Case 15037

Eurorad

Methylmalonic acidaemia (MMA) in a child

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ISSN: 1563-4086
Section: Neuroradiology
Area of Interest: Neuroradiology brain
Procedure: Diagnostic procedure
Procedure: Education
Imaging Technique: MR
Imaging Technique: MR-Diffusion/Perfusion
Imaging Technique: RIS
Special Focus: Metabolic disorders Case Type: Clinical Cases
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Patient: 6 years, male

Clinical History:

A six-year-old male child presented to the emergency room complaining about weakness, lethargy, abnormal respiration and episodes of vomiting together with dizziness one month before.
The parents admitted to developmental delay, eating disorders, seizures, iron-deficiency-anaemia under treatment, and surgical excision of adenoids 2 months ago. Workup revealed elevated ammonia and methylmalonyc acid levels and low vitamin-B12 levels in the blood.
Imaging Findings:

He was initially given magnetic resonance imaging (MRI) which revealed bilateral symmetric T2 hyperintensities in the lentiform nuclei (globus pallidi) and the cerebral peduncles. Isotropic diffusion imaging (DWI) showed no restriction of the lesions while the apparent diffusion coefficient [ADC] map showed hyperintensity, a sign of chronic lesions. Post-gadolinium images revealed mild peripheral enhancement of the basal ganglia lesions. The ventricular system was represented normal, with no dilation.
The abdomen ultrasound and chest X-ray showed no pathology.
Discussion:

Methylmalonic acidemia (MMA), also known as methylmalonic aciduria is an autosomal recessive metabolic disorder in which the body is unable to process certain proteins and fats properly. This condition was first characterised by Oberholzer et al and occurs in one in 48,000 live births [1].

It is caused by complete or partial deficiency of the enzyme methylmalonyl-CoA mutase (mut0 enzymatic subtype or mut– enzymatic subtype, respectively), a defect in the transport or synthesis of its cofactor, adenosyl-cobalamin (cblA, cblB, or cblD-MMA), or deficiency of the enzyme methylmalonyl-CoA epimerase [2]. These enzymes are essential for the body to convert the amino acids isoleucine, valine, methionine and threonine and also the cholesterol to propionic acid, methylmalonic acid and succinic acid.

It is estimated that as many as 60% of cases are the result of a mutated MUT gene encoding the protein

methylmalonyl-CoA mutase, which converts methylmalonic-CoA into succinyl-CoA. As a result of lack of this enzyme, methylmalonyl-CoA and other potentially toxic compounds accumulate in the body's organs, blood and tissues, causing the signs and symptoms of MMA [3]. Mutations in the MMAA, MMAB, and MMADHC genes can also hinder the proper function of methylmalonyl-CoA (each of these encodes a protein required for its proper function). Mut0 subtype, where there is complete lack of the enzyme, is the most severe form of MMA and has the poorest outcome. Whereas, mut- subtype, where mutations change the structure of the enzyme without eliminating its activity, is typically less severe and with variable symptoms than the mut0 form [3].

Onset of the manifestations of MMA ranges from the neonatal period (when proteins are added to the infant's diet) to adulthood and vary from mild to life-threatening [2,3,4]. It can present symptoms such as vomiting, lethargy, dehydration, hypothermia, hypotonia, respiratory distress, kidney failure, pancreatitis, seizures, stroke, progressive encephalopathy, severe ketoacidosis, hyperammonaemia, neurtropaenia, thrombocytopenia, and developmental delays [2,3].

Diagnosis is based on the high concentration of methylmalonic acid in urine and blood and can also be indicated through the use of CT and MR imaging of the brain. The most common findings of MMA on imaging is ventricular dilation, cortical atrophy, subcortical white matter abnormality, delay in myelination and abnormalities (T2 high intensity and diffusion restriction) in the basal ganglia, especially in the globi pallidi [5,6].The finding of biallelic pathogenic variants in one of the five genes associated with MMA can establish diagnosis [2].
Management consists of a protein-restricted diet, carnitine and parenteral vitamin B12 [2, 7].
Differential Diagnosis List: Methylmalonic acidaemia (MMA), Propionic acidaemia, Pyruvate dehydrogenase deficiency, Kernicterus, Carbon monoxide poisoning

Final Diagnosis: Methylmalonic acidaemia (MMA)

References:

