ABSTRACT

The normal development and growth of various structures in human body gives distinct appearance to the body with proper functions. Growth of individuals mainly depends upon the growth of long bones. Cartilage in epiphyseal end of long bones proliferates to form matrix which gets converted into bone by ossification and calcification. Continuous formation of matrix, conversion of bone helps the longitudinal growth of bone. Various factors disturb the endochondral ossification in various places including the long bones and the growth of bone is disturbed causing stunted growth with deformities in the individual. Thorough study of the facts and truths of disturbances of cartilage growth of long bones and other parts of bone would help in research to find out the possible remedies to solve the problem in cartilage dysfunction. Hence the present article is prepared to review the various aspects of cartilage, cartilage growth disturbances in endochondral ossification, stunted growth and deformities.

Key Words: Cartilage, Basicranium, Mandibular condyle, Epiphyseal cartilage

INTRODUCTION

Skeletal growth and growth in longitudinal direction of an individual depends upon proper cartilage function as cartilage plays a vital role in multiple growth centers of the body. Mesenchyme of embryonic germinal layer gives rise to formation of cartilage by producing cartilaginous matrix in which fibers are embedded to form homogenous cartilage. Depending upon the amount and type of fibers, the cartilage is called as hyaline cartilage, elastic cartilage and fibroelastic cartilage. Cartilage exists in pinna of the ear, nose, nasal septum, respiratory tract, ribs and articular surfaces of joints. In cartilage growth center cartilage proliferates and elaborates a matrix which is slowly replaced by ossification and calcification to form bone through endochondral ossification. This normal physiological function of cartilage turning into bone is affected by known and unknown causes. The development and growth of bone particularly the long bones are affected causing stunted growth and deformities. These disorders are being described and discussed in this article.

CARTILAGE GROWTH CENTERS

Cartilage growth centers exist in many places of the body but the following places are important for the growth of structure:

1. Basicranium
2. Condyle of mandible
3. Epiphyseal end of long bones

CARTILAGE IN BASICRANION

Cartilage growth center exist in the base of the skull in the form of synchondrosis. Cartilage synchondrosis is bipolar cartilage cells on either side with a central zone of persistent cartilage cells. Depending upon the amount and type of fibers, the cartilage is called as hyaline cartilage, elastic cartilage and fibroelastic cartilage. Cartilage exists in pinna of the ear, nose, nasal septum, respiratory tract, ribs and articular surfaces of joints. In cartilage growth center cartilage proliferates and elaborates a matrix which is slowly replaced by ossification and calcification to form bone through endochondral ossification. This normal physiological function of cartilage turning into bone is affected by known and unknown causes. The development and growth of bone particularly the long bones are affected causing stunted growth and deformities. These disorders are being described and discussed in this article.

Sphenoid bone in the anterior part is attached with pterygoid plates which in turn join the maxillary bone. Growth of sphenoid bone in basicranium pushes the pterygoid plates which in turn push to maxilla to form mid-
dle part of face. Any disturbances in the development of sphenoid bone in the anterior part of sphenoid-occipital synchondrosis causes arrested growth of sphenoid bone. Failure of forward growth of maxilla occurs due to the arrested growth in the base of the sphenoid bone [figure 1] and this causes the deformity of retracted maxilla in the midface.

**CLINICAL CHANGES DUE TO DISTURBANCE OF SPHENOID BONE FORMATION IN THE CRANIAL BASE**

In the craniofacial development, midface hypoplasia in cleidocranial dysostosis occurs and this is due to inadequate ossification of the cranial base\(^1\)\(^2\). As a result of the disturbance in formation of sphenoid bone in cranial base the forward movement of maxilla is not possible. In Crouzon\(^5\)\(^9\)\(^12\) syndrome [figures 4, 5 and 6] due to genetic disturbance, early closure of sphen-occipital synchondrosis occur due to failure in the development of the anterior part of sphenoid bone and posterior part of occipital bone. This results in short base of skull and midface hypoplasia[figures 4, 5 and 6]. Midface malformation due to cranial base disturbances also occurs in Apert syndrome\(^2\) and Turner's syndrome\(^12\). Midface hypoplasia occurs in achondroplasia due to the disturbances of cartilage growth in sphenoid-occipital synchondrosis\(^3\).

