

Imaging in osteogenesis imperfecta

Igor Borić, Renata Prpić Vučković*

Osteogenesis imperfecta (OI) is a congenital genetic disorder with skeletal or extra-skeletal manifestations. Phenotypic features and mode of inheritance, clinical features, and radiographic findings make the basis for the currently accepted classification system of OI. The antenatal and postnatal diagnosis of the disease using different radiographic methods (plain radiography, ultrasonography, computed tomography and magnetic resonance imaging) is described and characteristic appearances of bone and other deformities are analyzed. Distinctive bone manifestations of OI are illustrated using typical examples. Finally, we give a comment on differential diagnosis.

Key words: osteogenesis imperfecta, radiography, imaging

Osteogenesis imperfecta (OI) is a congenital, genetic disorder of collagen type I synthesis that involves connective tissues and bones, and is characterized by increased bone fragility and decreased bone density. There is extreme variation in clinical symptoms based on genetics and subtypes including blue sclera, dental fragility, and hearing loss. Depending on the disease severity, bone fragility may lead to perinatal death or can cause severe deformities that persist into adulthood (1, 2). Phenotypic features and mode of inheritance, clinical features, and radiographic findings make the basis for the currently accepted classification system of OI (2, 3).

Manifestations of OI may be skeletal and extra-skeletal.

Extra-skeletal manifestations are diverse and inconstant, i.e. blue sclera (mainly in type I OI); greyish or yellowish aspect of the teeth (dentinogenesis imperfecta, mainly in type III OI); skin fragility; joint and ligament hyperlaxity; early hearing loss; and cardiovascular abnormalities (particularly aortic valve disease). Less frequently, neurologic abnormalities related to basilar impression and platybasia (mainly in type IV OI) or direct involvement of neurovascular structures may be encountered.

Skeletal manifestations dependent on the severity of the disease include multiple, repeated or unexplained fractures that may lead to short stature and progressive deformities of the spine (kyphosis, scoliosis), rib cage or lower limbs (discrepancy in length, bone bowing) (4-6).

There are several radiographic methods that are used in detection and evaluation of OI in prenatal and postnatal peri-

od: radiography, ultrasonography (US), computed tomography (CT) and magnetic resonance imaging (MRI) (3, 7, 8).

The preferred radiographic examination for initial investigation of OI is plain radiography because most of the imaging characteristics of this disease are apparent on plain radiographs.

Prenatal ultrasonography plays a role in the diagnosis of OI; typical findings include fractures, decreased calvarial ossification, or fetal head compression by the ultrasound probe (4, 7).

The role of CT is limited because of ionizing radiation, especially in prenatal diagnostics, whereas MRI plays an important role in assessing for associated complications (3, 8).

PRENATAL DIAGNOSTICS OF OI

Ultrasonography

The diagnosis of OI may be made reliably using US by gestational week 17. Nonspecific signs such as intrauterine growth retardation or hydramnios may be seen. The diagnosis may be made by analyzing collagen synthesized by chorionic villus cells after US-guided chorionic villus sampling.

Severe forms of OI can be diagnosed by US during second trimester of pregnancy. Otherwise, examination may show

* Sv. Katarina Special Hospital, Zabok, Croatia

Correspondence to:

Igor Borić, MD, PhD, Sv. Katarina Special Hospital, Bračak 8a, HR-49210 Zabok, Croatia, e-mail: igor.boric@svkatarina.hr

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TABLE 1. Radiographic characteristics of osteogenesis imperfecta