Oberholzer VG, Levin B, Burgess EA, Young WF (1967) Methylmalonic aciduria. An inborn error of metabolism leading to chronic metabolic acidosis. Archives of Disease in Childhood 42: 492-504 (PMID:6061291)
Manoli I, Sloan JL, Venditti CP (2016) Isolated Methylmalonic Acidemia. Gene Reviews (PMID:20301409)
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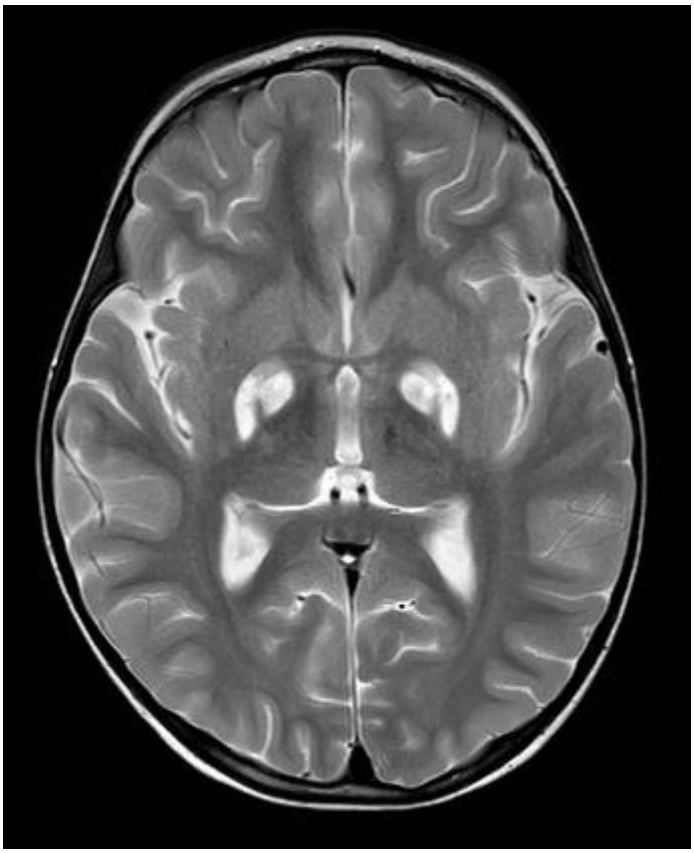
Radmanesh A, Zaman T, Ghanaati H, Molaei S, Robertson RL, Zamani AA (2008) Methylmalonic acidemia: brain imaging findings in 52 children and a review of the literature. Pediatr Radiol 38(10): 1054-61 (PMID:18636250)
Warren Chang, Neilesh Gupta, Dawn Duane, Patrick Barnes, Kristen Yeom (2012) Atypical imaging findings in the setting of methylmalonic acidemia in an infant. Radiology Case Reports Volume 7, Issue 4, Article 749 (PMID: 27330598)
Parayl Sankaran Bindu, Jerry M.E. Kovoor, Rita Christopher (2010) Teaching NeuroImages: MRI in methylmalonic acidemia.

