A Calcified Brain

Bilateral Basal Ganglia Calcification in a child with Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes (MELAS)

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Basal Ganglia

Deep Grey Structure between the lateral ventricle and insular cortex:

- Basal Ganglia
  - caudate
  - putamen
  - globus pallidus
- Thalamus

Core of the extrapyramidal system, integrating extrapyramidal motor activity.

http://www.radnet.ucla.edu/sections/DINR/index.htm
There is a normal aging process in T2-weighted MR images, due to iron deposition.
Metabolism of the Basal Ganglia

- Dynamic metabolism, especially in children
- Rich in mitochondria (ATP), vascular supply (O₂& Glucose), neurotransmitters and trace metal
- Vulnerable to metabolic abnormalities


Case report from PUMC Hospital

• A 13yo girl
• HPI: Presented to ER of a county hospital after 5 episodes of epilepsy-like symptom.
• PMH: early development is normal. **Failure to thrive** after 5 years of age.
• **Fatigability** after running.
• **Secondary sex development delay**.
• recurrent migraine headaches associated with episodic vomiting
• No childhood infection.
CT scan Head: basal ganglia calcification

Image from a county hospital in China
Common Causes of basal ganglia damage

Acute Causes:

- Hypoxia, CO poisoning, choke
- Hypoglycemia
- Vascular occlusion

--Unlikely considering the history

Chronic Causes?
Chronic causes of basal ganglia calcification

Table 2
Conditions Associated with Basal Ganglia Calcification

<table>
<thead>
<tr>
<th>Category</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocrine</td>
<td>Hypoparathyroidism, Pseudohypoparathyroidism, Pseudopseudohypoparathyroidism, Hyperparathyroidism, Hypothyroidism</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Leigh disease, Mitochondrial cytopathy, Fahr disease (familial cerebrovascular ferrocalcinosis)</td>
</tr>
<tr>
<td>Congenital or developmental</td>
<td>Familial idiopathic symmetric basal ganglia calcification, Hastings-James syndrome, Cockayne syndrome, Lipoid proteinosis (hyalinosis cutis), Neurofibromatosis, Tuberous sclerosis</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>Oculocraniosomatic disease, Methemoglobinopathy, Down syndrome, Toxoplasmosis, Congenital rubella, Cytomegalovirus, Measles, Chicken pox, Pertussis, Coxsackie B virus, Cysticercosis, Systemic lupus erythematosus, Acquired immunodeficiency syndrome</td>
</tr>
<tr>
<td>Toxic</td>
<td>Hypoxia, Cardiovascular event, Carbon monoxide intoxication, Lead intoxication, Radiation therapy, Methotrexate therapy, Nephrotic syndrome</td>
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</tbody>
</table>

Thorough Evaluation at PUMC Hospital
CT Scan Head

Patient transferred to Peking Union Medical College Hospital.

Basic biochemistry, Electrolyte level was normal.

No abnormality found in Parathyroid function

What is the possible relationship between basal ganglia calcification and developmental retardation?
A thorough history taking and tests revealed more information

- Mother was found to have neurosensory hearing loss at 28yo
- Mother had Ophthalmoplegia
- High lactate level in serum and CSF
- Pituitary hypoplasia
- GI discomfort (due to lactate acidemia)
- Myoclonus
Gene Diagnosis

- m.3243 A → G confirmed the diagnosis of MELAS
- The mitochondrial gene codes a functional protein in complex I of ETC
- Tissues with high energy requirements such as muscle and brain are particularly vulnerable
- The mitochondrial mutation confer maternal inheritance pattern of the mitochondrial encephalomyopathy
Maternal Inheritance Pattern of Mitochondrial disease
Interest Region

MR Spectrometry reveals focused on Basal Ganglia

This technique may detect elevated brain lactate elevations. The lactate signal is usually seen as a doublet at 1.3 ppm in H-MRS spectra changing its polarity, depending on the TE applied.
Pathophysiology of MELAS syndrome

Glucose is converted into Pyruvate in step 1 of oxidative phosphorylation (Glycolysis), which happened outside the mitochondria, upstream of the ETC.
Pathophysiology of MELAS syndrome

Abundant ATP is produced in the ETC, which requires normal function of complex I- complex V

Pathophysiology of MELAS syndrome

MELAS patients have a defect in complex I, so only glycolysis and citric-acid cycle produce very limited ATP, affecting development and body activity. Lactate accumulates as a by-product of anaerobic metabolism.
Mechanisms of Basal Ganglia Calcification

One hypothesis: may be due to iron accumulation from regenerated defective mitochondria?

Mineralization of the basal ganglia: implications for neuropsychiatry, pathology and neuroimaging

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MRI Scan Head
while the patient was stable...

T1 Flair

T2 FRFSE

Slight white matter lesions and T2-hyperintense lesions in the basal ganglia
The patient experienced 2 major Stroke-like episode 1 month after the diagnosis.

This is a characteristic of the disease, where symptom could present as hemianopia, hemiparesis.

The occipital regions are the most usually affected in such situation.

But a MR angiography (Time of Flight) will demonstrate normal bilateral posterior cerebellar arteries rulling out stroke.
MRI head (T2 Flair w/+ after the stroke like episodes)

Acute lesions appear as high intensity areas on the T2-weighted image
MRI head (T2 Flair w/+) after the stroke like episodes
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MRI head (T2 Flair w+/+) after the stroke like episodes
### Most common Imaging Findings in MELAS syndrome

<table>
<thead>
<tr>
<th>Finding</th>
<th>Frequency (%)</th>
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<tbody>
<tr>
<td>Reversible Infarct-like focal lesion</td>
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<tr>
<td>Parieto-occipital</td>
<td>58%</td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>28%</td>
</tr>
<tr>
<td>Temporal</td>
<td>10%</td>
</tr>
<tr>
<td>Generalized cerebral atrophy</td>
<td>38%</td>
</tr>
<tr>
<td>Focal cerebral atrophy</td>
<td>28%</td>
</tr>
<tr>
<td>Cerebellar atrophy</td>
<td>28%</td>
</tr>
<tr>
<td>White matter lesions (T2 high intensity)</td>
<td>24%</td>
</tr>
<tr>
<td>Ventricular dilation</td>
<td>10%</td>
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</tbody>
</table>

Reversible Infarct-like focal lesions in non-vascular territory, are part of the trade-marks of MELAS, not finding these lesions makes the diagnosis of MELAS less likely.

A comparative case report from literature

Sheng-Horng Chung, et. al., Symmetric basal ganglia calcification in a 9-year-old child with MELAS. Neurology. 2005
References

5. MG HARRINGTON, et. al., The significance of the incidental finding of basal ganglia calcification on computed tomography. Journal of Neurology, Neurosurgery, and Psychiatry1981 ;44:1168-1170
References

Acknowledgements

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