Part of the body	Radiologic changes
Head, neck and spine	Craniocervical junction abnormalities including basilar invagination
	Wormian bones
	Kyphoscoliosis
	Vertebral compression with/without fractures
	“Codfish vertebrae” – vertebral collapse (biconcave vertebral body)
	Platyspondyly – flattened vertebral body shape with reduced intervertebral space
Chest	Pectus excavatum
	Pectus carinatum
Pelvis	Acetabular protrusion
	Coxa vara
General bone changes	Severe osteoporosis
	Deformed, gracile (over-tubulated) bones
	Thinning of the cortical bone
	Hyperplastic callus formation
	“Popcorn” calcification: the metaphysis and epiphyses exhibit numerous scalloped radiolucent areas with sclerotic margins
	“Zebra stripe sign”: cyclic bisphosphonate treatment produces sclerotic growth recovery lines in the long bones
	Formation of pseudarthrosis in places of healing fractures – exuberant callus formation

abnormalities of the skull, decreased echoes from the calvarium with supervisualized intracranial structures, rib cage and multiple rib fractures, decreased echogenicity due to insufficient mineralization, increased bone plasticity, e.g., bowing and angulation of long bones, deformities related to fractures, callus formation, and micromelia (3, 7-10).

Magnetic resonance imaging

The role of MRI is in visualization of fetal brain or visceral organs to look for associated abnormalities or to assess fetal lung volume (3).

POSTNATAL DIAGNOSTICS OF OI

Radiography

In case of suspected OI, postnatal radiographs should include views of the long bones, skull, chest, pelvis, and thoracolumbar spine. Radiographic features are related to OI type and severity. Some findings, however, may be seen in all subtypes (8). Radiographic changes characteristic of OI are summarized by body regions in Table 1.

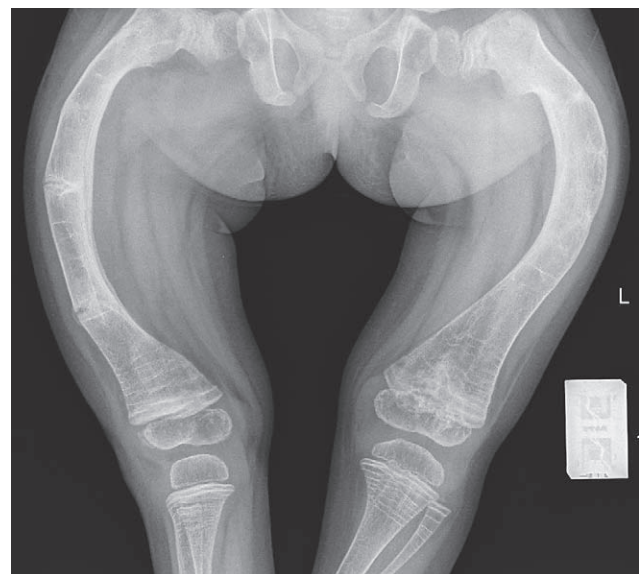


FIGURE 1. Anteroposterior radiograph of the thigh in a child with osteogenesis imperfecta shows considerable deformity of both proximal femurs with abnormal bone remodeling and associated multiple fractures caused callus formation.

A common radiographic finding in OI is generalized osteoporosis of both axial and appendicular skeleton. Milder forms of this condition result in overtubulated long bones with thin cortices and possible fractures. Short tubular bones may also be affected but they are less frequently fractured. In milder forms of OI, skull radiographs may show normal skull development.

If the hallmark bone findings of OI are detected on plain radiographs, the diagnosis may be made with a high degree of confidence and confirmation with other imaging modalities is not needed.

More severe forms of osteogenesis imperfecta, such as types II and III feature thickened, shortened long bones with multiple fractures (Figure 1). These conditions are often complicated by hyperplastic callus formation that is most often found around bone diaphysis and is often large, appearing as a dense, irregular mass arising from the cortex of the bone (Figure 2). This callus is associated with thickened periosteum, and its presence causes other differential diagnostic considerations, including osteosarcoma, *myositis ossificans*, chronic osteomyelitis, and osteochondroma.

In severe forms of OI, the skull demonstrates poor mineralization and multiple wormian or intrasutural bones are seen (Figure 3).

