Abnormal ossification as a cause the progression of adolescent idiopathic scoliosis

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ARTICLE INFO

Article history:
Received 1 October 2008
Accepted 26 December 2008
Available online xxxx

SUMMARY

Although, there is no generally accepted scientific theory for the etiology of adolescent idiopathic scoliosis (AIS), the relative anterior spinal column overgrowth has been postulated as a mechanism of AIS progression by many morphological studies. The normal spinal growth involves both kinds of ossification: endochondral and membranous ossification. Considering the uncoupled anterior–posterior column growth of AIS patients, the uncoupled endochondral–membranous ossification could possibly play an important role in the progression of AIS. Meanwhile, other observations found that the uncoupling of ossification was not limited to the spinal column, but a rather systemic phenomenon. This consideration leads us to carefully dissect the underlying abnormal molecular pathways, cytokines or receptors of ossification, such as BMP-Smads, Runx2, FGFR-3, and will raise the hope to detect the AIS progression potentiality and help to formulate the appropriately personalized treatment strategy for patients.

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Introduction

The adolescent growth spurt is the danger period for progression of adolescent idiopathic scoliosis (AIS); and relative anterior spinal overgrowth is believed to be a contributing cause of the hypokyphosis in the thoracic spine [1,2]. Many morphological studies have confirmed this relative anterior spinal column overgrowth phenomenon. Somerville [3] was the first to introduce the concept that AIS development is related to changes in the sagittal profile, namely lordosis. Smith et al. [4] described a transverse plane deformity and a bone-drift phenomenon towards the concavity of the curve. Disproportionate growth of the anterior and posterior spinal columns was also revealed in AIS by MRI studies. Cheng and coworkers [5] suggested that the longitudinal growth of the vertebral bodies of AIS girls is faster and disproportionate and a significant positive correlation was found between the difference in height between the anterior and posterior vertebral columns and the degree of the curve. Namely, the uncoupled anterior–posterior column growth plays an important role in the progression of AIS. Porter [6] proposed that the length of the spinal canal was shorter than the anterior length of the vertebral body, thus creating an effect similar to a posterior tether and causing “spinal buckling”, then the altered spine sagittal plane shape predisposes to an instability, then after a certain threshold of spinal curvature the scoliosis progresses in a relentless self-perpetuating manner, and finally the typical 3D deformity of scoliosis.

Hypotheses

There are two different types of bone formation: endochondral and membranous ossification. The former occurs by replacement of hyaline cartilage, and is the process responsible for much of the bone growth in vertebrate skeletons, especially in long bones. Whereas, the membranous ossification is the direct development of bone in one stage from connective, fibrous tissue, and the process responsible for the development of flat bones, especially those found in the skull and clavicles.

The normal spinal growth involves both kinds of ossification. The longitudinal growth of the anterior spine column, which includes the vertebral bodies, occurs at the growth plates by endochondral ossification and continues until the girl is between 16 and 18 years of age. In contrast, the endochondral ossification of the posterior elements is completed by the end of the first decade of life. Thereafter, the posterior columns grow circumferentially through membranous ossification [7]. The histological study [5] suggested that the disproportional growth of vertebral columns might due to the abnormal ossification of spinal columns.

Meanwhile, other observations found that the uncoupling of ossification was not limited to the spinal column, but rather a systemic phenomenon. It is well known that girls with AIS have

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a tendency to be taller and thinner than their peers. Previous studies [8–10] have shown that the mean bone mineral density (BMD) of patients with AIS is significantly lower than that of age or maturity matched healthy controls. The relatively increased height in patients with AIS reflects active longitudinal growth by endochondral ossification in these patients.

Taken together, these reports indicated that AIS progression was associated with the systemic change of ossification during the growth spurt. Cheng and coworkers [5] considered the uncoupling between the endochondral and membranous ossification was part of an intrinsic abnormality of skeletal growth in patients with AIS which may be genetic. At the same time, other researchers have found many signaling pathways, cytokines or receptors, such as BMP-Smads, Runx2, FGFR-3 play important roles in the regulation of ossification [11–13], which means the research include different local and systemic factors and the signal transduction pathways of ossification will raise the hope to detect the AIS progression potentiality and help to formulate the appropriately personalized treatment strategy for patients.

**Conclusion**

In summary, AIS progression was associated with loss of coupling between the endochondral and membranous ossification during the growth spurt. Future work will be the use of molecular biology techniques and animal models to carefully dissect the underlying abnormal molecular pathways of endochondral and membranous ossification. Besides providing new insight into the pathogenesis of AIS, it could result in long-term and large-scale consequences.

**Conflict of interest statement**

None declared.

**Acknowledgement**

This study was supported by National Natural Science Foundation of China (Grant No. 30571888).

**References**


