Case Report
https://doi.org/10.5115/acb.23.225
eISSN 2093-3673
Anatomy & Cell Biology acb

Atlanto-occipital assimilation: embryological basis and its clinical significance

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Abstract: Atlanto-occipital assimilation is an osseous embryological anomaly of the craniovertebral junction in which the atlas (C1) is fused to the occiput of skull. Embryologically, this assimilation may happen due to failure of the segmentation and separation of the caudal occipital and the cranial cervical sclerotome. The segmentation clock is maintained by NOTCH and WNT signalling pathways along with *Hox genes* and retinoic acid. This condition is likely to be a consequence of mutation in above mentioned genes. The knowledge of this assimilation may be crucial for the clinicians as it may lead to various neurovascular symptoms. The present case report involves the analysis of atlanto-occipital assimilation with its clinical significance and embryological basis.

Key words: Assimilation, Segmentation clock, Signalling pathways, Homeotic transformation

Received August 29, 2023; Revised October 24, 2023; Accepted October 30, 2023

Introduction

Atlanto-occipital assimilation is an osseous embryological anomaly of the craniovertebral junction in which the atlas (C1) is fused to the occiput of skull. This condition is also called atlanto-occipital assimilation, occipito-cervical fusion, craniovertebral synostosis, and occipitalization of the atlas (C1 vertebra). This condition was first described by Rokitansky in 1844, and Schullerin in 1911 demonstrated this anomaly roentgenographically [1]. Previous case reports described this condition as partial or complete assimilation based on the fusion of varying degrees between the atlas and occiput [2]. The incidence ranges from 0.14% to 0.75% in the population [3] and the prevalence ranges from 0.08% to 2.76% in the population [4]. The knowledge of this assimilation may be crucial for the clinicians as it may lead to various neurovascular symptoms. The present study involves the analysis of atlanto-occipital assimilation with its clinical significance and its embryological basis.

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Case Report

During routine undergraduate teaching, one skull with atlanto-occipital assimilation was encountered in the Department of Anatomy at All India Institute of Medical Sciences, New Delhi. Only one out of 24 skulls showed such anomaly (Fig. 1). The condylar part of occipital bone was partially fused with lateral parts of anterior arch and lateral masses of atlas (Fig. 1A) along with absent posterior arch (Fig. 1C). The two superior facets of atlas had completely fused with the occipital condyles and two inferior articular facets are normal and the fusion is more inclined towards right (Fig. 1A, B). The transverse processes on the right and left sides of the atlas were free from occipital bone (Fig. 1A, B). An incomplete foramen transversarium was visible on the left

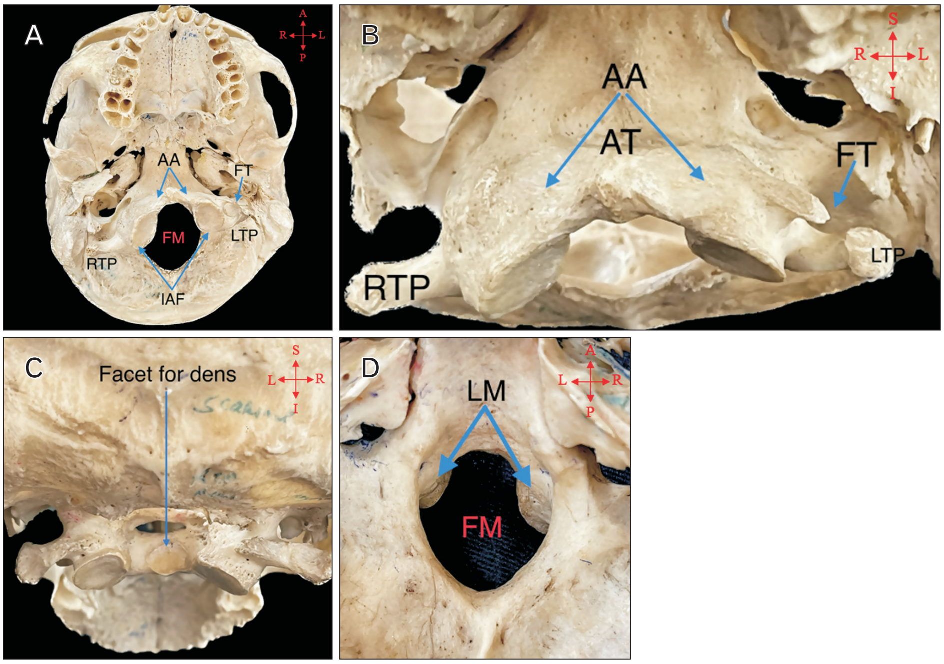

Fig. 1. Photographs showing different views of skull. (A) Inferior view. (B) Anterior view. (C) Posterior view. (D) Internal view. A, anterior; P, posterior; S, superior; I, inferior; R, right; L, left; AA, anterior arch of atlas (C1); FT, foramen transversarium; RTP, right transverse process; LTP, left transverse process; IAF, inferior articular facet; FM, foramen magnum; AT, anterior tubercle; LM, lateral mass.

