Embryology of the falco-tentorial dura mater

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Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Menu

1. Embryology of the dura mater encephali
2. Neural crest cell and falco-tentorial dura mater
3. Clinical consideration of falco-tentorial dura mater

Keywords: dura mater encephali, falx cerebri, tentorium cerebelli, neural crest, dura propria
Dura mater (Latin, dura mater = hard, tough mother)
The outer tough connective tissue meningeal coat of the 3 layers that cover the central nervous system of 3 layers (overlays the arachnoid mater middle layer and pia mater inner layer).
All three layers form from the meninx primitiva, a meningeal mesenchyme that is mesodermal and neural crest in origin.
Pia mater is medieval Latin meaning "tender mother".
Neurulation: Establishing the Neural Tube, the Rudiment of the Central Nervous System

DEVELOPMENT
- developed from the cells of the neural crest & mesenchyme (mesoderm and neural crest) forming the primitive meninges
- differentiate into ectomeninx (outer more compact layer) & endomeninx (inner more reticulated layer)

Larsen, W.J. Human Embryology 2009
neural tube (NT). DLHP, dorsolateral hinge point; HM, head mesoderm; N, notochord; MHP, median hinge point; SE, surface ectoderm.
F, Transverse section showing a slightly later stage in neurulation than shown in E. Neural crest cells (NC) are beginning to form and emigrate from the fusing neural folds.

Larsen, W.J. Human Embryology 2009
ectomeninx becomes more compact and with spaces (future sinuses)
dura mater (pachymeninx);

endomeninx becomes more reticulated with development of spaces (future SAS & cisterns) arachnoid & pia mater (leptomeninges)
mesoderm. Toward the end of the third week, the paraxial mesoderm proliferate to form longitudinal columns of paraxial mesoderm. The mesoderm on each side of the notochord and represent the most cephalic mesodermal contribution from the future occipital region of the embryo. Rostral to the first somite, differentiate to become sclerotome. The somites first appear in the notochordal process to organize into a third germ layer.

Table 1. Stages of human embryonic developments

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Days</th>
<th>No. of somite</th>
<th>Carnegie stage</th>
<th>Selected external features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1–7</td>
<td>0</td>
<td>1</td>
<td>Fertilization</td>
</tr>
<tr>
<td>2</td>
<td>8–14</td>
<td>0</td>
<td>6</td>
<td>Primitive streak develops</td>
</tr>
<tr>
<td>3</td>
<td>15–21</td>
<td>0–1</td>
<td>7</td>
<td>Gastrulation commences and notochordal process forms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1–3</td>
<td>8</td>
<td>Primitive pit, neural plate, neural groove, neural folds form</td>
</tr>
<tr>
<td>4</td>
<td>22–28</td>
<td>4–12</td>
<td>9</td>
<td>Somites begin to form</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13–20</td>
<td>10</td>
<td>Neural folds fuse, otic pits form</td>
</tr>
<tr>
<td></td>
<td></td>
<td>21–29</td>
<td>11</td>
<td>Cranial neuropore closes. The first four somites are beginning to be incorporate into the occipital segmentation. Oropharyngeal membrane rupture, optic vesicles develop, optic pit begin to form</td>
</tr>
<tr>
<td></td>
<td></td>
<td>29–35</td>
<td>12</td>
<td>Caudal neuropore closes. Pharyngeal arches 3 and 4 form</td>
</tr>
<tr>
<td>6</td>
<td>36–42</td>
<td>&gt;30</td>
<td>13</td>
<td>Otic vesicles form. The meninx primitiva is first seen as the first signs of the cranial vault. Occipital sclerotomal mesenchyme concentrates around the notochord</td>
</tr>
<tr>
<td>7</td>
<td>43–49</td>
<td>&gt;30</td>
<td>14</td>
<td>Cerebral hemispheres become visible</td>
</tr>
<tr>
<td>8</td>
<td>50–56</td>
<td>&gt;30</td>
<td>15</td>
<td>Sensory and parasympathetic cranial nerve ganglia begin to form</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>16</td>
<td>The skull has a membranous roof present during stage 16</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>17</td>
<td>Cerebellum begins to form. Conversion of the ectomenix mesenchyme into cartilage starts on 40–41 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>18</td>
<td>Pia mater is present around the brain</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>19</td>
<td>Skeletal ossification begins</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>20</td>
<td>The first indication of dura mater is found in the skull</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>21–23</td>
<td>Ossification continues until stage 20</td>
</tr>
</tbody>
</table>

Timing of some events and stage can vary by up to 4–5 days during stages 10–23.

by the end of 2nd month (57 days) the endomeninx covers significant portion of the brain and has develop into the arachnoid and the pia mater. Dural reflections begin to form.
Comparative anatomy of the meninges.

