Development and anomalies of the cranio-vertebral junction

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What is the Cranio-Vertebral Junction

- A segment of the spine dedicated to head motion - vision, smell, earing, seizing, eating, fighting
- Interposed between the “standard” spine and the “cephalized” spinal segment that constitutes the bony posterior fossa
- Derived from occipito-cervical somites
1. **Gastrulation**: notochord development and malformations
   - neuro-enteric canals/cysts
   - diplomyelia/diastematomyelia
2. **Neurulation**: neural tube differentiation and closure
   - Chiari III
3. **Somitic/vertebral segmentation disorders**
4. **Bony growth disorders**
   - Chiari 1 deformity commonly associated to both
Notochordodysraphism

Formation of the notochord
Neuro-enteric canal and cyst
Notochordodysraphism

Induction of the neurulation

Normal

Duplicate

Split cord
Notochordodysraphism at the CVJ

Diastematobulbia Herman, AJNR 1990

Foramen magnum diastematobulbia with triplobulbia Sandberg CNS 2007

Neuro-enteric canal and cyst
Open neurodysraphy (neural tube defect) at the CVJ

- Myelobulbo-meningocele = Chiari 3
- (Chiari 2 is a deformity secondary to a myelomeningocele, not a malformation)
Somitic segmentation process

- Ventral induction *SHH*
- Segmentation genes: Homeobox genes
  - "Segmentation clock" genes:
    - cyclic activation of *Notch, Wnt, FGF* makes up the somites
    - cyclic inhibition by *MESP2* = intersomitic-boundaries
Bony cranio-vertebral junction segmentation

- Vertebral “resegmentation” process
  - Somites = nerves, vertebrae between nerves
- Three cranio-vertebral specificities
  1. cephalized rostral “spine”: unsegmented posterior fossa
  2. bidirectional cranio-vertebral joint: un-divided C1-C2
  3. retention of C1 hypo-centrum for rotation socket
1) somitic levels correspond to nerves – vertebrae are between nerves
2) unsegmented occipital – CVJ segment – resegmented spine
3) retention of the O4 - C1 segmental hypocentra (hypochordal arches) to complete the multidirectional articulation (socket for the axis)
Segmentation process: beyond the somites

- Axial skeleton, paraxial mesoderm, neural tube are segmented
- Rostral-most notochord extends to mesencephalon
- Rhombomere 0 = isthmic organizer starts the segmentation
- Segments = somitomeres correspond to neuromeres
  - pharyngeal (branchial) arches = ventral portion of incomplete somites: no dorsal sclerotome, myotome, dermatome
  - occipital somites 1-3: no dorsal myotomes
  - pro-atlas: no dorsal sclerotome
  - C1: no dorsal dermatome (no sensory C1)
<table>
<thead>
<tr>
<th>neuro-mere</th>
<th>neural tube</th>
<th>somito-mere</th>
<th>somite</th>
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<th>derivative 2</th>
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Segmentation process

- Ventral induction *SHH*
- Segmentation genes: Homeobox genes
- "Segmentation clock" genes:
  - cyclic activation of *Notch, Wnt, FGF* makes up the somites
  - cyclic inhibition by *MESP2* = intersomitic-boundaries
- Specific causes, pathways, processes to explain why segmentation is abnormal in a given patient are lacking
- Specifics of CVJ unknown
- Segmentation disorders may be syndromic or sporadic
## Missegmentation of the bony CVJ