Table 1. Diameters of foramen magnum

S. no.	Diameter	Measurement (mm)
1	Anterio-posterior/sagittal diameter	32.16
2	Transverse diameter	18.28

while there was absence of right foramen transversarium (Fig. 1C). The anterior aspect of the foramen magnum was minimally decreased by the right and left lateral mass of the atlas (Fig. 1D). Bilaterally hypoglossal canals were normal. The shape of foramen magnum was nearly normal. A slight encroachment of the foramen magnum by the anterior arch as well as by the fused condylar parts with the lateral masses of the atlas vertebra was seen (Fig. 1D). The diameters of the foramen magnum were measured (Table 1). All measurements were done using a Vernier digital calliper and rounded off to the nearest millimetre.

Discussion

Occipitalization of atlas is an osseous embryological anomaly of the craniovertebral junction. It is a rare disorder of unknown etiology. The current study outlines the embryological basis and its clinical importance. This assimilation may be asymptomatic, but various signs and symptoms can be clinically manifested.

The probable embryological origins of atlanto-occipital assimilation are reported in the current study.

It is mentioned that at the beginning of 3rd week, paraxial mesoderm (presomite mesoderm) undergoes segmentation which is then called as somitomeres, and is maintained by a segmentation clock. After segmentation, the first pair of somite develops at the cephalic end at day 20. The segmentation clock is maintained by the cyclic expression of genes such as NOTCH and WNT in an oscillating pattern at the stage of presomite mesoderm. This overlapping expression gradient is very essential to maintain the segmentation clock [5]. Disturbances in the NOTCH and WNT signalling pathway may lead to the misexpression of genes and so there is disruption in the segmentation clock of somites and the failure of segmentation.

The majority of the vertebrae are specified by a special combination of Hox genes (homeobox genes), which ensures the formation of the normal segmental pattern along the cranio-caudal axis of the vertebral column. The expression of Hoxa1, Hoxa3, Hoxb1, and Hoxd4 defines the atlas (C1). The principal function of Hox genes is to establish structures along the main body axis. Hox genes were first described to function along the main body axis; sequential arrays of expression are present in the limbs, the internal and external genitalia, and the gut. At chromatin level, polycomb protiens silences Hox genes through chromatin remodeling. Defects in polycomb proteins, regulation, and mutation or misexpression of Hox genes result in homeotic transformations of the axial skeleton.

It is also documented that retinoic acid, or vitamin A, is also known to be produced and utilized in particular local areas at various points during fetal and postnatal development. Certain Hox genes are one of its clearly defined targets early in development. If retinoic acid is administered during particular developmental stages, it can result in changes to the overall segmental organization of the vertebrae, including changes to the cranial or caudal levels. Early administration of retinoic acid results in cranial shift (the last cervical vertebra is transformed into first thoracic vertebra) and late administration causes a caudal shift (the thoracic vertebra extends into first two lumbar vertebrae). These shifts in levels are called homeotic transformations [6].

Previous studies have suggested that the mutation in members of Hox (homeobox) gene family, mesenchyme homeobox 1 (MEOX1) is associated with the occipitalization of the atlas in a mouse model [7]. MEOX1, a protein-coding gene, plays a key role in somitogenesis and is also required for the maintenance of sclerotome polarity and the formation of craniocervical joints. It was suggested as a lack of segmentation and separation at the caudal most occipital sclerotome [8]. It was noted that only in cases of atlanto-occipital fusion does the dense caudal portion of the fourth occipital somite appear to fuse with the cephalic portion of the adjacent somite [9]. Early in the embryonic period, the differentiation of the occipito-cervical somites was interrupted, which was theorized to be the cause [10]. With the available embryological data regarding the occipitalization of the atlas, are inadequate.