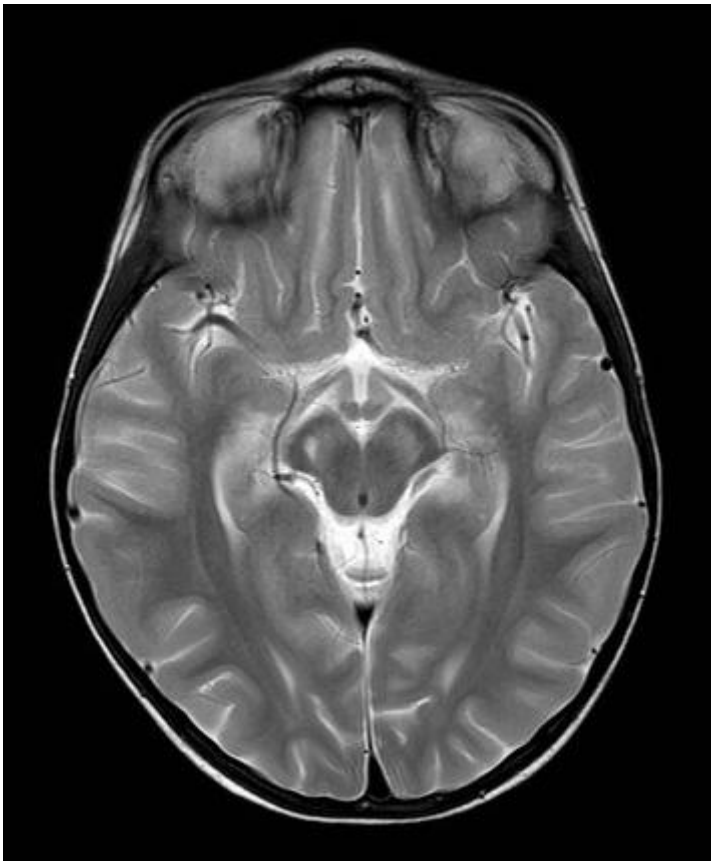
Figure 1

a



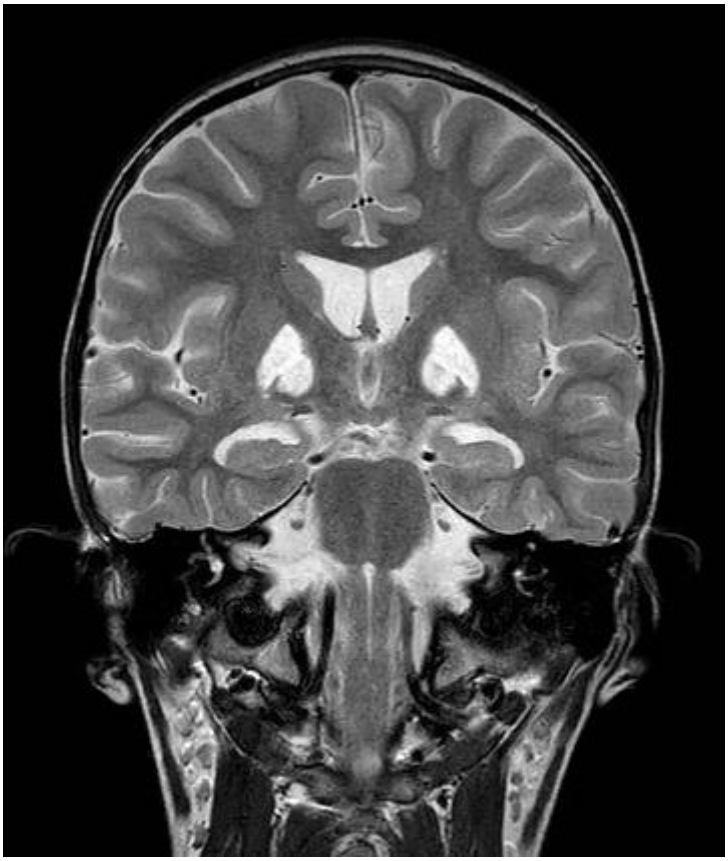
Description: Axial T2-weighted image showing hyperintensity in bilateral lentiform nuclei. **Origin:** Papageorgiou Hospital, Department of Radiology, Thessaloniki, Greece

b



Description: Axial T2-weighted image showing hyperintensity in bilateral cerebral penducles. **Origin:** Papageorgiou Hospital, Department of Radiology, Thessaloniki, Greece

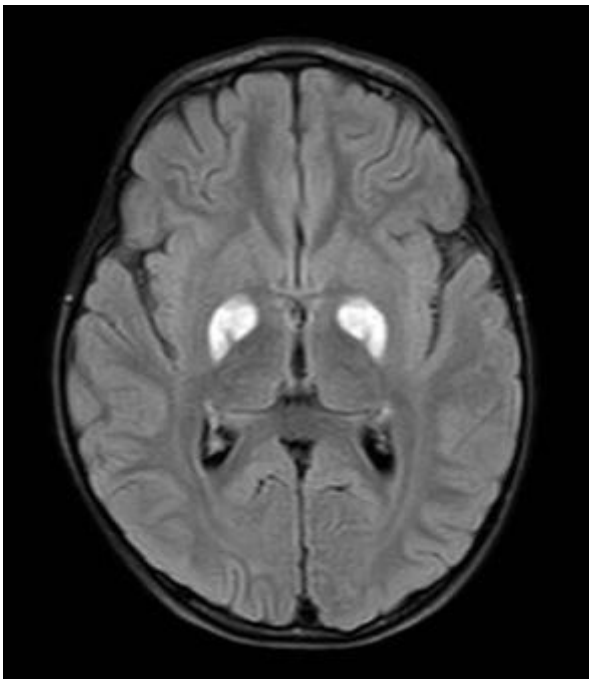
c



Description: Coronal T2-weighted image showing hyperintensity in the basal ganglia. **Origin:** Papageorgiou Hospital, Department of Radiology, Thessaloniki, Greece

