Developmental Posterior Fossa Abnormalities with Associated Supratentorial Findings

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Introduction

• Barkovich has classified posterior fossa developmental malformations into two subgroups, hypoplasia (incomplete formation) and dysplasia (abnormal formation)\textsuperscript{1}
• Each subgroup in turn can be broken into focal and diffuse, suggesting local insult compared with generalized process (e.g. genetic or metabolic)\textsuperscript{1}
• We also consider atrophy to represent a distinct subgroup
Introduction

• Our experience with developmental posterior fossa abnormalities has led us to realize that occasionally associated supratentorial anomalies are present.

• Lack of attention to the cerebellum has delayed understanding of cerebellar developmental abnormalities in general, let alone their associations with supratentorial anomalies.
Methods and Materials

• Review of our database of posterior fossa developmental abnormalities was performed to evaluate for associated supratentorial findings

• Attempt was then made to group the supratentorial abnormalities into various subtypes to better understand the potential associations
Results

• A total of 69 cases of developmental posterior fossa abnormalities were reviewed, revealing 17 cases with associated supratentorial findings.

• Supratentorial anomalies included: dysplasia, heterotopia, corpus callosal and septal malformations, white matter de/dysmyelination, polymicrogyria, microcephaly and volume loss, hippocampal unfolding, basal ganglia malformations, and encephalocele.
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Conclusions

• Various supratentorial findings can be seen with developmental posterior fossa abnormalities

• A better appreciation of observed associations and their imaging characteristics can improve search patterns within the supratentorium when a developmental posterior fossa abnormality is identified
Conclusions

• While it may be premature to attempt understanding of supratentorial anomalies associated with posterior fossa developmental abnormalities given the poor overall comprehension of posterior fossa development, ultimately, understanding relations between supratentorial anomalies and developmental posterior fossa abnormalities may aid in attaining a robust fundamental genetic understanding of brain development.
Case 1

- **Posterior Fossa Findings:**
  - Hypoplastic cerebellum
  - Note that the pons appears normal

- **Supratentorial Findings:**
  - Microcephaly
  - High T2 SI within medial frontoparietal cortex & subcortical white matter
  - Note that the corpus callosum is present
Case 1

- Posterior fossa finding:
  - High T2 SI within cerebellar white matter
Case 1

- Mosaic trisomy 21
- MRI obtained for severe developmental delay
- Posterior fossa findings could be considered generalized hypoplasia without cyst formation
- We believe that the posterior fossa findings and microcephaly are typical for trisomy 21\textsuperscript{11}, although the pons is not hypoplastic
- Aside from microcephaly, we believe that the supratentorial signal abnormalities may reflect a prior insult
Case 2

- Posterior fossa findings:
  - Hypoplastic vermis
  - High fastigium
  - Thin pontomesencephalic junction

- Supratentorial finding:
  - Mild atrophy
  - Note that the corpus callosum is formed
Case 2

• Posterior fossa findings:
  – Classic molar tooth sign seen with Joubert syndrome reflecting parallel, enlarged, horizontally oriented superior cerebellar peduncles
  – Severe vermian hypoplasia
Case 2

- MRI obtained for behavior problems, developmental delay, decreased muscular tone
- Sibling also has Joubert syndrome
- Posterior fossa findings considered focal cerebellar dysplasia of the vermis
- Molar tooth appearance is not diagnostic for Joubert and may be seen with other syndromes, some of which are associated with polymicrogyria, ocular anomalies, and hypothalamic anomalies\(^1\)
Case 3

- **Posterior fossa finding:**
  - Cystic dysplasia of the right cerebellar hemisphere inferior aspect
  - Note that the pons and peduncles appear normal

- **Supratentorial findings:**
  - Absent corpus callosum
  - Colpocephaly
Case 3

• Posterior fossa finding:
  – Cystic dysplasia of the right cerebellar hemisphere inferior aspect

