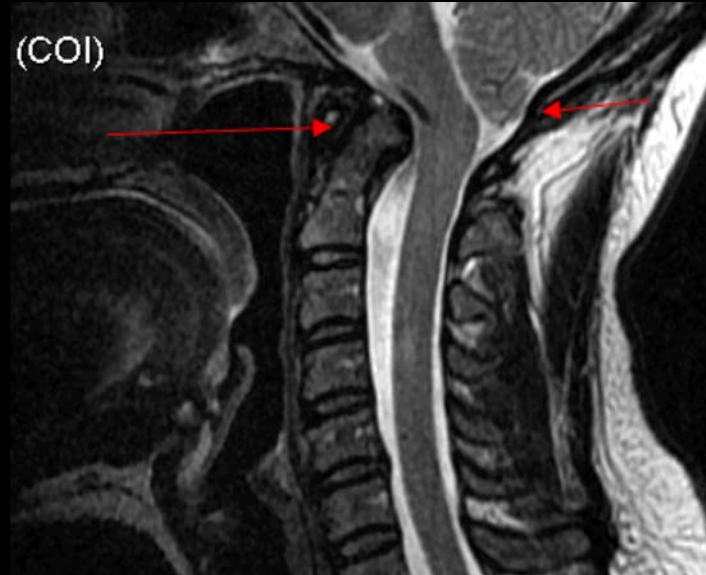


Diagnosis of headache in the EDS population requires a careful consideration and directed studies



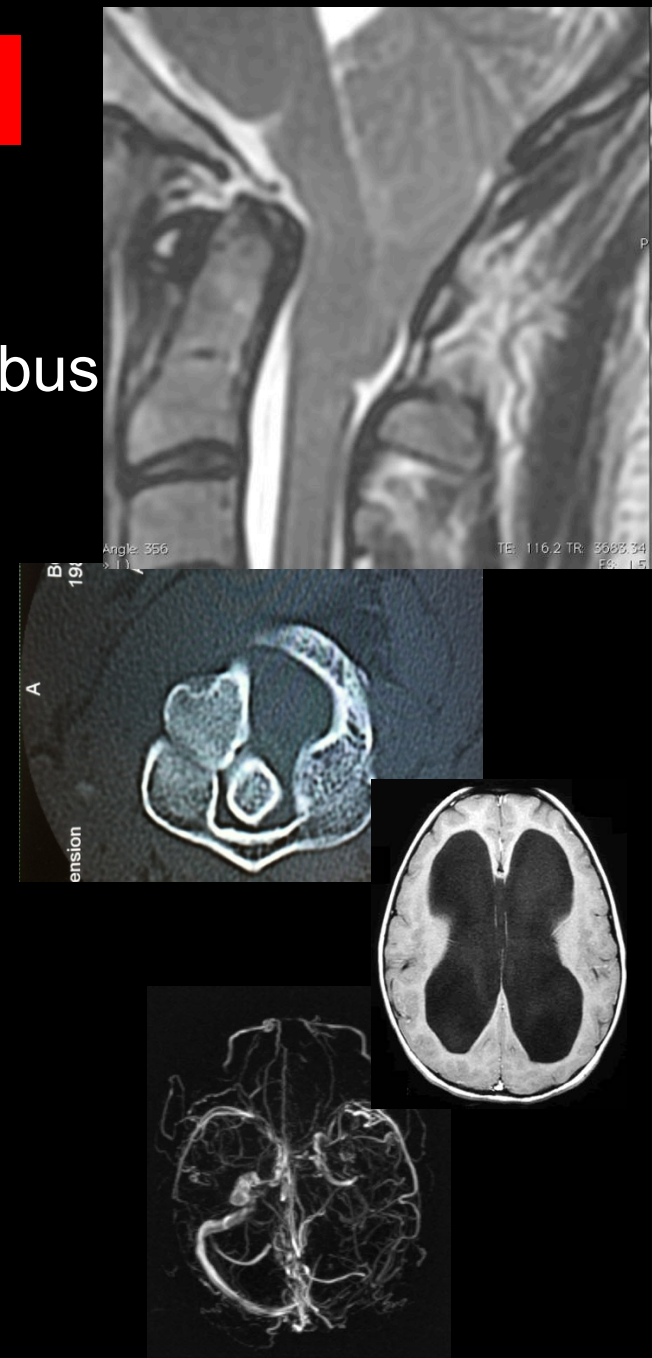
Fraser C. Henderson Sr, MD
Ehlers Danlos Society
Baltimore, Maryland
August 4th , 2018

Disclosure

- President, Computational BioDynamics, LLC
- Consultant , Life Spine , Inc
- Director, Wi2Wi Corp

Headaches that I am thinking of:

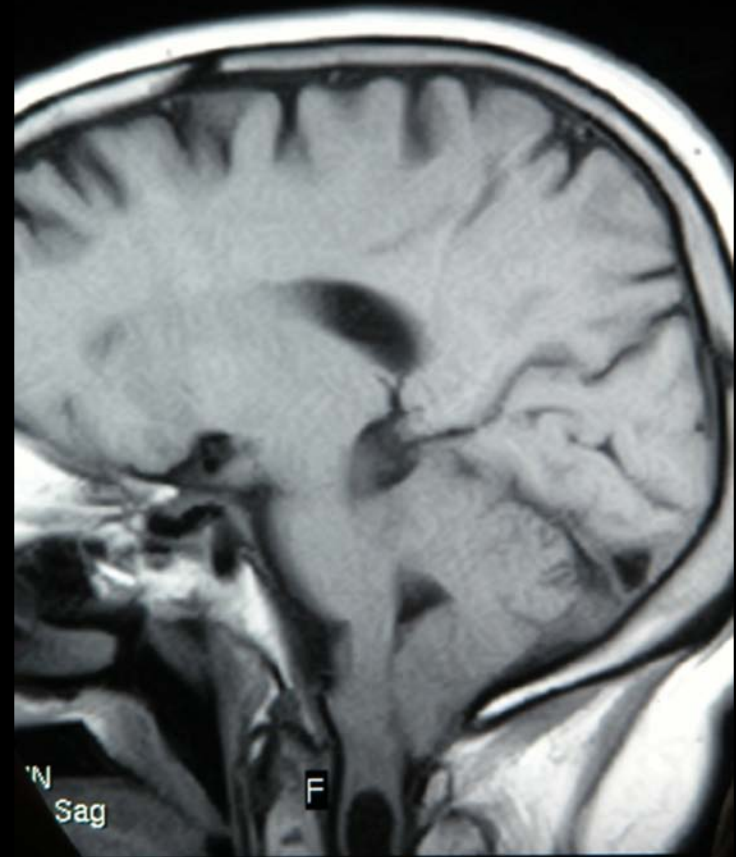
- Chiari Malformation
- Venous outflow obstruction/sinus thrombus
- Arterial disorders, dissection
- CSF increased or low pressure
- Instability – CCJ,AAJ, cervical spine
- Migraine or migrainous TIAs
- TMJ Syndrome
- Tethered cord syndrome
- Mast Cell activation syndrome
- Limbic encephalopathy, NeuroBehcet's



Chiari malformation Type 1

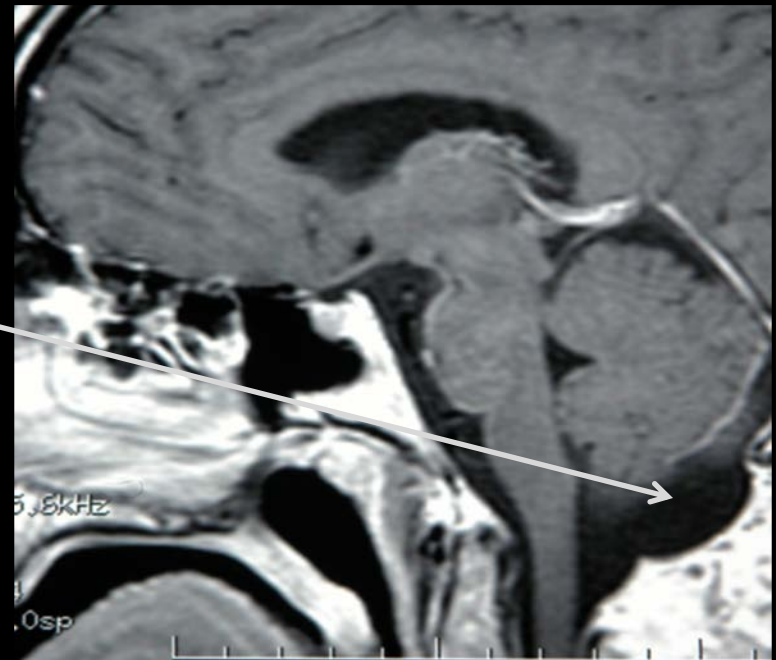
CMI Headache

1. precipitated by cough /or Valsalva maneuver
2. protracted (hours to days) occipital and/or sub-occipital headache
3. symptoms , signs of brainstem, cerebellar or cervical cord dysfunction

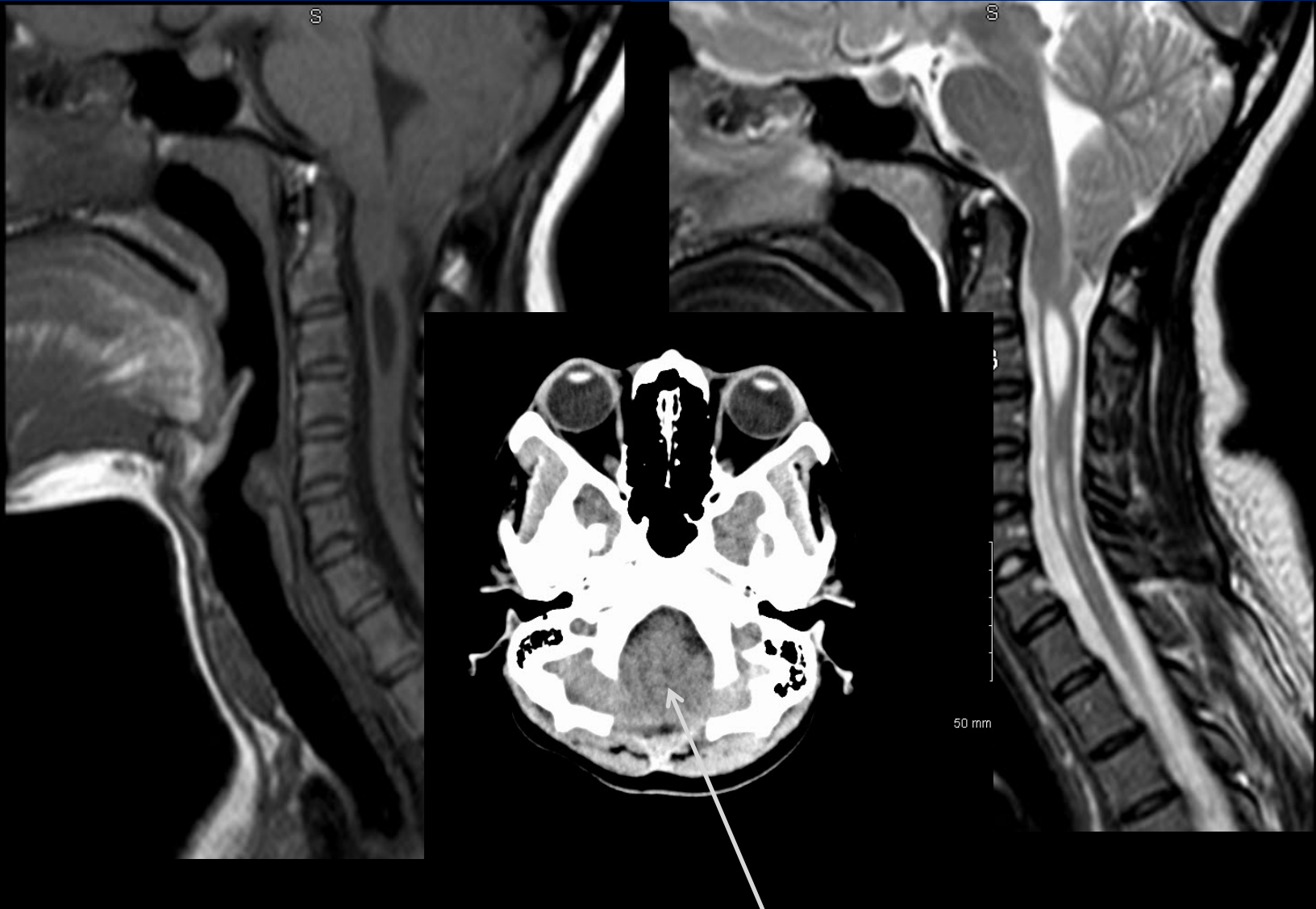


Treatment of Chiari malformation

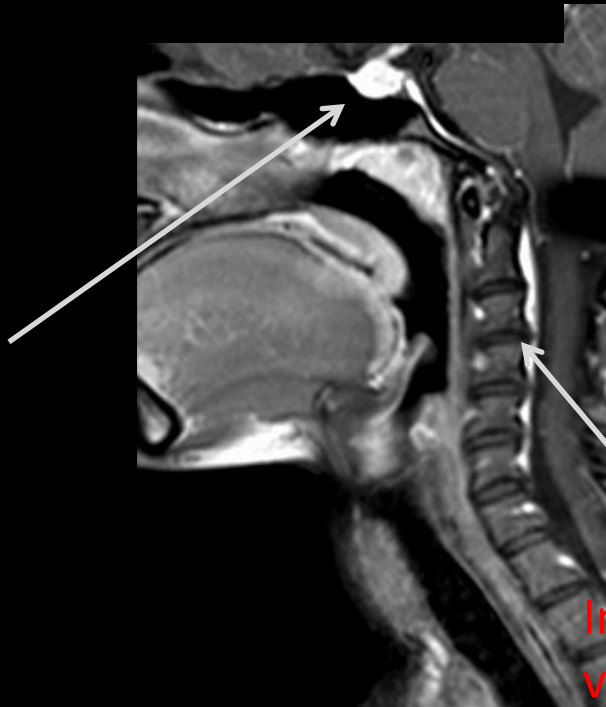
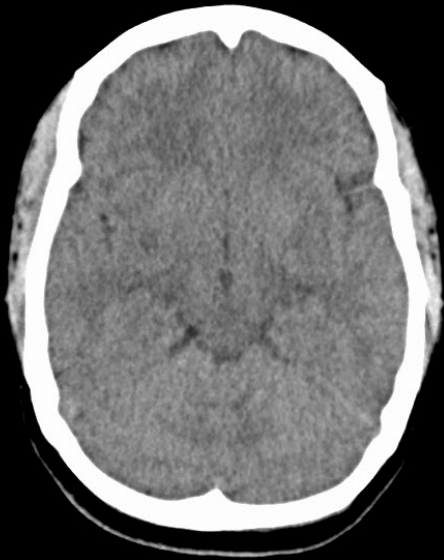
- Suboccipital decompression
- +/- dural patch (expansion duroplasty) to expand the space



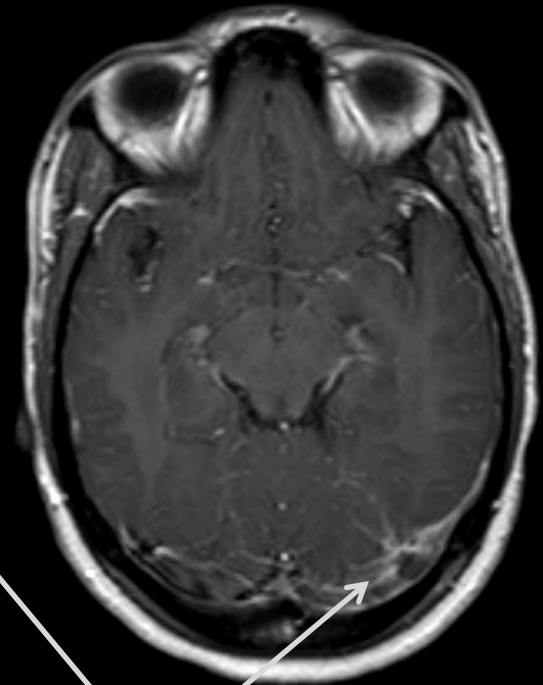
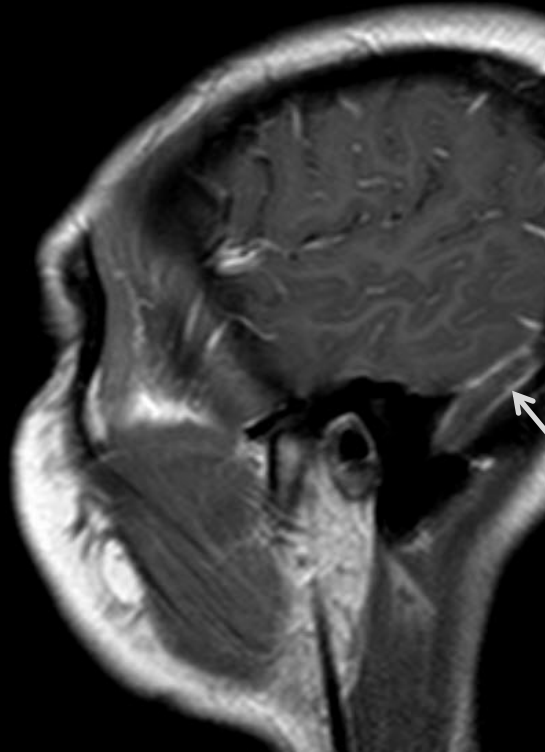
10 years s/p decompression:
Is recurrent Chiari malformation or syrinx
the cause of headache?



