Innovations

"Case Report and Review: Unveiling the Mysteries of Cervical Vertebral Fusion – Developmental, Radiological, and Genetic Insights"

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Abstract
Vertebral fusion is the fusion of bodies and the various elements of the vertebral arch of adjacent vertebrae Such vertebral fusion usually is seen in cervical and lumbar region, more so between the second and third cervical vertebrae, usually asymptomatic; but may also result in features suggestive of neurological compression and might also present difficulty in procedures like endotracheal intubation. This present case repors the discussion on fusion of C3 and C4 cervical vertebra. The Fused Cervical Vertebrae (FCV) studied is with respect to the degree and site of fusion. Partial fusion was seen in the specimen. This report aims at cervical vertebral fusion and the need for earlier detection to avoid the expected complications like degeneration of adjacent segments and neurological deficits. The report is compared with review analysis and the variable presentation and fusion of cervical vertebra.

Key Words: *Compression, Synostosis, Vertebral fusion*

Introduction

The human vertebral column is a critical component of the skeletal system, providing structural support, protecting the spinal cord, and enabling movement. The cervical region consists of seven vertebrae (C1 to C7), with the first two (C1 and C2) being atypical, and the remaining five (C3 to C7) classified as typical cervical vertebrae. Among the anomalies that can affect the vertebral column, congenital fusion of adjacent cervical vertebrae, particularly C2-C3 and C6-C7, is one of the most commonly documented issues. Such anomalies are often identified as incidental

findings during radiological imaging, with symptoms ranging from asymptomatic to potentially significant neurological deficits.

Cervical vertebrae are seven in number and first (C1), second (C2) and seventh (C7) are classified as atypical cervical bonesdue to their unique morphology and the remaining third to sixth (C3-C6) are considered typical vertebrae. These vertebrae are subject to numerous congenital anomalies like ponticulusposticus, osodontoideum and vertebral fusion to name a few [8]. FCV have been documented at two levels between: C2 and C3, C6 and C7 [9-11]. Vertebral fusions may be congenital isolated or part of KlippelFeil syndrome or acquired as a result of degenerative diseases, tuberculosis or trauma. Fused cervical vertebrae are said to have an incidence of 0.4%-0.7% [9, 11].

The occurrence of FCV may be asymptomatic or may result in compressive symptoms like neck pain, difficulty in movements of neck and occasionally motor or sensory deficits. Because of different varying clinical spectrum and presentations, the diagnosis of this condition is usually an incidental radiographic finding [1].

Cervical vertebral fusion may occur due to several factors, including congenital developmental defects, trauma, or degenerative diseases. This case report examines a rare occurrence of fusion between the third (C3) and fourth (C4) cervical vertebrae, highlighting the clinical significance, diagnostic implications, and management considerations associated with such anomalies. The review compares this finding with other studies in the literature, providing a comprehensive overview of cervical vertebral fusion [1, 2].The present reportbrings into view a case of FCV to stress upon the necessity for early detection and counselling of the patient to avoid them to improve the quality of life.

Aims and Objectives

1. To present a case of fused cervical vertebrae, specifically the fusion between C3 and C4 vertebrae.
2. To discuss the clinical significance of cervical vertebral fusion in terms of potential neurological implications, diagnostic challenges, and management strategies.
3. To review the literature on cervical vertebral fusion, exploring various documented cases and their outcomes.
4. To emphasize the importance of early detection and intervention to prevent degenerative changes and related complications.

Methodology

This case study was conducted at the Department of Anatomy, Sri DevarajUrs Medical College (SDUMC), Kolar, India. A detailed examination of cadaveric cervical vertebrae was undertaken during osteological demonstrations for first-year MBBS students. The specimen examined showed partial fusion between the bodies and elements of the vertebral arches of C3 and C4. The anatomical features studied included:

- Vertebral bodies
- Laminae
- Spinous processes
- Pedicles
- Transverse processes
- Foramenatransversaria

Photographs were taken to document the degree of fusion, and a review of relevant literature was conducted to contextualize the findings.

Results

During the examination of cervical vertebrae, a block vertebra, specifically a fused C3-C4, was identified. The fusion involved the vertebral bodies, which were completely fused anteroposteriorly. However, the laminae on either side of C3 and C4 were not fully fused, although partial fusion at the spinous processes was observed. The other vertebral arch elements, including pedicles and transverse processes, were fused. No other abnormalities such as spina bifida or malformations of foramina transversaria were observed in the specimen.