• Supratentorial findings:
  – Right frontal anterolateral aspect cortical dysplasia
  – Colpocephaly
Case 3

- **Posterior fossa finding:**
  - Cystic dysplasia of the right cerebellar hemisphere inferior aspect

- **Supratentorial findings:**
  - Right posterior frontal periventricular heterotopia
  - Colpocephaly
Case 3

- MRI obtained for infantile spasms/seizures
- Seizures resolved after right frontal resection
- Posterior fossa findings could be considered focal dysplasia, a poorly understood subject\(^1\)
Case 4

• Posterior fossa findings:
  – Cerebellar atrophy
  – Thin cerebellar peduncles
  – Note that the pons appears normal

• Supratentorial finding:
  – Low T2 SI within the globus palladi
Case 4

• Posterior fossa findings:
  – Cerebellar atrophy
  – Thin cerebellar peduncles
  – Note that the pons appears normal

• Supratentorial findings:
  – Atrophy
  – Periventricular white matter high T2 SI
Case 4

- MRI obtained for developmental delay and abnormal gait
- Mother also has developmental problems and is wheelchair bound
- Posterior fossa finding is considered atrophy with a normal sized pons
- Findings thought to represent cerebellar atrophy with ataxia, likely of a hereditary nature, although preliminary genetic tests have proven normal
Case 5

• Posterior fossa findings:
  – Inferior vermic hypoplasia
  – Enlarged 4th ventricle & foramen of Magendi
  – Note that the pons and cerebellar peduncles appear normal

• Supratentorial findings:
  – Microcephaly
  – Severe corpus callosal dysgenesis
  – Enlarged 3rd & prominent lateral ventricles
  – Simplified gyration
Case 5

• Child was born slightly premature
• Multiple congenital abnormalities are present
• Phenotypically, child resembles Cornelia de Lange syndrome, but genetic tests have proven normal
• Posterior fossa findings are felt to primarily represent focal hypoplasia of the vermis
Case 6

- **Posterior fossa finding:**
  - Left mid cerebellar polymicrogyria
  - Note that the pons and peduncles were normal in appearance (not shown)

- **Supratentorial findings:**
  - Right periventricular heterotopia
  - Bilateral frontoparietal polymicrogyria
Case 6

- MRI obtained for seizures, which started at age 2.5 years
- Child also demonstrated hypotonia, spastic paraparesis with right hemiparesis, cognitive difficulties, and sensorineural hearing loss
- Posterior fossa finding is felt to represent focal dysplasia, a poorly understood topic
Case 7

- **Posterior fossa finding:**
  - Rhomboencephalosynapsis, i.e. absent vermis with fused cerebellar hemispheres, dentate nuclei, and superior cerebellar peduncles

- **Supratentorial finding:**
  - Severe dysgenesis of the corpus callosum splenium & body
Case 7

- Child born slightly premature due to hydrocephalus
- Multiple congenital abnormalities and developmental delay noted
- Abnormal genetic test, with BNORMAL male microarray CGH result as follows: 
  arr cgh Xp22.31 (8040739→8223998)x2 [hg17; NCBI(B35)]
- Posterior fossa finding is considered focal dysplasia
- Various additional supratentorial findings have been noted, including fused thalami, absent septum pellucidum, olivary hypoplasia, limbic system anomalies, cortical malformations, and craniosynostosis
- Appreciation of supratentorial findings in the setting of rhomboencephalosynapsis is important given that they appear to dominate the clinical picture
- Fundamentally, this anomaly may represent a genetic malexpression affecting midline structures, as suggested by FGF8 gene activity in the cerebral midline (rostrodorsal septum) and the isthmic organizer (important in cerebellar induction)
Case 8

- **Posterior fossa finding:**
  - Right inferior cerebellar dysplasia
  - Note that the pons and peduncles were normal in appearance (not shown)

- **Supratentorial finding:**
  - Nodular subependymal heterotopia in the bilateral ventricular atrium region
Case 8