In fishes, only a single layer, the primitive meninx, is present.

Amphibians and reptiles have two meningeal layers, an outer dura mater (meaning "hard mother") and an inner thin layer, the secondary meninx.

In reptiles, the dura mater is fairly well separated from the underlying arachnoid and pia mater.

In mammals and birds, three meningeal layers are present.

The layer closest to the brain is a thin layer called the pia mater (meaning "tender mother"). The middle layer is a thin, avascular layer called the arachnoid due to its spider web-like appearance. The space between the pia mater and the arachnoid is the subarachnoid space.
Comparative anatomy of the meninges

Meninx primitiva
(Periosteal dura and meningeal dura)

Meninx secundaria
(arachnoid space and pia mater)

Nonvertebrate chordates

Invertebrate ancestor

Meninx secundaria

Meninx primitiva
Phylogeny of meninx

<table>
<thead>
<tr>
<th>Phylogenic Steps</th>
<th>FISHES</th>
<th>AMPHIBIANS</th>
<th>REPTILES</th>
<th>BIRDS</th>
<th>MAMMALS</th>
<th>PRIMATES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meninx</td>
<td></td>
<td>Meninx primitiva</td>
<td>Meninx secundaria</td>
<td>SUBARACHNOID SPACE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Illustration

buoyant (+)  buoyant (-)

Phylogenic Steps FISHES AMPHIBIANS REPTILES BIRDS MAMMALS PRIMATES

Meninx Meninx primitiva Meninx secundaria SUBARACHNOID SPACE

buoyant (+) buoyant (-)

Phylogeny of meninx

Meninx primitiva  Meninx secundaria

buoyant (+) buoyant (-)

Phylogenic Steps FISHES AMPHIBIANS REPTILES BIRDS MAMMALS PRIMATES

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buoyant (+) buoyant (-)

Phylogenic Steps FISHES AMPHIBIANS REPTILES BIRDS MAMMALS PRIMATES

Meninx Meninx primitiva Meninx secundaria SUBARACHNOID SPACE

buoyant (+) buoyant (-)
Prof. Ernst Haeckel (1834 - 1919)

“Die Ontogenesis ist eine kurze und schnelle Rekapitulation der Phylogenesi

“Ontogeny recapitulates phylogeny”
The Haeckelian form of recapitulation theory is considered defunct. However, embryos do undergo a period where their morphology is strongly shaped by their phylogenetic position, rather than selective pressures.
Carnegie stage 14  Week 5

Placental blood vessels are visible extending lower left from umbilicus.
MRI sagittal scan @4 week embryo

Development of the vision and hearing sensory vesicles (optic and otic) and their relative positions (optic at the diencephalon; otic at the metencephalon).

The lamina terminalis at the end of the neural tube (site of cranial/anterior neuropore closure).

Meninx primitiva becomes visible, but meninx secundaria has not come yet.
Embryo
CRL 4.2 mm  6 weeks
Sagittal section of human embryo crown rump length 4.2 mm

* showing amniotic sac, chorionic plate and chorionic villi
* brain region labels in the associated ventricular spaces
* only a single villi cross-section is labeled in each region
Human embryo is 27 mm (CRL) in size and approximately equal to day 54 - 56 of development (week 8).

Matrix layer of telencephalon starts to develop, but no marked dura mater encephalii is not yet emerged.
Week 8: Future’s tentorium cerebelli is formed.
Dural mater is formed around 12 weeks.
Meningeal dura (dura propria) developed earlier than osteal dura.
A 12-week-old fetus (65-mm crown-rump length).

1. Transverse sinus
2. Sigmoid sinus
3. Vein of Galen
4. Superior petrosal sinus
5. Superior sagittal sinus
6. Interna cerebral v.
7. Internal jugular v.
8. Straight sinus
9. Vein of Galen
10. SSS

Okudera et al. AJNR 1994
A 16-week-old fetus (115-mm crown-rump length)

1. Transverse sinus
2. Superior petrosal sinus
3. Tentorial sinus
begins from the lateral end of the sinus and proceeds medially to reach the torcular. Occasionally it further involves the posterior part of the superior sagittal sinus (SSS). The sigmoid (3) and jugular sinuses (4) are not yet developed, and their diameters remain small.