In this patient
venous sinus thrombosis was the
cause of headache

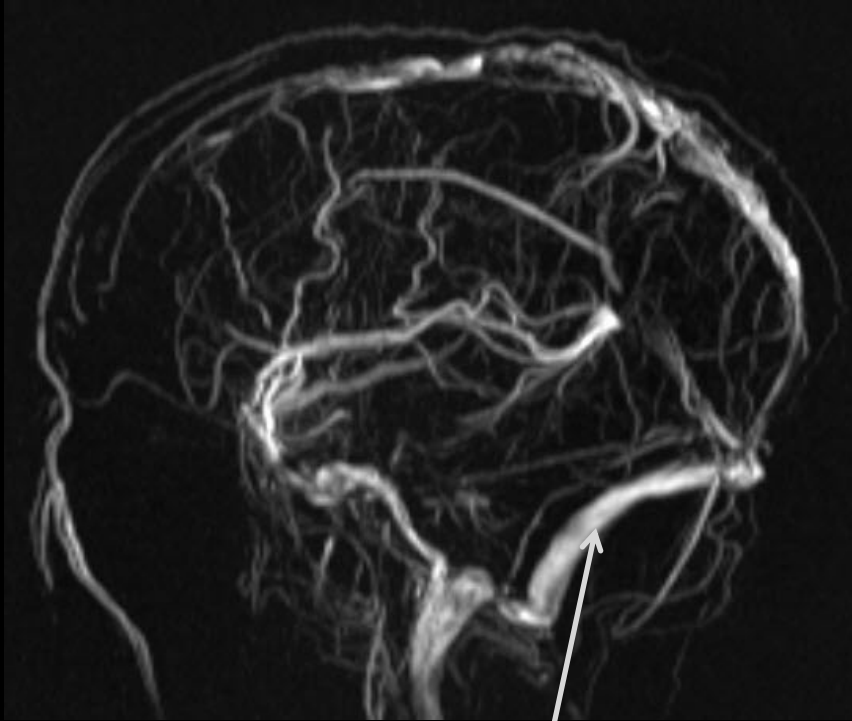


Increased blood flow through the
vertebral plexus

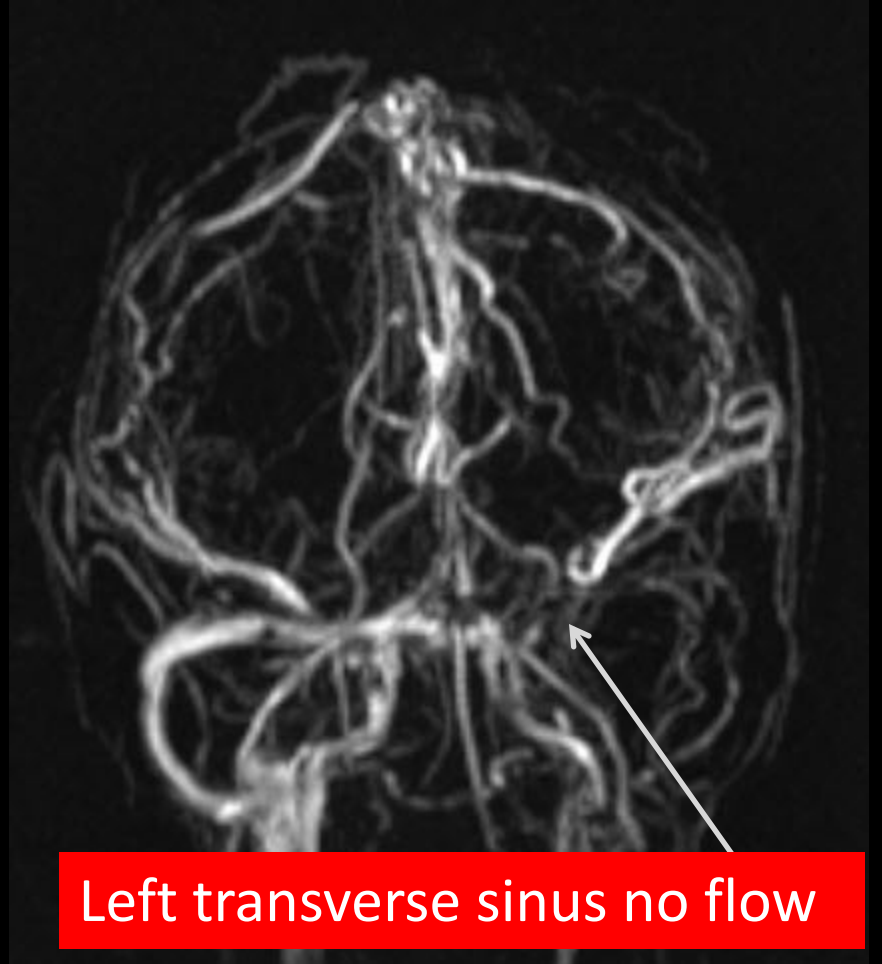


Blood clot

MR venogram



Right transverse sinus
Normal flow



Left transverse sinus no flow

after anti-coagulation with enoxaparin



Restoration of flow

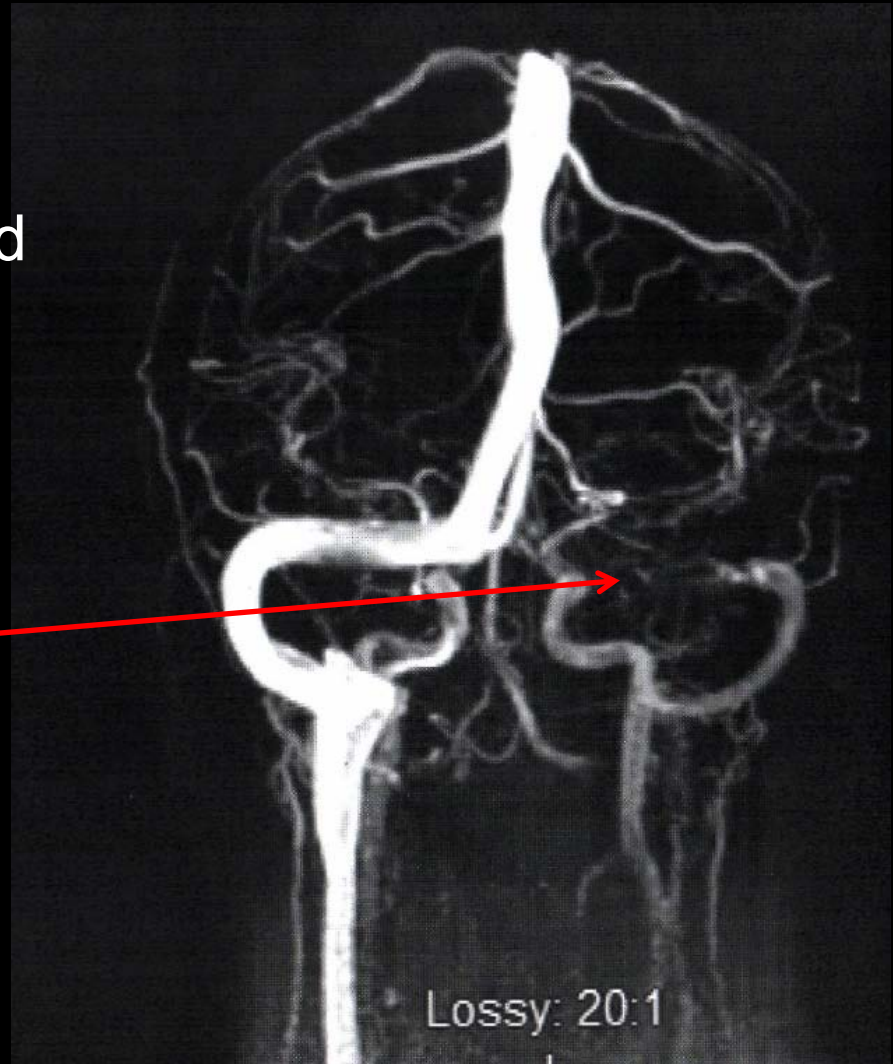
Sinus thrombosis

- 20 yo F with EDS,
- global headache increasing over several days
- Increasing leg weakness
- Urinary incontinence
- Personality change, loss of memory
- **Thrombosis of straight/transverse sinus**
- Rx with Lovenox
- Recovered in 2 days



Acute thrombosis with loss of consciousness

- 25 yo F
- Severe retro-orbital and global headaches
- Dystonic seizures
- loss of consciousness
- MRV – thrombosis of left transverse sinus
- Lovenox started
- Discharged from hospital 2 days later, Walking

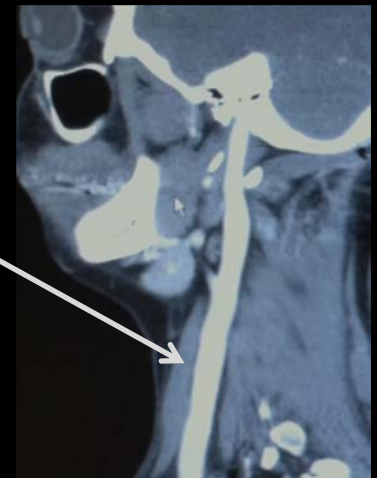


How does blood leave the brain?

- **upright posture:** Increased flow through Vertebral venous plexus

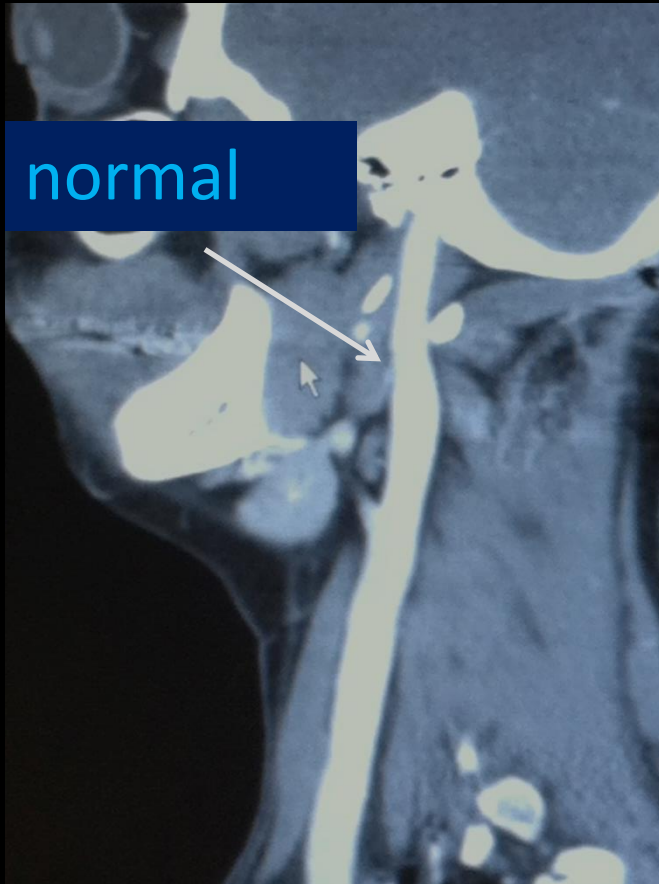


- in **supine posture** Increased flow in Jugular veins

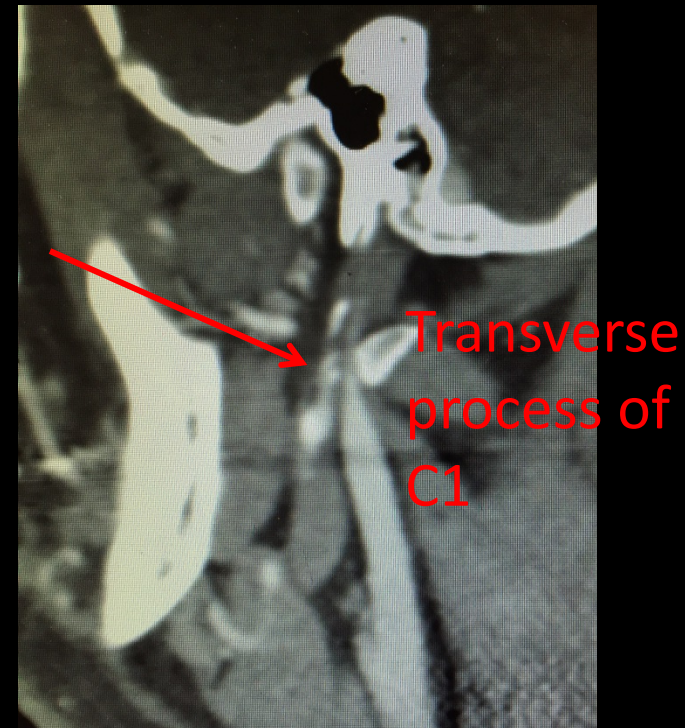


Doepp F, Schreiber SJ, Munster T. How does the blood leave the brain ? A systemic ultrasound analysis of cerebral venous drainage patterns. Neurorad 46: 565-574, 2004

Compression of the jugular vein

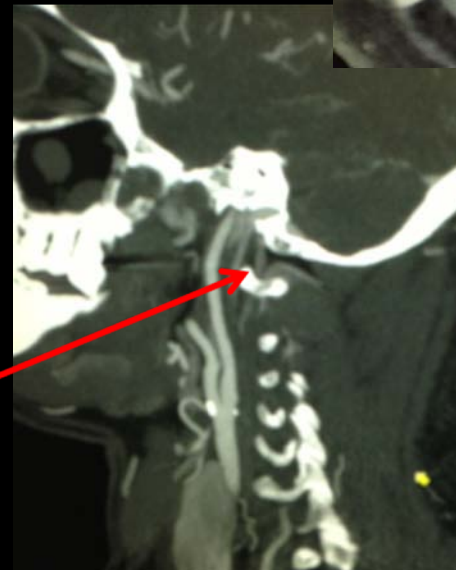


posterior belly of digastric
stylohyoid ligament

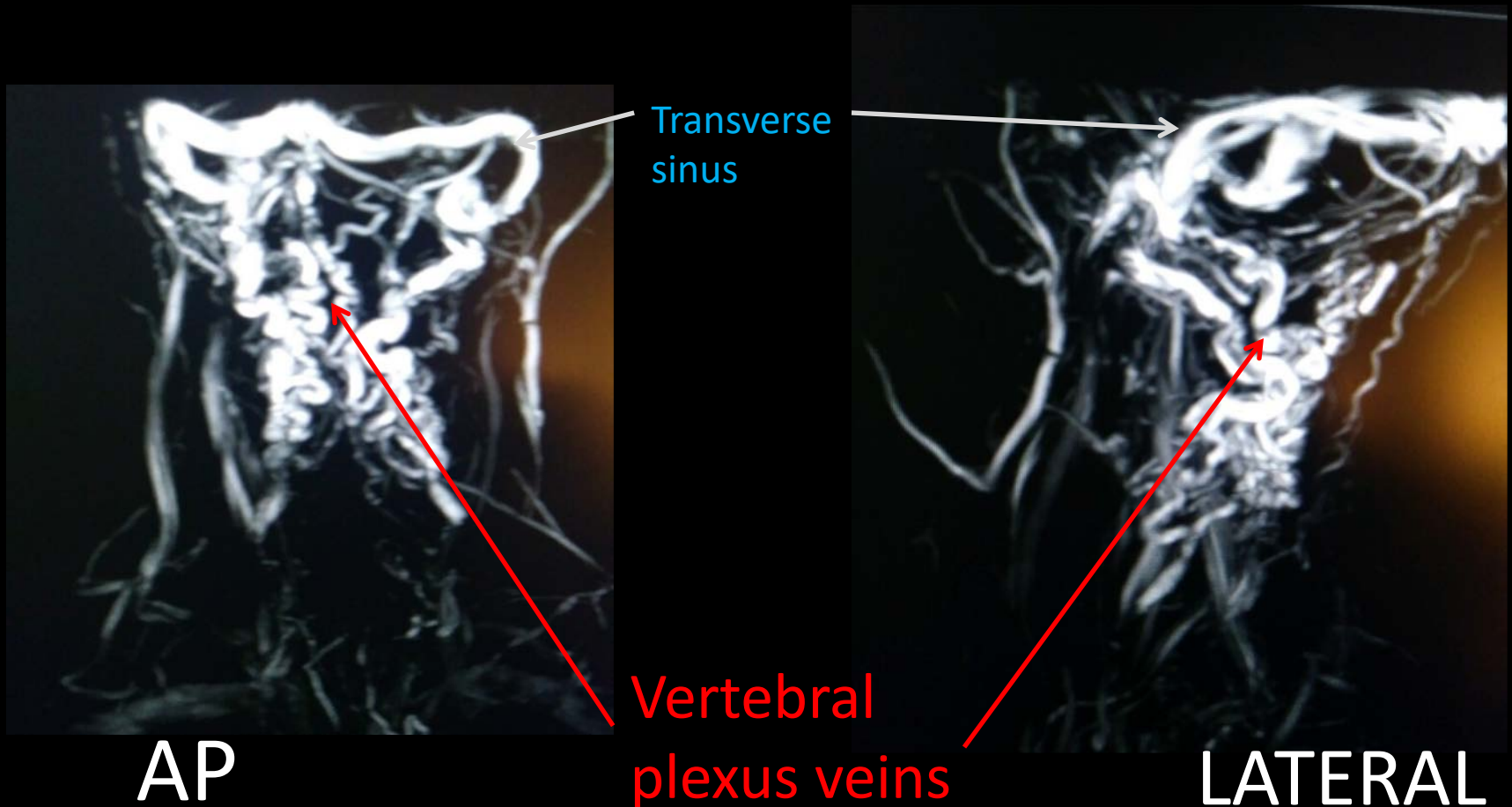


How common is jugular stenosis ?

- 35% CTA show jugular venous compression
- 18% severe stenosis
- 9% have collaterals through the ant+ post lateral condylar veins



Bilateral obstruction of the internal jugular veins may cause collateral flow through vertebral plexus



Raised intracranial venous pressure

- May cause intracranial hypertension
- Probably underlie many cases of IIH

Farb RI, Vanek I, Scott JN, Mikulis DJ, Willinski RA, Tomlinson G, Terbrugge KG. Idiopathic Intracranial Hypertension. *Neurology*, 60:1418-1424, 2003

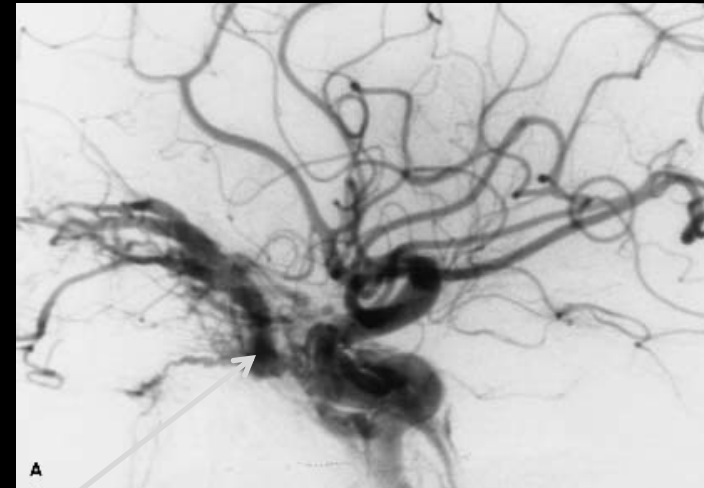
Treatment Intracranial Hypertension

- Weight loss
- Drugs
 - Acetazolamide
 - thiazide diuretic
- Serial lumbar punctures
- CSF diversion : LP or VP shunt
- Optic nerve fenestration
- Stenting
- anticoagulation

Arterial headaches

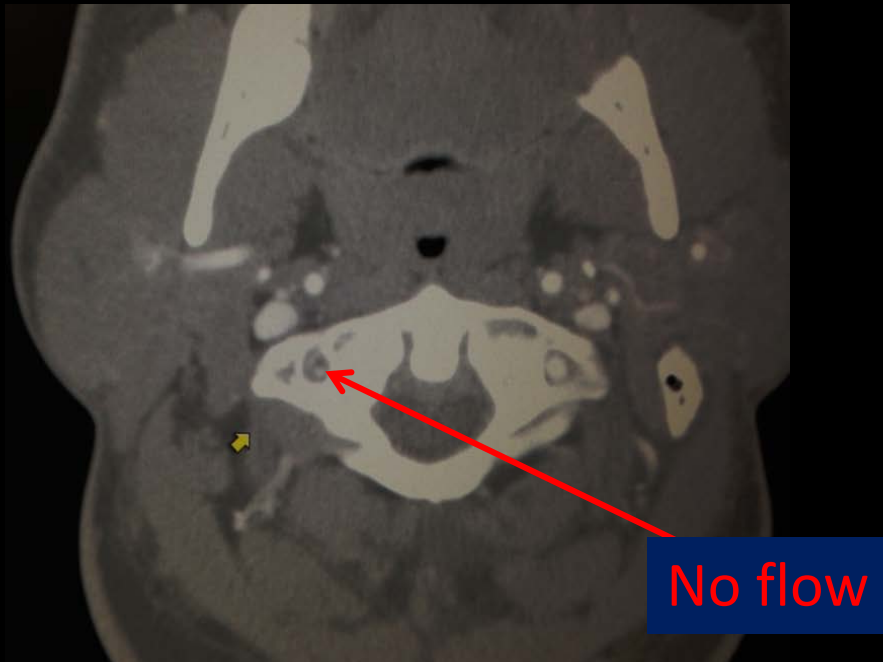
Carotid-cavernous malformations in EDS-Vascular type

- Ipsilateral blurred vision, diplopia , pulsatile tinnitus and periocular swelling
- blind, ophthalmoplegic
- afferent pupil defect
- Intraocular pressure (60 mmHg)
- 9mm proptosis
- left lid and conjunctival swelling
- 20/20 visual acuity in the other eye



Chuman et al., J Neuro-
Ophthalmol, 22-2, 2002

Vertebral artery dissection



Usu after physical trauma, blunt injury, manipulation, HMCTD

Suboccipital headache, altered vision, dysarthria, impaired coordination, stroke like symptoms