- Ocular motor apraxia noted
- Given findings in sibling, question of X-linked nature of anomalies was raised
- Posterior fossa finding is considered focal dysplasia, a poorly understood subject
Case 9

- Posterior fossa finding:
  - Inferior vermician hypoplasia
  - Dysplastic and hypoplastic cerebellar hemispheres
- Supratentorial finding:
  - Atrophy
Case 9

- Posterior fossa findings:
  - Inferior vermian hypoplasia
  - Enlarged 4th ventricle & foramen of Magendie
  - Note that the pons and peduncles are normal in appearance
Case 9

- Child demonstrated craniosynostosis with absent sphenoid wing and severe developmental delay, as well as a few other congenital anomalies
- Balanced 1:7 translocation (p22q31.2) found
- Posterior fossa finding is most likely classified as a generalized dysplasia
- The extent of the posterior fossa abnormalities compared with the relative lack of supratentorial findings is striking and unusual
Case 10

- **Posterior fossa finding:**
  - Dysplastic cerebellar hemispheres
  - Note the pons was normal in appearance

- **Supratentorial findings:**
  - Corpus callosal dysgenesis
  - Midline cyst in the quadrigeminal cistern
Case 10

- Posterior fossa finding:
  - Dysplastic cerebellar hemispheres

- Supratentorial findings:
  - Severe colpocephaly
  - Frontal polymicrogyria
Case 10

- Posterior fossa finding:
  - Dysplastic cerebellar hemispheres

- Supratentorial findings:
  - Colpocephaly
  - Mass-like subependymal heterotopia
  - Note that poor hippocampal folding was also seen (not shown)
Case 10

- Child had sensorineural hearing loss and mild motor developmental delay
- Case 11 is a sibling, with remarkably similar findings
- Possibility of Chudley-McCollough syndrome was raised
- Posterior fossa findings considered generalized dysplasia, in keeping with the severe supratentorial anomalies
Case 11

- Posterior fossa finding:
  - Dysplastic cerebellar hemispheres
- Supratentorial findings:
  - Corpus callosal dysgenesis
  - Midline cyst in the quadrigeminal cistern
Case 11

- Posterior fossa finding:
  - Dysplastic cerebellar hemispheres

- Supratentorial findings:
  - Colpocephaly
  - Mass-like subependymal heterotopia
  - Note that polymicrogyria and poorly folded hippocampi were also noted (not shown)
Case 11

- Child had sensorineural hearing loss
- Case 10 is sibling
- Possibility of Chudley-McCollough syndrome was raised
- Posterior fossa finding is considered generalized dysplasia, in keeping with the severe supratentorial anomalies
Case 12

- Posterior fossa findings:
  - Dysplastic vermis
  - Small right middle cerebellar peduncle

- Supratentorial findings:
  - Fused striatum
  - Large lateral ventricles
Case 12

- Posterior fossa finding:
  - Dysplastic vermis
Case 12

- Truncal hypotonia and developmental delay noted
- All genetic tests normal to date
- Posterior fossa finding likely represents focal dysplasia
Case 13

• Posterior fossa findings:
  – Cerebellar hypoplasia
  – Flat pons
  – High fastigium
  – Dysplastic superior vermis

• Supratentorial findings:
  – Dysgenetic corpus callosum
  – Hydrocephalus
  – Microcephaly
  – Bilateral medial occipital gliosis
Case 13

- **Posterior fossa findings:**
  - Cerebellar hypoplasia
  - Flat pons
  - High fastigium

- **Supratentorial findings:**
  - Fused striatum
  - Hydrocephalus
  - Note that partially absent septum pellucidum was also seen (not shown)
Case 13

- Child had severe developmental delay, cortical blindness, and seizure disorder
- Child clinically thought to demonstrate septooptic dysplasia
- Posterior fossa findings likely classified as generalized hypoplasia, (with presence of focal dysplasia), with a normal fourth ventricle and no posterior fossa cyst and a hypoplastic pons, although likely not of the classically known pontocerebellar hypoplasia types I or II
Case 14