The transverse sinus into the posterior part of the superior petrosal sinus. The torcular is plexiform, showing many cut surfaces of the veins toward the developed marginal sinus (3) around the foramen magnum. The marginal sinus then drains into the deep cervical veins channels. They stream inferiorly (from the primitive torcular area as well as from the medial portions of both transverse sinuses [2]).

The straight sinus (SS) opens into the medial portion (M) of the transverse sinus on the right side. The prootic sinus (3), and part of the occipital condyle (oc) are also labeled.

The vein (5) emerging from the jugular sinus (3) runs medially and inferiorly through the hypoglossal canal and joins the internal vertebral vein (4) are similar to those of the 7-month-old fetus (Fig 6), and the straight sinus (SS). The internal vertebral venous plexuses (1 to 2 mm), showing little changes in calibers as compared with those of a 3-month-old fetus. The occipital sinuses (7), and part of the occipital condyle (oc) are also labeled.

2. SPS
5. Tentorial sinus

A 17-week-old fetus (130-mm crown-rump length)

7-month-old (25-week) fetus (225-mm crown-rump length). 4. Tentorial sinus, 5.SPS

Okudera et al. AJNR 1994
Schematic illustration, focusing on the superior tentorial BVs and showing some of the many possible venous anatomic configurations, not necessarily coexisting in one individual.
The inferior tentorial BVs, including the petrosal BVs as seen from a caudal view. It shows some of the many possible venous anatomic configurations, not necessarily coexisting in one individual.
Falco-tentorial junction is a pivotal point for the development of telencephalon.

Falx cerebri is a very tough fascial membrane.

Arrows: developmental push of both cerebral hemispheres.
Embryo size approx. 29 mm. Modified from Blechschmidt, 1978
Sphenobasilar Articulation: The most important of the cranial articulations, the SB synchondrosis is formed at the juncture between the occiput and the sphenoid articulation.
Falco-tentorial membrane plays a role of biomechanics as the reinforce of skull bones.

Modified from Netter F. The CIBA Collection of Medical Illustrations. Summit, NJ: Ciba, 1983
Menu

1. Embryology of the dura mater encephali

2. Neural crest cell and falco-tentorial dura mater

3. Clinical consideration of falco-tentorial dura mater
What is the Neural Crest (NC)?

The neural crest (NC) is a transient, embryologic structure that was first found by a famous anatomist Wilhelm His in 1868.

NC is called the fourth germ layer and is characteristic to the vertebrates phylogenetically. Neural crest cells (NCCs) are pluripotent and give rise to a variety of derivatives after migration in early embryogenesis, such as neurons, glias, cartilage, connective tissue, pigment cells, and adrenal cells.
What is the Neural Crest (NC) ?

The blue stain is localized in small neurons of the neural crest cell–derived dorsal root ganglia and in the axons of these cells that penetrate the spinal cord in a region overlying the dorsal gray columns of the spinal cord (parasagittal stripes).
What is the Neural Crest (NC)?

Neural crest cells are a temporary group of cells unique to vertebrates that arise from the embryonic ectoderm cell layer, and in turn give rise to a diverse cell lineage—including melanocytes, craniofacial cartilage and bone, smooth muscle, peripheral and enteric neurons and glia.

These cells undergo an *epithelial-to-mesenchymal transformation* as they detach from the neural tube.
Multipotency and migratory capabilities of neural crest

Neural crest is called "The fourth germ layer" since the number of cell types that arise from the NC is truly astonishing as is the number of tissues and organs.
(A) Neural plate border specification

Neural crest specification

Non-neural ectoderm
Neural ectoderm
Notochord
Neural plate border
Neural fold
Neural plate

Neural crest EMT/delamination

Delaminating neural crest
Neural tube

Neural crest migration

Epidermis
Migrating neural crest

(B) Cranial neural crest

Chondrocytes
Osteocytes
Cranial sensory ganglia
Odontoblasts
Melanocytes
Ciliary ganglia

Vagal neural crest

Aorticopulmonary septum
Enteric ganglia
Sympathetic ganglia
Parasympathetic ganglia
Melanocytes
Cardiac ganglia

Trunk neural crest

Adrenal chromaffin cells
Dorsal root ganglia
Sympathetic ganglia
Schwann cells
Melanocytes

Sacral neural crest

Enteric ganglia
Sympathetic ganglia

Trends in Genetics
What is the Neural Crest (NC)?

