A temporary disc-like structure at the median atlanto-axial joint in human fetuses

Koichiro Sakanaka¹, Masahito Yamamoto¹, Hidetomo Hirouchi¹, Ji Hyun Kim², Gen Murakami¹,³, José Francisco Rodríguez Vázquez⁴, Shin-ichi Abe¹

¹Department of Anatomy, Tokyo Dental College, Tokyo, Japan, ²Department of Anatomy, Chonbuk National University School of Medicine, Jeonju, Korea, ³Division of Internal Medicine, Jikou-kai Clinic for Home Visits, Sapporo, Japan, ⁴Department of Anatomy and Embryology, School of Medicine, Complutense University, Madrid, Spain

Abstract: During observations of mid-term and late-stage fetuses, we found a joint disk-like structure at the anterior component of the median atlanto-axial joint. At mid-term, the disk-like structure was thick (0.1–0.15 mm) relative to the sizes of bones surrounding the joint. However, it did not completely separate the joint cavity, and was absent in the inferior and/or central part of the cavity. This morphology was similar to the so-called fibroadipose meniscoid of the lumbar zygapophysial joint that is usually seen in adults. In mid-term fetuses, there was evidence suggesting that a mesenchymal tissue plate was separated from a roof of the joint cavity. In late-stage fetuses, the thickness (less than 0.15 mm) was usually the same as, or less than that at mid-term, and the disk-like structure was often flexed, folded and fragmented. Therefore, in contrast to the zygapophysial meniscoid as a result of aging, the present disk-like structure was most likely a temporary product during the cavitation process. It seemed to be degenerated in late-stage fetuses and possibly also in newborns. Anomalies at the craniocervical junction such as Chiari malformations might accompany this disk-like structure at the median atlanto-axial joint even in childhood.

Key words: Median atlanto-axial joint, Disk, Meniscoid, Human fetuses

Received June 4, 2019; Revised August 9, 2019; Accepted August 17, 2019

Introduction

The median atlanto-axial joint is a pivot joint between the dens (odontoid process of the axis) and a ring formed by the anterior atlantal arch and transverse ligament of the atlas [1, 2]. A vertically ovoid facet on the anterior dens articulates with another on the posterior aspect of the anterior arch. The fibrous capsule, which is lined by the synovial membrane, is relatively weak and loose, especially superiorly. We have previously reported fetal development of the transverse atlantis and alar ligaments at the median atlanto-occipital joint [3]. We found that the joint cavity in the anterior compartment appears from the inferior part at 7–8 weeks of gestation and extends superiorly to reach a future apical ligament containing the notochord remnant. Because of a tight connection between the occipital and dens apex by the notochord, the growing dens temporarily rides over the occipital. Thus, the anterior joint cavity faces the apical ligament in the roof. In previous studies and later ones, we incidentally found a “rim” or disk-like structure in the anterior compartment of the median atlanto-axial joint. In the present study, we aimed to clarify the development and morphology of the disk-like structure in the fetus. Because no previous report has described the disk in the adult median joint, the structure is considered likely to disappear in the late-stage fetus or after birth.

Corresponding author:
Masahito Yamamoto
Department of Anatomy, Tokyo Dental College, 2-9-18 Misaki-cho, Chiyoda-ku, Tokyo 101-0061, Japan
Tel: +81-3-6380-9592, Fax: +81-3-6380-9664, E-mail: yamamotomasahito@tdc.ac.jp

Copyright © 2019. Anatomy & Cell Biology

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.
Materials and Methods

The study was performed in accordance with the provisions of the Declaration of Helsinki 1995 (as revised in Edinburgh 2000). We observed sagittal or horizontal sections of 44 human fetuses: 30 mid-term specimens (crown-rump length [CRL], 43–117 mm; approximately 9–15 weeks of gestational age [GA]) and 14 late-stage specimens (CRL, 250–310 mm; GA, 30–37 weeks). All specimens were part of the large collection kept at the Department of Anatomy and Embryology of the Universidad Complutense, Madrid, and had originated from miscarriages and ectopic pregnancies at the Department of Obstetrics of the University. The present mid-term specimens were sectioned serially, while the late-stage specimens were sectioned at intervals of 100 μm. Most sections were stained with hematoxylin and eosin, while a minor proportion were stained with Masson trichrome, azan, orange G or silver. The sectional plane was horizontal (25 mid-term, 4 late-stage) or sagittal (5 mid-term, 10 late-stage). The use of these specimens was approved by Complutense University ethics committee (B08/374). Most photographs were taken with a Nikon Eclipse 80 (Tokyo, Japan), whereas photographs

Fig. 1. Sagittal sections of the median atlanto-axial joint from two mid-term specimens. Panels A–C display a specimen of 82 mm crown-rump length (CRL), while panels D and E show a specimen of 100 mm CRL. Panel A (D) is the most medial side of the figure, whereas panel C (E) is the most lateral side. (A–C) A disk-like structure (arrows) is thick in lateral part of the joint cavity (C) and thin in the medial part (A). Likewise, in panels D and E, the structure appears to be complete at the medial part (D). Arrows in D and E indicate a disk-like structure. All panels were prepared at the same magnification. Scale bar=1 mm (D).
at ultra-low magnification (objective lens less than ×1) were obtained using a high-grade flat scanner with translucent illumination (Epson scanner GTX970, Tokyo, Japan).

