

Case Series

A rare characteristic neuroimaging pattern in hyperammonaemia.

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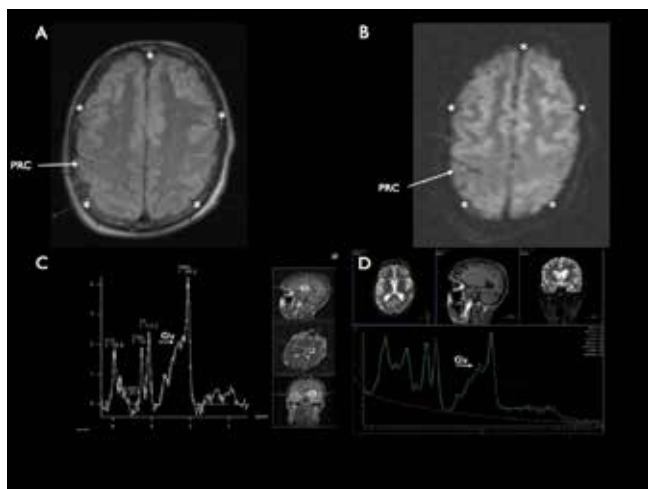
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INTRODUCTION

Hyperammonaemia is a potentially life-threatening condition that is often neglected diagnostically. It presents with non-specific symptoms, such as encephalopathy. Delayed recognition leads to potentially irreversible neurological damage. We report 3 patients who on magnetic resonance imaging (MRI) of brain demonstrated a rare pattern of cortical signal change, which spared the perirolandic cortex. This characteristic radiological pattern should prompt immediate testing for raised serum ammonia, facilitating early treatment for this disorder.

CASE SERIES

Case 1:



Case 1. (A) Axial FLAIR and (B) Diffusion sequences (B1000) are presented showing the diffuse cortical abnormality indicated with * adjacent to the abnormal cortex. The perirolandic cortex is spared from this signal abnormality (PRC with white arrow). (C) Short TE baseline and (D) Short TE 2 months post presentation indicate dynamic changes in glutamine/glutamate peaks across time on spectroscopy (peaks indicated with white arrow and GLU).

A 40 year-old malnourished man with history of roux-en-Y-gastrojejunostomy for pyloric stenosis secondary to analgesia overuse, presented with septic shock and hepatic

derangement. He developed refractory status epilepticus on day 2 of his hospital admission and received a loading dose of sodium valproate. Subsequently an ammonia level of 619 $\mu\text{mol/L}$ was reported (normal in all 3 cases presented $<52 \mu\text{mol/L}$). Emergency dialysis normalized the ammonia level by the next day but he remained encephalopathic. An MRI brain was performed 5 days after presentation showing a diffuse increase in T2 and FLAIR signal within the cortex of both cerebral hemispheres (Figure A). There was sparing of the perirolandic cortex and occipital cortex bilaterally. This cortical high signal with sparing of the perirolandic cortex was also well visualised on B1000 images of diffusion weighted imaging (Figure B) with no associated low signal on the ADC (apparent diffusion coefficient) map. The initial short TE (35ms) magnetic resonance spectroscopy (Figure C) at presentation revealed a slightly elevated glutamine/glutamate peak with a slight decrease in choline and myoinositol peaks. These findings have been described in hepatic encephalopathy with elevated ammonia¹.

At the time of the MRI, the cause of the ongoing encephalopathy was thought to have been due to sepsis but the diagnosis of hyperammonemic encephalopathy was suggested after MRI was performed even though his ammonia level was at that stage normal. The possibility of the cortical signal change relating to status epilepticus or hypoxia was also considered but both were felt to be less likely particularly given the pattern of signal change and the previously very markedly elevated ammonia level.

Repeat short TE MR spectroscopy was performed two months later (Figure D). Whilst it is difficult to directly compare these spectra due to the differences in the y-axis, using creatine peak as a reference, there is a reduced level of N-acetylaspartate (NAA). NAA is a marker of normal neuronal activity and the reduction of NAA is consistent with significant brain atrophy which was noted on other MR sequences obtained at that

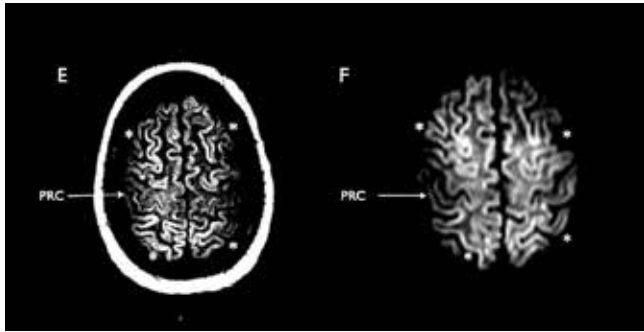
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time and which can be seen on the planning images for MR spectroscopy (Figure D). Although more equivocal, there was also a slight decrease in the glutamine/glutamate peak, which may reflect resolution of the hyperammonaemia.