1. The cranial (cephalic) neural crest from Rhombomere
2. The cardiac neural crest cells arise from the neural crest by somites 1–3;
3. The trunk neural crest
4. The vagal and sacral neural crest, whose cells generate the parasympathetic (enteric) ganglia of the gut.
Cardiac Neural Crest

Cranial Neural Crest
Vertebrates are characterized based on the endoderm, mesoderm, ectoderm and neural crest. Especially **head and neck consist from neural crest** that is so called the fourth germ layer. Pharyngeal system is also formed with neural crest.
Neural Crest–mesoderm interactions, D. M. Noden and P. A. Trainor

Progenitors of tongue muscles, which emigrate from somites 2–5 and move en masse as the hypoglossal cord (Fig. 2B) into the future tongue primordium, whose connective tissues are of neural crest origin. The significance of the interactions between mesoderm and neural crest cells during myogenesis is discussed below.

Movements and differentiation within head mesoderm: connective tissues

Later during embryonic development, cranial paraxial mesoderm produces cartilaginous and bony elements of the neurocranium, including the parietal, petrous and basisphenoid bones of the neurocranium (Fig. 5; chicks: Couly et al. 1992; mice: Jiang et al. 2002). Identifying the origins of calvarial elements has sparked controversy (Noden, 1975, 1978a, 1983a; LeLievre, 1978; Couly et al. 1992) in two aspects: the precise locations of the boundary between crest- and mesoderm-derived osteogenic precursors, and the correct nomenclature of avian vs. mammalian skull elements. Differing results based on quail-chick transplantations centered around the ability to graft neural crest or mesoderm progenitors exclusive of contamination by the other, which becomes increasingly difficult at progressively more caudal regions of the hindbrain. However, the use of replication-incompetent retroviral constructs containing a stable reporter construct (Mikawa & Gourdie, 1996) has substantiated the dual origin of the avian frontal bone and exclusively mesodermal origin of the avian parietal bone (Evans & Noden, 2005; Figs 3B and 5). Later, as the cerebral vesicles expand beneath the

Fig. 5

Schematic chick and mouse skulls showing the contributions of neural crest, paraxial and lateral mesoderms to the cranial skeleton. The avian map is based on transplantation and retroviral lineage tracings in the chick embryo; hyobranchial structures, all of which are derived from neural crest cells, are not shown. The mouse map is based largely on the location of neural crest cells, as identified by expression of \( \text{LacZ} \) driven by a \( \text{Wnt1} \) promoter in cre-lox transgenic embryos (Jiang et al. 2002). Origins of mouse laryngeal cartilages are by extrapolation from avian data, with the caveat that birds do not have a thyroid cartilage. Blue dots indicate the locations of crest cells present at sites of calvarial sutures. Abbreviations (Figs 5, 9 and 11): Ang, angular; Art, articular; Bs, basisphenoid; Den, dentary; Eth, ethmoid; Lac, lacrimal; Ls, laterosphenoid*; Mc, mandibular cartilage; Nc, nasal capsule; Os, orbitosphenoid*; Pal, palatine; Pfr, prefrontal; Po, postorbital; Ps, presphenoid; Ptr, pterygoid; Qd, quadrate; Qju, quadratojugal; San, surangular; Sqm, squamosal; *regions of the pleurosphenoid.

Dural membrane has two major Germ layers. One is Neural crest and the other is mesoderm.