The bodies of C3 and C4 were completely fused anteroposteriorly. With respect to the vertebral arch elements, laminae of the corresponding sides and the spinous processes of C3 and C4 were separate and partially fused at the spinous process. All other vertebral arch elements were fused [Table/Fig-1].

This finding is consistent with cases documented in the literature, where fusion commonly occurs at the C2-C3 or C6-C7 levels. The C3-C4 fusion observed in this case represents a rarer form of cervical vertebral fusion.

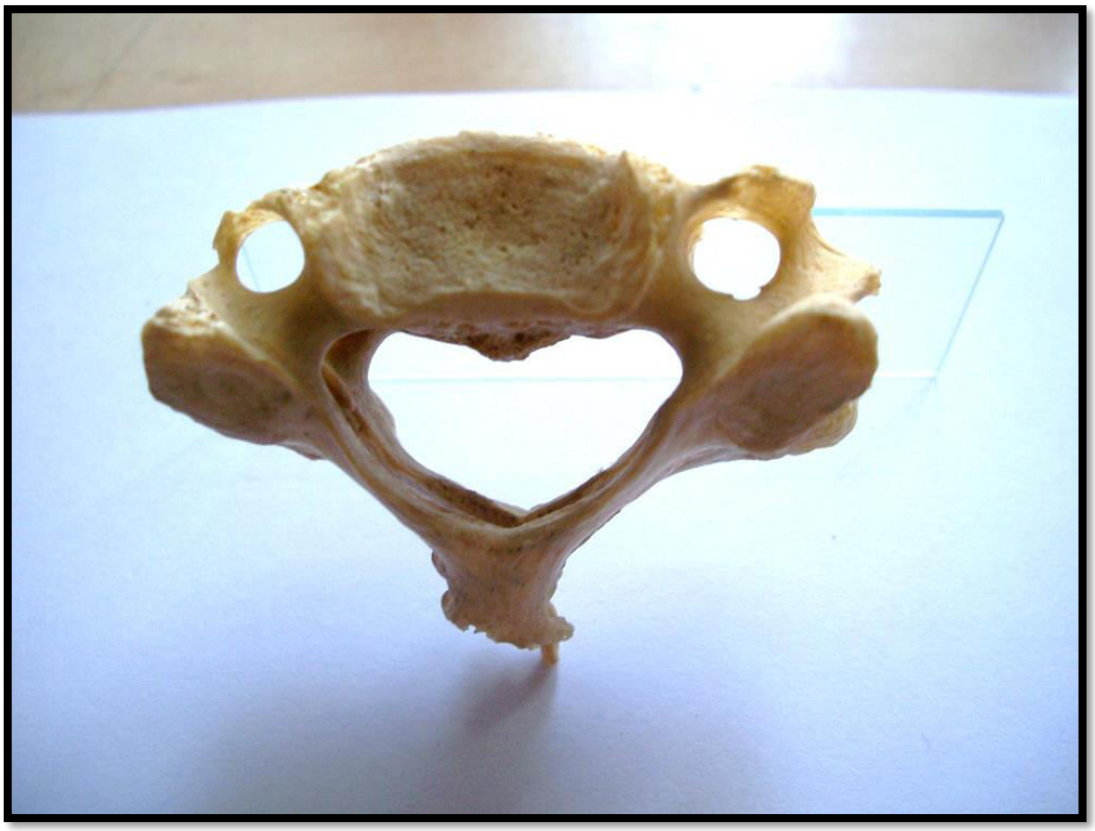

Figure1 showing fused C3 and C4 cervical vertebra

Discussion

The segmentation of the para-axial mesoderm is a critical process in the development of somites, which ultimately give rise to the vertebral column. The vertebrae are formed from the sclerotome of somites. Failure of normal segmentation of the cervical somites, particularly during the early intrauterine period (weeks 4-8), can lead to the fusion of cervical vertebrae, a condition known as cervical vertebral fusion (FCV). Failure of normal segmentation of the cervical somites during four to eight weeks of intrauterine period results in fusion of cervical vertebrae [5,6, 8, 12]. Congenital fusion of vertebrae is most commonly seen in the cervical region although it may involve other segments of vertebral column also. [9].

Congenital fusion of cervical vertebrae often coexists with other developmental anomalies, such as renal and limb abnormalities. This association is part of a broader group of VACTERL anomalies, which include vertebral defects, anal atresia, cardiac defects, tracheoesophageal fistula, renal anomalies, and limb abnormalities [1]. This is supported by multiple studies that have observed such associations, stressing the importance of a multidisciplinary approach to management in affected individuals.