A metabolic work up did not reveal any underlying urea cycle abnormality. His hyperammonaemia was attributed to a combination of malnutrition, acute sepsis, and poor hepatic reserve. Neurological recovery was poor at 6 months and he was quadriparetic and minimally responsive.



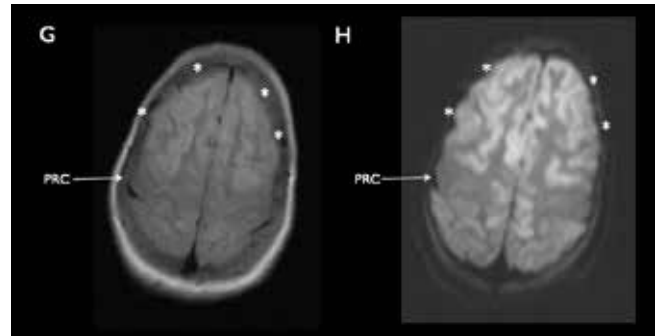
Case 2. (E) Axial FLAIR and (F) Diffusion sequence (B1000) imaging indicates the cortical abnormality with * and the spared perirolandic area of the cortex is indicated with PRC and a white arrow.

Case 2:

A 56 year-old man with a history of cirrhosis secondary to autoimmune hepatitis, presented with subacute lethargy, encephalopathy, and cortical blindness. Serum ammonia peaked at 133 $\mu\text{mol/L}$ and remained elevated for 6 days prior to normalizing. It remained normal for three days before becoming elevated (ranging between 69-86 $\mu\text{mol/L}$) for 1 further week. MRI of brain was performed two days after the last recorded elevated ammonia (81 $\mu\text{mol/L}$). This demonstrated subtle cortical high signal change on the axial T2 and FLAIR imaging within the posterior frontal and parietal lobes bilaterally (Figure E). This pattern was best appreciated on B1000 images of diffusion weighted imaging, with striking sparing of the perirolandic cortex (Figure F). There was no associated low signal on the ADC map. The basal ganglia were not involved. Magnetic resonance angiography was normal. Early treatment of the hepatic encephalopathy resulted in a full visual recovery.

Case 3:

A 27 year-old woman with alcoholic liver disease and oesophageal varices presented with a major upper gastrointestinal bleed. She developed encephalopathy and required mechanical ventilation. Serum ammonia was elevated at 167 $\mu\text{mol/L}$. At this time MRI brain was undertaken, demonstrating abnormal cortical T2 and FLAIR high signal change (Figure G). The cortical FLAIR high signal change spared both the parietal and perirolandic cortex and was visible on B1000 images of diffusion weighted imaging (Figure H) without corresponding low signal on the ADC map. Medical complications supervened and she died.



Case 3. (G) Axial FLAIR and (H) Diffusion sequence (B1000) imaging indicates the cortical abnormality with * and the spared perirolandic area of the cortex is indicated with PRC and a white arrow.

DISCUSSION

The neuroimaging presented from these 3 patients with hyperammonaemia demonstrated cortical high signal on the diffusion weighted and FLAIR images without evidence of diffusion restriction. There was striking sparing of the perirolandic cortex in all 3 cases.

Eight other cases were identified in the literature describing this radiological pattern in patients with raised serum ammonia levels²⁻³. These imaging findings of diffuse cortical T2, and FLAIR hyperintensities with sparing of the perirolandic cortex - occurred in all but 1 of the reported cases. There was also involvement of subcortical sites, including the periventricular white matter, the thalami, and striatum. It is currently unknown why a diffuse cortical insult such as hyperammonaemia should cause selective sparing of the perirolandic cortex.

It is possible that differences in the cortical cytoarchitecture and receptor characteristics lead to a differential sensitivity to the toxic insult of elevated ammonia. It has been suggested that lower T2 prolongation in the perirolandic cortex may relate to reduced extracellular space water content. Another possibility is the protective effect from perineuronal nets (containing proteoglycans), which surround the neurons of the perirolandic and visual cortices in abundance⁴.

The radiological differential diagnosis of cortical high T2 and FLAIR signals includes status epilepticus, hypoxic ischaemic injury, encephalitis and Creutzfeldt Jakob disease. Clinically, it can be difficult sometimes to differentiate between these conditions in the encephalopathic patient in an intensive care unit, who may have a combination of such clinical features. These radiological findings may however be of value in suggesting hyperammonaemia as a possible cause (as illustrated in our first patient). Further corroboration in larger series is however required.

CONCLUSION

Awareness of this characteristic neuroimaging pattern among physicians and radiologists will help identify hyperammonaemic encephalopathy, which, if not treated quickly, carries a high morbidity and mortality.

ABBREVIATIONS:

TE - echo time. FLAIR - Fluid attenuated inversion recovery.

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