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Cranio-cervical Instability in Patients with Hypermobility Connective Disorders

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Commentary

Cranio-cervical instability is well documented in connective tissue disorders such as rheumatoid arthritis, systemic lupus, and genetic disorders such as Down's syndrome and Osteogenesis Imperfecta. However, less understood are the more than fifty genetic disorders of collagen characterized by joint laxity, and of course, laxity of the ligaments of the spine. Given the propensity in these patients for spinal instability, it is not surprising that the most severe symptoms arise in the most mobile part of the spine, the cranio-cervical junction. The increased recognition of hypermobility syndromic disorders, of which Ehlers Danlos Syndome (EDS) is emblematic, has prompted questions and concern as to what constitutes pathological instability in this category of patients, and how to best diagnose this instability. These questions assume significant importance, given recent epidemiological evidence that the hypermobility syndromes, exemplified by EDS, are far more prevalent than previously thought.

Hypermobility is common. While hypermobile joints occur frequently in healthy children, they can also be severely disabling in others, wherein they constitute the Hypermobility Syndrome, characterized by pain in the joints and spine, and fatigue [1]. Ehlers-Danlos Syndrome, Loeys Dietz Syndome, Stickler Syndrome, Marfan Syndrome, Cleidocranial Dysostosis, Morquio Syndrome Down syndrome and many other less well known connective tissue disorders manifest as "lax ligament" syndromes. Pathological laxity of the cranio-cervical junction Results in what patients describe as "bobble head", with neck and suboccipital pain, bulbar symptoms and myelopathy. A recent Consensus Statement established that a group of symptoms-the Cervical Medullary Syndrome - may be associated with cranio-cervical instability (CCI) [2]. These symptoms are well established in the literature: altered vision, hearing , speech, swallowing and balance, the presence of vertigo , dizziness, altered sleep architecture, and signs of dysautonomia -such as Postural Orthostatic Tachycardia Syndrome-weakness and sensory loss. The Consensus concluded that the presence of the Cervical Medullary Syndrome should prompt consideration of a disorder of the cranio-cervical junction.

Whilst the clinical presentation of CCI is accepted in the population with conditions such as rheumatoid arthritis and osteogenesis imperfecta, the same clinical recognition has not been afforded to the hereditary hypermobility connective tissue disorders (HHCTD). Radiological measurements for degenerative connective tissue disorders are standard in the neuro-radiological lexicon. However, the diagnosis of cranio-cervical instability, such that occurs in EDS, more often requires images performed in flexion - extension, and careful measurement [3]. While advocates for HHCTD recommend the use of dynamic imaging, arguing that ligamentous instability is usually not apparent on routine imaging performed in the supine position, opponents argue that dynamic imaging is often not available, is not standard neurosurgical practice, and that the radiological diagnosis of pathological instability at the cranio-cervical junction has not been clearly established in the literature for the hypermobility population. Indeed, with the exception of osteogenesis imperfecta, there is a paucity of neurological literature referencing CCI in this group of disorders [1,3-7].

Notwithstanding that dynamic measurements of the cranio-cervical junction may be nuanced, the literature does support a scientific approach to the diagnosis of CCI in the HHCTD population. The diagnosis of instability should be predicated upon the presence of a supportive history and concordant, demonstrable neurological findings. Punjabi and White defined instability as the loss of the ability of the spine under physiological loads to maintain relationships between vertebrae in such a way that there is no damage or subsequent irritation of the spinal cord, brainstem or nerve roots. Additionally, that instability can be considered to exist where there is development of deformity or incapacitating pain due to structural change [8]. Standard metrics inform the surgeon of potential instability, in the form of basilar invagination, wherein the odontoid may broach McRae's line (across the foramen magnum), MacGregor's line (connecting the hard palate to the lowest point of the skull), Chamberlain's Line (palate to opisthion), Wackenheim's line (drawn along the clivus), digastric notch line, or the bimastoid line. In addition, one may determine basilar invagination by Ranawat's method, Lee's X lines (drawn from the basion to the mid-lamina of C2; the lines should be tangential to the odontoid process), and the Power's ratio, wherein the BC/OA ratio should be <1 (the numerator is the length of a line drawn from basion to the posterior C1 ring; the denominator is the distance from the opisthion to the anterior portion of C1). If the BC/OA ratio is greater than 1, cranio-vertebral instability is probable [9].