A case study by Shilpa et al. (2016) reported partial fusion of the C2 and C3 vertebral bodies, with no fusion of the laminae, and the presence of a right-sided spina bifida at C3 [10]. Similarly, in the present report, varying degrees of fusion between the C3 and C4 vertebrae were observed, but no spina bifida was noted. Another study by Freitas and Ventura (2021) documented a case of a C3 hemivertebra with partial fusion of C2 and C4 [14]. These reports emphasize the diversity in the degree of fusion in congenital anomalies of the cervical vertebrae and the importance of precise radiological examination for accurate diagnosis.

In the present report, there are varying degrees of fusion of C3 and C4 of vertebral bodies and parts of vertebral arches, spina bifida was not observed.

Developmental anomalies of vertebral column are common especially in the cervical region and thus become the point of keen interest from long time to the anatomists and related health professionals[2].

Among 93 axes in a study by George K P et al, a case of a congenitally fused second cervical vertebrae with the third and fourth cervical vertebrae was observed, which accounted for a frequency of 1.08%. There was an incomplete fusion of the vertebral bodies and almost complete fusion of the laminae and facet joints[3].

In severe cases, FCV may induce myelopathy presumably due to spinal stenosis. In some cases, it has been reported that intervertebral disc tear, rupture of the transverse ligament of the atlas, fracture of the odontoid process of the axis, and spondylolysis have been found. The presence of FCV may likely cause the laxity of the ligaments between the occiput and the atlas, leading to the brainstem or spinal cord compression with associated symptoms. Major neurological complications involve quadriplegia or death after minor trauma in high-risk patients. [3].

Sharma et al. studied 48 dried adult vertebral columns and noted FCV in 6.25%, fused thoracic vertebrae in 4.16%, and fused lumbar vertebrae in 2.08% [15].

Nazeer et al. examined 2,400 ossified dried vertebrae and encountered CFCV in 0.5%, fused thoracic vertebrae in 0.08%, and fused lumbar vertebrae in 0% [16].

Superior surface of sixth cervical vertebrae had uncal process for inferior surface of body of fifth vertebra. Inferior surface of seventh cervical Inferior surface of seventh cervical vertebra was flat. Pedicle, laminae and foramina transversarium were not fused on both the sides, Intervertebral foramina were patent. The inferior articular facet of C6 and superior articular facet of C7 were partially fused in a study by Vanitha et al.

Deepaet al. who studied 50 dry adult vertebral columns, the above-mentioned incidences were 2%, 4%, and 2%, respectively [17].

Ajay et al. found CFCV incidence of 1.4% in the material of 280 dried adult cervical vertebrae [22].

The fusion of thoracic vertebrae is usually associated with ossification of an anterior longitudinal ligament in diffuse idiopathic skeletal hyperostosis or ankylosing spondylitis [19].
Soni et al. reported for the fused C2-C3 an incidence of 0.4% to 0.7% with no sex predilection [11].
Shands et al. found an incidence of fused C2-C3 (0.5%) in the radiographic material of 700 patients [23].
Ajay et al. mentioned an incidenceof 0.36% for the fused C2-C3 [22], whereas Roy et al. found a frequency of 0.10% [20]. It has beennoted that up to 70% of atlantooccipital fusions have an associated C2-C3 fusion with instability at the atlantoaxialjoint [11].
In a radiological study by Ankith et al, 930 CT scans were screened, 308 (33.1%) had congenital anomaly. Of these, 184 (59.7%) were males and 124 (40.2.7%) were females, with a mean age of 44.2 years (range, 14–78 years). A total of 377 anomalies were identified, with 69 cases (7.4%) having more than one anomaly. Two hundred and fifty (26.8%) anomalies of the upper cervical region (occiput to C2–C3 disk space) were identified, with the most common upper cervical anomalies being high-riding vertebral artery (108 cases, 11.6%) and ponticulusposticus (PP) (75 cases, 8%). One hundred and twenty seven (13.6%) anomalies of the lower cervical spine (C3–C7) were noted, of which double foramen transversarium was the most common anomaly observed in 46 cases (4.8%)[8]

The occurrence of developmental anomalies in the cervical region is a significant point of interest for anatomists and clinicians alike. George et al. (2014) found that in a study of 93 cervical vertebral columns, a case of congenital fusion between the second and third cervical vertebrae was present in approximately 1.08% of the specimens. This study highlighted that incomplete fusion of the vertebral bodies and almost complete fusion of the laminae and facet joints were common in such cases [3]. This suggests that while the fusion may involve only certain parts of the vertebrae, other components, such as the laminae, may remain unaffected, influencing the clinical presentation and management of FCV.