**CARTILAGE IN CONDYLE OF MANDIBLE**

The head of mandibular condyle articulates within the glenoid fossa to form temporomandibular joint\(^4\). Mandible on either side develops separately and joins in the midline. During development, the anterior part of mandible develops from differentiation of fibrous tissue around the Meckel's cartilage through intramembranous ossification. The posterior part of mandible is formed by endochondral ossification of condyle of mandible [figure 2]. Condyle of the mandible is a growth center and consists of hyaline cartilage. Cartilage cells in condyle proliferate and elaborate a matrix downwards. The matrix gets calcified and bone is formed. Further proliferation of cartilage cells and further matrix formation pushes the bone downwards. Formation of cartilage matrix, conversion of matrix into bone continuously help to form the bone which helps in the forward growth of mandible. While the anteroposterior growth of mandible is formed by endochondral ossification of condyle, the horizontal growth of mandibular body is formed by surface apposition of bone in the preformed intramembranous ossification. Any disturbances to condylar cartilage growth center affect the development and growth of posterior part of mandible resulting in arrested growth of mandible. The following conditions are due to the disturbance of condylar growth center.

1. **Agenesis of condyle**

Agenesis of condyle is congenital absence of condyle due to failure of formation of condyle on one side. It is associated with hemifacial microsomia, where unilateral absence of condyle occurs. Clinically the individual has depression in the preauricular region with absence of auricle and external auditory meatus. The mandible in the affected side has arrested growth with deviation of mandible from unaffected side causing a shift in the midline. Palpation will reveal total absence of condyle and condylar movement in the affected side. Facial deformity with microstomia is a characteristic feature. Prenatal growth disturbance of condyle is the cause of agenesis of condyle.

2. **Aplasia of condyle**

Aplasia of condyle is an attempted formation of miniature condyle where the growth of condyle and endochondral ossification is affected. It may be unilateral or bilateral. In unilateral aplasia of condyle, the mandible will be small due to arrested growth in that side. On palpation the condyle will be small in size but the movement is not affected. On the unaffected side the growth of mandible is normal causing deviation of mandible and shift of midline towards the affected side. Bilateral aplasia of condyle causes arrested growth of mandible on both sides causing mandibular micromasthism.

3. **Hypoplasia of condyle**

Hypoplasia of condyle [figures 7, 8 and 9] is reduced size of condyle due to developmental disturbance\(^6\). This may occur unilaterally or bilaterally. As the condyle is hypoplastic and there is disturbance in endochondral ossification on one side, it causes arrested growth of mandible on one side and results in facial deformity [figures 7, 8 and 9]. The unaffected side of mandible grows normally but is deviated to affected side shifting the midline. If hypoplasia occurs on both sides, arrested growth occurs resulting in micrognathism. Due to arrested growth of mandible there is a depression at the junction of ramus and body called antegonial notch.

Thus when cartilage growth center in condyle of mandible is affected, arrested growth of mandible occurs causing deformity. The exact cause of prenatal disturbance of cartilage growth center is not fully understood but may be due to certain developmental disturbances.

4. **Unilateral condylar hyperplasia**

Disturbances in cartilage growth in many places occur as a deficiency or absence of growth of cartilage. But in condylar growth centers, cartilage overgrowth occurs resulting in condylar hyperplasia\(^7\) where cartilage produce excessive matrix and bone resulting in a large mandible
with excessive anteroposterior growth. In unilateral condylar hyperplasia there is bending of the lower border of mandible with deranged occlusion of teeth. The unaffected side is normal.

**CARTILAGE IN EPIPHYSEAL END OF LONG BONES**

The growth of long bone in vertical direction is purely due to the presence of cartilage in the epiphyseal end of long bones (figure 3). The cartilage proliferates and forms a matrix which gets calcified to form bone. Continuous proliferation of cartilage to form matrix and the matrix ossifying into bone causes growth in the length of bone. The growth of diaphysis in horizontal direction is by intramembranous ossification.

If the endochondral ossification in epiphyseal end is disturbed, different deformities occurs with a common sign of stunted growth/dwarfism.

Achondroplasia is a condition in which absence of cartilage growth occurs. Absence of cartilage growth in sphenoid-occipital synchondrosis causes midface hypoplasia and shortening of base of skull. Absence of cartilage growth in epiphyseal end in achondroplasia results in stunted growth of long bones in extremities with short stature of the individual [figures 10, 11 and 12].

Deficient ossification of cartilage matrix in epiphyseal end causes stunted growth with flattened vertebral body in Morquio Brailsford disease. Abnormal ossification of epiphyses causes stunted growth in dysplasia epiphyseal multiplex.

Osteopetrosis is a genetic disorder in which failure of bone resorption causes excess bone formation which obliterates the blood vessels and the viability of bone in that area is lost. Osteomyelitis can develop in the affected bone due to a compromised blood supply.

In osteopetrosis continuous bone formation occurs and failure of bone resorption causes unresorbed cartilage. This causes widening of bone with club shaped appearance of metaphysis of long bones. Thus the persistent cartilage causes defects in bone.

