Embryology

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Dimitrios-Stergios Evangelopoulos

1.1 Embryonic Phase

Development of the body's shape begins during gastrulation, a process in which a trilaminar embryonic disk is created from a bilaminar disk. In this phase, during the 3rd week, the primitive streak, well-defined germ layers and the notochord are developed. At this time, epiblastic cells migrate from the deep surface of the primitive streak and form the embryonic endoderm [1–4]. Subsequently, cells continue to migrate from the primitive streak, creating the embryonic mesoderm. The cells that remain on the epiblastic side of the embryonic disk form the embryonic ectoderm. Cells migrating through the primitive node, at the cranial end of the primitive streak, give rise to the notochordal process that would later develop into the notochord. On both sides of the notochord, the mesoderm differentiates into paraxial, intermediate and lateral mesoderm. Paraxial mesoderm divides into paired bodies, the somites, located bilaterally of the neural tube [1, 2, 4].

The notochord and somites are the most important structures for the development of the future vertebral column [1]. Initially, 42–44 pairs of somites are formed. Each one differentiates into sclerotomes, giving rise to vertebrae and ribs and dermomyotomes for the muscles and the overlying skin. During the 4th week, mesenchymal cells of the sclerotome migrate and surround the notochord and neural tube. Once surrounded, each level separates into cranial and caudal areas between which the intervertebral disk gradually develops. Two sclerotomes are required for the proper development of a complete vertebra [1, 4]. Fusion of cranial and caudal parts of the adjacent sclerotomes creates the centrum that will further develop into the mesenchymal vertebral body. Similarly, mesenchymal cells surrounding the neural tube will give rise to the development of the vertebral arch [4].

During the 6th week, following cell migration and the onset of fusion of vertebral structures, vertebral bodies are subjected to an initial phase of chondrification followed by a second phase of ossification after the disintegration of the notochord. During this period, the developing vertebra enlarges and is subjected to structural changes, preserving its original shape. Chondrification starts at the beginning of the 6th week, at the level of the cervicothoracic junction and then proceeds cranially and caudally transforming somites into primary vertebrae. Four centers can be detected: two in each centrum that will fuse at the end of the embryonic period, contributing to the development of the vertebral body and two at the isthmus, bilaterally, for the development of vertebral arches. Fusion between body and arches occurs at the end of the 8th week at the initiation of the ossification phase [1–5].

D.-S. Evangelopoulos (✉)
Third Department of Orthopedic Surgery,
University of Athens, 48, Lamesou Street,
15669 Papagos, Athens, Attika, Greece
e-mail: ds.evangelopoulos@gmail.com

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1.2 Prenatal Period

During this period, ossification centers can be found in three main vertebral regions: one in the centrum and one on each side of the vertebral arch [4, 5]. The vertebral body will articulate with the vertebral arch at the neurocentral joints at birth. Fusion occurs later on, between the age of 5 and 8 years. The two pieces of the arch begin to fuse during the first year of life with complete fusion occurring by the age of 6 years [1, 4]. The five secondary ossification centers that will form after birth, as described by Moore et al. are one for the tip of each transverse process, one for the extremity of the spinous process, one for the upper and one for the lower surface of the body (Fig. 1.1) [1, 2, 4]. Ossified bone deriving from the secondary centers will contribute to the formation of growth plates. Absence and/or asymmetry of growth plates is believed to contribute to the development of congenital defects. Additionally, defects in both chondrification and ossification may lead to the development of known congenital abnormalities.

Molecular signals from the notochord are responsible for the differentiation, chondrification and ossification of the vertebrae [6]. The notochord along with several genes as well as the involved signaling pathways enables the proper development of the vertebrae and the nervous system.