The chest volume is usually small with multiple rib fractures (Figure 4); these can cause the ribs to become broad and deformed. In addition, spinal abnormalities in all OI subtypes include platyspondyly and scoliosis that may have influence on chest volume (Figure 5) (3, 8).



FIGURE 2. Anteroposterior (a) and lateral (b) radiograph of the calf in a child with osteogenesis imperfecta shows hyperplastic callus formation around tibial and fibular fracture in bone diaphysis.

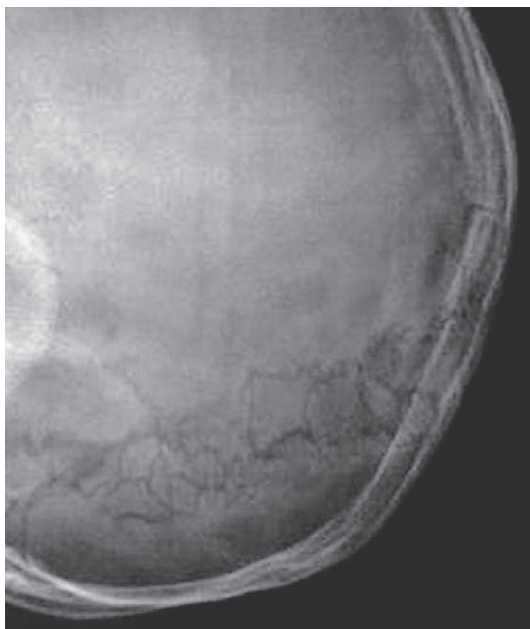


FIGURE 3. Lateral radiograph of the occipital part of the skull shows multiple wormian bones in the lambdoid sutures.

Recent advances in the treatment of OI with bisphosphonates have resulted in specific imaging findings. The “zebra stripe sign” producing sclerotic growth recovery lines in the spine and long bones occurs when children with OI have been treated with cyclic bisphosphonate therapy, e.g., pamidronate. In long bones, these dense lines (Figure 6) are

parallel to the growth plate; they are located in the metaphysis and move towards the diaphysis in step with bone growth. Each dense line corresponds to one intravenous course of therapy, and the space between two lines depends on the bone growth rate and delay between two courses (9). In differential diagnosis of these dense bone lines, the “growth arrest lines” (growth resumption lines, Harris lines or Park lines), i.e. transverse rings of sclerosis at the metaphysis of a long bone as a sign of growth arrest of long bones have to be considered. The radiographic finding results from alternating cycles of osseous growth arrest and growth resumption. This appears to result from pathologic levels of stress during bone development (e.g., disease, malnutrition) (9).

Some radiographic findings are more specific to certain OI subtypes than others, as follows (1, 3, 8):

a) Type I-specific radiographic features of osteogenesis imperfecta

In type I osteogenesis imperfecta, bone fragility is mild, and there are minimal bony deformities; kyphoscoliosis is found in almost 20% of patients (Figure 5) (8).

b) Type II-specific radiographic features of osteogenesis imperfecta

Type II osteogenesis imperfecta is further categorized into 3 subtypes on the basis of radiographic features of long

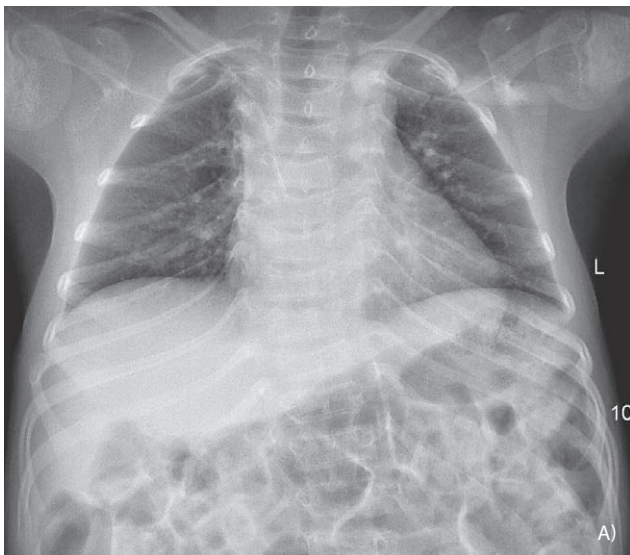


FIGURE 4. Anteroposterior radiograph of the chest (a) in two children with osteogenesis imperfecta shows multiple rib fractures with callus formation (I, II, VII left ribs, and VII and IX right ribs) in one child, and (b) marked thinning of the posterior ribs associated with right VII and VIII rib fractures developing callus in another child.