**Ethical statement**

The authors declare that all procedures contributing to this work complied with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1995, as revised in 2000, and that the study was approved by the relevant institutional committees (No. 1428).

**Results**

In the present specimens, we did not find anomalies at the craniocervical junction such as Chiari malformations and neurocentral synchondrosis. The transverse atlantis and alar ligaments appeared to develop normally in comparison with our previous observations [3]. Sagittal sections allowed better visualization of the topographical anatomy of the joint cavity, whereas horizontal sections readily demonstrated the presence or absence of the disk-like structure along the supero-inferior axis. Indeed, sagittal sections demonstrated the entire extent of the structure along the long axis, but we needed to carefully identify whether the site was marginal or central in the joint.

**Thirty mid-term specimens**

In the anterior component of the median atlanto-axial joint, i.e., between the anterior aspect of the dens and the anterior atlantal arch, we found vascularized synovial tissue projecting from the superior and/or lateral margins to the joint.

![Fig. 2. Horizontal sections of the median atlanto-axial joint from two mid-term specimens. Panels A–E display a specimen of 96 mm crown-rump length (CRL), while panels F–I show a specimen of 100 mm CRL. Panel A is the most superior side of the figure, whereas panel E is the most inferior side. In the former specimen, a disk-like structure (D, E; arrows) is continuous with mesenchymal tissue at the irregular superior margin of the joint cavity (A, B). In the latter specimen, the roof of the joint cavity is separated from the atlas between panels F and G. In both specimens, the structure was not a complete septum but was considered to be a superior marginal fold (E, I). Arrows in G, H, and I indicate a disk-like structure. All panels were prepared at the same magnification. Scale bar=1 mm (A).](https://doi.org/10.5115/acb.19.128)
cavity. Thus, the disk-like structure was not a complete septum but appeared to be a superior or superolateral marginal fold. The smallest specimen containing the disk-like structure was CRL 52 mm (approximately GA, 10 weeks) and the structure was consistently present in specimens larger than CRL 82 mm (GA, 12 weeks) (Figs. 1, 2). Although it was absent or interrupted in the central or median area, the structure appeared to represent a complete septum depending on the sections chosen (such as horizontal sections across the superior part of the joint) (Fig. 1A, D).

The maximum thickness was 0.1–0.15 mm, being relatively thick and corresponding to more than 10% of the supero-inferior diameter of the anterior atlantal arch (0.8–1.3 mm). Notably, in four specimens (CRL, 90 mm, 96 mm, 100 mm and 120 mm), we found evidence suggesting that a mesenchymal tissue plate was separated from a roof of the joint cavity, providing the disk-like structure. The roof was located close to the apex of the dens. As shown in Fig. 2A and B, the disk-like structure was continuous with mesenchymal tissue at the irregular superior margin of the joint cavity. As shown in Fig. 2F and G, the roof of the joint cavity was separated from the atlantal arch. The fovea dentis of the atlas had not yet not developed in any of the specimens. The transverse ligament provided a deep notch on the dens.

Fourteen late-stage specimens

Instead of a disk, we found a short membranous structure in all specimens. In the majority (10 specimens) (Figs. 3–5), it was a short, thin synovial fold projecting from the roof of the joint cavity in association with tissue fragments scattered within the cavity. Usually, the short fold was highly flexed and pushed to the roof of the joint cavity by the convex surface of the anterior atlantal arch (Fig. 3E, F). In a minority of specimens (4 in all), the membranous structure appeared to provide an incomplete septum (Fig. 4E) interrupted in the central or median area (Fig. 4F). In two of the four specimens showing the septum, the dens did not reach the level of the upper margin of the atlantal arch (Fig. 4C). Thus, in the two specimens, the joint cavity extended above the apex of the dens and the transverse ligament was attached to the apex, rather
than appearing as a neck-like depression. The fovea dentis of the atlas had not yet developed in any of the specimens. The fold or septum was vascularized, at least at the base.

In late-stage specimens, the maximum thickness of the fold or septum was less than 0.15 mm: it appeared to be very thin compared with the size of the surrounding bony structures. The atlas and axis were 2–3 times larger than at mid-term (e.g., the anterior atlantal arch, 2.4–2.9 mm), and the maximum thickness of the joint cavity increased from 0.2 mm to 0.8 mm.