Torklus et al. accurately described the development of the axis body. The authors reported a detailed description on the five centers of ossification of the axis vertebra. The process initiates at the second fetal month, through perichondral ossification, on the two posterolateral centers from the arch of the axis [6, 7]. Their anterior expansion contributes to the ossification of the vertebral body. At the fifth fetal month, one median ossification center gives rise to a significant section of the vertebral body while two primary ossification centers arising cranially to the median center give rise to the dens axis through cranially directed ossification, remaining separated from the body's ossification center through subdental synchondrosis.

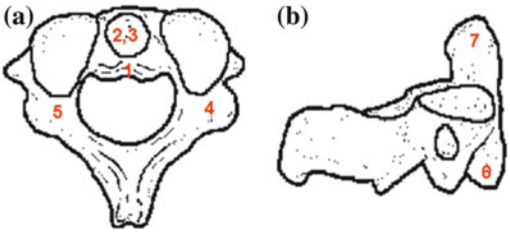

Fig. 1.1 Development of the axis. The five primary [Fig. 1.1a: body (*1*), dens (*2*, *3*), lateral masses (*4*, *5*)] and two secondary [Fig. 1.1b: inferior epiphyseal plate (*6*), Bergmann's (*7*)] centers

The odontoid process represents a distinct process lying separated cranially to the body of the axis since its primitive development. Wang et al. reported that this synchondrosis is restricted to the medial border of the superior articular facets of the axis [8]. However, in the study of Torklus et al. during development, the odontoid process together with the subdental synchondrosis is shown to countersink into the corpus of the axis as being an independent anatomical structure, the basis of the odontoid process [5, 7]. Several authors concluded that the syndesmosis represents a bipolar growth zone located below the level of the atlantoaxial articulation, contributing to the height of the base of the dens and the vertebral body [9–11]. Highlighting these results, Cokluk et al., in their MRI study on the upper cervical spine of pediatric and adult patients, demonstrated the independent structure of the odontoid process and recognized the remnants of the subdental syndesmosis as a hypointense ring located well below the level of the superior articulating facets [12].

The distinct development of the odontoid process compared to the body of the axis necessitates reconsideration of the Anderson-D'Alonso classification of odontoid process fractures [13, 14]. Additionally, the base of the odontoid process and the subdental region, apart from the unique anatomy, distinct anatomical features of the region and different origin, demonstrates delayed ossification, compared to the body and the neck of the odontoid process, leading to altered age-related structural and biomechanical properties (Fig. 1.2) [14]. For the above-mentioned, to achieve optimal treatment

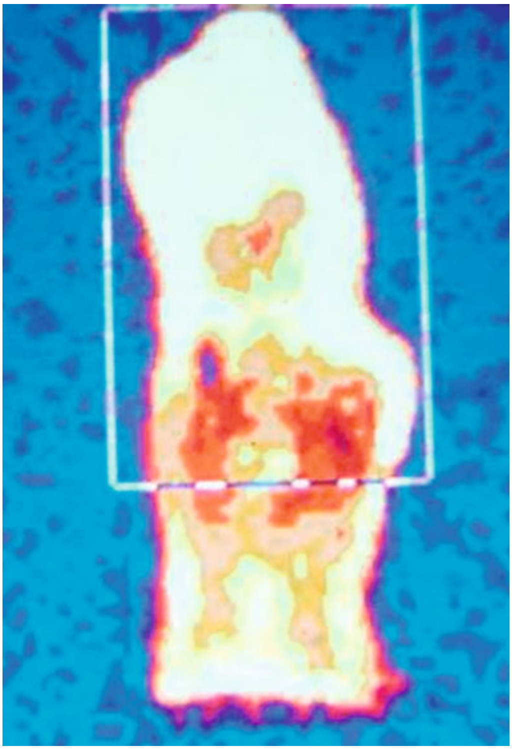

Fig. 1.2 pQ-CT analysis demonstrating delayed ossification of the basis of the dens and the subdental region, compared to the body and the neck of the dens

and allow accurate prognosis, fractures at the base of the odontoid process should be considered as a separate trauma entity in the different fracture classification systems and not as an extension of fracture lines from the body of the axis.

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