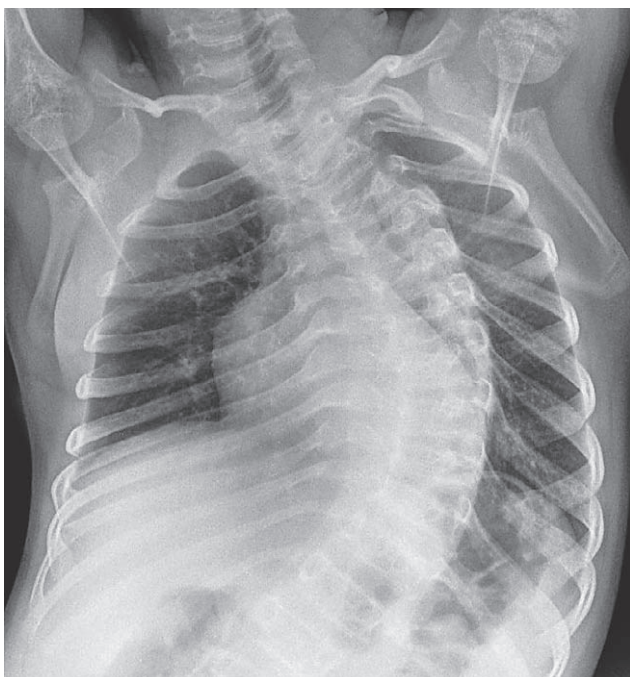


FIGURE 5. Anteroposterior radiograph of the chest in a child with osteogenesis imperfecta shows severe thoracic spine deformity, i.e. kyphoscoliosis.



FIGURE 6. Anteroposterior radiograph of the thigh in a child with osteogenesis imperfecta shows marked deformity of the femur. Multiple dense lines in the distal femur and proximal tibia associated with dense metaphyseal bands along the cartilaginous plates related to bisphosphonate therapy ("zebra stripe sign").

bones and ribs. In types IIA and IIB, the long bones are short and broad because of undermodeling; the bones are also crumpled (Figure 1). In type IIC, the long bones are thinner and longer than in other subtypes, although they are still undermodeled.

In type IIA, the ribs are short and broad with continuous beading. In type IIB, beading is absent or minimal and discontinuous. In type IIC, the ribs are thin and beaded.

c) Type III-specific radiographic features of osteogenesis imperfecta

Scoliosis of the thoracolumbar spine is specific to type III osteogenesis imperfecta; approximately 25% of patients with

type III osteogenesis imperfecta have scoliosis. Most affected patients have an S-shaped scoliosis (Figure 5) (6, 10).

Severe platyspondyly with vertebral compression fractures and “codfish vertebrae” are more common in this type of OI than in other types (Figure 7, 8).