• Posterior fossa findings:
  – Cerebellar atrophy
  – Small cerebellar peduncles
  – Note that the pons appears normal

• Supratentorial findings:
  – Severe corpus callosal thinning
  – Severe atrophy
  – Simplified gyration
  – High T2 SI within white matter representing de/dysmyelination
Case 14

- Global developmental delay and seizure disorder noted
- Two siblings demonstrated similar MR findings, one of whom died before 2 years of age
- Possibility of a muscle-eye-brain autosomal recessive disorder raised
- Posterior fossa finding is considered atrophy with a normal sized pons
Case 15

- Posterior fossa findings:
  - Inferior vermian hypoplasia
  - Kissing cerebellar tonsils
  - Note that the pons and cerebellar peduncles appear normal

- Supratentorial finding:
  - Left temporocipital subependymal heterotopia
Case 15

- Posterior fossa findings:
  - Inferior vermian hypoplasia
  - Kissing cerebellar tonsils
  - Note that the pons and cerebellar peduncles appear normal

- Supratentorial finding:
  - Left temporocipital subependymal heterotopia
Case 15

• Posterior fossa finding is considered to be focal vermian hypoplasia
Case 16

• Posterior fossa finding:
  – Rhomboencephalosynapsis, i.e. absent vermis with fused cerebellar hemispheres, dentate nuclei, and superior cerebellar peduncles
  – Note that there was normal appearing pons and cerebellar peduncles (not shown)

• Supratentorial finding:
  – Thinned corpus callosum & absent septum pellucidum
Case 16

- Child demonstrated ataxia and craniosynostosis
- Posterior fossa finding is considered to be focal dysplasia
- Various additional supratentorial findings have been noted, including fused thalami, olivary hypoplasia, limbic system anomalies, cortical malformations
- Appreciation of supratentorial findings in the setting of rhomboencephalosynapsis is important given that they appear to dominate the clinical picture
- Fundamentally, this anomaly may represent a genetic malexpression affecting midline structures, as suggested by FGF8 gene activity in the cerebral midline (rostromedial septum) and the isthmic organizer (important in cerebellar induction)
Case 17

- Posterior fossa finding:
  - Absent pons
- Supratentorial finding:
  - Simplified gyration
Case 17

- Child thought to demonstrate primary dysgenesis of the neural tube at the level of rhombomere-1 due to defective expression of homeobox gene EN2 for WNT1.
- Gene En2 appears to play a role in specifying cerebellar domains in embryos\(^5\).
- Wnt family of signaling molecules appears to be involved in cerebellar development, restricting cerebellar granule cell migration, thus acting to guide axons within the developing brain\(^3,4,9\).
- Additional congenital anomalies noted.
- Both posterior fossa and supratentorial findings fail to fall within the classification schemes we have used, but we wanted to share this amazing case.
Case 18

• Posterior fossa findings:
  – Severe cerebellar atrophy
  – Small superior cerebellar peduncles
  – Note that the pons appears normal

• Supratentorial findings:
  – Severe atrophy
  – Periventricular white matter high T2 SI representing de/dysmyelination
Case 18

- Constellation of severe postnatal growth failure, developmental delay, light sensitivity, hearing loss, calcification of the basal ganglia, and retinal degeneration all suggest Cockayne syndrome
- Posterior fossa finding is considered atrophy with a normal appearing pons
Case 19

• Posterior fossa findings:
  – Classic Dandy-Walker syndrome, with enlarged posterior fossa with 4th ventricle communicating with cystic space & absent vermis
  – Flat pons
  – High tentorium

• Supratentorial findings:
  – Hydrocephalus
  – Dysgenetic corpus callosum
  – Absent septum pellucidum
Case 19