In more severe cases, FCV can lead to complications such as spinal stenosis and myelopathy. The fusion of cervical vertebrae may result in constriction of the spinal canal, potentially causing compression of the spinal cord. Other complications, including intervertebral disc tear, rupture of the transverse ligament of the atlas, and fractures of the odontoid process of the axis, have also been documented [3]. These complications highlight the need for careful monitoring and management, particularly in individuals with unstable cervical fusions, to avoid neurological deficits and other severe outcomes.

Bodies of Axis & third vertebra were not completely fused on anterior aspect showing a clear gap but on posterior aspect they were completely fused. Pedicles, transverse processes & intervertebral foramen appeared to be normal. Even the laminae were completely separate. Foramenatransversaria of both vertebrae were normal in a study by Shilpa et al[10].

The chromosomal address of Human Pax1 gene is 20p11.2 [7] . Alterations in expression of this gene have been associated with some vertebral anomalies. Hox genes encode transcriptional regulatory proteins that play a key role in control of axial skeletal formation. HoxPG3, HoxPG4 and HoxPG5 are examples of Hox family genes involved in establishing morphologies in the cervical skeleton (17). Mutations in some members of Hox genes family have been associated with cervical vertebrae anomalies.

Overall, while FCV remains a relatively rare condition, its implications for both clinical practice and research are significant. The variety in the degree of fusion, potential for associated anomalies, and the risk of neurological complications necessitate a comprehensive approach to diagnosis, management, and treatment. Early detection, particularly through advanced imaging techniques, plays a key role in minimizing potential risks associated with FCV. Further research into the genetic and embryological origins of these anomalies will continue to enhance our understanding and improve outcomes for affected individuals.

Table1 : Summary of Studies on Fused Cervical Vertebrae (FCV)

S.No.	Study	Summary	References
1	Suganya Saminathan & Amudha Govindarajan (2022)	This study highlights the clinical significance of fused cervical vertebrae (FCV) and presents a case series. The authors emphasize the importance of early detection and potential complications such as neurological deficits. They also discuss the management of FCV in clinical practice.	[1]
2	Singh, A., & Bhadwar, M. (2021)	The authors focus on the anatomical considerations of cervical vertebral fusion. They discuss the developmental abnormalities leading to FCV and its clinical importance in diagnosis and management.	[2]

3	Paraskevas GK et al. (2019)	This osteological study discusses congenital synostosis of cervical vertebrae. It reviews the frequency of fusion between C2 and C3 and its clinical implications. The paper emphasizes the need for radiological identification of FCV to avoid future complications.	[3]
4	Vanitha, C. et al. (2015)	The study reports a congenital fusion of C6 and C7 vertebrae. It also addresses the potential clinical implications such as spinal stenosis and neurological deficits, and suggests early diagnosis to prevent severe outcomes.	[4]
5	Singh A, Sekhon J, Abhilash et al. (2016)	This study examines congenital fusion of typical cervical vertebrae and reviews the embryological origin of the condition. It also highlights potential complications like myelopathy due to spinal stenosis, particularly in cases involving C2-C3 fusion.	[5]
6	Nallathambi, A. (2014)	This case report discusses a fused typical cervical vertebra and reviews its embryology. The paper emphasizes the rarity of FCV and the clinical consequences, especially during surgical procedures.	[6]
7	Mardani, M., SaeediBorujeni, M.J. et al. (2016)	This review focuses on the embryological etiology of congenital cervical vertebral fusion, explaining the causes of malformation during fetal development and the genetic factors associated with these defects.	[7]
8	Ankith NV, Avinash M, Shrivijayanand KS et al. (2019)	This radiological study screened 930 CT scans and identified cervical anomalies, including FCV. The study reports that the most common anomalies involved the upper cervical region, such as ponticulusposticus and high-riding vertebral artery, providing important data for diagnosis.	[8]
9	Yadav Y, Goswami	This case report discusses C2-C3 synostosis,	[9]

