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Atypical imaging findings in the setting of methylmalonic acidemia in an infant

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Classically, methylmalonic acidemia (MMA) is characterized on imaging by abnormalities in the basal ganglia, specifically the globus pallidi, as well as occasional signs of delayed maturation. We report a case of MMA in which abnormal signal and diffusion restriction occurred in the subcortical white matter, sparing the classically involved globus pallidi, a situation that has not been previously reported in the literature. This report demonstrates that diffusion abnormality can be seen in the white matter in MMA, in the absence of basal ganglia involvement, and that MMA may be considered when the diagnosis of metabolic acidemias is raised.

Introduction

Methylmalonic acidemia (MMA) is a rare autosomal recessive disease that is caused by mutations in several different genes. Briefly, isoleucine, valine, methionine, and threonine are normally converted to propionic acid, methylmalonic acid, and succinic acid, the last step of which requires methylmalonyl CoA mutase and a coenzyme, adenosyl cobalamine. A deficiency in either the enzyme or coenzyme, in an autosomal recessive manner, results in the accumulation of methylmalonic acid. This buildup further results in the inhibition of succinate dehydrogenase, the enzyme that facilitates mitochondrial aerobic glucose oxidation. The globus pallidus is particularly sensitive to mitochondrial dysfunction. Classically, MMA presents with T2 high intensity and diffusion restriction (1-4) in bilateral basal ganglia, correlating with symptoms presenting in early childhood. Previous reports describe signs of delayed brain maturation such as delays in myelination, an immature gyral pattern, and incomplete perisylvian opercularization, as well as changes in the brainstem and cerebellum (5).

Case report

A 6-day-old female infant presented to the emergency room with a history of lethargy, poor feeding, and abnormal respiration. Workup revealed elevated ammonia levels and glucose less than 30. CBC revealed a WBC count of 1100, with absolute neutrophil count of 100 and platelets of 127. Blood, urine, and CSF cultures were negative. Continuous venovenous hemodiafiltration was started, as well as ampicillin and cefotaxime, and a noncontrast CT scan of the brain was performed, followed by contrast-enhanced MRI. Shortly after the patient was admitted to the pediatric ICU, the laboratory results revealed that the newborn screen was positive for C3 acylcarnitine, suggestive of an organic acidemia. See Figures 1-7.

Discussion

In prior case reports on MMA, the basal ganglia have been described as primary regions of abnormality, either presenting with T2 high intensity or diffusion restrictions (6-8). While some cases have reported scattered white-matter abnormalities, this pattern of diffuse symmetric subcortical diffusion restriction with peri-Rolandic sparing has not been previously described, and is thought to represent a form of global energy failure. Diffusion abnormality

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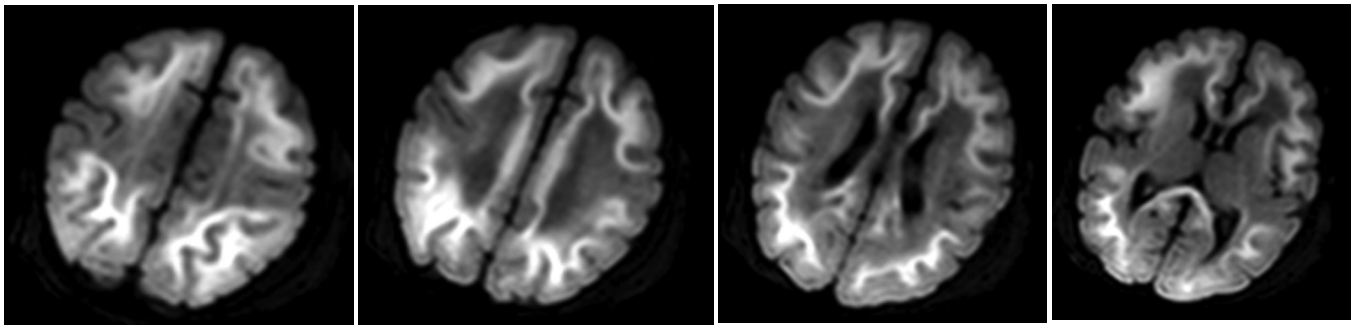
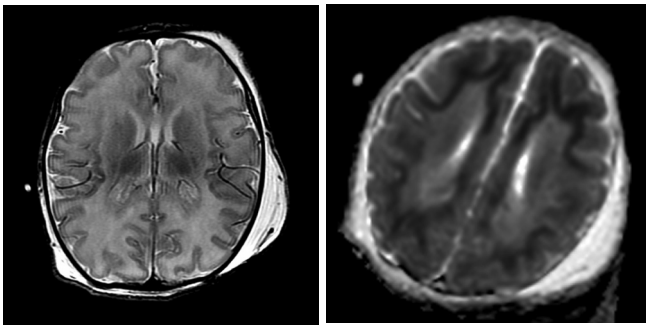


Figures 1-4. 6-day-old infant with methylmalonic acidemia. Sequential mean diffusion images derived from diffusion tensor imaging showed symmetric diffusion restriction in the subcortical white matter of bilateral cerebral hemispheres, with sparing of the peri-Rolandic regions. Note that there was no abnormal signal along the basal ganglia, and specifically along the globus pallidi.



