic findings revealed osteopenia and markedly decreased ossification of the skull (Fig. 2 a), disproportionately small maxillofacial structures, flattening of the occipital bone (Fig. 2 b) and platyspondyly (Fig. 3 a-c). The thoracic cage was narrowed and the ribs showed a beaded appearance (Fig. 3 b). There were multiple fractures of the long bones with surrounding callus resulting in shortening, bowing and deformity (Fig. 4).

Discussion:

Based on the antenatal findings on ultrasound and the postnatal radiographic findings, the diagnosis of osteogenesis imperfecta (OI) type 2 according to the Silence and Glorieux classification was suggested. The diagnosis was confirmed postnatally by genetic testing consisting of analysis of COL1A1 and COL1A2 genes. OI is a genetic disorder characterized by bone fragility due to a defect of type I collagen. There are 7 types of OI, varying from mild to lethal (Fig. 5). The most common symptoms are bone fractures, skeletal deformity and short stature. Type 2 is a lethal form of OI incompatible with life. The cause of death is usually due to severe hypoxemia caused by pulmonary hypoplasia, leading to cardiac arrest or due to multiple fractures [1].

OI is a relatively uncommon disorder, affecting approximately 1 in 10,000 to 20,000 births [1]. Type 2 OI is rare, with an incidence of 1-2:100,000 [2]. As a perinatal lethal condition it always presents as a de novo mutation [2].

Prenatal diagnosis can be made in severe forms of OI, such as type 2, by ultrasound during the second trimester. Ultrasound may show non-specific signs such as growth retardation and polyhydramnios. Other ultrasound findings include decreased echogenicity and increased plasticity of bone due to insufficient bone mineralization and micromelia. Intrauterine fractures with surrounding callus are readily detected. The role of other antenatal imaging modalities such as CT and MRI is limited [1].

Postnatal diagnosis of OI can be made solely on clinical findings only in severe cases. Conventional radiography is usually mandatory. Radiographic findings of type 2 OI consist of osteopenia of the skull with disturbance of
intramembranous ossification, platyspondyly, small beaded ribs, severely deformed extremities and broad, crumpled, bent femurs [1-3].

Fig. 6. shows characteristic radiographic features of some other types of OI.

Confirmation of the diagnosis of type 2 OI can be obtained either with direct COL1A1/COL1A2 gene sequencing or biochemical analysis of type 1 collagen in cultured fibroblasts from a skin biopsy [2].

The prognosis of OI type 2 is poor, with some of the fetuses already dead in utero. Most infants will die in the perinatal period, 60% during the first day. Because of this infaust prognosis, the management is mainly supportive, with assisted ventilation and pain control [2].

**Differential Diagnosis List:** Osteogenesis imperfecta type 2 according to the Sillence and Glorieux classification., Other types of OI, Hypophosphatasia, Thanatophoric dysplasia, Campomelic dysplasia, Achondrogenesis.

