AUTOPSY FINDINGS IN PONTINE TEGMENTAL CAP DYSPLASIA

Andrew Gao¹, Susan Blaser³, David Chitayat², Felice D’Arco³, Patrick Shannon¹

¹Depts. of Laboratory Medicine and ²Medical Genetics, Mount Sinai Hospital; ³Dept. of Medical Imaging, Hospital for Sick Children
University of Toronto | Toronto, Ontario
1. Flat ventral pons
2. Pontine tegmental “cap” projecting into IVth ventricle
3. Subtotal absence of MCPs
4. “Molar tooth” SCPs
5. Hypoplastic vermis
6. Absent or hypoplastic ION

Pontine tegmental cap dysplasia: a novel brain malformation with a defect in axonal guidance

Peter G. Barth,1 Charles B. Majoie,2 Matthan W. A. Caan,2 Marian A. J. Weterman,3 Marten Kyllerman,4 Leo M. E. Smit,5 Richard A. Kaplan,6 Richard H. Haas,7 Frank Baas,5 Jan-Maarten Cobben8 and Bwee Tien Poll-The1
Absence of normal transverse pontine fibres

Ectopic transverse pontine fibres in pontine tegmentum

1 corticospinal tract
2 transverse pontine fibres
3 ectopic transverse fibre tract
4 middle cerebellar peduncle
5 fibres passing from ectopic transverse bundle to cerebellum
# Additional (variable) features

18 publications, 34 cases; 1997-

<table>
<thead>
<tr>
<th>Sex</th>
<th>15 M, 19 F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmission</td>
<td>Sporadic; 1 case of consanguineous parents; no affected siblings</td>
</tr>
<tr>
<td>Age of onset</td>
<td>Congenital to early infancy</td>
</tr>
<tr>
<td>Clinical</td>
<td>Respiratory, feeding difficulty</td>
</tr>
<tr>
<td>Supratentorial</td>
<td>Ventriculomegaly</td>
</tr>
<tr>
<td>Brainstem</td>
<td>Small cerebellum</td>
</tr>
<tr>
<td>Spine</td>
<td>Vertebral defects</td>
</tr>
<tr>
<td>Systemic</td>
<td>Congenital heart defect (ASD, VSD, Tetralogy of Fallot)</td>
</tr>
</tbody>
</table>
Female fetus, termination of pregnancy at 22 weeks gestational age

Mother: healthy 35 yo G2P1
Father: healthy 38 yo
Non-consanguineous

Conceived via IVF

Coxsackievirus infection at 8 weeks

Hindbrain abnormalities detected on imaging at 21 weeks
MRI

CT reconstruction
duplication of IAC bilaterally

CT
Autopsy findings

- General autopsy and placenta: vertebral segmentation defect
- Brain weight: 85.9 g (expected 64 ± 12 g)
- Supratentorial: sulcation compatible with 22 weeks; mildly dilated ventricular system; normal architecture
- Cerebellum: reduced rostral-caudal diameter; vermis present
- CNs: III, IV, V, VI, VII present; questionable VIII
- Spinal cord: normal
Relatively normal caudal midbrain
Rostral pons
Poorly formed SCPs
Cerebral peduncles split
Midline pontine tegmentum occupied by wedge of neurons

Splaying of the tegmental elements laterally

Nucleus basis pontis absent
Tegmentum obscured by tangentially running tracts, obscuring the floor of IVth ventricle

Corticospinal tracts descend as compact masses without dissection by nucleus basis pontis
Nucleus basis pontis appears displaced into medulla.
Hypoplastic inferior olivary nuclei
Summary of findings

- Ectopic transverse fibres form pontine cap
- Absence of normal transverse pontine fibres
- Descending corticospinal tracts displaced dorsally by apparent nucleus basis pontis in caudal pons and medulla
- Midline pontine tegmentum occupied by wedge of neurons
- Poorly developed SCP, MCP, dentate nucleus, inferior olive
32-month-old boy

Flattened ventral pons

Band of tissue in floor of IVth ventricle in dorsal pons (cap)

CN VII and VIII absent

No olivary prominences
Neurofilament, Luxol fast blue-cresyl violet
P. Jissendi-Tchofo
D. Doherty
G. McGillivray
R. Hevner
D. Shaw
G. Ishak
R. Leventer
A.J. Barkovich

Pontine Tegmental Cap Dysplasia: MR Imaging and Diffusion Tensor Imaging Features of Impaired Axonal Navigation

CONTROL

PATIENT

1. Rhombic lip progenitors
2. Ventral migration
3. Decussation
4. Radial (dorsal) migration
5. Enter MCP

B: Decreased ventral migration
C: Increased radial migration
D: Abnormal axon guidance
Genetic studies

- Netrin 1/DCC – no pathogenic mutations identified (Barth et al. 2007)
- NPHP1 (2q13) 96 kb deletion – detected in 1 patient (Macferran et al. 2010), subsequently not detected in 3 patients (Briguglio et al. 2011)

Macferran et al. Semin Pediatr Neurol 2010;17:69-74
Briguglio et al. Orphanet Journal of Rare Diseases 2011;6:36
Summary

Transverse fibres forming dorsal pontine cap

Architectural disarray of brainstem

Aberrant neuronal migration