The sagittal suture is formed from neural crest cells and separates the two mesodermally derived parietal bones. The coronal suture is derived from mesoderm.
Innervation of falco-tentorial dura mater

- Lamina cribrosa
- Vorderer Schädelgrube
- Mittlere Schädelgrube
- Hintere Schädelgrube
- Rr. meningei (N. ethmoidalis anterior/posterior)
- R. meningeus (N. spinosus/V₃)
- Rr. meningei (Nn. cervicales 1 u. 2)
- Rr. tentorii (N. ophthalmicus/N. maxillaris)
- Tentorium cerebelli
- Magnus raphe nucleus
- Superior salivatory nucleus
- Locus ceruleus
- Thalamus
- Dorsal raphe nucleus
- Hypothalamus
- Cortex
- Pterygopalatine ganglion
- Trigeminal ganglion
- Dura
The innervation of falco-tentorial dura mater is trigeminal nerve V1.
V1 was stimulated with devices and it caused trigeminal cardiac reflux.
Menu

1. Embryology of the dura mater encephali

2. Neural crest cell and falco-tentorial dura mater

3. Clinical consideration of falco-tentorial dura mater
neural crest cells

Trabeculum
Developing pituitary
Hypophysial cartilage
Parachordal cartilage
Otic capsule
Notochord
Occipital somites

Interorbital nasal septum
Orbitosphenoid
Alisphenoid
Internal carotid artery
Embryological background of skull and dural membrane

Base of the skull in adult showing the various embryonic components that participate in its formation. Part derived from neural crest cells (blue) and paraxial mesoderm (red) (Sadler, 2010).
Embryology of ossification in relation with Membranous bone and Endochondral (cartilaginous) bone

Neurocranium

Vicerocranium

Membranous neurocranium
Cartilaginous neurocranium
Membranous viscerocranium
Cartilaginous viscerocranium

by courtesy of Dr. Mitsuhashi modified from W.J. Larsen, Human Embryology
SKULL of the NEWBORN

Flat bones are connected through seams of connective tissue SUTURES.

Sagittal suture- neural crest cells
Coronal suture- paraxial mesoderm

FONTANELLES—more than two bones meet, sutures are widened.
Introduction of embryological concept of domains

Neural crest cells

Endochondral bone

Membranous bone

Neural crest

Paraxial mesoderm

dorsal mesoderm

Paraxial mesoderm

Dorsal mesoderm
Cephalic neural crest as the risk factor of dural AVFs

**Purpose:**
This study retrospectively analyzed the correlation between the distribution of DAVFs and the dural membrane derived from neural crest cells (NCC).

**Material and Methods:**
Sixty-six consecutive of DAVFs (32 men and 34 women, mean 68.4 years) were analyzed. Superselective digital subtraction angiography and high-resolution cone beam CT were performed in order to identify the shunt point. The topographical area derived from NCC was reviewed and identified from the literatures.
Neural crest contributions to the skull
Proposed classification of DAVFs

- **FT group:** Falx and Tent of the cerebellum group derived from neural crest cells
- **VE group:** Ventral group on the surface of Endochondral bone
- **DM group:** Dorsal group on the surface of Membranous bone

**neural crest origin**

**paraxial mesoderm origin**

**dorsal mesoderm origin**
Proposed classification of DAVFs

- **FT group:** Falx and Tent of the cerebellum group derived from neural crest cells

- **VE group:** Ventral group on the surface of Endochondral bone

- **DM group:** Dorsal group on the surface of Membranous bone
Three different domains of dural membrane

Dura propria alone
(inter dural space between two layers of dura propria)

YES

NO

FT group

Periosteal dura and Dura propria on the surface of endochondral bone

YES

NO

VE group

Located on the surface of membranous bone

DM group
Result 1

Neural crest derived (Neurocristopathy)
### Result 2

<table>
<thead>
<tr>
<th></th>
<th>FT: Falx and tent of the cerebellum derived from neural crest cells</th>
<th>VE: Ventral group derived from endochondral bone</th>
<th>DM: Dorsal group derived from membranous bone</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (male/female)</td>
<td>15 (87% / 13%)</td>
<td>30 (27% / 73%)</td>
<td>21 (62% / 38%)</td>
</tr>
<tr>
<td>Mean age (year)</td>
<td>65.1</td>
<td>78.4</td>
<td>59.8</td>
</tr>
<tr>
<td>Cortical venous reflux</td>
<td>93%</td>
<td>37%</td>
<td>52%</td>
</tr>
<tr>
<td>Major symptoms</td>
<td>headache, neurological deficit associated with venous infraction, hemorrhage, paraplegia (central myelopathy)</td>
<td>diplopia, chemosis, bruit</td>
<td>headache, tinnitus</td>
</tr>
<tr>
<td>Mode of embolization</td>
<td>TAE 93%, TAE+TVE 7%</td>
<td>TVE 60%, TAE 7%</td>
<td>TVE 52%, TAE 19%</td>
</tr>
</tbody>
</table>