In the HHCTD, Wackenheim's line and Lee's X-lines may show anterior slippage of the skull on the spine [3], due to forward rotation of the skull upon the spine. The resulting translation of skull upon spine can be measured by the basion-dens interval- the distance between the basion and the top of the odontoid. In the normal person, the basion lies over the midpoint of the odontoid process, with a separation of approximately 5 mm. A basion to dental interval greater 10 mm is abnormal, and predicts occipito-atlantal instability [10]. The Consensus Statement on Basilar Invagination and Cranio-Cervical Instability includes three metrics which may be useful in the identification of CCI and basilar invagination: the clivo-axial angle, the Harris measurement and the Grabb, Mapstone, Oakes method [2].

The Clivo-Axial Angle (CXA) is that angle formed between a line drawn along the posterior aspect of the lower clivus and the posterior axial line. The angle of less than 135 degrees is pathological [11-19]. Increasing acuteness of clivo-axial angle creates a fulcrum by which the odontoid deforms the brainstem [11,20]. The medulla becomes more kinked as the angle becomes more acute, and this results in deformative stress of the neuraxis.

The Harris measurement is that distance from the basion to the Posterior Axial Line (PAL) [21]. Instability is suspected when the basion to the PAL exceeds 12 mm. This measurement, used in conjunction

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with dynamic flexion and extension images of the cervical spine, also measures the dynamic translation between the basion and the odontoid [2]. In the normal individual there is a pivoting movement between the basion and odontoid, but there should be no measureable translatory movement (sliding movement). Translation between the basion and odontoid reflects cranio-vertebral instability [8, 22-24]. Translation of greater than 1mm may in some circumstances warrant evaluation for stabilization [24].

The Grabb, Mapstone, Oakes measurement assesses the risk of clinically significant ventral brainstem compression, and has been statistically correlated with clinical outcome [25]. This methodology draws a line from basion to the posterior inferior edge of the C2 vertebra; a perpendicular distance from this line to the dural edge exceeding 9 mm suggests high risk of ventral brainstem compression. Some authors use a threshold of 8 mm, rather than 9 mm. The finding of ventral brainstem compression by this method prompted transoral odontoidectomy in children, to alleviate the ventral brainstem compression [25].

The importance of dynamic imaging is that ventral brainstem compression may exist in flexion of the cervical spine, but appear normal on routine imaging. For instance, in a survey of Chiari malformation treatment via foramen magnum decompression, surgical failures were thought to range from 20-50% [19]. Klekamp looked at forty-five revision decompressions for Chiari I malformation, of which ten underwent cranio-spinal fusion. He stated that deterioration after decompression, for Chiari I malformation was related to untreated basilar invagination cranio-cervical instability or recurrent CSF flow obstruction. He emphasized the importance of signs of instability and stressed the importance of "functional studies in flexion and extension to demonstrate hypermobility at the cranio-cervical junction.

The presence of cranio-cervical instability is thought to cause pain and neurological findings through three mechanisms: stretch of the lower cranial nerves; stretch of the vertebral arteries and deformative stretching or deformation of the brainstem and upper spinal cord. Neurobiological evidence of deformative stress is manifested in clumping of the neuro-filaments and microtubules and loss of axonal transport [26], the formation of axon retraction balls similar to those seen in diffuse axonal injury [27], pathological calcium influx [28], and altered gene expression [29].

Ligamentous laxity, inherent in HHCTD, may result in cranio-cervical instability, kyphosis of the clivo-axial angle and ventral brainstem compression. In some patients, this causes disabling pain and neurological deficits. Dynamic imaging appears to be helpful in the diagnosis of these challenging conditions. The growing body of knowledge regarding the prevalence of hypermobility connective tissue disorders should lead to more widespread recognition of the lax ligament syndromes arising in the context of HHCTD at the cranio-cervical junction.

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