Figures 5-6. 6-day-old infant with methylmalonic acidemia. On figure 5, the T2-weighted image demonstrated lack of intensity abnormality in bilateral basal ganglia, including the globus pallidi. On figure 6, an apparent diffusion coefficient map again illustrated markedly reduced diffusion.

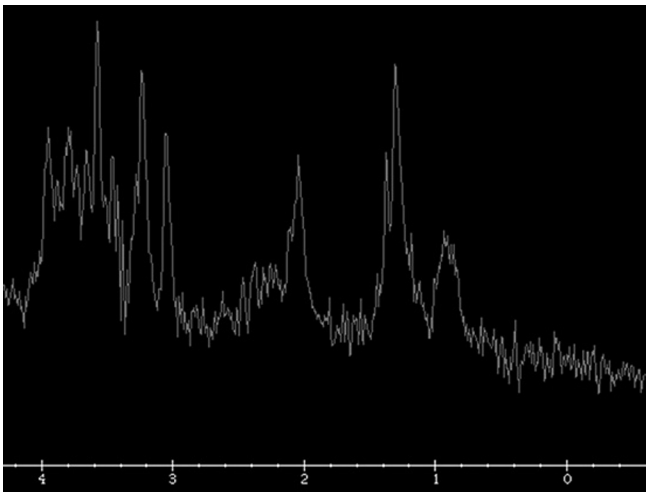


Figure 7. 6-day-old infant with methylmalonic acidemia. Spectroscopy demonstrated an elevated lipid/lactate peak (1.3 ppm), a finding commonly seen in the setting of methylmalonic acidemia.

of the white matter has been described in mitochondrial disease, leukodystrophies, and other metabolic disorders, but never in a case of MMA (9). It has been proposed that in acidemias, the mechanism of diffusion restriction is secondary to excitotoxicity due to the buildup of excitotoxic metabolites such as glutaric acid in glutaric aciduria (10) or global energy failure leading to the failure of the sodium-potassium pump in conditions such as maple syrup urine disease (11). This case highlights the importance of considering MMA when symmetric diffusion restriction of the white matter in a neonatal brain is observed, and the diagnosis of inborn errors of metabolism is raised.

References

1. Bindu, P., Kovoor, J., and Christopher, R. Teaching NeuroImages: MRI in methylmalonic academia. *Neurology* 2010; 74:14. [PubMed]
2. Hendriksz, C., Pediatric Inborn errors of metabolism for the diagnostic radiologist. *Pediatr Radiol* 2009; 39:211–220. [PubMed]
3. Prust, M., Gropman, A., and Hauser, N. New frontiers in neuroimaging applications to inborn errors of metabolism. *Molecular Genetics and Metabolism*; 2011. [PubMed]
4. Michel S., Given C., and Robertson W., Imaging of the brain, including diffusion weighted imaging in methylmalonic acidemia. *Pediatr Radiol.* 2004; 34:580-582. [PubMed]
5. Harting, I., Seitz, A., Geb, S., et al. Looking beyond the basal ganglia: The spectrum of MRI changes in methylmalonic acidaemia *J Inherit Metab Dis* 2008; 31:368–378. [PubMed]
6. Takeuchi M., Harada M., Matsuzaki K., et al. Magnetic resonance imaging and spectroscopy in a patient with treated methylmalonic acidemia. *J Comput Assist Tomogr.* 2003; 27:547-551. [PubMed]
7. Yesildag A., Ayata A., Baykal B., et al. Magnetic resonance imaging and diffusion weighted imaging in methylmalonic acidemia. *Acta Radiol.* 2005;46:101-103. [PubMed]

8. Gao Y., Guan W., Wang J., et al. Fractional anisotropy for assessment of white matter tracts injury in methylmalonic acidemia. *Chin Med J* (Engl) 2009; 122:945-949. [PubMed]
9. Strauss, K., and Morton, D. Type I glutaric aciduria, part 2: A model of acute striatal necrosis. *American Journal of Medical Genetics Part C: Seminars in Medical Genetics* 2003;121C:53–70. [PubMed]
10. Jan, W., Zimmerman, R., Wang, Z, et al. MR diffusion imaging and MR spectroscopy of maple syrup urine disease during acute metabolic decompensation *Neuroradiology* 2003; 45(6):393-399. [PubMed]
11. Zimmerman, R. Neuroimaging of inherited metabolic disorders producing seizures. *Brain and Development*, 2011; 33(9): 734-44. [PubMed]