TVE 33%  
TAE+TVE 29%
<table>
<thead>
<tr>
<th></th>
<th>FT: Falx and tent of the cerebellum derived from neural crest cells</th>
<th>Non FT: Independent from Neural crest cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (male/female)</td>
<td>$15$ (87% / 13% )</td>
<td>$51$ (45% /55%)</td>
</tr>
<tr>
<td>Mean age (year)</td>
<td>65.1</td>
<td>68.3</td>
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<td>TVE 60%, TAE 7% TAE+TVE 33%</td>
</tr>
</tbody>
</table>
Result 3

- **FT group**: Green
- **VE group**: Red
- **DM group**: Yellow

Bar chart showing the distribution of male and female patients in the FT group, VE group, and DM group.
Result 4

All of FT group presented with aggressive clinical course

- **FT** (Falx and tent group derived from neural crest cells)
- **VE** (Ventral group of endochondral bone)
- **DM** (Dorsal group of membranous bone)
Falx, tentorium, olfactory groove and spinal canal consist only from dura propria.
Periosteal dura

Dura propria

SSS

Transverse sinus

Spinal canal is covered with only dura propria

Tentorium cerebelli

Falx cerebri

Tentorium cerebelli is covered with only dura propria

Transverse sinus
Schematic illustration of the venous exits in the ethmoidal area, anterior to and at the lamina cribrosa.

Notice the direct duro-leptomeningeal venous connections at the level of the olfactory bulbs as well as the BV exiting at the lowermost end of the superior sagittal sinus.

direct duro-leptomeningeal venous connections
Primitive marginal sinus (future’s falx and SSS) is derived from neural crest.

~48 days, 18 mm, Carnegie Stage 19
The pathologies on the surface of falco-tentorial region can be considered as the neurocristopathy.

FT group: Falx, tent of the cerebellum and lateral surface of spinal canal group derived from neural crest cells.
Discussion based on embryology

ACC, olfactory groove, lateral spinal

Geibprasert S et al. 2008

ACC, Cavernous, sigmoid

Tanaka M, 2016
Summary 1

1. Dural membrane on the falx, tentorium cerebelli, olfactory groove and spinal cord are derived from neural crest.

2. Dural AVFs associated with neural crest have always pial cortical venous reflux and character of demographic with male predominant.

3. Falco-tentorial, olfactory groove and spinal cord DAVFs can be considered as the neurocristopathy with aggressive clinical course.
Embryological Consideration of Dural Arteriovenous Fistulas

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Abstract

The topographical distribution of dural arteriovenous fistulas (DAVFs) was analyzed based on the embryological anatomy of the dural membrane. Sixty-six consecutive cases of intracranial and spinal DAVFs were analyzed based on the angiography, and each shunt point was identified according to the embryological bony structures. The area of dural membranes was categorized into three different groups: a ventral group located on the endochondral bone (VE group), a dorsal group located on the membranous bone (DM group) and a falco-tentorial group (FT group) located in the falk cerebri, tentorium cerebelli, falk cerebelli and diaphragm sellae. The FT group was designated when the dural membrane was formed only with the dura propria (meningeal layer of the dura mater) and not from the endosteal dura. Cavernous sinus, sigmoid sinus, and anterior condylar confluence was categorized to VE group, which had a female predominance, more benign clinical presentations, and a lower rate of cortical and spinal venous reflux. Transverse sinus, confluence, and superior sagittal sinus belonged to the DM group. Olfactory groove, falk, tent of the cerebellum, and nerve sleeve of spinal cord were categorized to the FT group, which presented later in life and which had a male predominance, more aggressive clinical presentations, and significant cortical and spinal venous reflux. The DAVFs was associated with the layers of the dural membrane characterized by the two different embryological bony structures. The FT group was formed only with the dura propria as an independent risk factor for aggressive clinical course and hemorrhage of DAVFs.