<table>
<thead>
<tr>
<th>Classification of bony malformations of the CVJ according to embryogenesis</th>
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<tr>
<td>Clinically significant CVJ bony malformations</td>
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<tr>
<td>Malformations of central pillar</td>
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<td>Disturbance of axial component of occipital sclerotome, proatlas and C₁ resegmented sclerotome</td>
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<td>Odontoid dysgeneses</td>
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<td>- Aplasia/hypoplasia of odontoid components</td>
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<td>- Disturbance of odontoid synchondroses (IBZ)</td>
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<td>- Os odontoideum</td>
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<td>- Os odontoideum persistens</td>
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<td>- Abnormal resegmentation of proatlas centrum</td>
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<td>- Failed midline integration of basal dental segment</td>
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<td>Basioccipital dysgeneses</td>
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<td>C₁ sclerotome anomalies</td>
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<td>- Aplasia of hypochordal bow of C₁</td>
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<td>- Aplasia and hypoplasia of anterior C₁ arch</td>
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<td>- Aplasia/hypoplasia of lateral sclerotome</td>
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Pang and Thompson Childs Nerv Syst 2011
Missegmentation of the bony CVJ
Abnormal bony posterior fossa

Normal occipital alignment

Unilateral occipital hypoplasia

Basal impression (invagination)
Neural CVJ: Chiari 1 deformity

Chiari 1 may appear or regress spontaneously
May be secondary to lumbar shunt or CSF over-drainage

Chiari 1 is a deformity, not a malformation
Chiari 1 deformity: terminology

- Hans Chiari 1891
  - Chiari 1: tonsillar ectopia
  - Chiari 2: low, abnormal hindbrain with myelomeningocele
  - Chiari 3: occipito-cervical cephalocele
  - Chiari 4: extreme cerebellar hypoplasia, now PCH (degenerative)
- Tortori-Donati 1996
  - Chiari 4: Chiari 2 + small cerebellum, now “vanished cerebellum”
- Alabama’s group, 2000s
  - Chiari 0: no Chiari but syringomyelia
  - Chiari 1.5: tonsillar + brainstem descent
  - Chiari 5: Chiari 3 + occipital lobes
Chiari 1: pathogenetic postulates

- Hans Chiari: congenital hydrocephalus
- 1970’s-1980’s: Chiari 2 in children, Chiari 1 in adults
- 1990’s: abnormal ventro-dorsal patterning
- Now: small posterior fossa
Chiari 1: small posterior fossa

- Poorly developed posterior fossa (Aydin 2005, 60 adults; Sekula 2005, 20 adults)
- Posterior fossa normal without syringomyelia, small with syringomyelia (Sgouros 2006, 42 children)
- Abnormal skull base morphometry (Sgouros 2007, 30 children)
- Small posterior fossa (Trygilidas 2007, 61 children)
- Basi-occipital shortness (Noudel 2009, 17 adults; Dagtekin 2011, 15 adults)
- Posterior fossa normal in children but abnormal in adults (Furtado 2009, 21 children, 21 adults)
Chiari 1 deformity: a discrepancy content/container

- Large brain/hindbrain
  - Sotos, HME, NF1, congenital hydrocephalus etc.
- Small skull, and/or small posterior fossa
  - craniosynostoses, platybasia, basal impression etc.
- Short clivus (most common)
  - pro-atlas hypoplasia
- Mis-segmentation (e.g., Klippel-Feil)
  - occipital vertebra, other complex malformations
In all, posterior fossa is small, therefore cisterns are effaced and foramen magnum is crowded
PMG +
ACC +
dysplasia

Large brains/hindbrains

Soto's congenital hydrocephalus
Small skull or small posterior fossa

Crouzon
- early closure of coronal sutures and basal synchondroses

Cavalier King Charles Spaniel
- small skull
- flat skull base - PF
- Chiari 1 deformity
- syringomyelia (no hydrocephalus)
Anatomic landmarks of bony posterior fossa

• Chamberlain, McRae
  – same plane
• Other landmarks
  – synchondrosis – midpons
  – basion -- obex
• Incisural line
Anatomic landmarks of bony posterior fossa

- Chamberlain, McRae
  - same plane
- Other landmarks
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- Incisural line

Tip of dens and occipito-atlantal joints are aligned along the flexion axis of the head
Achondroplasia