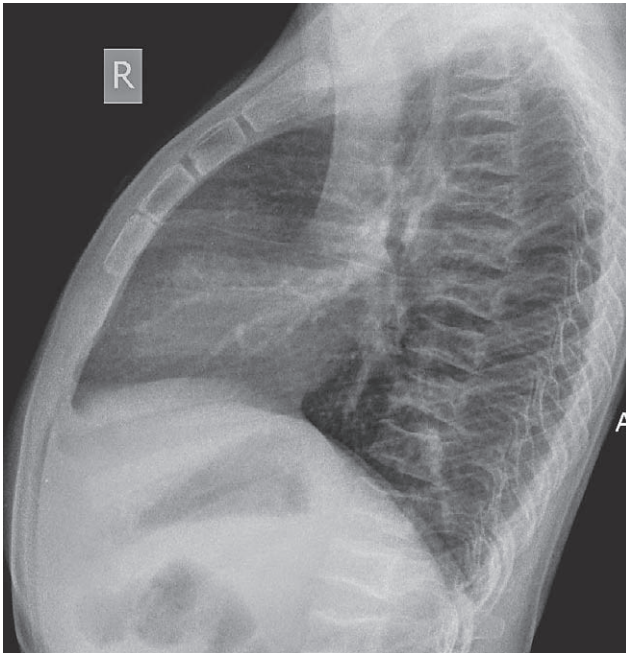
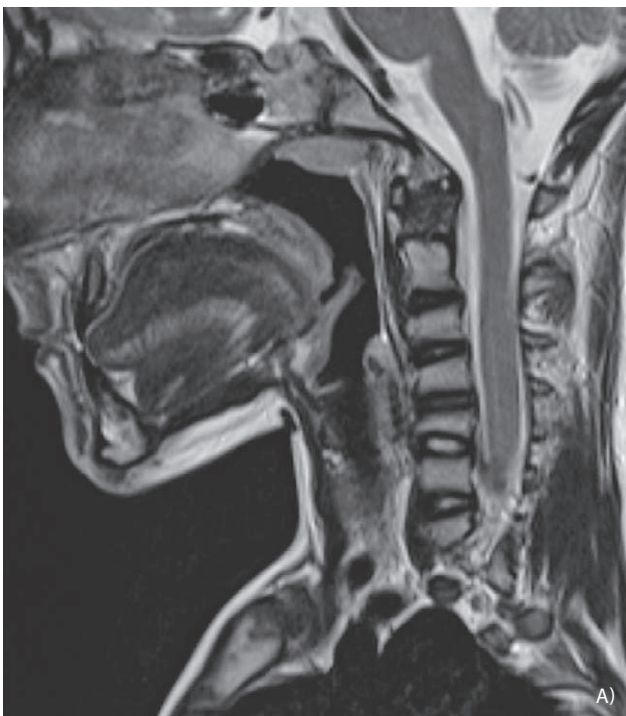


FIGURE 7. Lateral radiograph of the chest in a young child with osteogenesis imperfecta shows severe and multiple vertebral collapses (“codfish vertebrae”).



“Popcorn calcifications” are commonly seen in the metaphyseal-epiphyseal region of long bones, most commonly at the knee and ankle (Figure 9). This results from repeated microfractures at the growth plate (10).

Soft craniofacial bones with a large, thin calvarium cause triangular facies.

d) Type IV-specific radiographic features of osteogenesis imperfecta

Radiographic findings of type IV osteogenesis imperfecta are similar to the general findings and findings specific to type I disease but the severity of bone fragility is slightly increased. The feature that is more commonly associated with type IV than other types is basilar invagination with or without brainstem compression (Figure 10): projection of the tip of the odontoid process above the McGregor line (straight line connecting the upper surface of the posterior edge of the hard palate to the most caudal point of the occipital curve) suggests the presence of basilar invagination (11, 12).

e) Type V-specific radiographic features of osteogenesis imperfecta

The type V category has been added to include patients with osteoporosis or interosseous membrane ossification of the forearms and legs, as well as patients who are prone to the development of hypertrophic calluses (13, 14).



FIGURE 8. Sagittal (a) and coronal (b) magnetic resonance imaging of the cervical spine in a child with osteogenesis imperfecta showing severe and multiple vertebral collapses associated with kyphoscoliosis.



FIGURE 9. Anteroposterior radiograph of the knee in a child with type III osteogenesis imperfecta and a history of femoral osteosynthesis shows "popcorn" calcifications with sclerotic margins.