Key words: dural arteriovenous fistulas, dura propria, osteal dura, endochondral bone, membranous bone
Spinal DAVF

Why posterior spinal vein is always dilated rather than anterior spinal vein?
Embryo@8 week

- **Vertebrate neural crest development**
  - Neural plate border
  - Premigratory neural crest
  - Migratory neural crest

- **Anatomical layers:**
  - Dorsal root
  - Ventricular layer
  - Intermediate layer
  - Alar Plate
  - Basal Plate
  - Marginal layer
  - Floor plate
  - Sulcus limitans
  - Dorsal root (spinal) ganglion
  - Arachnoid mater
  - Pia mater
  - Dura mater

- **References:**
Artery of Davidoff-Schechter
A 64 year-old-man presented with progressive paraplegia with bladder and rectal disturbance.
What causes Cobb syndrome?

The cause of Cobb syndrome is not completely understood. It is believed that somatic mutations in the neural crest or mesoderm are responsible for its development fairly early in the development of the embryo.
Cobb syndrome is associated with the migration of neural crest pericyte.
Neurocristopathy

The neural crest (NC) is a transient, embryologic structure that was first found by a famous anatomist Wilhelm His in 1868. NC is called the fourth germ layer and is characteristic to the vertebrates phylogenetically. Neural crest cells (NCCs) are pluripotent and give rise to a variety of derivatives after migration in early embryogenesis, such as neurons, glia, cartilage, connective tissue, pigment cells, and adrenal cells. It was proposed to call the diseases of NC origin as neurocristopathy (crista = crest, ridge), which is divided into dysgenetic and neoplastic forms.

Canadian pediatric pathologist Bolande proposed that diseases of NC should be called "neurocristopathy" in 1974.
Neurocristopathy was further classified into dysgenetic and neoplastic forms.

Dysgenetic neurocristopathy, for example, includes congenital melanotic nevi, cafe au lait spots, albinism, Pierre Robin syndrome, Treacher Collins syndrome, facial clefting syndrome, and Hirschsprung's disease,

The neoplastic form is typified by neuroblastoma, pheochromocytoma, carotid body tumor, paraganglioma, peripheral neuroectodermal tumor, and meningioma.
Treacher Collins syndrome as a neurocristopathy mutation p.Lys643GlufsX38 (c.1927dupG) in the TCOF1 gene

SKELETAL DERIVATIVES OF BRANCHIAL ARCHES

I. MANDIBULAR ARCH - forms
   a) BONES OF MIDDLE EAR (malleus, incus, also ant. lig. of malleus);
   b) STRUCTURES ASSOCIATED WITH MANDIBLE
      sphenomandibular lig., (Meckel's cartilage, framework of mandible)

   note: FIRST ARCH SYNDROME (TREACHER COLLINS) - genetic disorder; Neural crest cells do not migrate into Arch 1:
   - mandibular hypoplasia
   - conductive hearing loss
   - facial malformation

   TREACHER COLLINS SYNDROME

II. HYOID ARCH -
    a) ONE BONE OF MIDDLE EAR (stapes);
    also
    b) STYLOID PROCESS and stylohyoid lig.
    c) part of HYOID BONE (upper half of body of hyoid bone)

III. THIRD ARCH -
     REST OF HYOID BONE - lower half of body of hyoid

IV. FOURTH ARCH -
    cartilages of larynx
Population of neural crest cells migrates to many areas of embryonic body to differentiate to various structures including pharyngeal arches, which are a base for formation of some facial, cervical, laryngeal and pharyngeal structures.

Decreased amount of migrating cells to the first and second pharyngeal arches leads to malformations of mandibulofacial and auricular areas typical for Treacher–Collins syndrome.

Mutation of TCOF1 gene

↓ Treadle phosphoprotein

↑ p53 and activation of proapoptotic genes

↑ neuroepithelial apoptosis of neural crest cells

Normal TCOF1 gene — normal amount of migrating cells from neural crest area

Mutation of TCOF1 gene — decreased amount of migrating cells from neural crest area

Down-slanting „antimongolid“ palpebral fissures

Coloboma of the lower lid

Microtia, malformed ears

Macrostomia

Micro/retrognathia

Cleft palate
Treacher Collins syndrome has potential risk of dysgenesis on the falco-tentorial region as a neurocristopathy.
Flow diagram of the current model of the pathogenesis of Treacher Collins syndrome.

Nature medicine 2008

Right panel shows rescue of most apoptosis in the neuroepithelium, normal neural crest migration and normal bone structure in Tcof1+/− mice lacking one copy of Trp53.
Segmental neurovascular syndromes in children.