The cartilage matrix formed in the epiphyseal end fails to calcify and more amount of cartilage accumulates in the metaphysis affecting the longitudinal growth of long bone in Ollier’s disease. Shortness of affected extremities due to chondrodystrophic calcification congenita and stippled epiphyses is a rare congenital disease with discrete spots of calcification affecting cartilaginous structure. A single limb may be affected.

Cartilage growth disturbances occurs in epiphyseal end of long bones due to genetic disturbances resulting in stunted growth of extremities with a clinical appearance of a long trunk and short extremities, polydactyly with cardiac changes in Ellis-van Creveld syndrome.

Growth of any organ depends upon the metabolic activities of growth hormones, pituitary hormone and thyroid hormone. Epiphyseal cartilage growth is also suppressed when there is a deficiency of these hormones and cause stunted growth in hypopituitarism and hypothyroidism.

Stunted growth occurs in Gargoylism due to chondroosteodystrophy and is associated with mental retardation, cloudy cornea and enlargement of liver and spleen.

**DISCUSSION**

It is true that proper growth of an individual depends upon the proper growth of cartilage in the cartilage growth centers, since midface deformity is due to the disturbance in growth of sphenoid-occipital synchondrosis. Arrested growth of mandible is due to defective condylar growth and stunted growth is due to failure of cartilage growth center in epiphyseal end of long bones.

Craniofacial deformities are due to disturbances in growth centers of cranial base. Cartilage growth disturbance in sphenoid-occipital synchondrosis may be only a local disturbance without involving other growth centers as we find that in Crouzon’s disease only face is affected. But in achondroplasia, cartilage growth disturbances occur both in sphenoid-occipital synchondrosis and in the epiphyseal cartilage growth center resulting in midface deformity and stunted growth of long bones. Anterior cranial base is affected more than posterior cranial base and the skull base is shortened in the cartilage growth disturbances of the cranial base. Since cranial base growth disturbance is due to mutation of genes, a thorough research study may be helpful to solve this problem.

Arrested growth of mandible due to disturbances in cartilage growth center of condyle appears to be an independent disorder without involving other cartilage growth centers. Arrested growth of mandible is not associated with other skeletal deformities like midface hypoplasia or stunted growth. This appears to be more of prenatal disturbances rather than genetic involvement. Cartilage growth disturbances in condyle cause aplasia and hypoplasia of condyle resulting in arrested growth of mandible. But condylar hyperplasia also occurs with the formation of large body of mandible for which the reason in not known.

The major cause of individual stunted growth/dwarfism is mainly due to disturbed growth of epiphyseal cartilage of long bones. This may be a physiological alteration due to pituitary and thyroid deficiency or due to genetic disturbances. There is no absence of cartilage in epiphyseal growth center but the existing cartilage does not grow.
or grows abnormally. In the abnormal cartilage, there is failure of ossification and calcification. The reason behind failure of growth, ossification and calcification of cartilage is not fully understood but genetic changes have been proposed. Cartilage growth in the epiphyseal end without ossification and calcification may occur as masses in the long bone. Single long bone may also be affected. In certain conditions, epiphyseal cartilage growth is affected in association with ectodermal dysplasia and cardiac manifestations in Ellis-van Creveld syndrome and mental retardation, cloudy cornea, spleen and liver enlargement are seen in Gargoylism. The systemic symptoms do not have any relevance in the failure of cartilage growth. Disturbances in epiphyseal cartilage growth are not associated with condylar cartilage growth but is seen in cranial base disorders as in achondroplasia.

**CONCLUSION**

Disturbances in cartilage growth centers causing stunted growth and deformity have been explained. Stunted growth of long bones, arrested growth of mandible and sphenoid bone are the features of cartilage growth disturbances. Disturbances are not uniform and may vary for every growth center. Continuous and constant research in genetics and prenatal disturbances pertaining to the cartilage growth disturbances may be carried out and this research may reveal some newer concepts which may help to prevent the cartilage growth disorders. This review article would act as a basis for further evaluation and research of cartilage growth disturbances.

1. **Cartilage growth centers**

2. **Midface deformity in Crouzon syndrome due to disturbances of cartilage growth in sphenoorbital synchondrosis**
3. Jaw deformity in cartilage growth disturbances in condyle – condylar hypoplasia in right condyle

Figure 7: Arrested growth of right mandible with normal growth of left mandible deviating towards right

Figure 8: Hypoplastic growth of right condyle

Figure 9: Normal growth of left condyle

4. Stunted growth of long bones due to cartilage growth disturbances in achondroplasia

Figure 10: Stunted growth

Figure 11: Stunted growth of upper extremities

Figure 12: Stunted growth of lower extremities

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