Krabbe disease in a 6-month old male presenting with neurodevelopmental regression and psychomotor delay: A case report

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Section: Neuroradiology
Area of Interest: Neuroradiology brain
Procedure: Contrast agent-intravenous
Imaging Technique: MR
Special Focus: Metabolic disorders Case Type: Clinical Cases
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Patient: 6 months, male

Clinical History:
A 6-month-old male patient was born full-term to a G1P1 mother via vaginal delivery, with unremarkable prenatal and birth history. Early development was unremarkable. At 4 to 6 months of age, blank stares, poor head control and signs of developmental regression such as loss of previously made sounds were noted.

Imaging Findings:
Contrast-enhanced MRI of the brain showed prominence of the subarachnoid spaces in both the supra- and infratentorial region, more along the anterior temporal lobes.
Evaluation of the grey matter and hippocampi regions were unremarkable. Evaluation of the white matter on T2-weighted images showed abnormal bright signals in the frontal and parietal corona radiata. Cystic foci are likewise noted in the posterior limb of both internal capsules. Similar findings are noted in the cerebral peduncles, brainstem, and in the white matter of both cerebellar hemispheres, with cystic foci in the medullary pyramids. These findings are distributed symmetrically, and exhibit no enhancement upon gadolinium administration. Analysis of the involved regions indicate an abnormality of the corticospinal tract. Analysis of deep grey matter nuclei showed hypointensity of the thalami on T2-weighted images. Diffusion-weighted imaging revealed no areas of differentation. Susceptibility-weighed imaging showed no evidence of haemorrhage nor abnormal calcifications. The cerebral vascular pattern is likewise unremarkable.

Discussion:
Krabbe disease (globoid cell leukodystrophy), is a rare autosomal recessive disorder with an incidence ranging from one in 100, 000 to one in 200, 000 live births worldwide. This is due to a deficiency in lysosomal enzyme, galactosylceramidase, which is responsible for the degradation of galactolipids found in myelin such as galactosylphingosine (psychosine). Enzyme deficiency would result in abnormal accumulation of galatosylcerebroside which is extremely toxic to oligodendroglia, and induces macrophages to become globoid cells. This would eventually result in demyelination and severe astrogliosis [3, 6].

Clinical manifestations of Krabbe disease are non-specific and progressive. Initial symptom includes interruption or
regression of psychomotor development. It is clinically classified based on age of onset and includes: early infantile form (1 to 12 months), late infantile form (1-3 years of age), and juvenile variety manifesting in older children. The early infantile form is the most common form. Other signs and symptoms that could be seen in cases include multiple spontaneous spasms, Babinski sign, lack of deep reflexes, vomiting, and head growth retardation [4]. Imaging is done to localise the involved anatomic region that could explain the aetiology of the neurologic symptoms. MRI is the imaging modality used for evaluating possible neurometabolic conditions due to its ability to detect small brain tissue abnormalities that is superior compared to other imaging modalities [1].

CT features known to characterise Krabbe disease are increased attenuation in cerebellum, brainstem, thalami, caudate nuclei and corona radiata on non-contrast images. This is due to the alterations in the ratio of lipids, water and proteins, secondary to the breakdown of myelin and the associated astrogliosis [3, 6]. On MRI, the areas of hyperdensities seen in CT scan will be seen as prominent T2 hyperintensity and T1 hypointensity within the white matter, with parietooccipital lobe or periventricular predominance. A definitive diagnosis is usually made through an enzymatic assay which would reveal a deficiency in the galactosylceramidase enzyme [5].

Currently, enzyme replacement therapy (ERT) or haematopoietic stem cell transplantation (HSCT) are the primary therapeutic approaches available for the treatment of Krabbe disease. Despite the available treatment, prognosis remains poor. Patients experience progressive neurologic deterioration, until coma and death ensues with an average of 24.1 months [2].

In paediatric patients with developmental regression and psychomotor delay, clinical clues and laboratory examinations are not enough to establish the diagnosis. Characteristic neuroimaging findings and patterns together with clinical and laboratory correlation aids in clinching the diagnosis.

**Differential Diagnosis List:** Krabbe disease (globoid cell leukodystrophy), Gangliosidoses (GM1 and GM2), Metachromatic leukodystrophy

**Final Diagnosis:** Krabbe disease (globoid cell leukodystrophy)

**References:**

**Figure 1**

a

**Description:** At the high frontal and parietal lobes showing cerebral volume loss as evidenced by the prominence of the subarachnoid spaces. **Origin:** Department of Radiology, Philippine General Hospital, Manila, Philippines

b

**Description:** At the level of the basal ganglia, across the temporal lobes, showing cerebral volume loss as evidenced by the prominence of the subarachnoid spaces. **Origin:** Department of Radiology, Philippine General Hospital, Manila, Philippines
Description: At the cerebellar hemispheres showing cerebral volume loss as evidenced by the prominence of the subarachnoid spaces. Origin: Department of Radiology, Philippine General Hospital, Manila, Philippines
**Figure 2**

Description: At the level of the hippocampi showing no abnormal signals or volume loss within the said structure. Evaluation of the entire limbic system was likewise unremarkable. **Origin:** Department of Radiology, Philippine General Hospital, Manila, Philippines.
Figure 3

Description: At the level of the corona radiata showing white matter hyperintensities. Origin: Department of Radiology, Philippine General Hospital, Manila, Philippines
Description: At the level of the basal ganglia showing white matter hyperintensities. Origin: Department of Radiology, Philippine General Hospital, Manila, Philippines
Description: At the level of the corona radiata showing no enhancement in the contrast-enhanced images. Origin: Department of Radiology, Philippine General Hospital, Manila, Philippines
Description: At the level of the basal ganglia showing no enhancement in the contrast-enhanced images. Note the well-defined cystic lesions in the posterior limb of both internal capsules. Origin: Department of Radiology, Philippine General Hospital, Manila, Philippines
Description: At the level of the basal ganglia showing relative hypointensity of the thalami. No lesions suggestive of gray-matter heterotopia is detected in the rest of the white matter. Origin: Department of Radiology, Philippine General Hospital, Manila, Philippines
Description: Abnormal bright signals in the cerebral peduncles. These regions, along with the involved portions of the supratentorial brain, point to involvement of the corticospinal tract. Origin: Department of Radiology, Philippine General Hospital, Manila, Philippines
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