Left anterior circulation fed from the right ICA



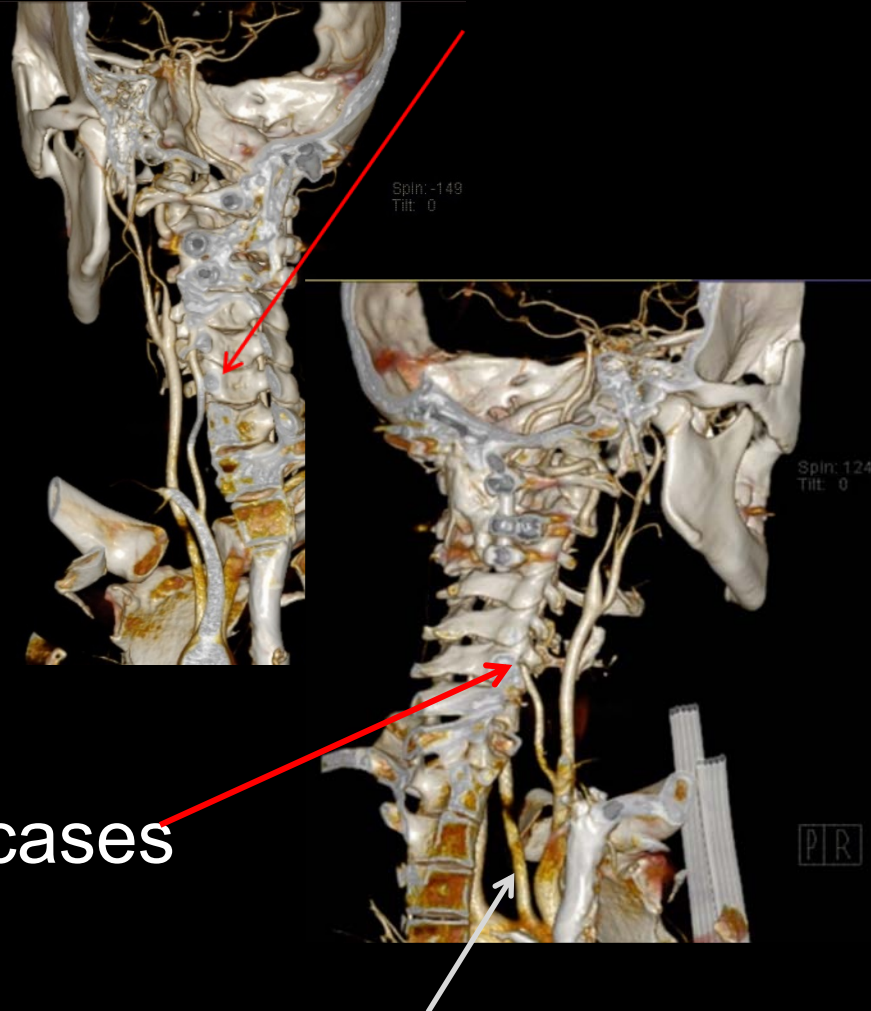
Transient ischemic events
headache

Carotid dissection

Dx on neck CTA, or MRA

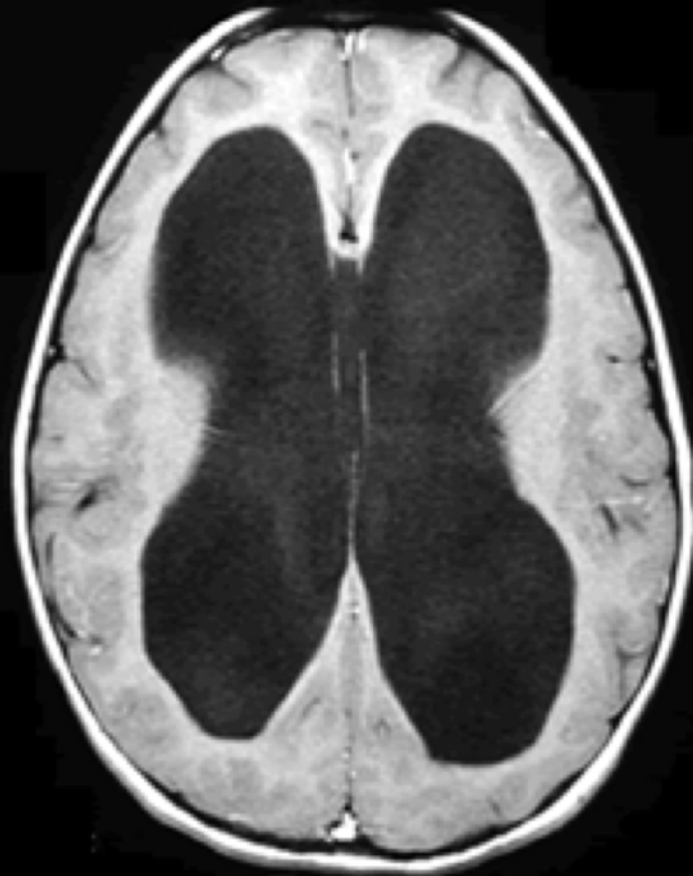
Characteristically:

- temporal h/a, neck or
or eye pain
- miosis/Horner's Syndrome
- ipsilateral vision loss
- Ipsilateral stroke in some cases



Disorders of CSF flow

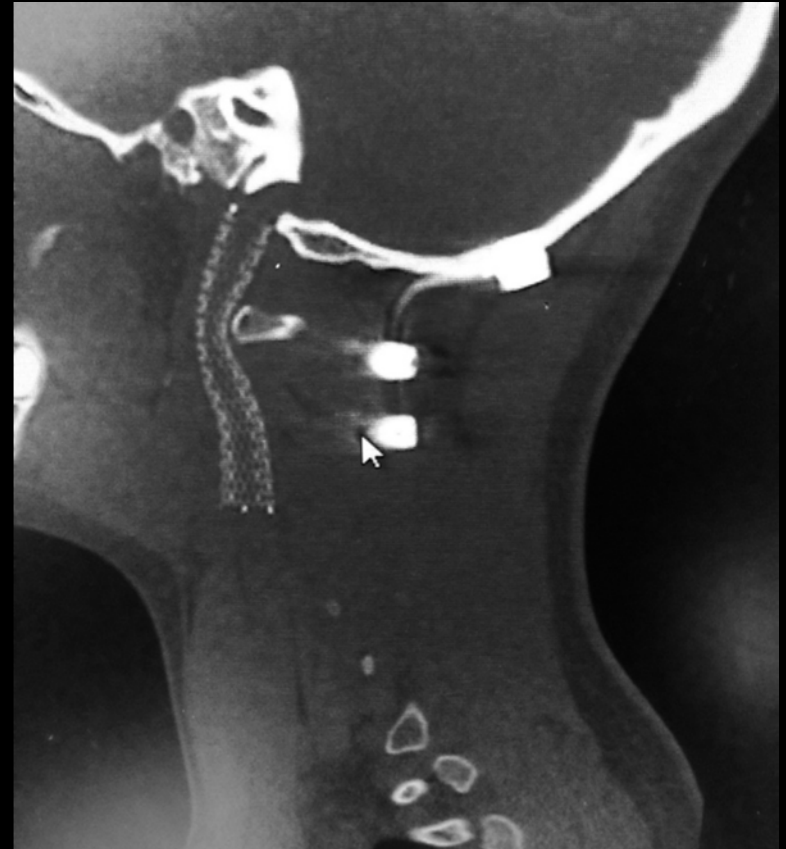
- Hydrocephalus



Idiopathic intracranial Hypertension (IIH)

- Usually 3rd and 4th decades
- Women > men
- Headache (94%)
- visual obscurations/blurring (68%)
- Retro-orbital pain (44%)
- Diplopia (38%)
- Visual loss (30%)
- Pulse synchronous tinnitus or whooshing noise (58%)
- Standard imaging is normal
- CSF pressure by lumbar puncture >20 cm H₂O (or 25 for obese pt)
- Normal CSF composition, no evidence of inflammation

Stenting the transverse sinus and jugular vein to treat IIH

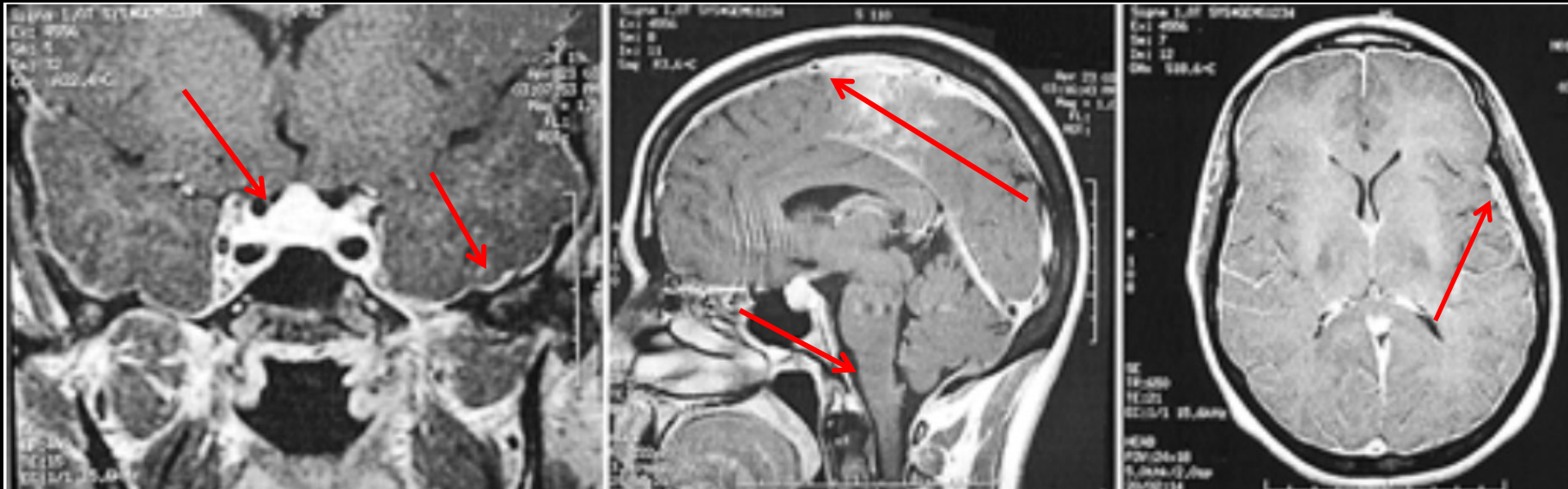


Intracranial Hypotension Syndrome

- Persistent csf leak with Orthostatic Headache
- nausea, vomiting, anorexia, neck pain, dizziness
- horizontal diplopia, changes in hearing, galactorrhea,
- Orthostatic facial or radicular sensorimotor sx
- exacerbated by laughing, coughing, jugular venous compression
- Resistant to analgesic
- LP Pressure < 6 cm H₂O, xanthochromia, lymphocytosis increased RBCs, and protein, h/o LP, trauma, shunt overdrainage

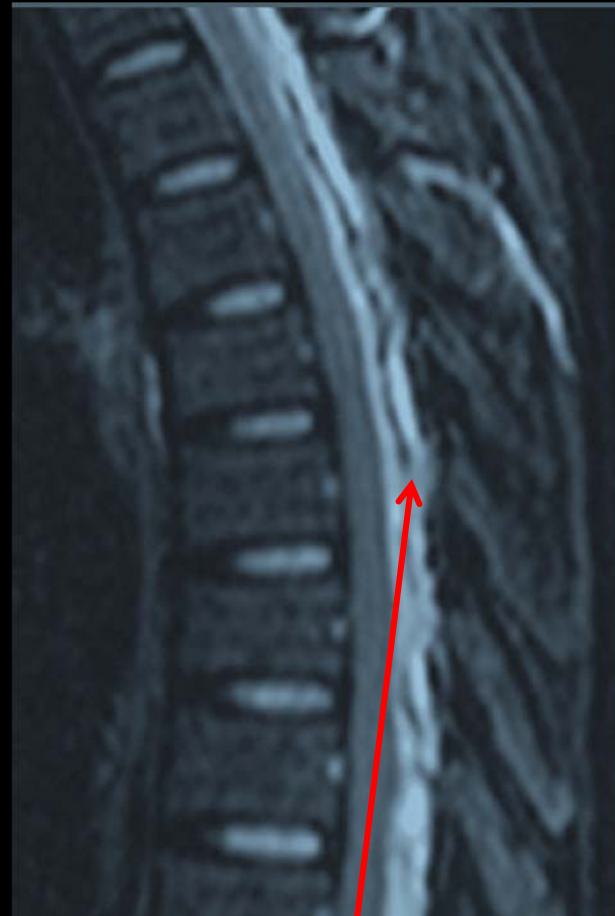
Intracranial hypotension syndrome: a comprehensive review. Paldino, M, Mogilner AY, Tenner MS. Neurosurg Focus (16) 1-8, 2003

IHS - Findings on contrasted MRI



venous engorgement, enlarged pituitary ,
pachymeningeal +/- crescentic subdural fluid,
effacement of the prepontine and other
cisterns; inferior displacement of optic chiasm;
descent of the iter , cerebellar tonsils

Spontaneous Intracranial Hypotension



CSF leak in mid thorax : note extradural fluid and dilated veins

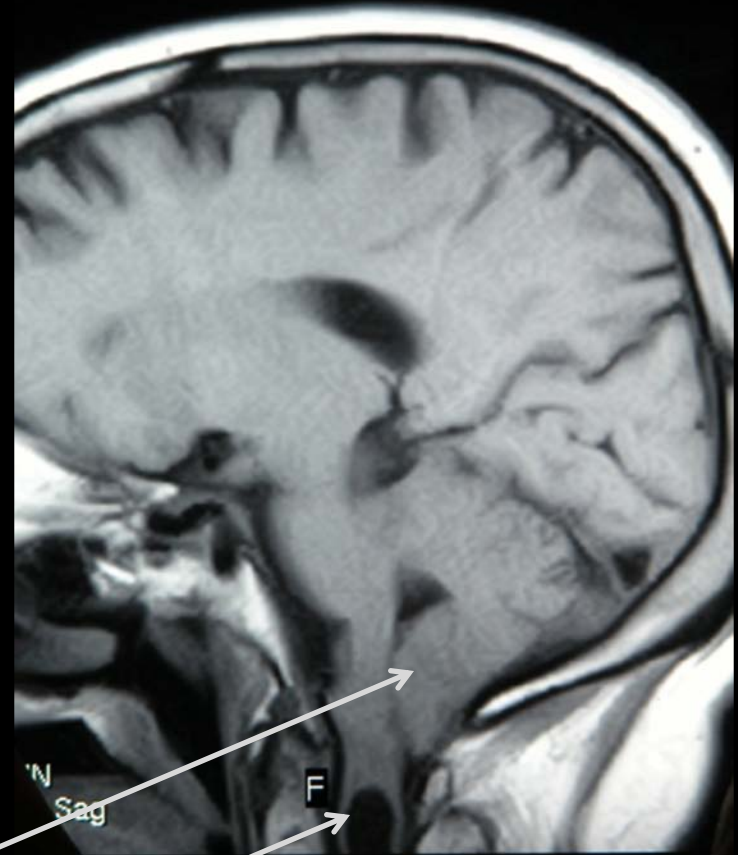
Spontaneous intracranial hypotension

- Note large amount of venous blood flow



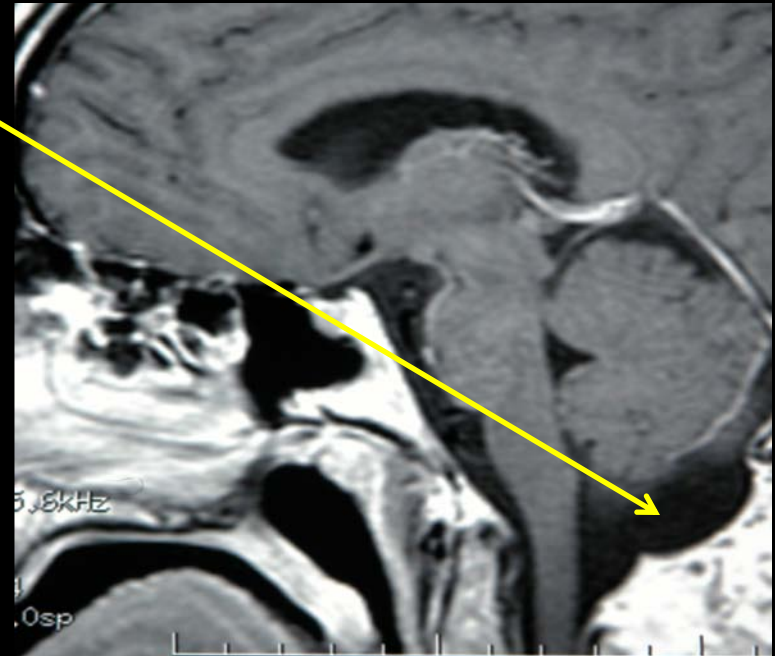
Chiari malformation with headache

Is it the result of syrinx
and Chiari malformation?



Ligamentous Laxity may be one of the reasons that Chiari decompression is not successful

- The treatment of Chiari malformation is foramen magnum decompression
- A literature survey of CM treatment via foramen magnum decompression revealed surgical failure rates ranging from 20% to 50%



Naftel RP, Tubbs RS, Menendez JY, Wellons JC III, Pollack IF, Oakes WJ: Worsening or development of syringomyelia following Chiari I decompression. Clinical article. J Neurosurg Pediatr 12:351–356, 2013 [Abstract](#), [Medline](#)

Failure after decompression of CM1 may occur because of ligamentous laxity

- Of 45 revision decompressions for Chiari 1 Malformation, 10 underwent Cranio-spinal fusion
- “Deteriorationrelated to untreated basilar invagination ...or craniocervical instability
- “of particular importance are signs of instability”
- If “functional studies in flexion extension demonstrate hypermobility of the craniocervical junction.. then decompression should be combined with the appropriate fusion”

Hypermobility connective tissue syndromes and Chiari malformation are co-morbid conditions

- 12.7% of Chiari malformation patients have a connective tissue disorder
- However, many EDS pts have Chiari sx without Chiari malformation



Milhorat TM, et al. Syndrome of occipitoatlantoaxial hypermobility, cranial settling, and Chiari malformation Type I in patients with hereditary disorders of connective tissue. J Neurosurg Spine 7:601-609, 200

CM and EDS

- increased incidence of hereditary disorders of the connective tissue among patients with Chiari malformation [Milhorat et al., 2007]

Milhorat TM, et al. Syndrome of occipitoatlantoaxial hypermobility, cranial settling, and Chiari malformation Type I in patients with hereditary disorders of connective tissue. J Neurosurg Spine 7:601-609, 2000

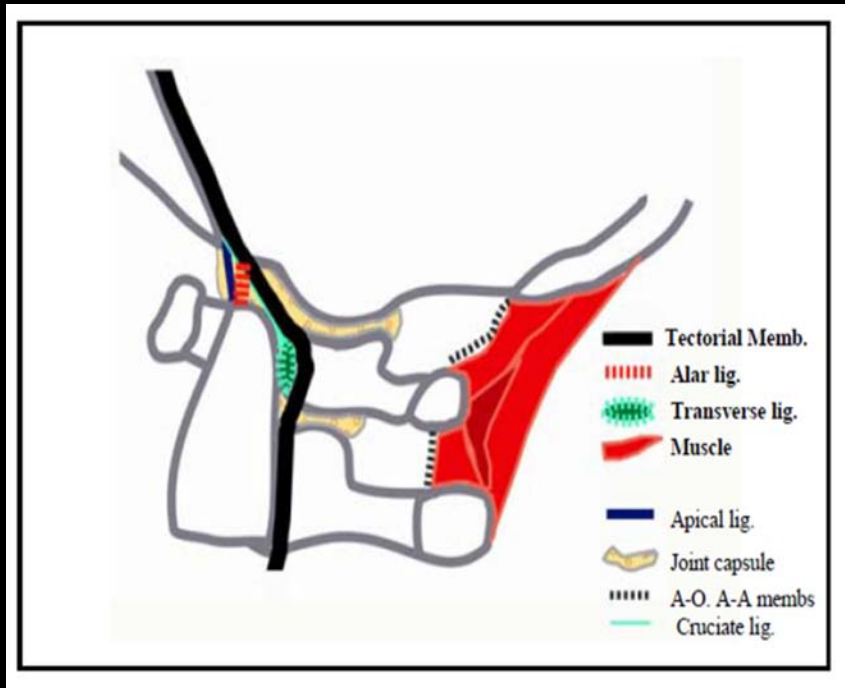
- Chronic headache is a major complaint in EDS

Natural History and Manifestations of the Hypermobility Type Ehlers–Danlos Syndrome: A Pilot Study on 21 Patients
Marco Castori, Camerota Am J Med Genet Part A 152A:556–564, 2010

- The hypothesis that CM is more symptomatic in EDS as a consequence of occipito-atlanto-axial instability, is supported by the increased rate of headache

Jacome ,1999,2001

Ligaments are the major occiput- C1 stabilizing structures



- the condylar – C1 capsular ligaments
- the tectorial membrane
- The alar and transverse ligaments

How does Ligamentous instability give rise to basilar invagination ?