**Final Diagnosis:** Osteogenesis imperfecta type 2 according to the Sillence and Glorieux classification.

**References:**


Description: Post-mortem anteroposterior radiograph of the skull shows decreased ossification of the calvaria. Origin: Vanhoenacker F. M. Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
Description: Post-mortem lateral radiograph of the skull showing decreased ossification, flattening of the occipital bone (arrows) and disproportionately small maxillofacial structures. Origin: Vanhoenacker F, Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
Description: Post-mortem anteroposterior radiograph of the trunk showing marked demineralization of the skeleton and abnormal bowing of the humeri, radii and ulnae (arrows). Origin: Vanhoenacker F.M., Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
**Description:** Enlarged view of the chest revealing beaded appearance of the multiple ribs (as demonstrated with arrowheads on the course of rib 8 R/L). Note also presence of an umbilical vein catheter. **Origin:** Vanhoenacker F, Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
Description: Post-mortem lateral radiograph showing flattening of the vertebral bodies (as demonstrated on a lumbar vertebra (thick arrow); Note also bowing fractures of the long bones (small arrows). Presence of an umbilical vein catheter. Origin: Vanhoenacker F, Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
Description: Post-mortem radiograph of the right limbs showing shortening, bowing and callus formation of the long bones due to fractures (arrows). This results in a typical accordion-like appearance of the tubular bones. Origin: Vanhoenacker F.M., Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
Description: Type I OI. Note osteoporosis, mild overmodelling of the long bones and fractures sequelae of a different date at the left distal femoral diaphysis (arrow) and medial proximal tibia diaphysis (arrowhead). Origin: Vanhoenacker F.M., Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
Description: Type III OI in a 1 year-old male. Note osteoporosis, marked deformities of the femora with bilateral fracture sequelae of the femoral diaphyses. There is hypertrophic callus at the right femoral diaphysis (arrow). Origin: Vanhoenacker F.M., Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
**Description:** Type III OI. Note popcorn calcifications of the proximal humeri (arrows) and severe kyphoscoliosis. **Origin:** Vanhoenacker F.M., Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
Description: Type IV OI in an adult patient. Note spontaneous fracture at the left femoral diaphysis and dense metaphyseal bands in the distal femur (arrow) and proximal tibia due to bisphosphonate treatment. Origin: Vanhoenacker F.M., Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
Description: Type V OI. There is an incompletely healed fracture at the middiaphysis of the right femur with hyperplastic callus formation (arrow). Note dense metaphyseal lines within the distal femur and proximal tibia. Origin: Vanhoenacker F.M., Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
Description: Transverse image of the skull. Note soft, depressible skull, with flattening of the parietal bone on pressure with the ultrasound transducer (arrow). Origin: Leroij Y., Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
**Description:** Axial image of the chest. The fetal cardio-thoracic circumference ratio is 0.55 (normal value < 0.5), indicating relative narrowing of the chest. Note deformed ribs (arrows) due to fractures.

**Origin:** Leroij Y., Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
Description: 3D-ultrasound image of the chest depicting irregular delineation of multiple ribs in keeping with rib fractures (arrows). Origin: Leroij Y., Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
Description: Longitudinal image of the femur showing shortening of the diaphysis compared to gestational age, broadening and bowing. Origin: Leroij Y., Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
Description: Marked shortening of the ulna and radius compared to gestational age. Origin: Leroij Y., Department of Radiology, Antwerp University Hospital, Edegem, Belgium.
**Figure 6**

<table>
<thead>
<tr>
<th>Type</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (mild)</td>
<td>Fractures, minor deformities, Wormian bones, codfish vertebrae, osteopenia</td>
</tr>
<tr>
<td>II (perinatal/lethal)</td>
<td>Fractures in utero, severe deformities, beaded ribs, small thorax, platyspondyly</td>
</tr>
<tr>
<td>III (severe)</td>
<td>Fractures, major deformities, popcorn calcifications (metaphyses), Wormian bones, codfish vertebrae, kyphoscoliosis, severe osteopenia</td>
</tr>
<tr>
<td>IV (moderate)</td>
<td>Fractures, Wormian bones, codfish vertebrae</td>
</tr>
<tr>
<td>V, VI, VII and VIII have recently been added. (These types do not have a characteristic type I collagen mutation)</td>
<td></td>
</tr>
<tr>
<td>Type V</td>
<td>Fractures, hyperplastic callus formation, metaphyseal dense lines, interosseus membrane ossification</td>
</tr>
<tr>
<td>Type VI</td>
<td>Looser striations mimicking fractures</td>
</tr>
<tr>
<td>Type VII</td>
<td>Fractures, coxa vara</td>
</tr>
<tr>
<td>Type VIII</td>
<td>Fractures at birth, severe osteopenia</td>
</tr>
</tbody>
</table>

**Description:** Table showing the different types of OI according to the Sillence and Glorieux classification and most characteristic (imaging) features. **Origin:** Vanhoenacker F.M., Department of Radiology, University Hospital Antwerp, Edegem, Belgium.