The present case report also explains the relevant clinical significance of this kind of assimilation. Atlanto-axial instability occurs in about 50% of patients with atlanto-occipital fusion [11]. In most cases, patients with cranio-cervical junction defects do not experience neurological symptoms and signs until they are 20 years old. Although atlas assimilation may be asymptomatic, those who have it may experience a variety of indications and symptoms at the 3rd or 4th decade of the life. These include a headache, neck pain (the most common type), pain and numbness in the limbs, weakness, ataxia, and indications of vertebral artery compression and dissection [12], which may manifest independently or concurrently with signs of spinal cord compression [13]. The diameters of the foramen magnum are an important landmark in symptomatic patients. According to Hayes et al. [14] the measurement is accepted abnormal when its sagittal diameter is less than 30 mm and according to Greenberg [15], when the sagittal spinal canal diameter behind the odontoid process is less than or equal to 14 mm, spinal cord compression will always occur. However, in the present case report, the sagittal diameter was measured as 32.16 mm and transverse diameter was 18.28 mm, so spinal cord compression could be due to less transverse not because of sagittal diameter.

In this case, there is reduction in the shape and size of the foramen magnum with an incomplete foramen transversarium for the vertebral artery to reach the brain may lead to clinically manifesting symptoms and due to compression of the brain stem, the nerves and the vessels, there will be instability and mechanical immobility. Additionally, one of the clinical cases was compared to the findings. A 64-year-old male patient was identified and managed at a neurology department for supranuclear palsy and multiple cerebellar infarcts prior to his death. His additional diagnoses included high blood pressure, atherosclerosis, chronic pancreatitis, pancreaticogenic diabetes, polyneuropathiadiabetica, and dementia. According to the patient's anamnesis, he had gait ataxia for the previous five years [4].

Klippel-Feil syndrome is the result of fusions of the cervical vertebrae such that the head appears to rest on the shoulders. This kind of assimilation can also be associated with Klippel-Feil syndrome. There were no other abnormal features in the skull.

It may cause anaesthetic problems also. Impairment of atlanto-occipital extension will have difficulty in positioning for intubation for any surgeries. With head positioning and manipulation, an unstable cervical spine increases the risk of neurological injury. Mask ventilation would be difficult. Due to the cervical spine's limited mobility, direct laryngoscopy and tracheal intubation may be extremely challenging or impossible, so video laryngoscopes are always preferred. Maintain spontaneous ventilation through awake or sedated fibreoptic intubation. Depending on the type of surgery, a tracheostomy may be required.

Atlanto-axial instability and immobility causes the compression of the medullary cord and it is termed as cervical myelopathy (International Classification of Disease, 10th version code M50.02 for cervical disc disorder with myelopathy). Therefore, after receiving an magnetic resonance imaging diagnosis, the patient with instability will undergo occipitocervical fusion using occipital wiring and screws, whereas the patient without instability will undergo straightforward decompression surgery.

Atlanto-occipital assimilation findings from earlier case reports, this case report, and its related findings, were compiled (Table 2).

The knowledge of atlanto-occipital assimilation may be of

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Table 2. Other tables published in the journal

S. no.	Journal (yr)	Authors	Topic	Findings
1	European Journal of Anatomy (2008)	Sharma et al.	Occipitalization of atlas with other associated anomalies of skull	The atlas vertebra was almost completely fused with the occipital, except at the transverse processes on both sides. Partial fusion
2	International Journal of Anatomical Variations (2009)	Vineeta et al.	Occipitalization of the atlas: its occurrence and embryological basis	Case 1 1. Complete fusion of the atlas vertebra with the occipital bone. 2. Both the right and the left transverse process were free from the occipital bone. 3. The right transverse process had no foramen transversarium. 4. The hypoglossal canals on both sides were normal. Case 2 1. Hemi-fusion of the atlas vertebra to the axis and the other half to the occipital bone. 2. The entire left side of the atlas vertebra was assimilated into the occipital bone. 3. The left transverse process was completely assimilated in the occiput. 4. The right side of the posterior arch superior aspect was free but its inferior aspect displayed vertebralisation. Complete and partial fusion
3	Journal of Biomedical Science and Research (2010)	Hussain et al.	Occipitalization of Atlas: A case report	1. The lateral mass and both anterior& posterior arches were completely fused with the occipital bone. 2. The transverse processes of the atlas were also fused to the occipital bone. Complete fusion
4	International Journal of Science and Research (2012)	Girish et al.	Occipitalization of the Atlas - A Case Report	The lateral and both anterior and posterior aches were completely fused with the occipital bone and the transverse processes of the atlas were also fused to the occipital bone. Complete fusion
5	International Journal of Anatomy and Research (2014)	Sween et al.	Occipitalization of Atlas	Case 1 1. Skull showed completely fused atlas vertebra with the occipital bone, except at the transverse processes on both sides. 2. The right and the left transverse process of the atlas each containing complete transverse foramen was not fused with the occipital bone. Case 2 Atlas vertebra was completely fused with the occipital, except the right transverse process. Case 3 1. Partial and asymmetrical occipitalization of atlas vertebra with occipital bone was found. 2. The skull showed midline defect in posterior arch of atlas because of failure of fusion of right and left halves of posterior arch. Complete and partial fusion
6	Curr Trends Diagnosis and Treat (2017)	Lalit et al.	Occipitalization of Atlas: A Case Report with its Ontogenic Basis and Review of Literature	Partial assimilation of the atlas with the occipital bone on the right and left sides. Partial fusion
7	Present case report (2023)	Hanusun et al.	Atlanto-occipital Assimilation: Embryological Basis and its Clinical Significance	1. The condylar part of occipital bone was partially fused with lateral parts of anterior arch and lateral masses of atlas along with absent posterior arch. 2. The transverse processes on the right and left sides of the atlas were free from occipital bone. 3. An incomplete foramen transversarium was visible on the left while there was absence of right foramen transversarium. 4. Bilaterally hypoglossal canals were normal. Partial fusion