- Instability causes **micro-trauma** to the nervous system, decreased neuromuscular control with a result of progressive instability
- Pathophysiology exacerbated by **malnutrition, vitamin deficiencies**, degenerative changes
- **Deconditioning**

Hypermobility connective tissue disorders are associated with CNS injury

Developmental coordination disorder,
headaches, quadriparesis, clumsiness....
suggests possibility of CNS involvement in EDS

El-Shaker and Watts, 1991

Kirby and Davies, 2006; Jelsma, 2013

Easton, 2014

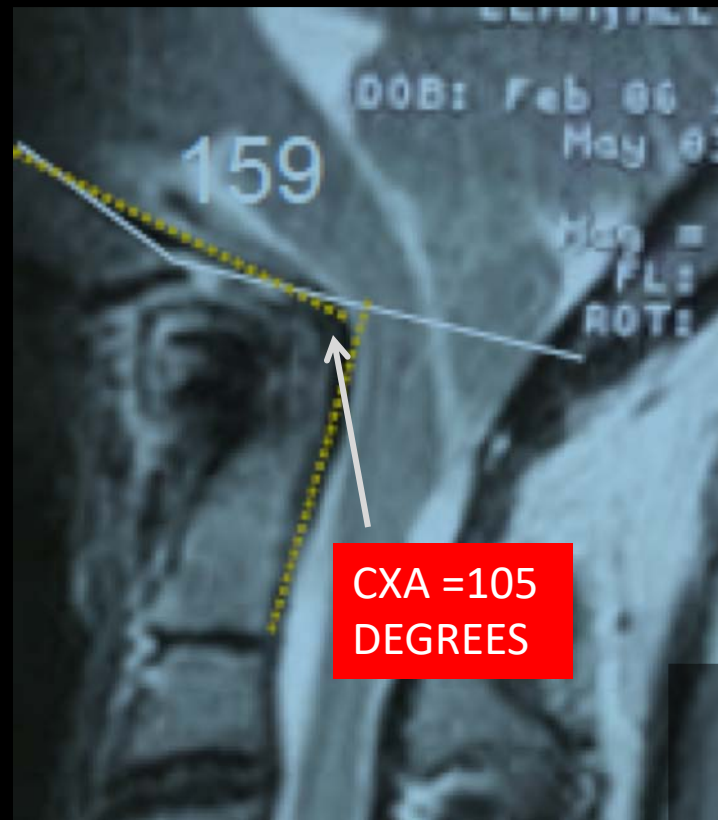
DiPalma, 2005

Nagashima, 1981; Halko, 1995

Galan, Koussef, 1995

N. Adib, K. Davies, R. Grahame, P. Woo and K. J. N. Adib, and K. J. Murray
Joint hypermobility syndrome in childhood.
Rheumatology 2005;44:744–750

Ligamentous laxity results in deformation of the nervous system in EDS



Van de Paepe A, Malfait F: , Clin Genet : 82: 1–11, 2012
Voermans et al, Annals of Neurol, 2009

Brainstem deformity occurs in 20% of treated Chiari malformation = the Complex Chiari

- Retrospective study of 101 Chiari pts
- 19 occipito-cervical fusion +/- transoral odontoidectomy

Risk Factors :

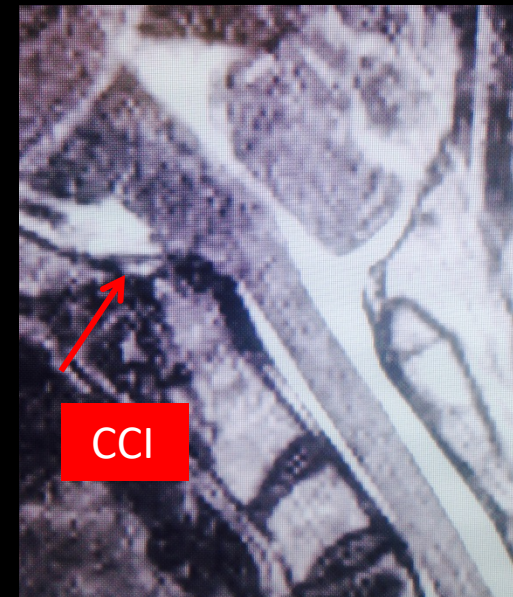
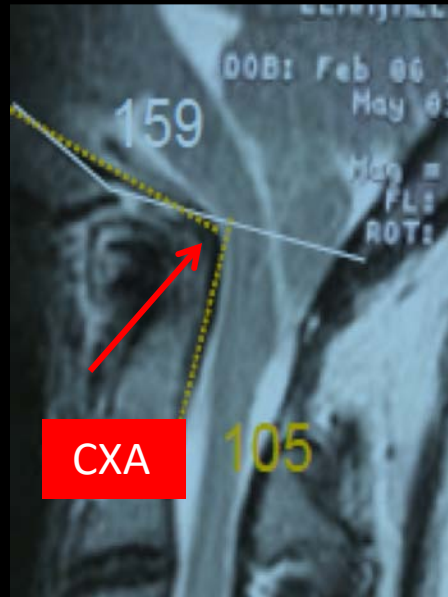
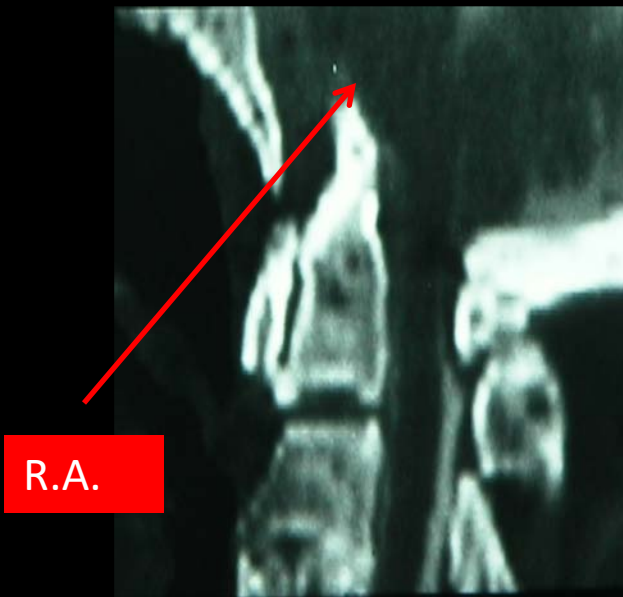
- Kyphotic CXA <125 degrees
- basilar invagination
- Chiari 1.5



Doug Brockmeyer Neurol Sci 32 S345-347 2011
Robert Bollo J NSGY Ped 10(2): 134-141, 2012

When does ligamentous laxity at the craniocervical junction become pathological ?

- Brainstem compression due to ligamentous laxity



The Consensus Statement

CSF Multi-disciplinary Colloquium for Basilar Impression and Craniocervical Hypermobility

San Francisco, October 19th, 2013

University College ,London, GB

General Hospital of Chinese People's Armed Police Forces, Beijing, China

Moriguchi -Ikuno Memorial Hospital, Japan

Johns Hopkins

Cleveland Clinic

University of Utah Health Care

UCLA

Tufts

Medical University of South Carolina

Georgetown University

University of Washington/ Seattle Children's Hospital

North Shore University Hospital

Greater Baltimore Medical Center

University of Maryland

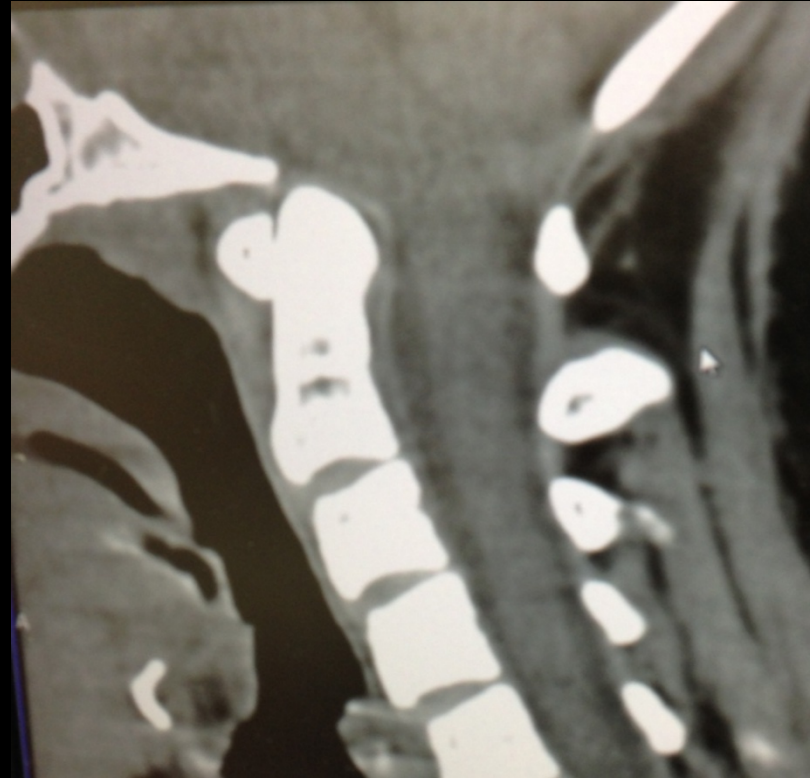
Doctor's Hospital, Maryland

Advocate Children's Hospital, Chicago

The Canine Chiari Institute

3 additional radiological metrics to assess basilar invagination and cranio-spinal instability

- Clivo-axial angle
- Grabb-Mapstone-Oakes measurement
- Harris' measurement

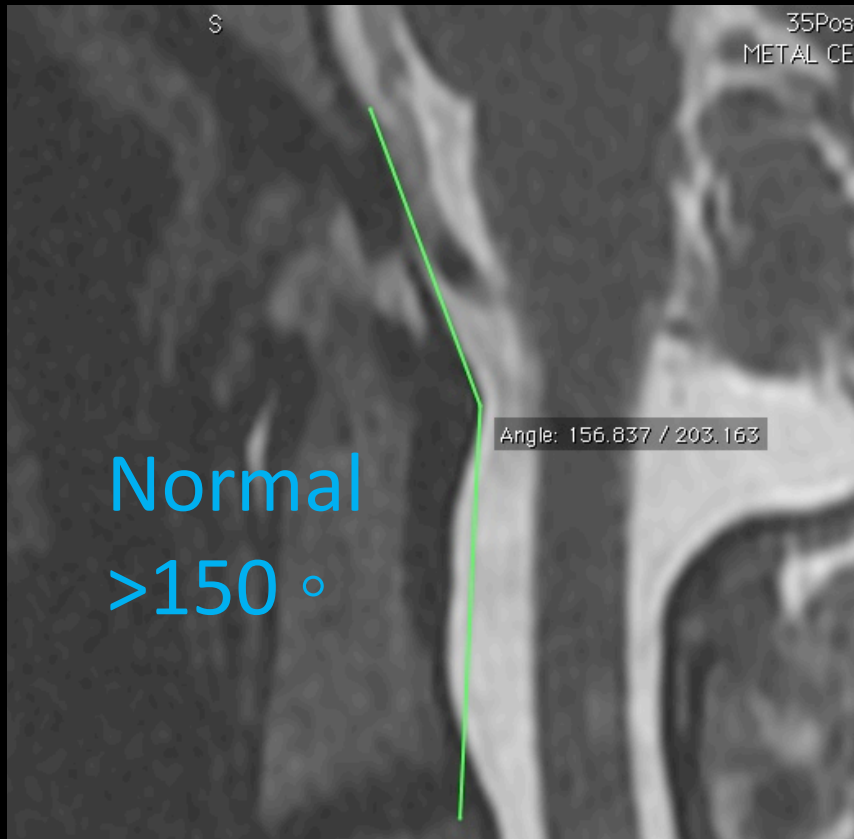


The Consensus Statement

Chiari Syringomyelia Foundation Multi-disciplinary

Colloquium Craniocervical Hypermobility Francisco, Oct 19th, 2013

1. Clivo-axial angle (CXA)

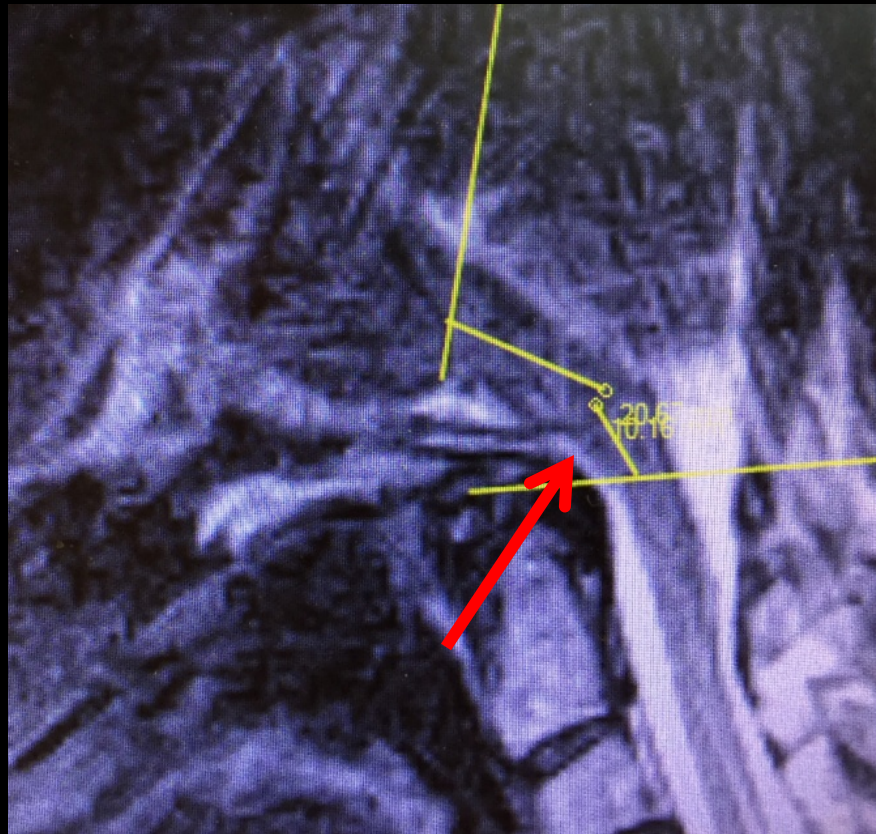


NORMAL

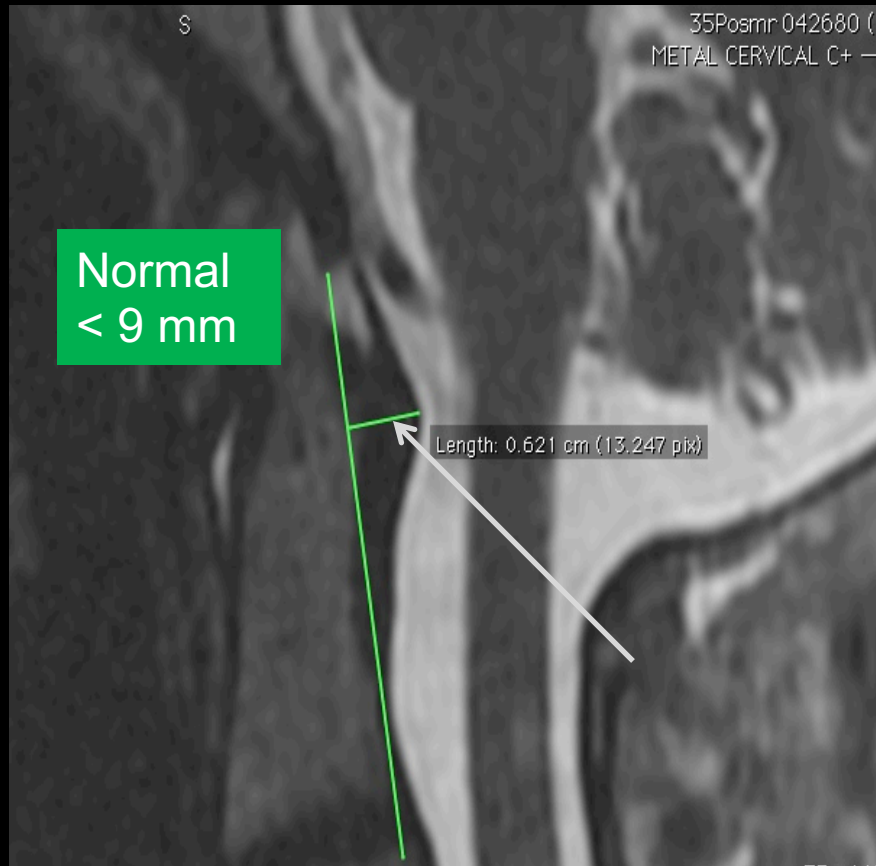


PATHOLOGICAL

Kyphosis of the clivo-axial angle (CXA)
results in a medullary kink

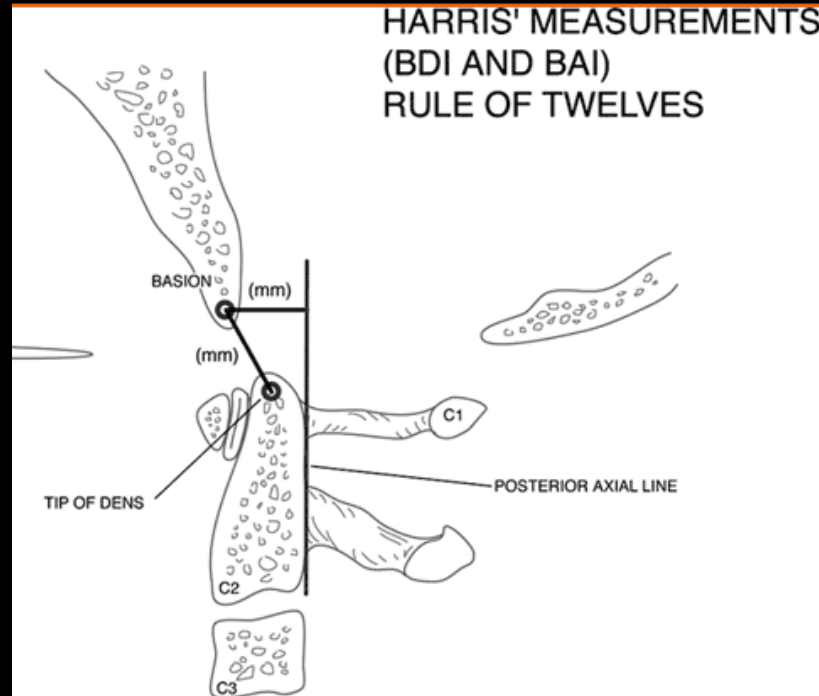


2. Grabb Oakes Measurement >9mm = high risk for ventral brainstem compression



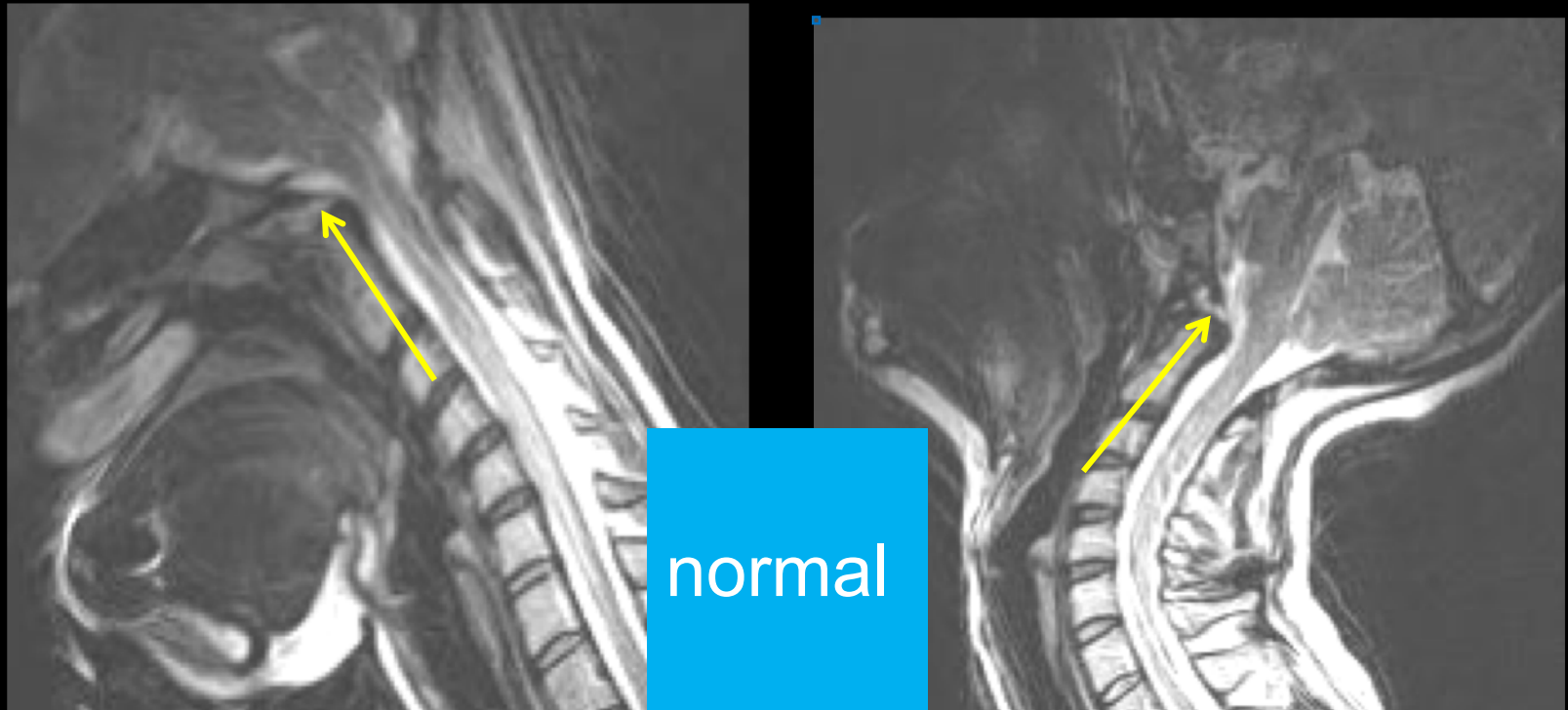
3. Harris Measurement (basion axis interval)

- Of 400 normal subjects, basion to PAL < 12mm
- The Harris measurement should not change from flexion to extension



Harris JH, Carson GC, Wagner LK: Radiological diagnosis of traumatic Occipitovertebral Dissociation

In flexion and extension, the basion pivots over the mid -odontoid, translational movement is < 1 mm



Translation >1-2 mm between basion and odontoid is pathological

Flexion-extension is the only motion at the normal OA jt

Fielding JW Cinerentgenography of the normal cervical spine J BJT Surgery 39A1280-1288

There is no horizontal translation at the OA jt

Werne S:Studies in spontaneous atlas dislocation Acta Orthoped ScandSuppl 23,1957

