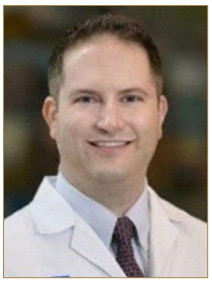
Neurospine 2020;17(4):859-861.
https://doi.org/10.14245/ns.2040548.274

Neurospine
pISSN 2586-6583 eISSN 2586-6591

Editorial

From Anatomic to Genetic Understanding of Developmental Craniovertebral Junction Abnormalities



Corresponding Author
Alexander E. Ropper

Department of Neurosurgery, Baylor College of Medicine, Houston, TX. 77030, USA
E-mail: Alexander.Ropper@bcm.edu

See the article "Weak Ligaments and Sloping Joints: A New Hypothesis for Development of Congenital Atlantoaxial Dislocation and Basilar Invagination" via https://doi.org/10.14245/ns.2040434.217.

The anatomically complex, yet compact, craniovertebral junction (CVJ) is the site of multiple congenital and developmental abnormalities including basilar invagination (BI) and atlantoaxial dislocation (AAD). The dizzying array of radiographic measurements; such as Wackenheim's line, McRae's line, Modified Ranawat's line, etc. has created debate among neurosurgeons and radiologist as to the exact definitions of BI and AAD. While traumatic instability at the CVJ has a simpler treatment paradigm, the diagnosis and treatments for developmental CVJ pathology, which can be accompanied by central nervous system disease, remains more challenging.

The clinical implications of abnormalities at the CVJ became more apparent after Chamberlain's report in 1939 titled "Basilar Impression (Platybasia): A Bizarre Developmental Anomaly of the Occipital Bone and Upper Cervical Spine with Striking and Misleading Neurologic Manifestations".[1] Chamberlain, a American radiologist, credited the earlier description of these characteristic bony CVJ abnormalities to Virchow, Rokitansky and Grawitz in the latter half of the 19th century; all based on autopsy. They believed that while bony and ligamentous anatomic variations may have caused spastic quadriparesis in some patients, many of the clinical presentations were due to other causes such as syphilis. Homen[2] noted the focal effects of the dorsal odontoid on the central cervicomedullary junction in autopsy studies and correlated those with the patients' clinical symptomatology before death.

In 1905, Schiiller[3] published the first description of a living patient with a confirmed CVJ anomaly (as seen on radiograph) with lower cranial nerve dysfunction, compression of the aqueduct and cerebellum resulting in hydrocephalus and the stenosis at the foramen magnum resulting in long tract signs. Chamberlain's 1939 monograph summarizes his predecessor's findings and offers multiple case reports of similar patients who underwent posterior fossa and upper cervical spine decompressions, with improvement in their symptoms. He also hypothesized that symptoms rarely present in the first decade of life since children's brains can accommodate this compression, but as young adults, neurological deficits progress rather quickly. And therefore, basilar impression must be considered in cases where "disseminated sclerosis" and synringomelia are thought to be causative.[1]

During the mid-20th century, posterior decompression of the foramen magnum remained the mainstay of surgical treatment for many cases, however, it was unsuccessful in cases of irreducible ventral compression. Transoral approaches for ventral decompression were pioneered in the 1950s and 1960's by Scoville and Sherman[4] and Greenberg et al.[5] and added a necessary surgical approach to treat severe pathology. With advances in imaging techniques, understanding CVJ pathology improved. Combined with modern spinal instrumentation

and biomechanical models, the surgical approaches and indications to treat diseases such as BI and AAD has improved outcomes. While the exact relationship between the bony and ligamentous disorders of the CVJ to central nervous system pathology such as Chiari malformation remains controversial. Substantial literature exists on the relationship of CVJ pathology with genetic syndromes such as Goldenhar syndrome, Klippel-Fiel syndrome, Larsen syndrome, and Pierre-Robin syndrome.[6] These genetic syndromes are thought to have a Mendialian genetic inheritance pattern and a multitude of pathognomonic systemic findings. This genetic analysis has been taken a step further with advanced genotyping.

Chauhan et al.[7] have published an interesting extension of this work in the current issue. Their experience with a large population of developmental CVJ patients has led them to identify candidate genes for the laxity of ligaments and sloping of the CVJ joints resulting in developmental abnormalities. The goal of such work is to perform early detection of asymptomatic carriers for these genes, since mild bony and ligamentous disease may remain clinically dormant in children until neurological deficits develop as young adults. As the authors explain, the incomplete penetrance observed in some familial studies makes this work even more challenging.

The authors' work extends research using GWAS (genome-wide association) and single-nucleotide polymorphisms which identified the fibrillin 1 gene (*FBN1*) on chromosome 15 as a possible gene involved in Chiari malformation. They then hypothesized that since fibrillin is a major component of microfibrils, that *FBN1* mutations may also be related to BI and AAD. Correlation was performed between the exons implicated in neonatal Marfan's Syndrome and Occ–C1 and C1–2 joint morphology in patients with BI and AAD and controls. 64% of patients demonstrated sequence variations in the intronic region of the *FBN1* gene and a this was associated with increased joint obliquity and severity of BI and AAD. Chauhan and colleagues concluded that this "double hit" hypothesis; the presence of lax ligaments (from *FBN1* gene alterations) combined with abnormal joint morphology may contribute to the development of nonsyndromic BI and AAD.

This report suggests a relationship between these gene mutations and CVJ abnormalities, but appropriately stops short of concluding a direct causal relationship. These results will likely be expanded with future studies to better define this association. The authors leverage the genetic technology available to modern clinicians to investigate possible causes of a complex and heterogenous disease entity, just as their predecessors used cadaveric dissection in their era to further the field's understanding.

CONFLICT OF INTEREST

Dr. Ropper receives consulting fees from Stryker and Globus Medical, but these have no bearing on the content of this report.

REFERENCES

1. Chamberlain WE. Basilar impression (platybasia): a bizarre developmental anomaly of the occipital bone and upper cervical spine with striking and misleading neurologic manifestations. Yale J Biol Med 1939;11:487-96.
2. Homen EA. Zur kenntnis der rhachitischen deformationen der schädelbasis und der basalen schädelhyperostosen. Dtsch Z Nervenheilkd 1901;20:1. (German).
3. Schiiller A. Die schadelbasis im rontgenbilde. fortschr. a. d. Geb. d. Rontgenstrahlen, 1905. (German).
4. Scoville WB, Sherman IJ. Platybasia, report of 10 cases with comments on familial tendency, a special diagnostic sign, and the end results of operation. Ann Surg 1951;133:496-502.
5. Greenberg AD, Scoville WB, Davey LM. Transoral decompression of atlanto-axial dislocation due to odontoid hypoplasia. Report of two cases. J Neurosurg 1968;28:266-9.
6. Menezes AH, Vogel TW. Specific entities affecting the craniocervical region: syndromes affecting the craniocervical junction. Childs Nerv Syst 2008;24:1155-63.
7. Chauhan AK, Chandra PS, Goyal N. Weak ligaments and sloping joints: a new hypothesis for development of congenital atlantoaxial dislocation and basilar invagination. Neurospine 2020;17:843-56.

 https://doi.org/10.14245/ns.2040548.274

Title: Great Still life on pedestal
Artist: Pablo Picasso
Year: 1931