The concept of segmental vascular syndromes with different, seemingly unrelated, diseases is based on the embryology of the neural crest and the mesoderm migration of cells that share the same metameric origin.

Migrating patterns of these cells link the brain, the cranial bones, and the face on the same side.

A somatic mutation developing in the region of the neural crest or the adjacent cephalic mesoderm before migration can, therefore, be postulated to produce arterial or venous metameric syndromes, including PHACES, CAMS, Cobb syndrome, and Sturge-Weber syndrome.

Although these diseases may be rare, their relationships among each other and their postulated linkage with the development of the neural crest and the cephalic mesoderm may shed light on the complex pathology and etiology of various cerebral vascular disorders.
The PHACE acronym refers to the association of:

**P**osterior fossa anomalies- Includes Dandy-Walker malformation, cerebellar hypoplasia or agenesis as well as other central nervous system (CNS) abnormalities

**H**emangiomas- segmental facial

**A**rterial cerebrovascular anomalies- agenesis, aneurysms, occlusion or anomalies of arteries or persistence of fetal circulation

**C**ardiac abnormalities and Coarctation of the Aorta- structural heart defects and/or coarctation, aneurysm or aberrant anatomy of the aorta or the vessels that arise from the aorta

**E**ye abnormalities- persistent fetal vasculature and morning glory disc anomalies, microphthalmia, optic nerve hypoplasia and other ocular abnormalities

This is not an all-inclusive list. Recently, a review detailed findings in each of the above categories that can be associated with PHACE and defined consensus criteria to diagnose PHACE syndrome.

PHACE syndrome should be suspected clinically whenever a newborn exhibits a segmental hemangioma greater than 5 cm of the face and/or scalp. Subtle skin changes involving the skin overlying the sternum or above the umbilicus can also be a clue to PHACE syndrome. These include linear scars, clefts, pits, dimples, or papules.
In a review of 108 patients with large facial hemangiomas (images from Haggstrom), it was found that the highest risk for PHACE syndrome seems to be in patients who have hemangiomas involving the S1 and S3 segments. S4 segmental involvement also confers risk but PHACE rarely occurs with solely S4 presentations without S1 or S3 involvement. Isolated S2 involvement seems to have a lower risk of PHACE as well.


This patient with a segmental hemangioma of the back manifested cardiac and aortic arch anomalies.
Cardio-cephalic neural crest syndrome
CRANIOSYNOSTOSIS

Craniosynostosis, the premature closure of sutures, affects approximately 1 in 2500 children and occurs in many syndromes, including Crouzon, Apert, Pfeiffer, Muenke, and Saethre-Chotzen syndromes.

The coronal suture is derived from mesoderm and separates the neural crest cell-derived frontal bone and the mesoderm-derived parietal bone. The sagittal suture is formed from neural crest cells and separates the two mesodermally derived parietal bones.
The typical dysgenetic form includes Hirschsprung disease, DiGeorge syndrome, coarctation of the aorta, and agenesis/ hypogenesis of the internal carotid artery (ICA), and the neoplastic form includes neuroblastoma, paraganglioma, and neurofibromatosis type 1 (NF1).

Interestingly, it is reported that Moyamoya disease co-exists with Hirschsprung disease, coarctation of the aorta, and NF1. In addition, PHACE syndrome may present with agenesis of the ICA, coarctation of the aorta, cardiac anomaly, and segmental facial hemangioma as well as Moyamoya disease.
Anterior circulation is derived from neural crest

Posterior circulation is derived from mesoderm.

 neural crest origin
ICA system
including Pcom a and entire PCA

Primitive internal carotid artery system

mesodermal origin
VB system

Ventral longitudinal arteries

Moyamoya disease affects only the arterial system derived from neural crest pericytes.

→ Moyamoya disease is a sort of neurocristopathy.
Conclusions

1. Falx cerebri, tentorium cerebelli, olfactory groove and dura mater of spinal canal can be categorized to the same domain derived from neural crest. These dura maters consist of only dura propria (meningeal dura).

2. Falco-tentorial, olfactory groove and spinal DAVFs can be defined as the neurocristopathy that is a category of diseases associated with neural crest development.

3. A thorough knowledge of NCC may help in understanding a disease process and address these pathological issues associated with falco-tentorial dura mater.
Neural crest gives us another point of view to know underlying pathology of falco-tentorial system.

Thank you…

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