Discussion

The present disk-like structure at the anterior component of the median atlanto-axial joint was similar to the so-called fibroadipose meniscoid present in adult lumbar zygapophysial joints [4]. Like the zygapophysial meniscoid, the present disk-like structure did not form a complete septum in the joint cavity. The zygapophysial meniscoid is considered to be a result of aging, and it develops to increase joint congruity. According to our unpublished observations, fetal lumbar zygapophysial joints sometimes carry a very short fold or rim. However, in contrast to the zygapophysial meniscoid, the present atlanto-axial disk appeared to degenerate in late-stage fetuses and possibly also in childhood. Other than real growth, the present measurements suggested that the disk became stretched and fragmented between the mid-term to late stages (approximately 16–29 weeks). We found evidence suggesting that a tissue plate was separated from the roof of the joint cavity at mid-term. In adults, the roof of the joint is characterized by a weak and loose capsule [1, 2].

The elbow (humeroradial) joint always carries synovial folds or rims in late-stage fetuses as well as in adults [5]. In the human fetal elbow joint at 9–10 weeks, Mérida-Velasco et al. [6] found that the rim or fold develops from interzone mesenchymal tissue filling the future joint cavity before cavitation. Likewise, in the fetal knee joint, both the synovial fold and meniscus are sculpted from interzone tissue of the future joint cavity [7]. In the median atlanto-axial joint at mid-term, when the cavitation reached the roof, the mesenchymal tissue...
A temporary disc-like structure appeared to become separated from the superior margin of the cavity to provide a disk-like structure. The roof of the joint cavity seemed to correspond to the initial sheath of the notochord or the base of the future apical ligament [3]. Therefore, there seemed to be traction stress against the roof of the joint cavity between the occipital and the dens during their bony growth at and after mid-term, resulting in easy separation of the roof. Consequently, rather than creating increased joint congruity, the present disk-like structure appeared to be a temporary structure during the process of cavitation and later growth.

We found that a relatively lower or shorter dens accompanied a thicker and larger disk in the median atlanto-axial joint. Without compression from the dens, incomplete degeneration might occur. Currently there is no information on the association of the disk with anomalies of the craniocervical junction, such as Chiari malformations and neurocentral synchondrosis [8-12]. Therefore, further detailed examinations of the relationship between bone anomalies and the persistent disk-like structure would be warranted.

ORCID

Koichiro Sakanaka: https://orcid.org/0000-0002-0796-8212

www.acbjournal.org
Author Contributions

Conceptualization: GM. Data acquisition: KS, MY, HH. Data analysis or interpretation: KS, HH, JHK. Drafting of the manuscript: GM, JFRV, SIA. Critical revision of the manuscript: MY. Approval of the final version of the manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Acknowledgements

This work was supported by JSPS KAKENHI (grant number 18K17180).

References

1. Cave AJ. On the occipito-atlanto-axial articulations. J Anat 1934;68:416-23.
2. Cave AJ. The morphology of the mammalian cervical pleurapophysis. J Zool 1975;177:377-93.
3. Abe H, Ishizawa A, Cho KH, Suzuki R, Fujimiya M, Rodríguez-Vázquez JF, Murakami G. Fetal development of the transverse atlantis and alar ligaments at the craniovertebral junction. Clin Anat 2012;25:714-21.
4. Engel R, Bogduk N. The menisci of the lumbar zygapophysial joints. J Anat 1982;135:795-809.
5. Isogai S, Murakami G, Wada T, Ishii S. Which morphologies of synovial folds result from degeneration and/or aging of the radiohumeral joint: an anatomic study with cadavers and embryos. J Shoulder Elbow Surg 2001;10:169-81.
6. Mérida-Velasco JA, Sánchez-Montesinos I, Espín-Ferra J, Mérida-Velasco JR, Rodríguez-Vázquez JF, Jiménez-Collado J. Development of the human elbow joint. Anat Rec 2000;258:166-75.
7. Gray DJ, Gardner E. Prenatal development of the human knee and superior tibiofibular joints. Am J Anat 1950;86:235-87.
8. Azahraa Haddad F, Qaisi I, Joudeh N, Dajani H, Jumah F, Elmashala A, Adee N, Chern JF, Tubbs RS. The newer classifications of the chiari malformations with clarifications: an anatomic review. Clin Anat 2018;31:314-22.
9. Pang D, Thompson DN. Embryology and bony malformations of the craniovertebral junction. Childs Nerv Syst 2011;27:523-64.
10. Prescher A. The craniocervical junction in man, the osseous variations, their significance and differential diagnosis. Ann Anat 1997;179:1-19.
11. Shoja MM, Johal J, Oakes WJ, Tubbs RS. Embryology and pathophysiology of the Chiari I and II malformations: a comprehensive review. Clin Anat 2018;31:202-15.
12. Shoja MM, Ramdhan R, Jensen CJ, Chern JF, Oakes WJ, Tubbs RS. Embryology of the cranio cervical junction and posterior cranial fossa, part I: development of the upper vertebrae and skull. Clin Anat 2018;31:466-87.