Imaging in Genetic Skeletal Dysplasias

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Abstract:

Skeletal dysplasias (SD) are clinically a heterogeneous group of genetic disorders characterized by the presence of generalized disorder of bone growth. The incidence of SD in India is not known. In US, it is one case per four thousand to five thousand births. However, prenatal deaths due to SD are about nine thousand. There are about 372 SDs and 215 of which are associated with 140 genes. In this article the imaging diagnostic criteria of some of the dysplasias are described.

Hereditary sclerosing SDs result from disturbance in the pathways involving osteoblast/osteoclast regulation, leading to excessive bone formation. Hereditary sclerosing SDs include osteopetrosis, pycnodysostosis, osteopoikilosis, osteopathia striata, progressive diaphyseal dysplasia, hereditary multiple diaphyseal sclerosis, hyperosteosis corticalis generalizata and melorheostosis.

In many instances, plain radiography is enough for diagnosis. Rarely, other imaging methods are needed.

In osteopetrosis generalized increase in bone density is noted while pycnodysostosis is a hybrid between osteopetrosis and cleidocranial dysostosis. Hence, besides increase in bone density, Wormian bones in the skull, dysplasias of clavicles, mid line defects and acroosteolysis are noted. Osteopiklisis consists of multiple dense islands of bone mostly scattered around joints. Osteopathia striata shows multiple linear striations of bone. Progressive diaphyseal dysplasia consists of dense thick tubular bones. Melorheostosis consists of dripping candle appearance of new bone along the shafts.

Keywords:

Sclerosing Skeletal Dysplasias (SSD), genetics-plain radiography.

Imaging in Genetic Skeletal Dysplasias:

Skeletal dysplasias (SD) are clinically a heterogeneous group of genetic disorders characterized by the presence of generalized disorder of bone growth. The incidence of SD in India is not known. In US, it is one case per four thousand to five thousand births. However, prenatal deaths due to SD are about nine thousand. There are about 372 SDs and 215 of which are associated with 140 genes. Radiology and imaging play a great role in confirming the clinical diagnosis of all the imaging plain radiography is the best screening method for diagnosis. The lethal dysplasias are generally diagnosed by ultrasonography of fetus.

Among the non lethal sclerosing SDs and their imaging findings are described here. The minimum radiographs required include skull, chest, pelvis, long bones, hands and spine. The recent classification of the SDs is best on the genes responsible for the disorder. The classification of sclerosing dysplasias is given in table I

Table I - SCLEROSING DYSPLASIAS

- Osteopetrosis
- Pycnodysostosis
- Osteopoikilosis
- Osteopathia striata
- Dysosteosclerosis
- Worth’s sclerosteosis
- Van buchem’s dysplasia
- Camurati Engelman’s dysplasia
- Ribbing’s dysplasia
- Pyle’s metaphyseal dysplasia
- Melorheosteosis
- Osteoectasia with hyperphosphatasia
- Pachydermoperiosteosis (Touraine-Solente-Gole Syndrome)

Time / space does not permit to describe all the entities. Hence, some of the entities are dealt with.

Osteopetrosis (Marble Bones). Three forms are reported. The most common form is autosomal dominant. The second common is malignant form which is autosomal recessive. The rare form is associated with tubular acidosis. In all the forms generalized increased in bone density is noted (fig.1). The normal trabeculae are obliterated. With trauma, banana type of fractures are noted in long bones (fig. 2). The normal bone density and the increased density produce transverse bands in long bones and flat bones. A bone within a bone pattern is noted particularly in innominate bones, calcaneum and ribs (fig. 3). Modeling deformities of long bones are also noted (fig.4). In spine, sandwich vertebra is common. Changes in skull or variable with increased density at the base (fig.5). In osteopetrosis associated with tubular acidosis rachitic changes are noted.

Fig. 1: Osteopetrosis - Generalized bone density in the feet of a child
Fig. 2: Osteopetrosis – Osteosclerosis with obliteration of the trabeculae. Note the “banana” type of fracture in the left femur.

Fig. 3: Osteopetrosis – “Bone in bone” in the hand.

Fig. 4: Osteopetrosis - Modeling deformity simulating Erlenmyer Flask appearance.
Pycnodysostosis (Toulouse-Lautrec) - French Artist had similar features

It is a hybrid between osteopetrosis and Cleidocranial dysostosis. Major sites include skull, mandible, clavicles and spine. All the bones are uniformly sclerotic. However, skull findings include frontal bossing, persistent fontanels, wormian bones an obtuse angle of mandible is noted (6). There is clavicular hypoplasia (fig. 7). Acro osteolysis is noted (fig. 8).

Fig. 5: Osteopetrosis – lateral view of skull. Note the dense bones at the base of the skull

Fig. 6: Pycnodysostosis – Note the obtuse angle of the mandible
Fig. 7: Pycnodysostosis – Note the hypoplasia of the clavicles

Fig. 8: Pycnodysostosis – Note acro osteolysis

The major differences between osteopetrosis and pycnodysostosis include persistent fontanels and wormian bones in the skull, obtuse angle of mandible, clavicular hypoplasia and acro osteolysis, which are present in pycnodysostosis.

OSTEOPOIKILOSIS – Autosomal dominant
It is relatively uncommon familial disorder and seen at any age. Punctuate or even short linear densities of compact bone varying in size from 1-10mm are noted. These are common towards long bones particularly articular ends (fig.9). Common in pelvic bones (fig.10ab). Spine, skull and ribs rarely show the findings. Findings are similar to bone islands, which are inclusions of cortical bone in spongiosa.