- **Posterior fossa findings:**
  - Dandy-Walker syndrome, with enlarged posterior fossa with 4th ventricle communicating with cystic space & absent vermis

- **Supratentorial finding:**
  - Hydrocephalus
Case 19

- Dandy Walker malformation is an example of generalized hypoplasia with cyst formation in Barkovich’s classification
- Presence of supratentorial anomalies in Dandy Walker malformation is associated with poorer prognosis
- Hydrocephalus is present in 90% at time of diagnosis
- Callosal anomalies are present in 32-55%
- Polymicrogyria is present in 5-10%
- Occipital encephalocele is present in 16%
- Dandy Walker malformation likely results from a genetic predisposition, with an observed sibling recurrence rate of 6%
Case 20

- **Posterior fossa findings:**
  - Pontocerebellar hypoplasia

- **Supratentorial findings:**
  - Thinned corpus callosum
  - Absence of myelin
  - Hippocampal unfolding
  - Simplified gyration
Case 20

- **Posterior fossa findings:**
  - Pontocerebellar hypoplasia
- **Supratentorial findings:**
  - Small basal ganglia
  - Enlarged ventricles
  - Absence of myelin
  - Simplified gyration
  - Thinned corpus callosum
Case 20

• Posterior fossa findings:
  – Pontocerebellar hypoplasia

• Supratentorial findings:
  – Absence of myelin
  – Enlarged ventricles
  – Simplified gyration
  – Thinned corpus callosum
Case 20

- Sibling of Case 21, with remarkably similar imaging findings
- Posterior fossa findings considered generalized hypoplasia with a small pons
Case 21

- Posterior fossa findings:
  - Pontocerebellar hypoplasia

- Supratentorial findings:
  - Thinned corpus callosum
  - Absence of myelin
  - Simplified gyration
Case 21

- Posterior fossa findings:
  - Pontocerebellar hypoplasia
- Supratentorial findings:
  - Small basal ganglia
  - Ventriculomegaly
  - Absence of myelin
  - Simplified gyration
  - Thinned corpus callosum
Case 21

• Posterior fossa findings:
  – Pontocerebellar hypoplasia

• Supratentorial findings:
  – Absence of myelin
  – Simplified gyration
  – Thinned corpus callosum
Case 21

• Posterior fossa findings:
  – Pontocerebellar hypoplasia

• Supratentorial findings:
  – Hippocampal unfolding
  – Absence of myelin
  – Simplified gyration
  – Thinned corpus callosum
Case 21

• Sibling of Case 20, with remarkably similar imaging findings

• Posterior fossa findings considered generalized hypoplasia with a small pons
Case 22

- **Posterior fossa findings:**
  - Right greater than left cerebellar hemisphere hypoplasia
  - Dandy-Walker syndrome, with enlarged posterior fossa with 4th ventricle communicating with cystic space & severely hypoplastic vermis
  - Flat pons
  - High tentorium

- **Supratentorial finding:**
  - Occipital encephalocele
Case 22

- **Posterior fossa findings:**
  - Right greater than left cerebellar hemisphere hypoplasia
  - Dandy-Walker syndrome, with enlarged posterior fossa with 4th ventricle communicating with cystic space & severely hypoplastic vermis

- **Supratentorial findings:**
  - Occipital encephalocele
  - Simplified gyration
Case 22

- Dandy Walker malformation is an example of generalized hypoplasia with cyst formation in Barkovich’s classification
- Presence of supratentorial anomalies in Dandy Walker malformation is associated with poorer prognosis\(^1\)
- Occipital encephalocele is present in 16\(^\%\)\(^2\)
- Hydrocephalus is present in 90\(^\%\) at time of diagnosis\(^7\)
- Callosal anomalies are present in 32-55\(^\%\)\(^2,8\)
- Polymicrogyria is present in 5-10\(^\%\)
- Dandy Walker malformation likely results from a genetic predisposition, with an observed sibling recurrence rate of 6\(^\%\)\(^6\)