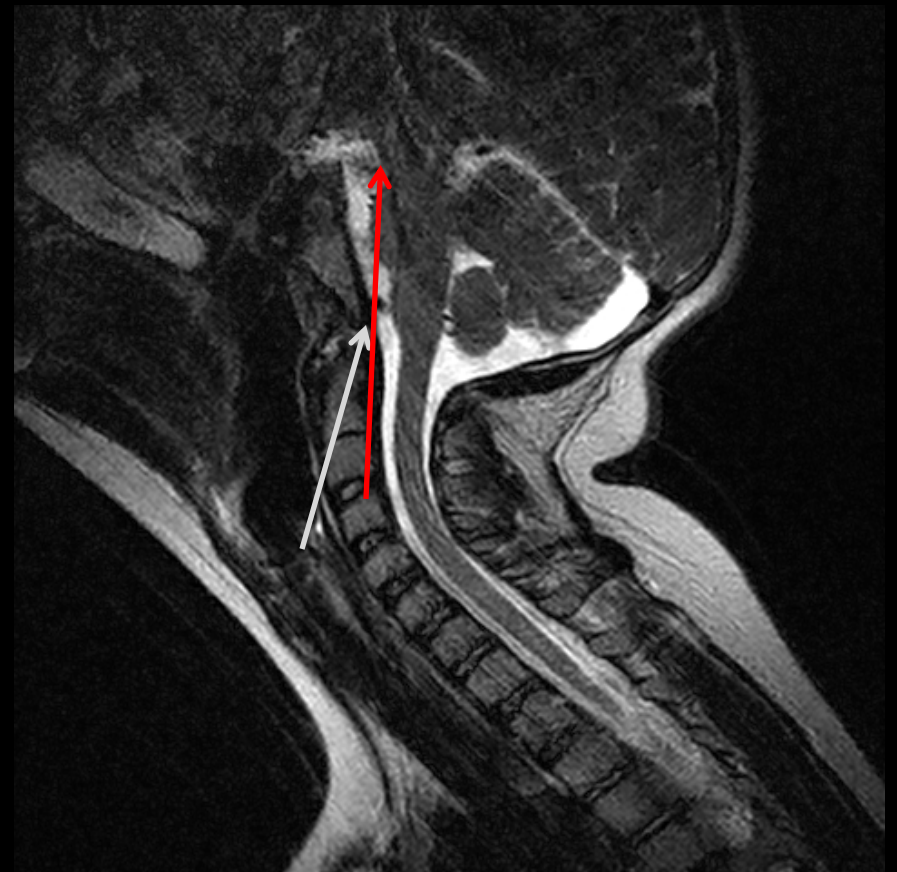
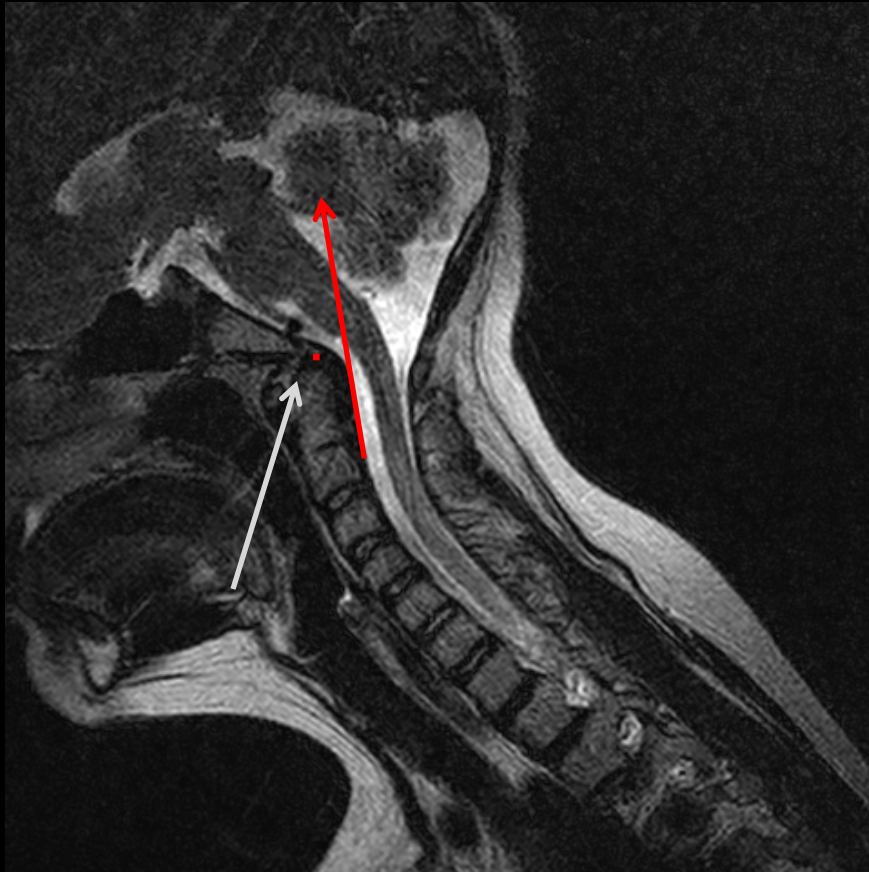
The normal range of horizontal translation in flexion/ extension is no more than 1 mm . Movement >1mm is clinically significant . Treatment by posterior cranio-cervical fusion has proved successful

Weisel SW ,Rothman RH: Occipito atlantal Hypermobility .Spine 4:187-191, 1979

>more than 1 mm of translation in flexion /extension is an important and useful criterion. Symptoms of weakness of the limbs and occipital pain are additional indications of instability

White AA, Panjabi MM Clinical Biomechanics of the Spine :p284-286 ,2ND Edition Lippincott1990

Horizontal Harris measurement
translation >1 mm is pathological



Harris measurement Abnormal >12mm

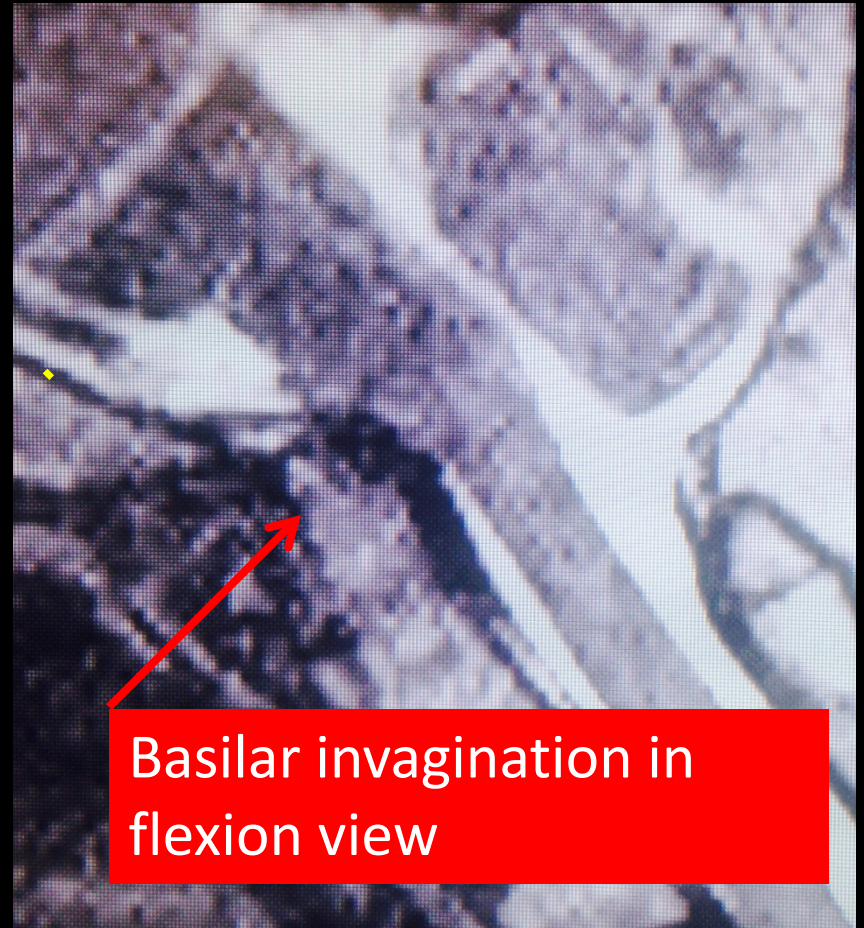
Horizontal Harris
measurement
= 15 mm
= **unstable**



Pitfall : craniocervical instability is often only seen on Dynamic imaging



Relatively
Normal in
supine view



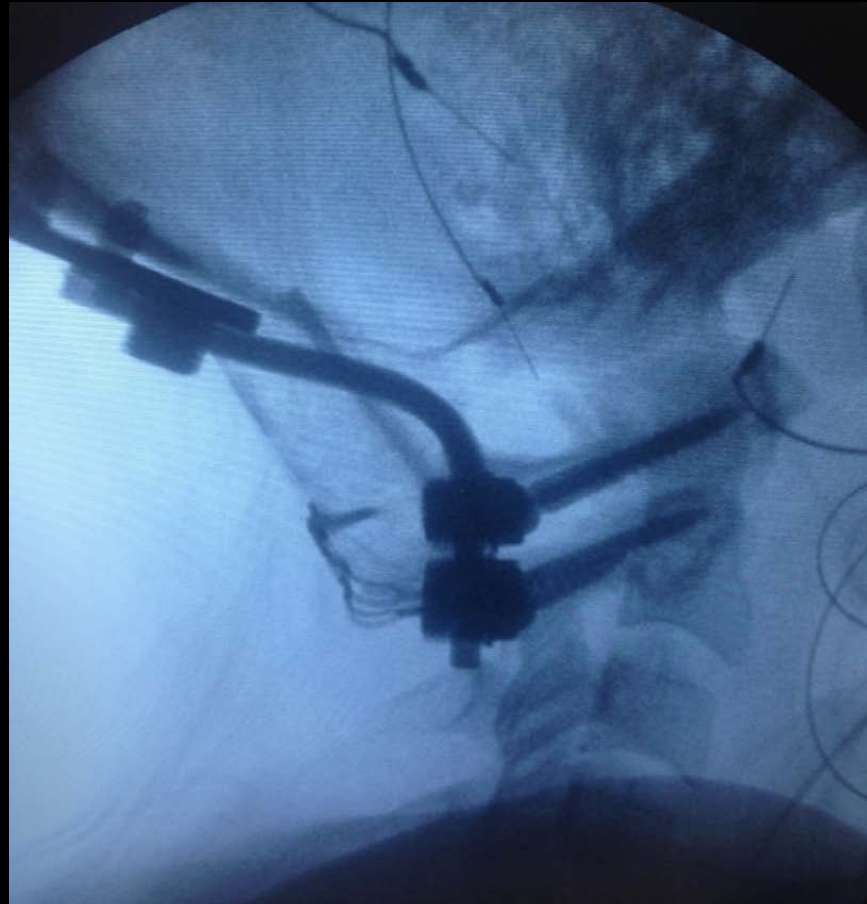
Basilar invagination in
flexion view

Cranio-cervical instability causes headache

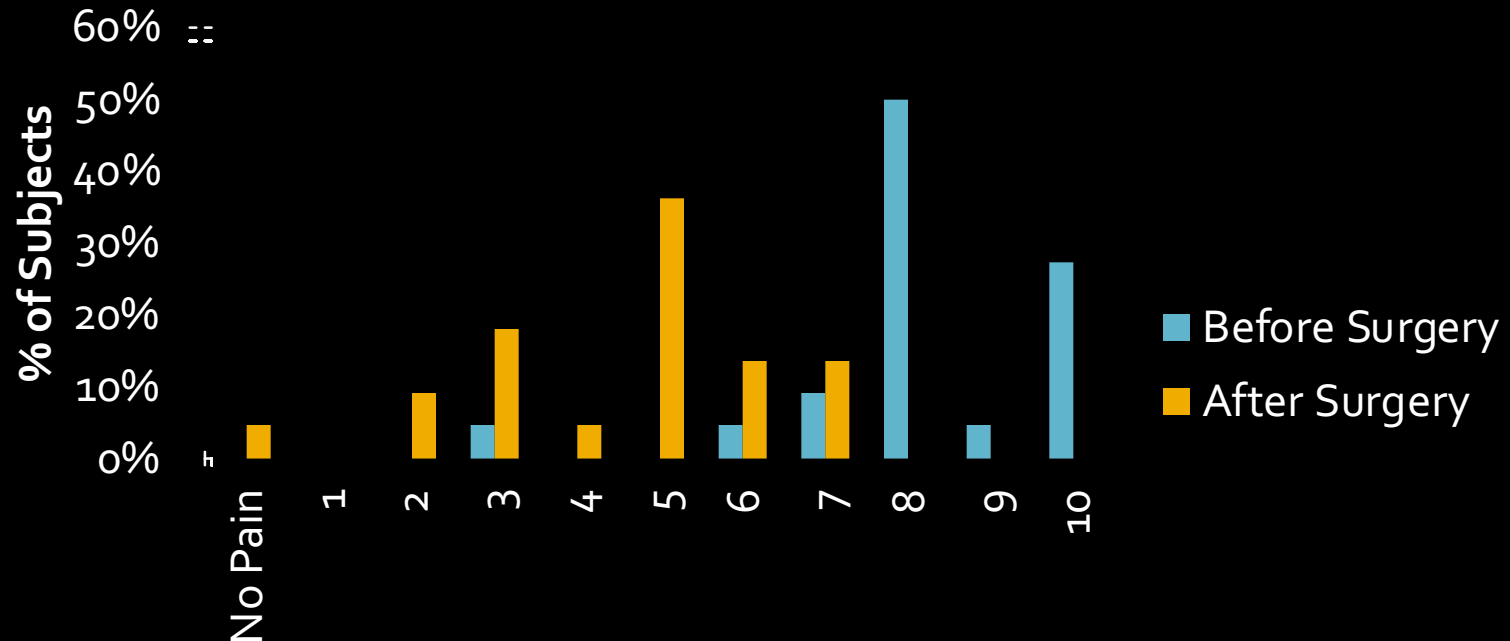
How does craniocervical instability headache present ?

- 100% suboccipital , 70% also have neck pain
- often radiates to some or all cranium
- throbbing, shooting, stabbing, sharp
- Worse exertion, looking up
- Truncal ataxia, poor tandem gait
- dysmetria, dysdiadochokinesia,
- Decrease fine motor hands
- Nausea
- imbalance

Reduction, fusion and stabilization
decrease headache



Average Headache



■ Headache preop
postop

$M = 8.18,$ $SD = 1.62$
 $M = 4.50,$ $SD = 1.82$

$t(21) = 6.532,$ **$p < 0.001$**

$M_{diff} = 3.68, SD_{diff} = 2.64),$
95% CI [2.51-4.85]

HOX D3 homeotic transformation mutation can cause severe headache

- Hox genes encode transcription factors to regulate the body plan.
- Inactivation of *Hox d-3*, shifts the transitional sclerotomal properties from C₁ to C₂

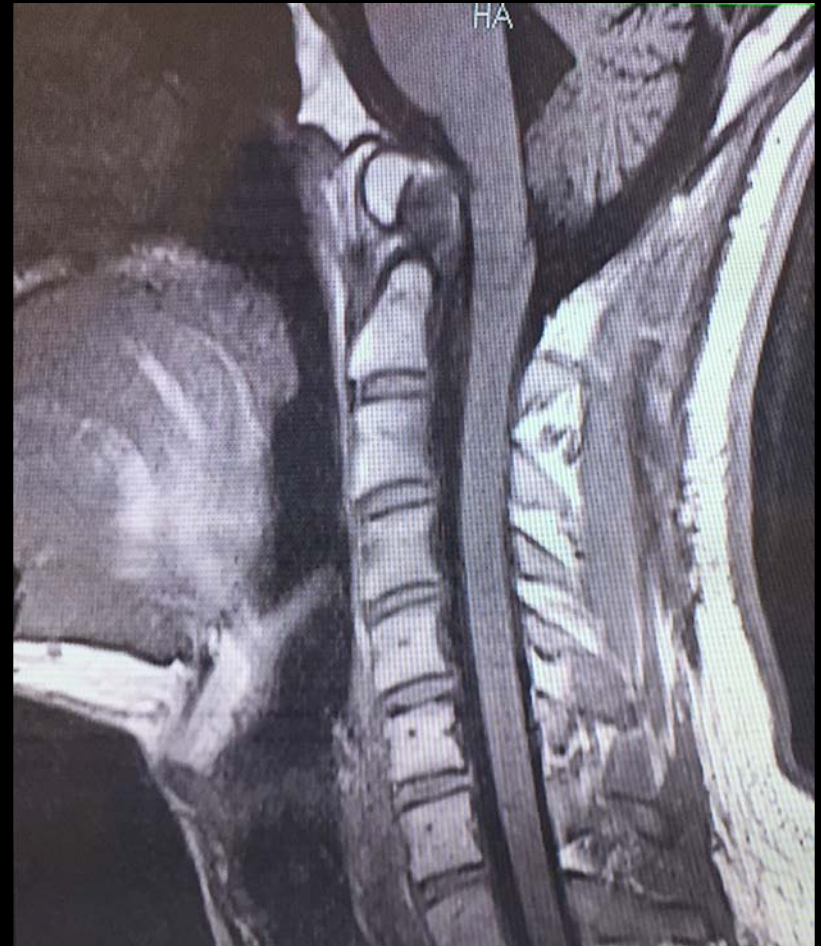


A French horn player with EDS, HOX D3 Homeotic transformation and Chiari malformation



Dachling Pang & Dominic N. P. Thompson. Embryology and bony malformations of the craniovertebral junction Childs Nerv Syst 27:523–564 (2011)

Hox D3 homeotic transformation in an EDS pt: 2 yr s/p decompression with no fusion



Pitfall: The radiological metrics are guidelines, not rules

pathological radiological metrics *per se* are not indications for surgery

Surgery should proceed

- disabling pain,
- appropriate symptoms
- neurologic findings, and
- failed non-operative treatments



Pitfall: assuming that all headaches originate in the head

- Many headaches are cervico-genic

Mechanical instability of the cervical spine Is a recognized cause of headache

- At least 25% of patients after Chiari malformation surgery continued to complain of headache at Johns Hopkins. The headache is occasionally clearly related to upper cervical instability
- ..I .. want to reemphasize that mechanical instability is ...important in explaining the symptoms that our patients have. .. the neurophysiological basis is much more complex than simple compression and disruption of spinal fluid flow.

Cervicogenic headache have a greater 'quality of life' burden

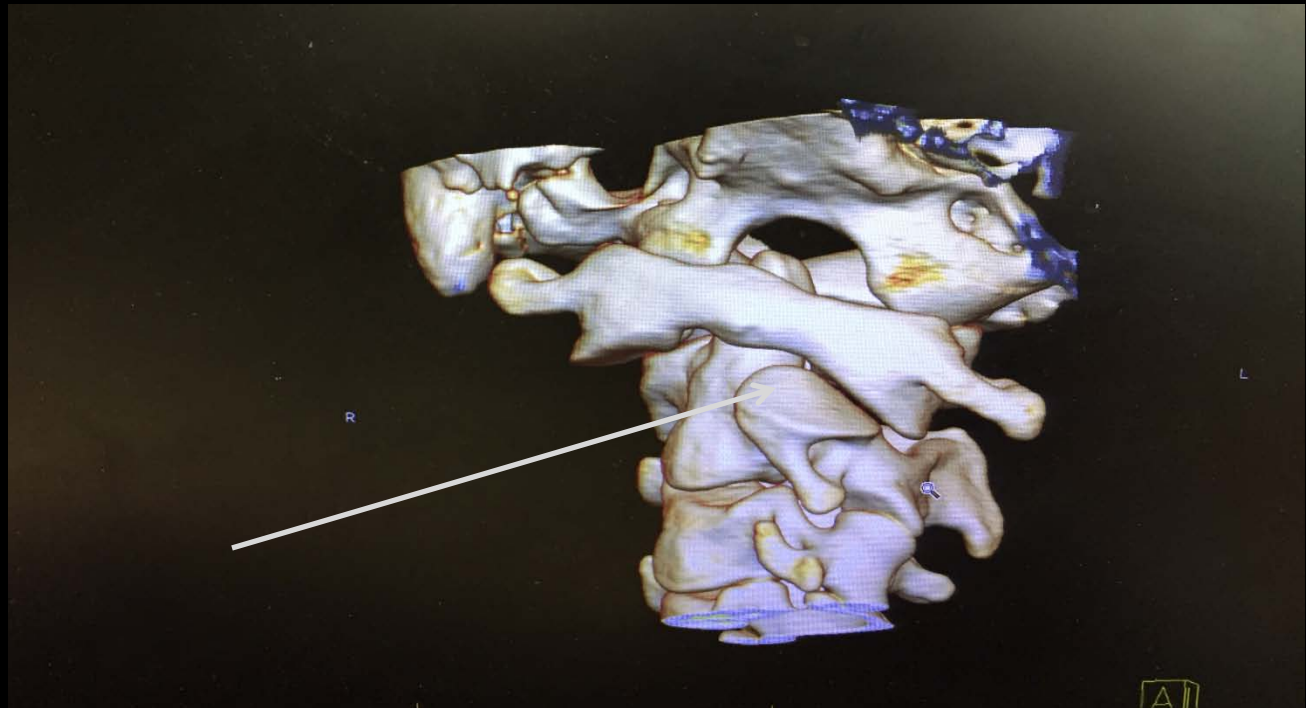
- 66 % population have headaches
- incorrect headache diagnosis > 50% of cases
- **Cervicogenic headache** (2.5– 4.1%)

have a substantial higher quality-of life burden

van Suijlekom, Lame et al. Quality of life of patients with cervicogenic headache: A comparison with control subjects and patients with migraine or tension-type headache. *Headache* 2003;43:1034–1041.