importance to anaesthesiologist, orthopaedic/neurosurgeons dealing with the pathologies of upper cervical spine.

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Conceptualization: JJP. Data acquisition: AS, PP. Data analysis or interpretation: JJP, HHHN, HG, SS. Drafting of the manuscript: HHHN. Critical revision of the manuscript: NR, HG, SS. Approval of the final version of the manuscript: all authors.

Conflicts of Interest

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

Funding

None.

References

1. Jadhav SD, Ambali MP, Patil RJ, Doshi MA, Roy PP. Assimilation of atlas in Indian dry skulls. J Krishna Inst Med Sci Univ 2012;1:102-6.
2. Ranade AV, Rai R, Prabhu LV, Kumaran M, Pai MM. Atlas assimilation: a case report. Neuroanatomy 2007;6:32-3.
3. Guebert GM, Yochum TR, Rowe LJ. Congenital anomalies and normal skeletal variants. In: Yochum TR, Rowe LJ, editors. Essentials of Skeletal Radiology. Williams and Wilkens; 1987. p.197-306.
4. Bodon G, Glasz T, Olerud C. Anatomical changes in occipitalization: is there an increased risk during the standard posterior approach? Eur Spine J 2013;22(Suppl 3):S512-6.
5. Sadler TW. Langman's medical embryology. 14th ed. Wolters Kluwer; 2019.
6. Carlson BM. Human embryology and developmental biology. 6th ed. Elsevier; 2019.
7. Leucht P, Kim JB, Amasha R, James AW, Girod S, Helms JA. Embryonic origin and Hox status determine progenitor cell fate during adult bone regeneration. Development 2008;135:2845-54.
8. Harcourt BT, Mitchell TC. Occipitalization of the atlas. J Manipulative Physiol Ther 1990;13:532-8.
9. Tachdjian MO. Congenital anomalies of the occiput and cervical spine. In: Tachdjian MO, editor. Pediatric orthopedics. WB Saunders; 1990. p.874-5.
10. Chandraraj S, Briggs CA. Failure of somite differentiation at the cranio-vertebral region as a cause of occipitalization of the atlas. Spine (Phila Pa 1976) 1992;17:1249-51.
11. Warner WC. Pediatric cervical spine. In: Canale ST, Campbell WC, editors. Campbell's operative orthopaedics. 10th ed. Mosby; 2003. p.1736-1737.
12. Wang S, Wang C, Liu Y, Yan M, Zhou H. Anomalous vertebral artery in craniovertebral junction with occipitalization of the atlas. Spine (Phila Pa 1976) 2009;34:2838-42.
13. Hensinger RN. Osseous anomalies of the craniovertebral junction. Spine (Phila Pa 1976) 1986;11:323-33.
14. Hayes M, Parker G, Ell J, Sillence D. Basilar impression complicating osteogenesis imperfecta type IV: the clinical and neuroradiological findings in four cases. J Neurol Neurosurg Psychiatry 1999;66:357-64.
15. Greenberg AD. Atlanto-axial dislocations. Brain 1968;91:655-84.