Fig. 9: Osteopoikilosis – Note the spotty bones at the juxta articular region of the hip

Fig. 10ab: Osteopoikilosis – a. CT, b. MRI (over investigations)
Patients having both osteopoikilosis and osteosarcoma have been described. Osteosarcoma is related to active osteogenesis. It has been proposed that perhaps the chronic remodeling of osteopoikilosis has resulted in malignant degeneration.

Osteopathia striata

It is another sclerosing dysplasia affecting the secondary spongiosa, generally detected incidentally. It is characterized by multiple linear densities of varying widths. These are prominent in the ends of long bones within medulary cavities. They may extend into epiphysis (fig.11ab). Linear striations may also occur in other sclerosing dysplasias.

Fig. 11ab: Osteopathia Striata, knee – a. Child, b. Adult

DYSOSTEOSClerosis

Radiological findings include progressive marked hyperostosis of the skull and mandible (fig. 12). The vertebral endplates, pedicles and the bones of the pelvis are sclerotic (fig. 13ab). The long bones are enlarged, with cortical hyperostosis. Moderate alteration of the bone contours, and lack of normal diaphyseal constriction and pathologic fractures do not occur.
WORTH’S SCLEROSTEOSIS

It is another variant of dysostosclerosis. Radiographic findings include endosteal thickening in the cortex of the tubular bones with encroachment on the medullary cavity. Osteosclerosis begins in the base and subsequently involves the facial bones, especially the mandible. The latter bone lacks the normal antegonial notch, and the mandibular canal may be prominent.
Van Buchem's Type of Endosteal Hyperostosis - Hyperostosis corticalis generalisata. It is a rare hereditary autosomal recessive disorder. Calvaria, mandible, clavicles, innominate bones and extremity bones are involved (fig.14). Specific abnormalities include periosteal excrescences in the tubular bones, osteosclerotic and enlarged ribs, and clavicles, and increased radiodensity of the spine, particularly prominent in the spinous processes.

Fig. 14: Van Buchem’s - Hyperostosis corticalis generalisata - Note the sclerosis of the cranio-mandibular bones

Camurati –Engelmann disease - Progressive diaphyseal dysplasia

This is an autosomal dominant disorder which manifests during childhood. The disease begins in the diaphysis of long bones. Bilateral and symmetrical cortical findings are noted. It may eventually spread to the metaphysis (fig. 15ab).
Fig. 15a: Camurati–Engelmann disease - Progressive diaphyseal dysplasia involving the bones of the lower limbs

Fig. 15b: Engelmann’s disease – Widened diaphyses with new bone indicating progressive diaphyseal dysplasia
The disease is always symmetric and the lower extremities are usually more affected than the upper extremity. In mild cases there is only slight thickening of the cortex in the mid-diaphysis (fig. 16ab). In more advanced cases midshaft sclerosis is more pronounced and widespread and involve the diaphysis as well as the metaphysis approaching the epiphysis. Intra articular spaces are not involved. The sclerotic process is accompanied by uniform thickening of cortex. Irregular endosteal and periosteal apposition, and narrowing of the medullary canal. Valgus and Emlenmeyer flask deformities are seen in advanced cases. In severe cases there is sclerosis of the skull base and sometimes mandibular involvement, especially in the region of the temporomandibular joint, in addition to the other findings. In the most severe cases the sclerotic changes involve the entire skull, the vertebral column, metacarpal and metatarsal bones, and the shoulder girdle. The pelvic, carpal, and tarsal bones are not involved.

Fig. 16ab: Progressive diaphyseal dysplasia starting at the mid diaphyses of bones of lower extremities

Ribbing's

This is hereditary and autosomal dominant recessive. Symetrical, fusiform, diaphyseal, osteosclerosis and hyperostosis are noted (fig. 17). Single long bone may also be involved.
Differential diagnosis of Ribbings include, progressive diaphyseal dysplasia, (Camurati-Engelmann dysplasia), haemato-diaphyseal dysplasia (Ghosal syndrome) and infantile cortical hyperostosis (Caffey’s disease) which is not bilateral and symmetrical. Engelmann disease presents during childhood with bilateral and symmetrical bone involvement, whereas ribbing disease may be unilateral and asymmetrical. In Engelmann's the skull is involved whereas in Ribbing’s disease only long bones are involved. Engelmann is autosomal dominant while ribbing is autosomal recessive in fact both of them may represent phenotypic variation of the same disorder.

Pyle’s Disease - Metaphyseal Dysplasia

Radiological findings include wide metaphyses with florentine flask deformity of long bones. Wide medial ends of clavicles are also noted (fig. 18ab). In craniometaphyseal dysplasia, mild hyperostosis of skull is noted, with poor aeration of sinuses and prominent supraorbital ridges (fig. 19).
Fig. 18ab: Pyle’s – a. flaring of the medial ends of clavicles and proximal ends of femora, b. Note the sclerosis in the pubic bones and coxavara deformity.

Fig. 19: Cranio Metaphyseal Dysplasia. Note the sclerosis in the base of the skull and mandible

Melorrheostosis (Flowing Hyperostosis)
It may be monostotic, monomelic or polyostotic. Radiologically the hyperostosis appears like wax dripping down on one side of the burning candle. Linear and segmental, flowing hyperostosis corresponding to sclerotomes is noted. The hyperostosis skips joints (fig. 20abc). Hyperostotic bone is also noted in soft tissues. The bony over growth simulates osteochondroma (fig. 21).

Fig. 20abc: Melorrheostosis – a. Knee, b. Hand, c. Femur.

Note the hyperostosis and dripping wax of a burning candle
Fig. 21: Melorrheostosis - Simulates exostosis of Ischium

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