Pfaffenrath , Kaube . Diagnostics of cervicogenic headache. *Funct Neurol* 1990;5:159–164.

Pitfall : Failure to diagnose C1-C2 instability – in the EDS population



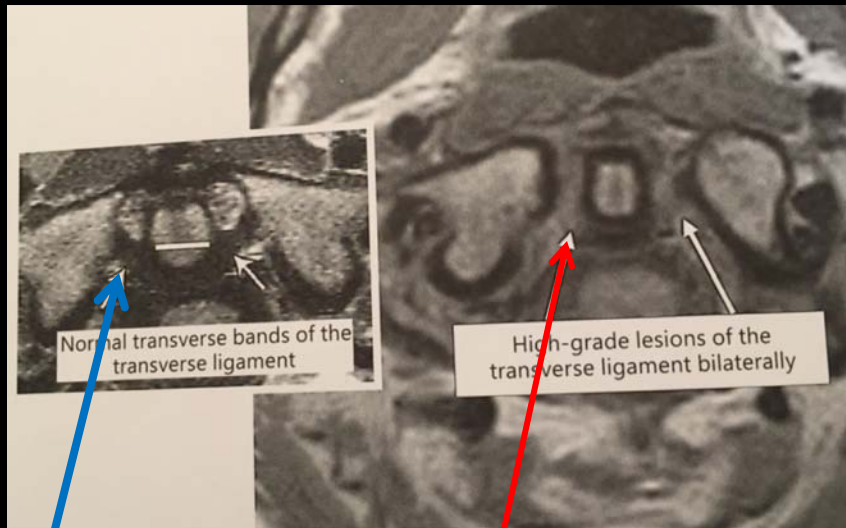
Halko GJ, Cobb R, Abeles M. Patients with type IV Ehlers-Danlos syndrome may be predisposed to atlantoaxial subluxation. *J Rheumatol*. 1995;22(11):2152-2155.

Nagashima C, Tsuji R, Kubota S, Tajima K. Atlanto-axial, atlanto-occipital dislocations, developmental cervical canal stenosis in the Ehlers-Danlos syndrome (author's transl).

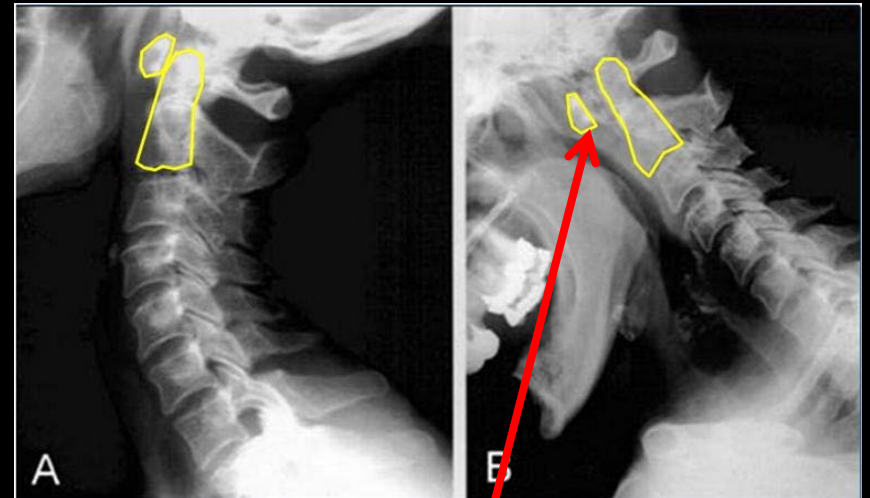
Mo Shinkai Geka. 1991;9(5):601-609.

Menezes, A. H. (2008). Specific entities affecting the craniocervical region: Down's syndrome. *Child's Nervous System*, 24(10), 1165-1168.

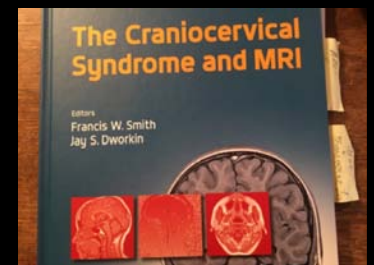
Incompetence of the Transverse odontoid ligament seen on flex extension x-rays



Normal

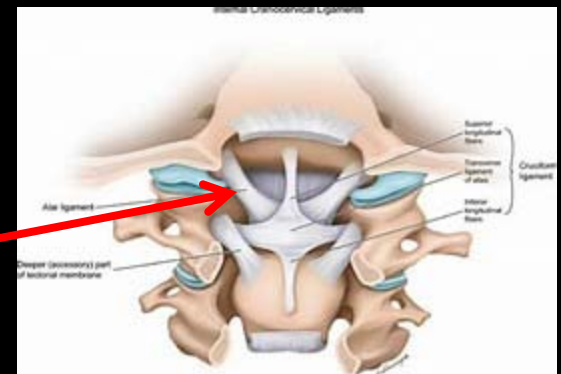


High grade lesion of transverse ligament



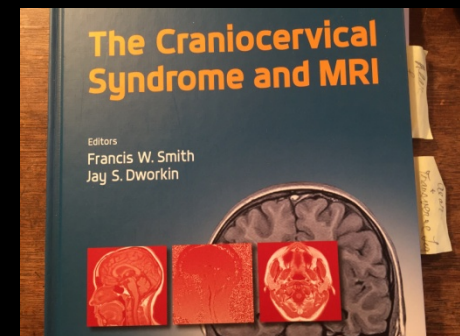
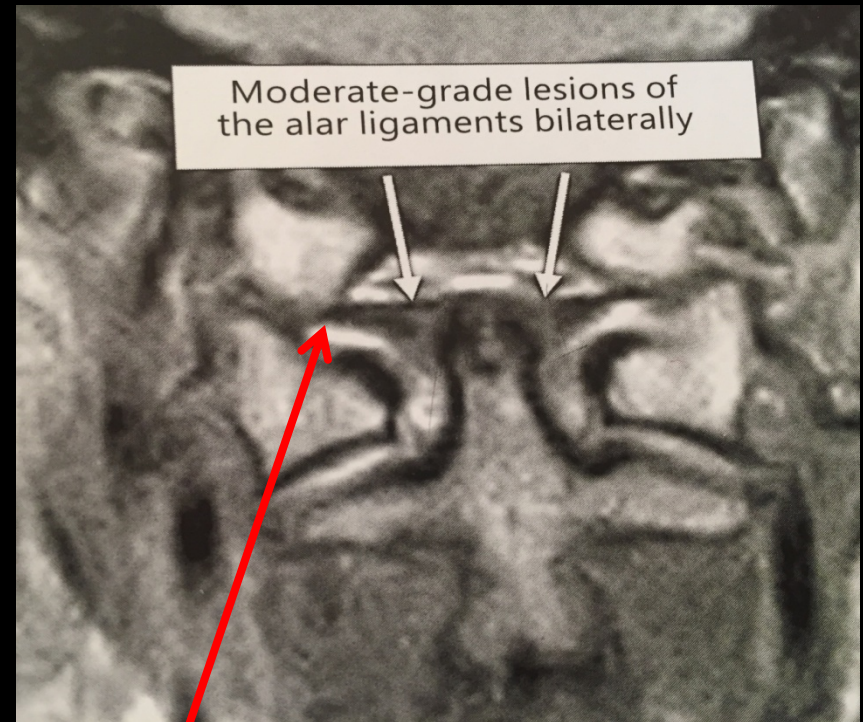
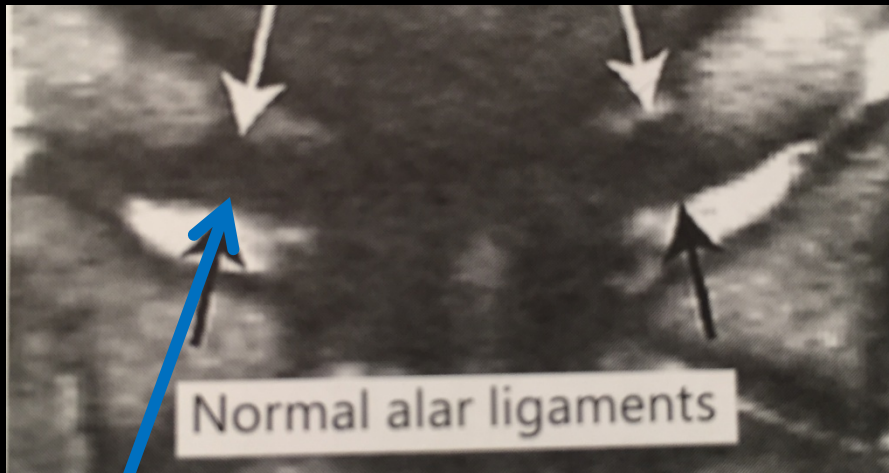
Alar ligament incompetence is a cause of AAI

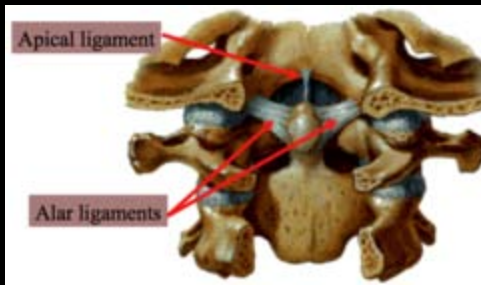
- Mean rotational movement 23-39 degrees, limited by the transverse, capsular and **contralateral alar ligaments**
- “It is concluded that overstretching or rupture of the alar ligaments can result in rotary hypermobility or instability”
 - Harold Hoffman



Dvorak JRI, Panjabi M, Gerber M, Wichmann W. CT Functional diagnostics of the Rotary Instability of Upper Cervical Spine , Spine ,1987

AAI due to incompetent alar ligaments





Diagnosis of AAI

- Sub-occipital headache (occipital neuralgia)
- “Ice pick eyes”
- Worse looking up, rotation
- Tension band around base
- Syncope or pre-syncope
- Nausea, dizziness
- Cervical medullary syndrome – diplopia, clumsy hands, memory
- Tenderness over C1
- Spastic reflexes, vocal cord spasm, clumsiness, dystonia
- C,T,L,S sensory deficits to pp
- **Radiologic: excessive rotation**
>42 degrees of C1 on C2

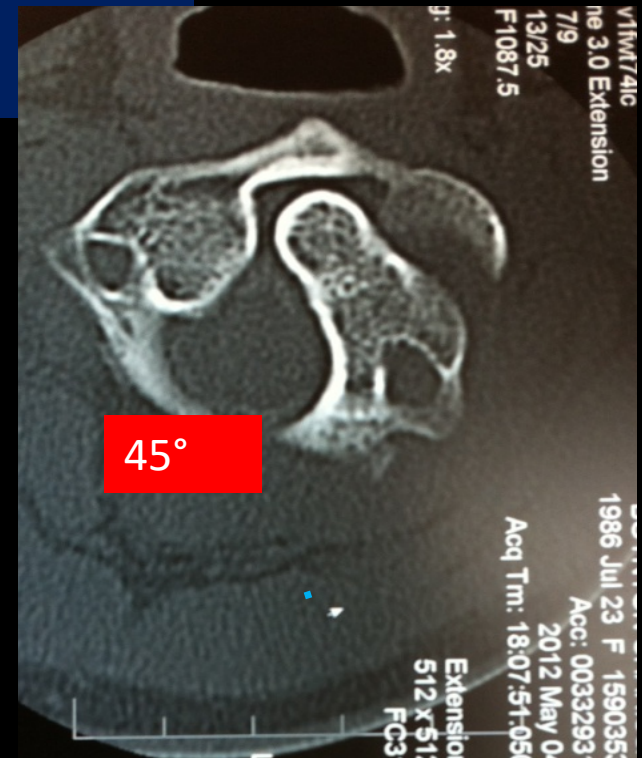


Supine CT occiput c1c2 with neck rotated 90 degrees to left and then 90 degrees to right

Atlantoaxial instability

A 40 degree rotation
cause VA stretch/ kink
At 45 degrees there is
occlusion of VA

<20% facet overlap

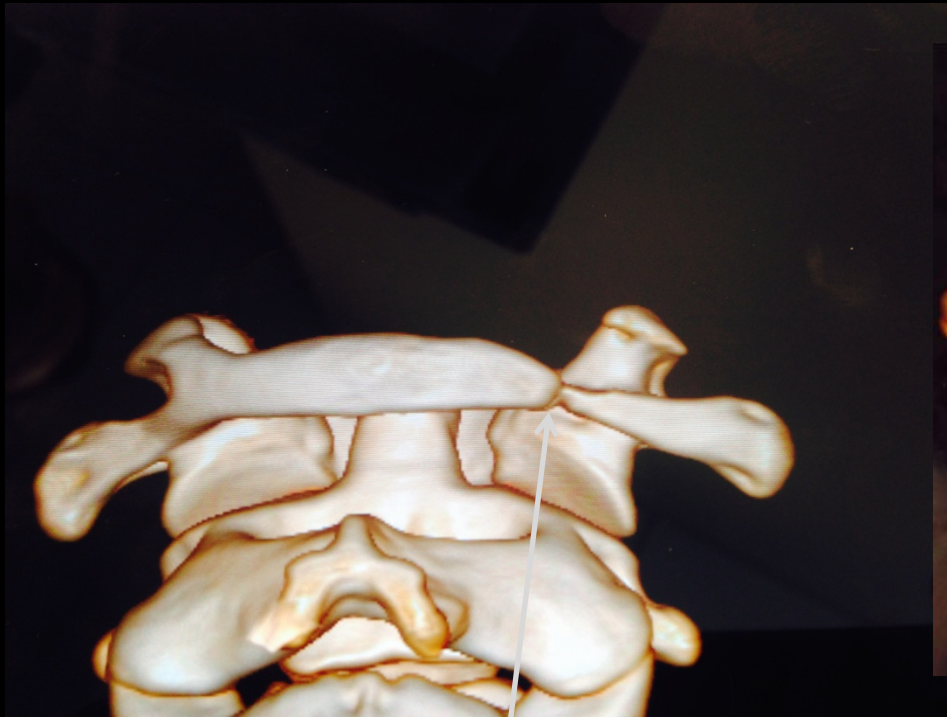


Zang H, Bai J. Spine 32: 968-974, 2007

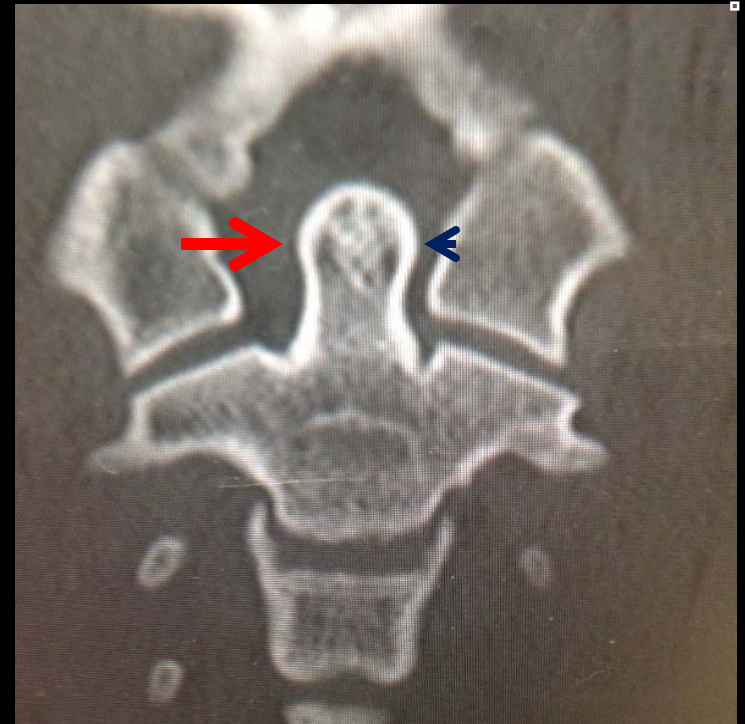
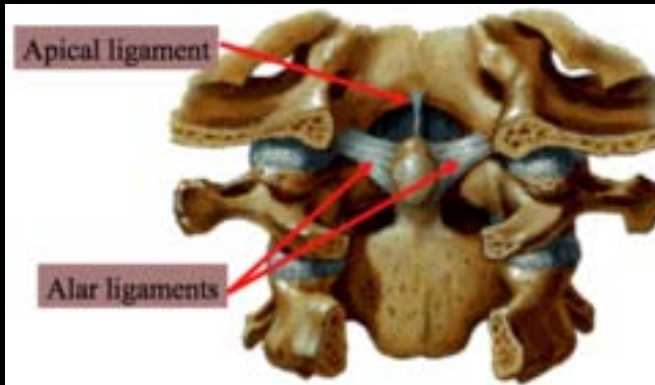
Punjabi, Dvorak, Crisco, Oda, Wang, Grob. Effects of alar ligament transection, J Orthop Res 9 : 584-593, 1991

Menezes AH, Traynellis VC Childs Nervous System 24: 1091-1100, 2008

Incomplete C1 ring - AAI



Atlanto-axial instability due to alar ligament incompetence



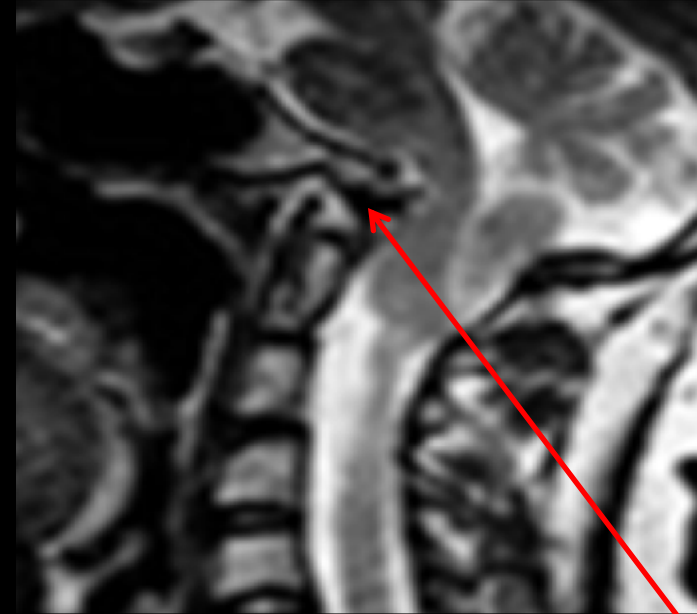
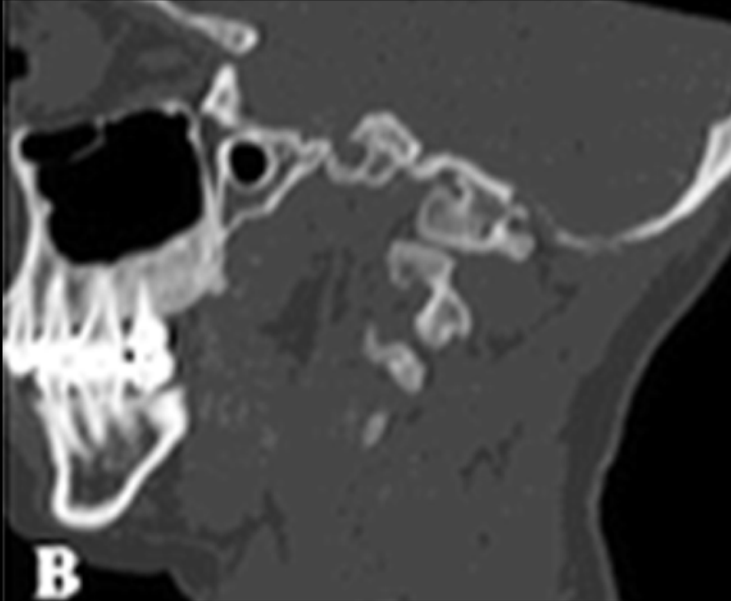
AAI with normal atlanto-dental interval



- Goel Type III: 17/65 pts
no facet malalignment but
unstable intraoperatively “Vertically unstable”

Goel A, Shah A, Rajan S: Vertical mobile and reducible atlantoaxial dislocation.
Clinical article. J Neurosurg Spine 11:9–14, 2009