Synchondroses closed, not sutures

Posterior fossa small, vault gives way, hindbrain ascends

Bony abnormalities: posterior fossa landmarks

Short clivus

Small posterior fossa

Abnormal CVJ dynamics
Anatomical landmarks of posterior fossa

- Posterior fossa sagittal osteo-dural pentagon: regular and symmetric
- Standard measuring bar: clivus
Abnormal bony posterior fossa

Normal occipital alignment

Unilateral occipital hypoplasia

Basal impression (invagination)

Sagittal pentagon AND coronal evaluation
- effaced cisterns
- asymmetric pentagon = short supra-occiput

- effaced cisterns
- flat pentagon = flat posterior fossa

- gelastic seizures
- low forebrain, effaced cisterns, McRae & Chamberlain
- asymmetric pentagon
- high midbrain, filled cisterns,
- small, flat pentagon: short clivus & supraoccipital,

- high midbrain, filled cisterns, wide basal angle
- platybasia, flat asymmetric pentagon & short supraoccipital

- distorted pentagon: short clivus, "retroverted" dens (tilted head)
  = hypoplastic pro-atlas
Short clivus: proatlantal hypoplasia and retroverted dens

- Proatlas: **anterolateral** margin of foramen magnum
- Hypoplasia of clivus & condyles, not of opisthion
- Head tilted forward, relative ascent of the dens, which abuts medulla
- Occipito-atlantal joints ascend in relation to brainstem
  - not a “basilar impression”
Abnormal segmentation: occipital vertebra

Prominent dens & short clivus
Associated hypoplasia of jugular tubercles-condyles
Neo-articulation with unknown ligamentous anatomy
Hypogenesis, condylus tertius: new joint, what ligaments?

High segmentation, undivided O4, fused hypocentra, prolonged invaginated dens; ligamentous apparatus?
Chiari 1: pathophysiology

• Chiari I deformity: chronic tonsillar downward displacement
  – four main causes: 1) large hindbrain, 2) short / flat posterior fossa,
    3) proatlantal hypoplasia, 4) occipital vertebra
• Not a cause of hydrocephalus, but most common cause of hydromyelia
  and medullary/low cranial nerve compression (plugging of foramen
  magnum)
• CVJ *bony malformations* have complex consequences:
  – abnormal osteo-neural biomechanics (specific brainstem exposure)
  – unknown anatomy of ligamentous apparatus (stability)
Neural cranio-vertebral junction: tumors

- Neural cranio-vertebral junction is biologically different from upper medulla
- Like in cord, cranio-cervical gliomas involve the whole neural thickness; upper medullary gliomas are tegmental or ventral
- Genome of ependymomas is different in different locations—genetically similar to cord and like them, lower fourth ventricular ependymomas are rather benign (type B)
  - lateral recess ependymomas different, with poor prognosis (type A)
Arterial cranio-vertebral junction: functional adaptation

- Lower medulla and upper cord supplied by anterior midline channel
- Development of the hindbrain first, then of cerebral hemispheres led to capture of the cervical supply through longitudinal paravertebral anastomoses
- The mobility of the CVJ imposed peri-atlantal collateral loops via the pro-atlantal arteries
Venous cranio-vertebral junction: cranio-spinal continuity

- Supratentorial venous drainage: through remaining ends of the primary head sinuses: cavernous sinus and jugular foramen, and peripheral dural collaterals (sinuses)
- Like the spine, posterior fossa characterised by an anterior epidural plexus and lateral outlets (mastoid and posterior condylar emissary channels)
- Continuous with sigmoid sinuses and spinal epidural plexuses
- Jugular foraminal stenosis → high ICP only if associated with cervical canal stenosis (and non-efficient emissary veins)
In summary

- CVJ: a developmentally transitional zone between pharyngeal arch and somitic systems, retaining vestigial hypocentrum
- Bony, neural, arterial and venous transitional segment as well
  - in addition to being a specifically joint for a complex motion
- Chiari deformity a consequence of CVJ abnormalities, not a malformation
  - clinical impact: compression (cord, cranial nerves, CSF dynamics) and abnormal biomechanics (osteo-medullary conflict)