	P, Bharihoke V. (2014)	presenting an incidence of 0.5%. The report highlights the importance of recognizing the condition in radiographic findings to prevent future spinal complications, including nerve root compression.	
10	Shilpa S, Praful N, Madhuri D. (2016)	This case study reports a partially fused C2-C3, with a right-sided spina bifida observed at C3. The authors discuss its clinical implications and the role of imaging in early diagnosis.	[10]
11	Soni P, Sharma V, Sengupta J. (2008)	This study highlights the incidence of cervical vertebral anomalies, including FCV, as incidental findings in radiographic evaluations. The authors mention that cervical anomalies are often asymptomatic but may require attention during surgical procedures.	[11]
12	Sadler TW, Langman J. (2012)	This textbook provides a foundational understanding of embryology, including the segmentation of somites and the formation of the vertebral column. The failure of normal segmentation is identified as the cause of cervical vertebral fusion.	[12]
13	Moore KL, Persaud TVN, Torchia MG. (2013)	This textbook on human development offers an overview of the skeletal system's formation, including cervical vertebrae. It explains how abnormalities like FCV result from disruptions in somite segmentation during embryonic development.	[13]
14	Freitas MM, Ventura LC. (2021)	This study documents a case of a hemi vertebra at C3 with partial fusion of C2 and C4, emphasizing the importance of understanding the varying degrees of fusion for diagnosis and treatment.	[14]
15	Sharma M, Baidwan S, Jindal AK, Gorea RK. (2013)	This study examines the prevalence of FCV in 48 dried adult vertebral columns. The authors report that the frequency of FCV was 6.25%, underlining the need for awareness of	[15]

		congenital cervical anomalies in clinical settings.	
16	Nazeer M, Soni S, Sreekanth T et al. (2014)	This study reviews the occurrence of cervical fusion anomalies in 2,400 ossified dried vertebrae. The authors report a lower incidence of FCV, with notable cases of thoracic and lumbar vertebral fusion.	[16]
17	Deepa S, Rajasekar SS. (2014)	This study investigates a series of vertebral synostosis cases, focusing on clinical implications, including potential neurological issues like nerve root compression and spinal stenosis.	[17]
18	Ajay N, Tejaswi HL, Rajendra R, Makandar UK. (2015)	This study on cervical vertebral synostosis in dried adult vertebrae reports a 1.4% incidence, providing valuable data on the prevalence of FCV and its clinical significance.	[18]
19	Elster AD. (1989)	The study discusses Bertolotti's syndrome and its association with congenital vertebral anomalies, including thoracic vertebral fusion. The author emphasizes the clinical importance of identifying vertebral fusion to prevent complications during surgery.	[19]
20	Roy PP, Arun DM, Shedge SA. (2018)	This study reports a case of fusion between C2 and C3. The authors provide insights into the frequency of cervical vertebra fusion and discuss the potential clinical impact, particularly regarding instability at the atlantoaxial joint.	[20]

Conclusion

Cervical vertebral fusion, although relatively rare, can have significant clinical implications. Early detection and awareness of the fusion, such as that observed between C3 and C4 in this case, are essential for preventing complications associated with this anomaly. These include potential neurological deficits, degenerative changes in adjacent vertebrae, and difficulties in performing certain medical procedures.

It is critical for healthcare professionals, particularly those involved in spine surgery and anesthesiology, to be aware of the potential for cervical vertebral fusion in their patients. Early diagnosis, patient counseling, and regular monitoring can greatly improve the patient's quality of life and reduce the risks of degenerative complications in the long term. Furthermore, this case underscores the need for greater understanding and research into the embryological origins and clinical significance of congenital vertebral anomalies.

The awareness about the complications as a result of FCV helps in anticipating these during procedures involving the cervical spine and also during anaesthetic manoeuvres of neck to avoid them. Majority of the fusion reported in literate were between C2 and C3 and rarely C3 and C4. So diagnosis of congenital fusion of C3-C4 is helpful in treating and managing the related complicated outcomes yet to be appeared and its knowledge can further assist in planning the surgeries of head &neck.Also upon earlier diagnosis of this condition, the patients can be properly counselled as to its presentations and risks, ensuring proper followup and improving their quality of life.

Though the fusion may appear silent, but in advanced age it causes degenerative changes in non-segmented cervical regions and also leads to development of hypermobility and degenerative arthritis above and below the fused cervical region, webbed neck, kyphosis, torticollis, compression of nerve roots resulting in and paralysis of the concerned parts of the body. Early diagnosis can help in the prevention of degenerative process by motivating the patients to change their lifestyle.The detailed knowledge on variations of spleen is important in clinical practice to avoid and prevent any complications and to obtain a good operative, as well as diagnostic intervention.

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