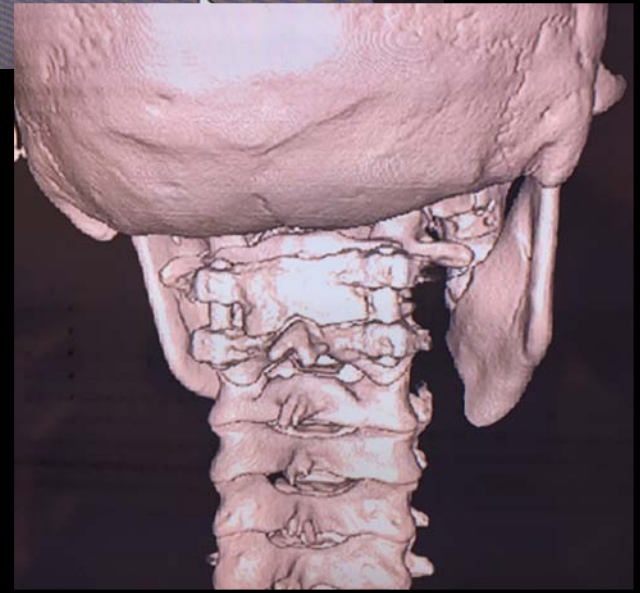
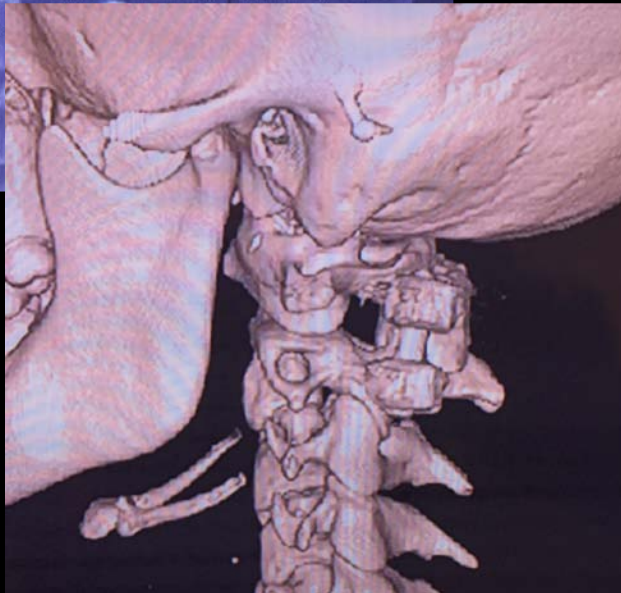
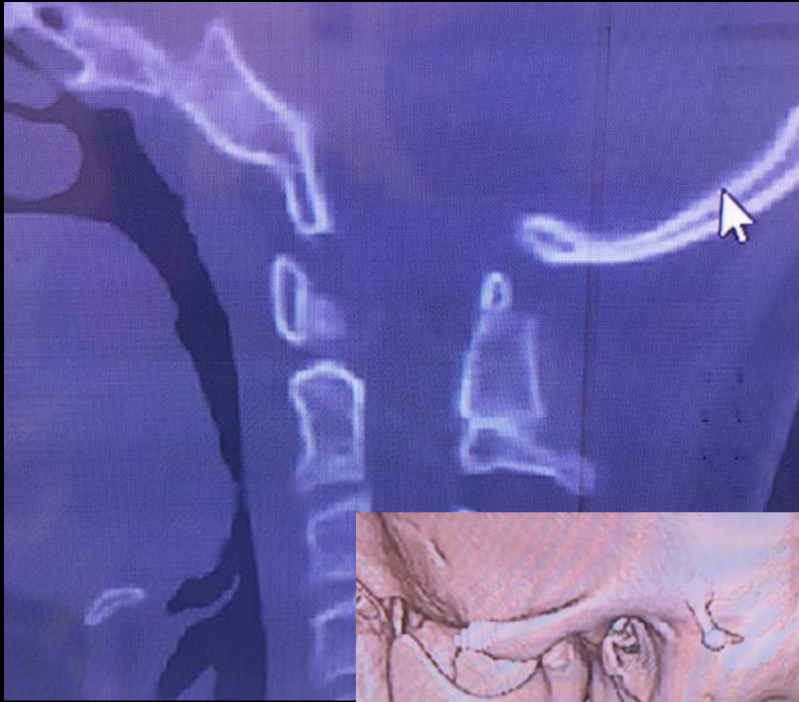
AAI with normal atlanto-dental interval



- Yin: Type IV= retroversion of facet causes “posterior-olisthy”

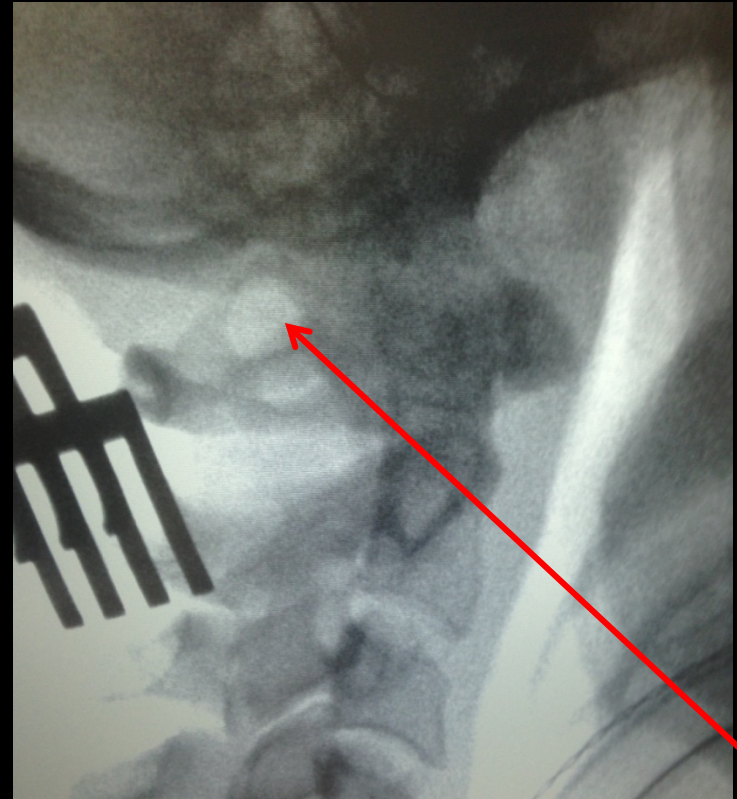
Yin YH, Yu XG, Zhou DN\B, Wang P, Zhang YZ, Ma XD et al: 3Dconfiguration and morphometric analysis of the lateral atlanto axial articulation.. Spine 37: E170-173, 2012

Treatment: C1-C2 fusion stabilization



Kimmerle anomaly

- Bone ring around the VA
- 14% of the population
- Due calcification of the fibrous ligament of the condyle entraps the vertebral artery and suboccipital nerve
- deafness, dizziness, drop attacks, paresthesia, arterial dissection



Cusching KE et al. "Tethering of the vertebral artery in the congenital arcuate foramen of the atlas vertebrae : a possible cause of vertebral artery dissection in children. Dev Med Child Neurol 43:491-2001

Elliot RE, Tanweer O. The prevalence of the arcuate foramen and its importance. World Neurosurg 82:335, 2014

Pitfall: Failure to recognize dynamic instability in the cervical spine



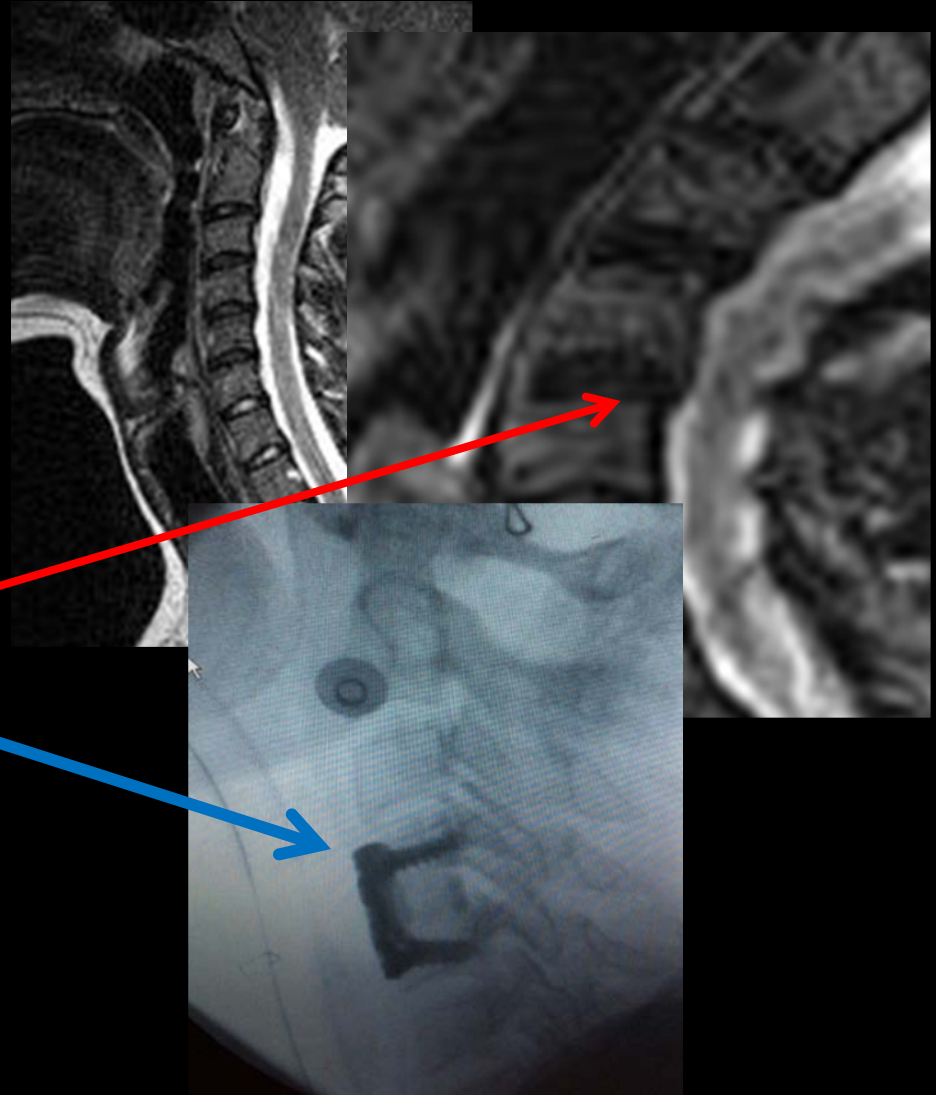
Standard supine
MRI –looks NL



**Same pt in a
Dynamic extension
view**

Cervicogenic headache due to cervical instability

- Suboccipital headache
- Interscapular burning
- +/- dyspnea
- Visual accommodation impaired
- deltoid weakness
- Hypoesthesia over the shoulders
- Dynamic imaging: subluxation, angulation
- Reduction and fusion: resolution of neurological findings



The importance of dynamic imaging for ligamentous degeneration



Kyphosis causes **stretching of the spinal cord**
A form of **tethering** via the “sagittal bowstring effect”

Cervical Spondylosis anatomy: pathophysiology and biomechanics
Shedid D, Benzel EC. Neurosurg 60 : SI-7 to SI-13, 2007

Clinical instability mid / lower cervical spine

5 pts or more = unstable

2 points each

- Positive stretch test = traction sign
- Total angulation on sagittal plane f/e > 20 degrees
- sagittal plane angulation > 11 degrees in one image
- Sagittal plane subluxation > 3.5 mm (or 20% vert width)
- Spinal cord injury

1 pt each

- Stenosis sagittal diameter < 13 mm or Pavlov's ratio < 0.8
- Abnormal disc narrowing
- radiculopathy
- Dangerous loading anticipated

Headache may arise from **neurogenic pain** which is difficult to diagnose by neurological exam

Neural disorders causing headache may arise from **peripheral nerve sensitization, but normal neurological function**

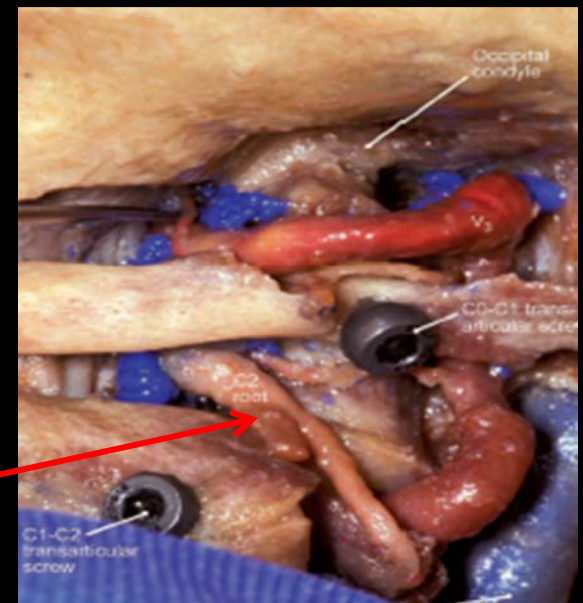
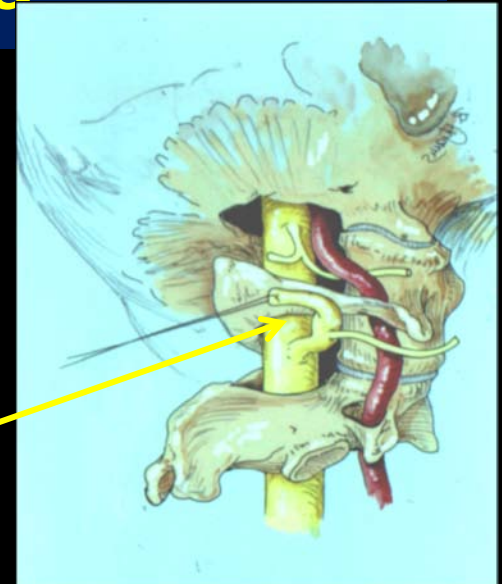
- greater occipital nerve, lesser occipital or third occipital nerve

Therefore, we cannot diagnose these through the standard neurological exam

- Provoked by palpation, provocative movts esp flexion, sometimes extension

Occipital Neuralgia

- Misdiagnosed as tension headache
- pain upper neck, occiput, retro-orbital
- Pain is sharp, shooting, shocking, stabbing
- May last seconds or continuous, usu hours to a day
- Usu neurologically intact
- Photo- phono-sensitivity
- Occ slurred speech
imbalance
nausea
- Diagnosis by hx,
nerve block



Migraine Headaches from patent foramen ovale

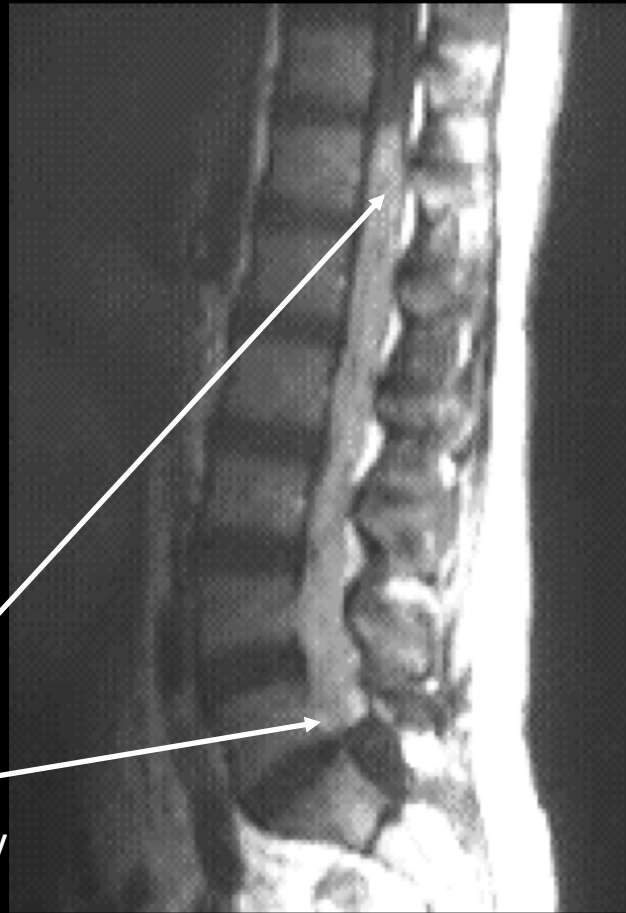


- Women with EDS 3 x higher rate of MIGRAINES
- ECHO with bubble technique may show bubbles passing through the septum
- Other causes of migraine: r/o TMJ, corneal and retinal conditions with asthenopia (eye strain)

Castori M, Morlino S, Celletti C. *Am J Med Genet A*. 2012;158A(8):2055-2070.

Remote causes of headache

Remote extramedullary tumors cause headaches



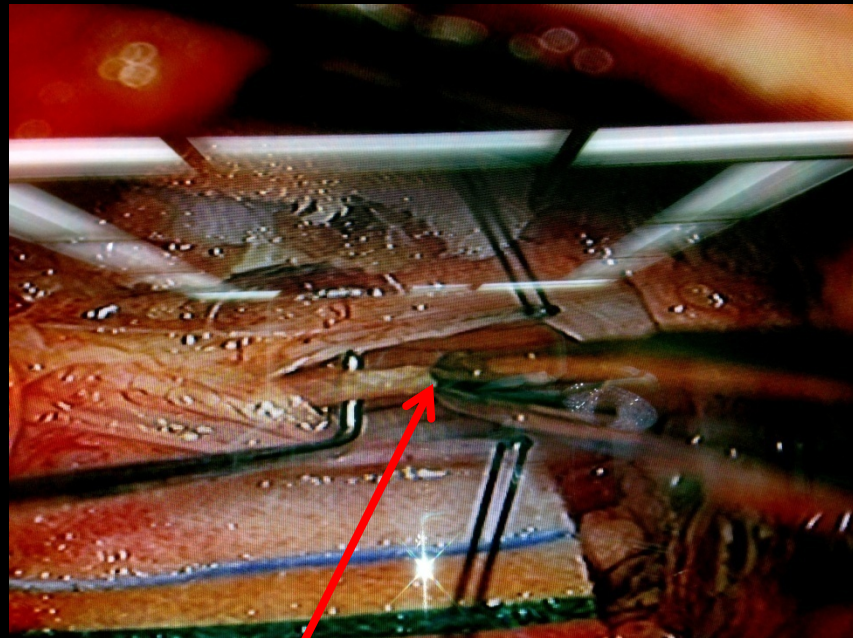
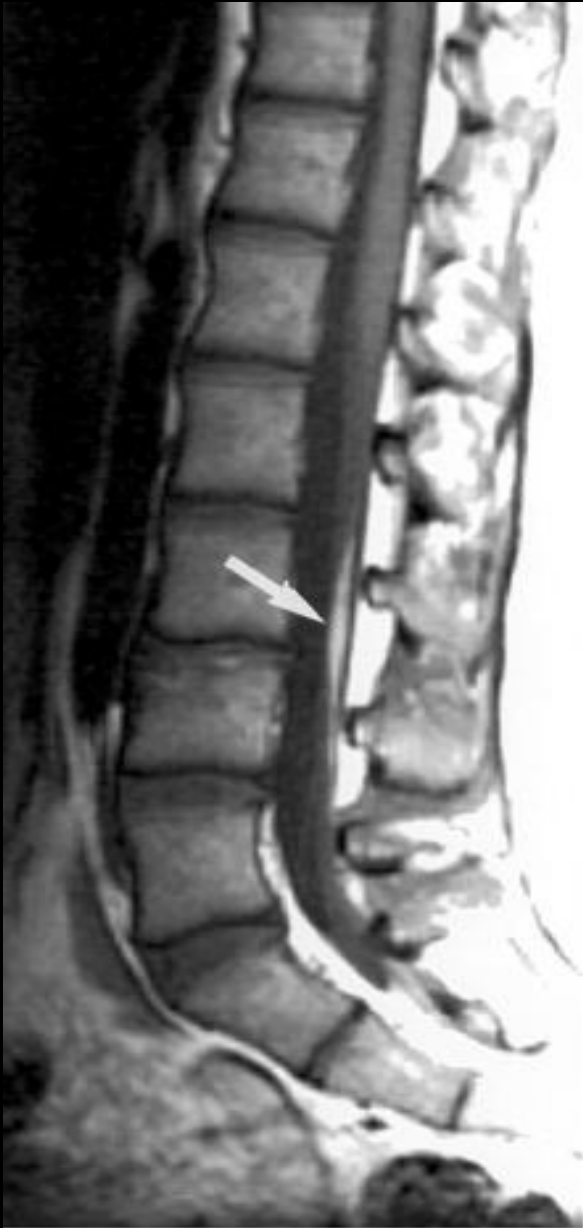
Myxopapillary
ependymoma

Headaches due to tethered cord

- 1/2 of tethered cord pts report “pulling down the back of the head”
- Headache worsens with traction - straight leg raising, neck flexion
- Moderate severe pain



Tethered cord syndrome (may be radiologically occult)



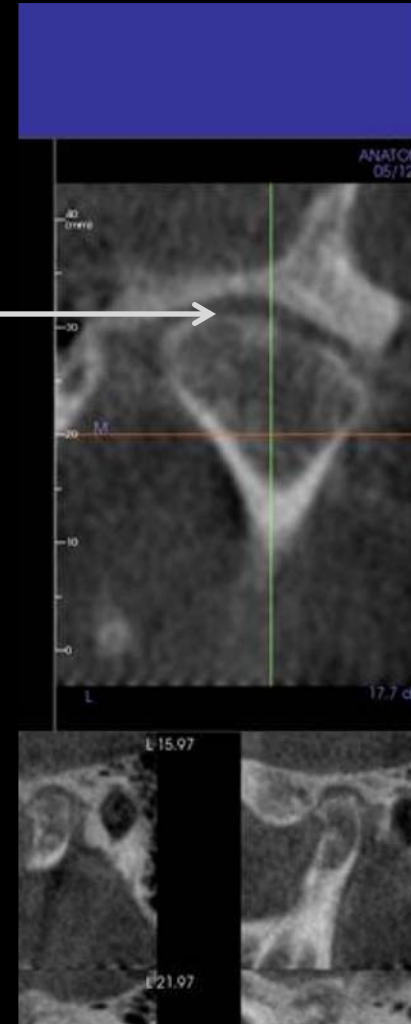
Diagnosis occult tethered cord syndrome

- Lumbo-sacral pain, weakness and sensory decrease, bowel bladder dysfunction
- Urodynamics: increased bladder volume, detrusor spincter dyssynergia
- prone MRI - 62% sensitivity
- 18% of pts had Occult TCS (Warder, Oakes, 1993)
- Harold Hoffman: “The authors have demonstrated that patients with the traditional clinical findings of a tethered cord can have a conus in the normal position.

