Glut-1 deficiency with Leukoencephalopathy on MRI in a 2 months old

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Introduction:

Glut-1 deficiency can presents with epilepsy, movement disorder and developmental delay due to the inability to transport glucose through the blood brain barrier via the Glut-1 transporter due to the SLC2A1 gene mutation [1]. There are usually no MRI brain changes in Glut-1 deficiency [1] but here we present a case with leukoencephalopathy changes on the MRI.

Case Presentation: A 2 month old girl presented with afebrile focal seizures with left sided jerking of upper limbs and leg, eye deviation to the left and twitching of the lip which would last up to 15 minutes. She also had vacant episodes where she would zone out, stiffen and holds her breath for a few seconds and return to her usual self. Seizures were more frequent if intervals between feeds were longer. She also has paroxysmal eye-head movements and startle myoclonus.

Past medical history: Born at 37 weeks by normal vaginal delivery. IUGR and abnormal dopplers antenatally. Reflux secondary to suspected cow's milk protein intolerance.

Family history: 3rd child. Grandmother with epilepsy. Parents non-consanguineous.

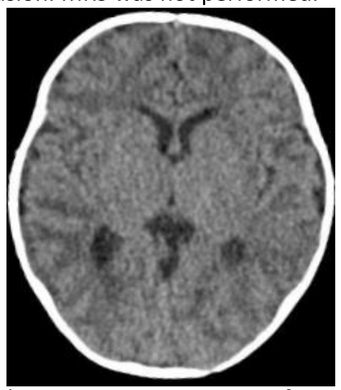
On examination: Microcephaly on 2nd centile. Reduced tone with head lag. She was also noted to have developmental delay with no social smile and not visually fixing and following. Incidental grade 2/6 systolic murmur.

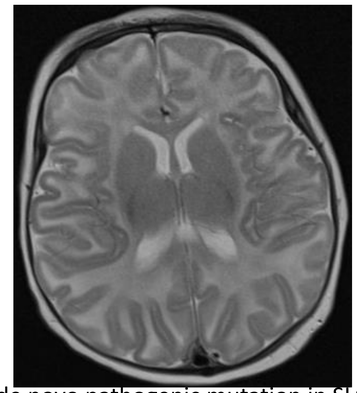
Investigations:

Interictal EEG showed sharp waves over posterior region especially right temporal regions.

Lumbar puncture performed showed WCC<1, RBC 312, protein 0.71g/L, CSF glucose 1.1mmol/L, blood glucose 6.1mmol/L, CSF to blood glucose ratio 0.19 indicating hypoglycorrhachia, viral PCR negative. Hypoglycorrhachia was not present when lumbar puncture was repeated 3 days later but 6 hour fasting was not undertaken before the procedure (CSF glucose: 3.9mmol/L, serum glucose 5.1, CSF to blood glucose ratio 0.76, WCC 8, RBC 636, protein 1.8g/L, viral PCR negative).

CT head showed bilateral frontal lobe hypodensity. MRI head was performed which showed no gross structural abnormalities but subtle changes indicating leukoencephalopathy with oedematous frontal lobes but no restricted diffusion. MRS was not performed.





Left: CT head showing frontal hypodensities

Right: MRI head T2 imaging leukoencephalopathy with oedematous frontal lobes.

Whole genome sequencing confirmed a de novo pathogenic mutation in SLC2A1 gene (pathogenic copy number loss with break points in 1p34.2 and 1p34.1) confirming a diagnosis of Glut-1 deficiency.

Management:

The patient was initially treated for possible infection with IV cefotaxime, amoxillicin and acyclovir until this was ruled out. For seizures, levetiracetam was started and later clobazam was added. Ketogenic diet (3:1) has been started since GLUT1 deficiency was genetically confirmed as a precision therapy and seizure freedom has been achieved on this with good ketosis and no side effects.

She remains under on-going ophthalmology follow up for her delayed visual maturation. There are no concerns with her hearing on auditory brainstem response testing.

Discussion:

MRI brain is usually performed to rule out other structural and neurometabolic causes of epilepsy and there are usually no changes detected in Glut-1 deficiency [1]. However, there is now increasing case reports (7 cases as far as we are aware) published of MRI T2 hyperintensity in patients with Glut-1 deficiency [2][3][4][5][6][7]. In the published literature, these resolve with time with ketogenic diet in 3 cases reports [5][6][7] although the timing of this varies from 6 month to 2.8 years. There is a described case that reduction rather than resolution of the leukoencephalopathy is observed from initial scan over a 27 month period [4]. There is also one report that these hyperintense white matter lesions can increase with time (over a 2 year period) despite being on a ketogenic diet for 6 months [3]. The mechanism of these MRI changes are not fully understood.

There are also reports about the MR spectroscopy findings alongside the leukoencephalopathy but the findings are variable from no changes detected [3] to a reduced NAA peak [4][5].

Conclusion:

This case highlights the rarer MRI changes that can be seen in Glut-1 deficiency with leukoencephalopathy and the importance of rapid genetic testing in securing a diagnosis, as this is linked with improved seizure control and neurodevelopmental outcomes with the use of ketogenic diet as precision therapy.

Consent: Parents consent for presentation.

Reference:

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