Computed tomography

The role of CT imaging in OI is in adjunctive problem-solving. This modality may be used to further assess for basilar impression, to evaluate the petrous bone for narrowing of the middle ear or otosclerosis, and to support bone mineral densitometry (BMD) (15).

Because of ionizing radiation, it is recommended to use other imaging methods instead of CT to skip harmful effect of x-rays.

Magnetic resonance imaging

The major role of MRI in OI is in problem-solving. MRI is also used to image complications of the disease, such as basilar impression that is frequently associated with type IV osteogenesis imperfecta. Although cervical spine radiography and CT scanning may demonstrate this abnormality well, MRI has the advantage of detecting associated compression of the spinal cord. Other associated conditions that may better be imaged using MRI than plain radiography include syringohydromyelia and communicating hydro-



FIGURE 10. Sagittal magnetic resonance imaging of the craniocervical junction shows basilar invagination without brainstem compression.

cephalus, especially if these conditions develop after fontanelle closure. MRI may show intracranial anomalies and anomalies of visceral organs or spine as a prenatal diagnostic tool (16).

DIFFERENTIAL DIAGNOSIS

Because osteoporosis and multiple fractures are hallmark features of OI, other disorders that cause multiple fractures or decreased bone mineralization may be considered in the differential diagnosis, such as child abuse, juvenile osteoporosis, steroid-induced osteoporosis, Menkes (kinky-hair) disease, hypophosphatasia, battered child syndrome (syndrome X) and temporary brittle-bone disease. It is important to differentiate OI from non-accidental injury (NAI), and radiographic examination including skeletal survey can be helpful in differentiating these two pathologic entities. In NAI, some fractures are very suggestive of abuse (i.e. posterior rib fractures, metaphyseal corner fractures and complex skull fractures).

Rib fractures usually result from anteroposterior compression of the rib cage when the child is held around the chest and shaken back and forth. The posterior involvement is due to excessive leverage of the posteromedial part of the rib over the transverse process of the spine and is highly specific of abuse.

Long bone fractures may be encountered in NAI, but in contrast to OI, where the fractures most commonly affect the diaphyseal regions, they classically involve the metaph-

ysis, especially that of the distal femur, the proximal and distal tibia and, less frequently, the proximal humerus. Metaphyseal corner fractures, also known as classic metaphyseal lesions, are pathognomonic for abuse.

Skull fractures result from direct trauma. Bilateral fractures, fractures involving more than one cranial bone, fractures with complex configuration, fractures that cross suture lines, depressed fractures, and fractures associated with underlying intracranial lesions all suggest NAI (17-19).

List of abbreviations

OI – osteogenesis imperfecta
MRI – magnetic resonance imaging
CT – computed tomography
US – ultrasonography
BMD – bone mineral densitometry

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Nema/None

ETIČKO ODOBRENJE/ETHICAL APPROVAL

Nije potrebno/None

SUKOB INTERESA/CONFLICT OF INTEREST

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SAŽETAK

Slikovne metode kod osteogenesis imperfecta

Igor Borić, Renata Prpić Vuković

Osteogenesis imperfecta (OI) je nasljedni genetički poremećaj koji nije povezan sa spolom, a ima koštane i ne-koštane manifestacije. Fenotipska obilježja i način nasljeđivanja, klinička obilježja i radiografski nalazi čine osnovu za danas prihvaćeni sustav klasifikacije OI. Opisuje se antenatalna i postnatalna dijagnostika ove bolesti pomoću različitih radiografskih metoda (radiografija, ultrazvuk, kompjutorizirana tomografija i magnetska rezonancija), uz analizu znakovitih pojavnosti koštanih i drugih deformacija. Osobite koštane manifestacije OI ilustrirane su tipičnim primjerima. Na koncu se nalazi komentar autora o diferencijalnoj dijagnostici kod OI.

Ključne riječi: osteogenesis imperfecta, radiografija, slikovne metode