Warder DE, Oakes WJ. Tethered cord syndrome: the Low Lying and Normally Positioned Conus. (1994) Neurosurg 34 (4) 597-600.

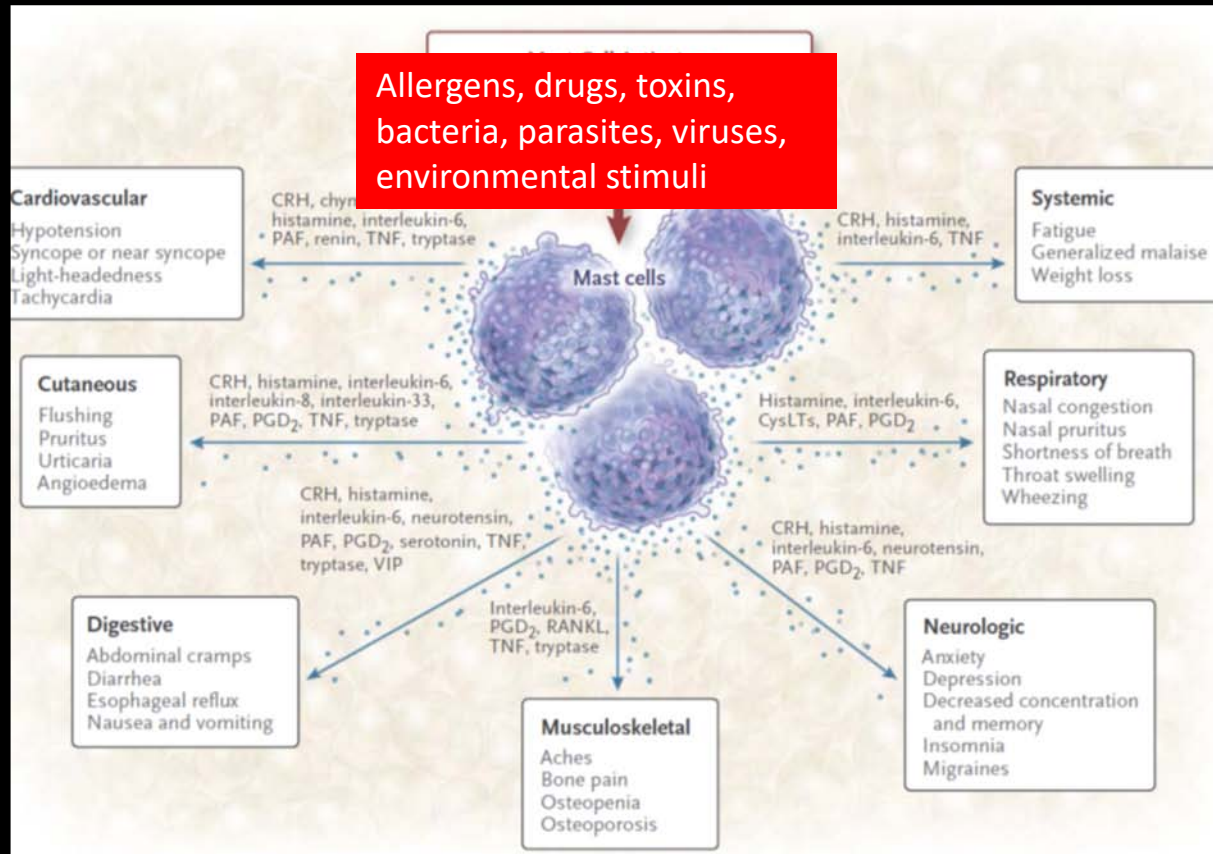
TMJ Dysfunction

- very common in the EDS population
- Temporo-mandibular joint is highly innervated
- Refers pain to
 - subocciput
 - Levator scapulae and trapezius mm
 - temporalis muscle
 - supraorbital region
- Pain may be severe
- Awaken pt in middle of night
- Worsened with neck brace, chewing, talking
- sleep apnea, weakness of arm abductors

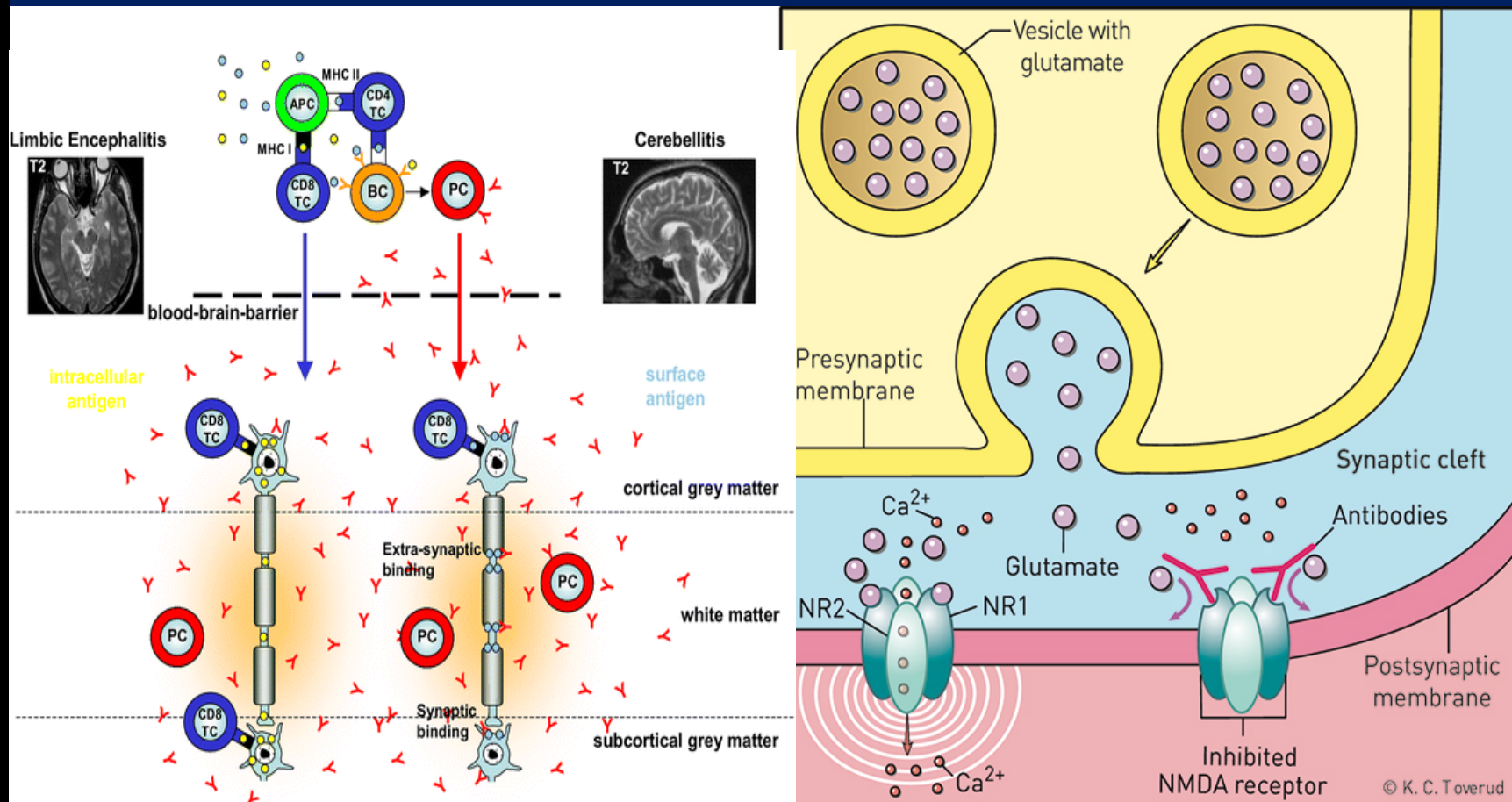


Disorders of Immunity

Pitfall : failure to recognize Mast cell activation syndrome

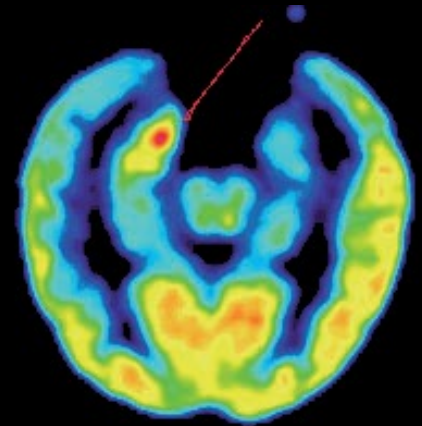


Immune problems: PANDAS , Neuro- Behcets Paraneoplastic Limbic Encephalopathy



anti-NMDA-receptor encephalitis

- potentially lethal disorder in which serum antibodies react with brain receptors, predominantly expressed in limbic structure
- And temporal lobes
- More often in women
- development of sudden behavioral and personality changes ,seizures ,mood
- sleep disturbances,hallucinations
- short-term memory loss that can progress to dementia
- EEG focal slowing or epileptiform activity



DALMAU J, GLEICHMAN AJ, HUGHES EG et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. Lancet Neurol 2008;7:1091–8.

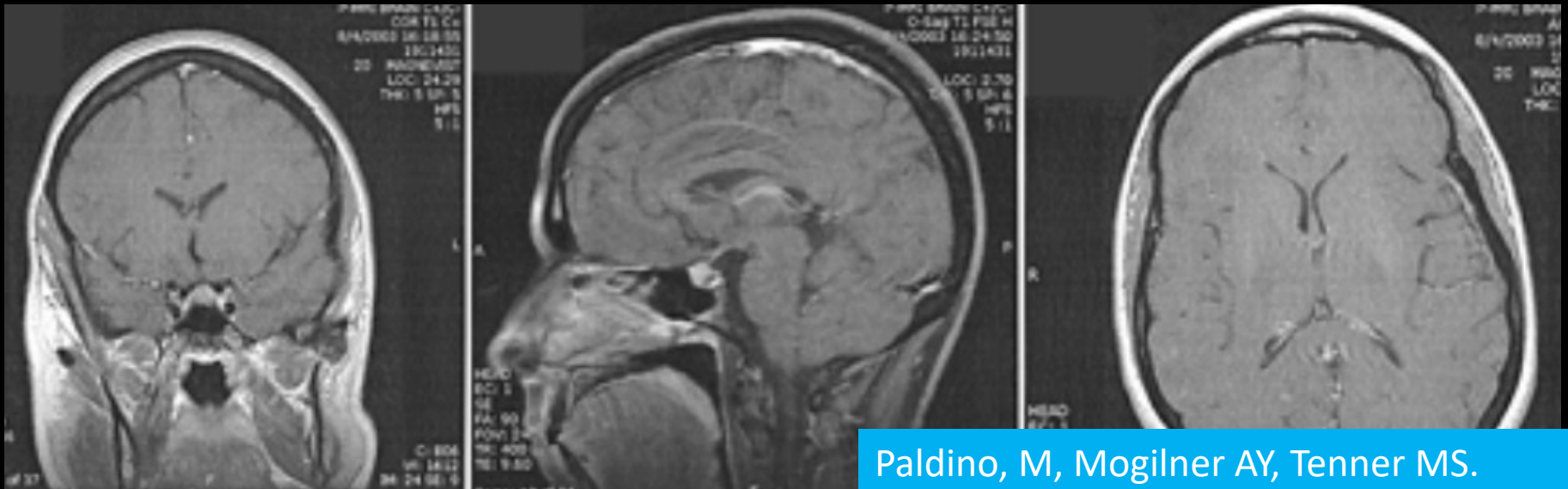
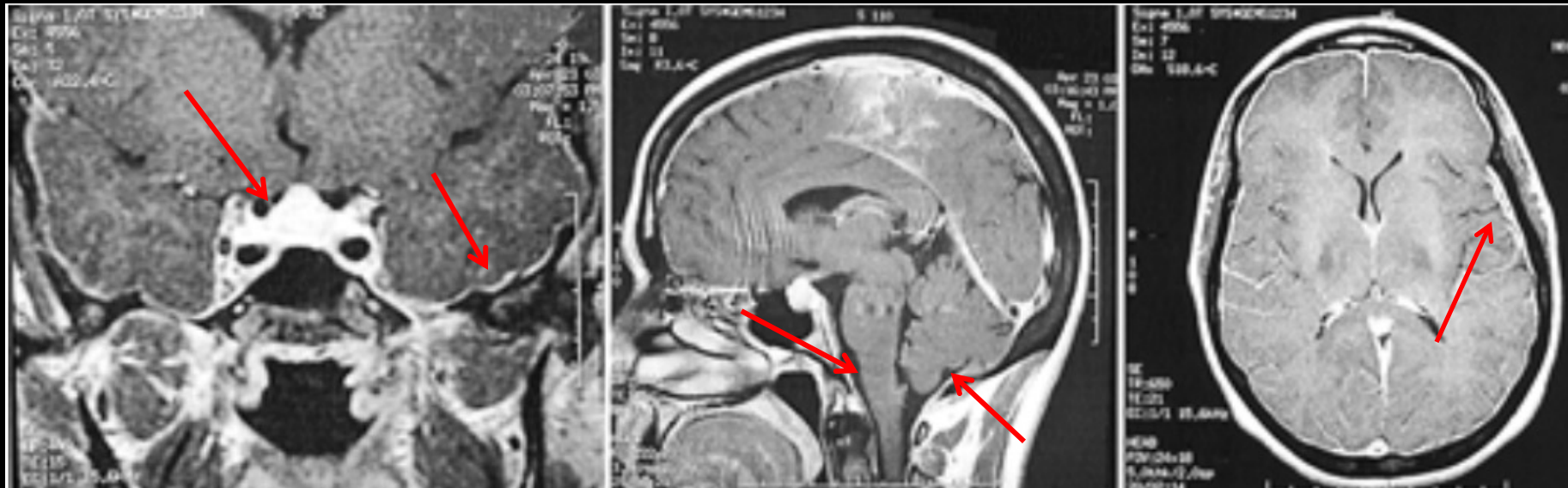
Preliminary conclusions

- Though a useful measure of disability and suffering, headaches are highly variable and non-specific
- Because these diagnoses are not obvious or intuitive, they must be considered and searched for
- Awareness of the many co-morbid conditions of EDS is important to establish the origin of the headache
- **Ligamentous laxity** is an important feature in many of the conditions that generate headache

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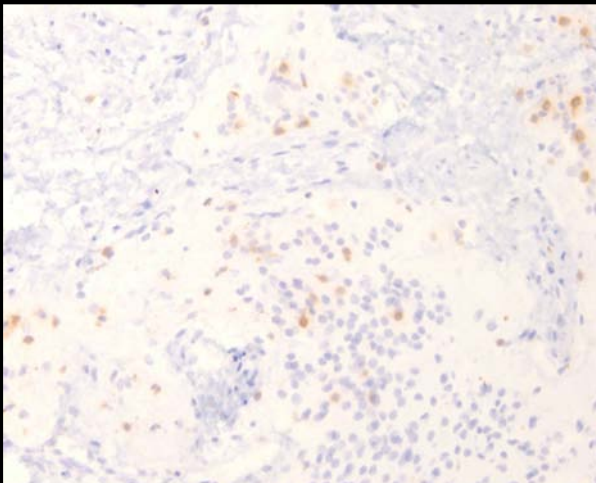
IHS - Findings on contrasted MRI



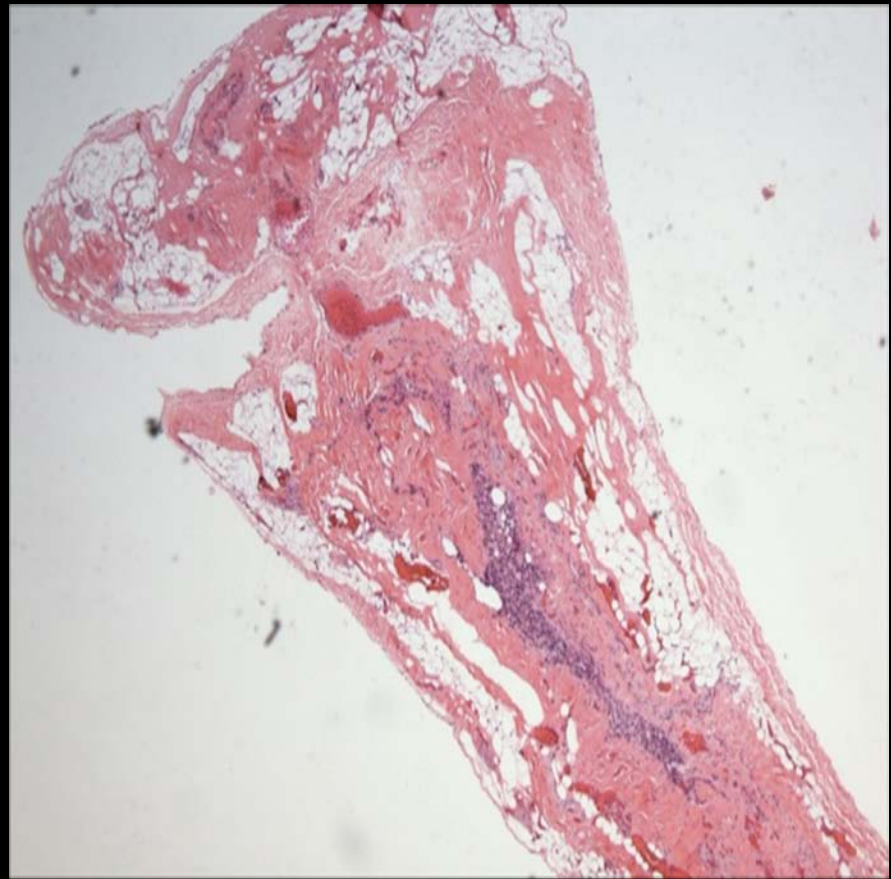
Paldino, M, Mogilner AY, Tenner MS.
Neurosurg Focus (16) 1-8, 2003

Features that differentiate normal fila from fila of TCS

- adipose tissue
- fibrosis
- abundant collagen
- meningo-epithelial proliferation
- Activated microglial cells
- Mast cells



Klinge P , Pension M 2016 in prep



Izci,Y. J Neurosurg :Pediatrics 13, 2014.

Occult tethered cord syndrome

Table 1 Details of published series of OTCS

Author	Duration of follow up (months)	Number of patients in study	Number with urologic dysfunction	Number with improved urologic symptoms post op	Number with worse symptoms post op
Khoury et al. (1990)	Mean 13.3	31	31	22	0
Warder and Oakes (1993)	Range 6–72	13	13	13	0
Nazar et al. (1995)	Range 2–48	32	32	22	0
Selcuki et al. (2000)	Mean 18	17	17	10	0
Selcuki et al. (2003)	Range 3–84, mean 31.7	8	8	5	0
Komagata et al. (2004)	Not reported	37	37	25	0
Wehby et al. (2004)	Mean 13.9	60	60	40	0
Metcalfe et al. (2006)	Mean 49	36	36	20	0
Selden et al. (2006)	Range 3–30, mean 15.6	6	6	6	0
Steinbok et al. (2007)	Range 12–120, mean 37.2	8	8	7	1

13 Studies
289 Patients
239 Improved
9 Worse

Conclusions: As occult tethered cord syndrome becomes increasingly recognized, it is important to be aware of the potential benefits of operative intervention for appropriately selected patients.