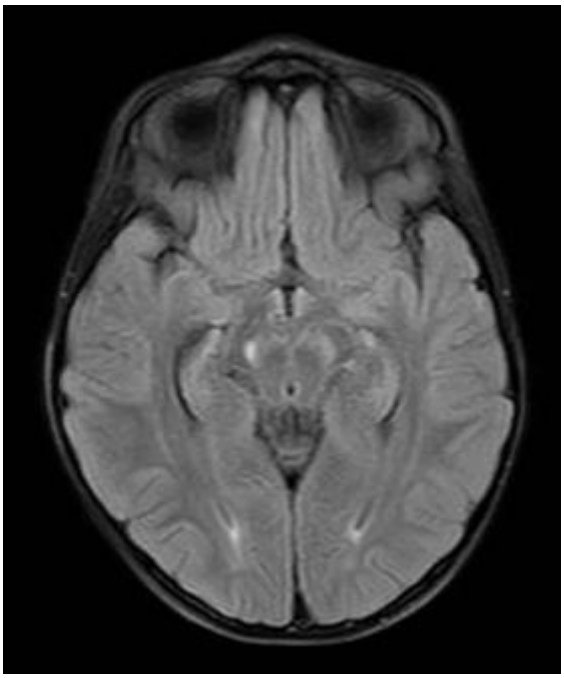
Figure 2

a



Description: Axial FLAIR image depicting hyperintensity in the basal ganglia. **Origin:** Papageorgiou Hospital, Department of Radiology, Thessaloniki, Greece

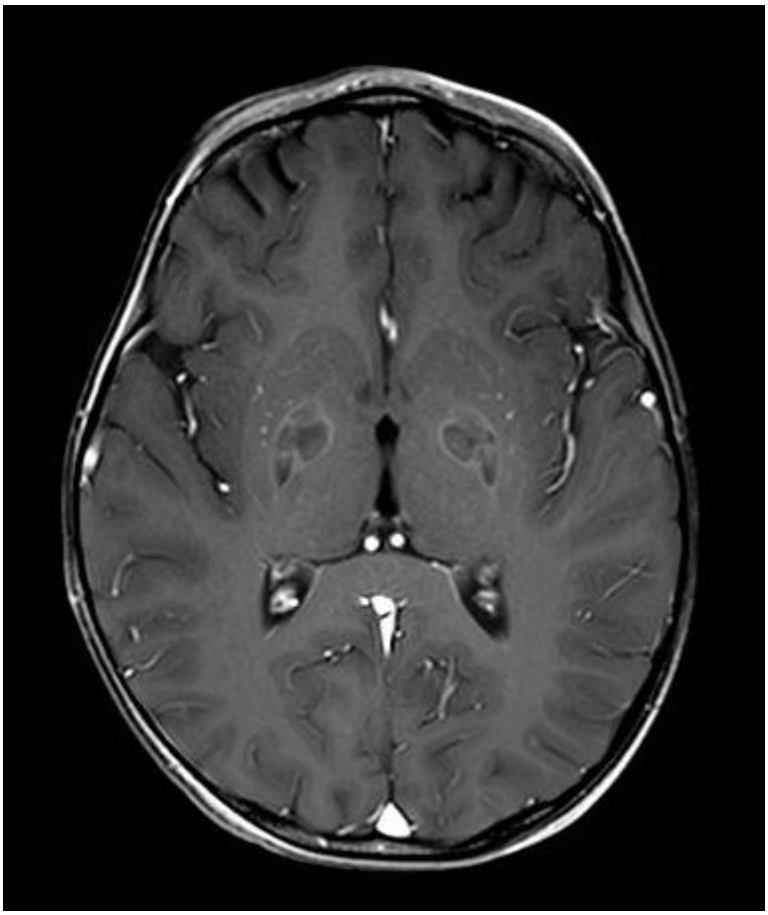
b



Description: Axial FLAIR image showing hyperintensity in the brainstem. **Origin:** Papageorgiou Hospital, Department of Radiology, Thessaloniki, Greece

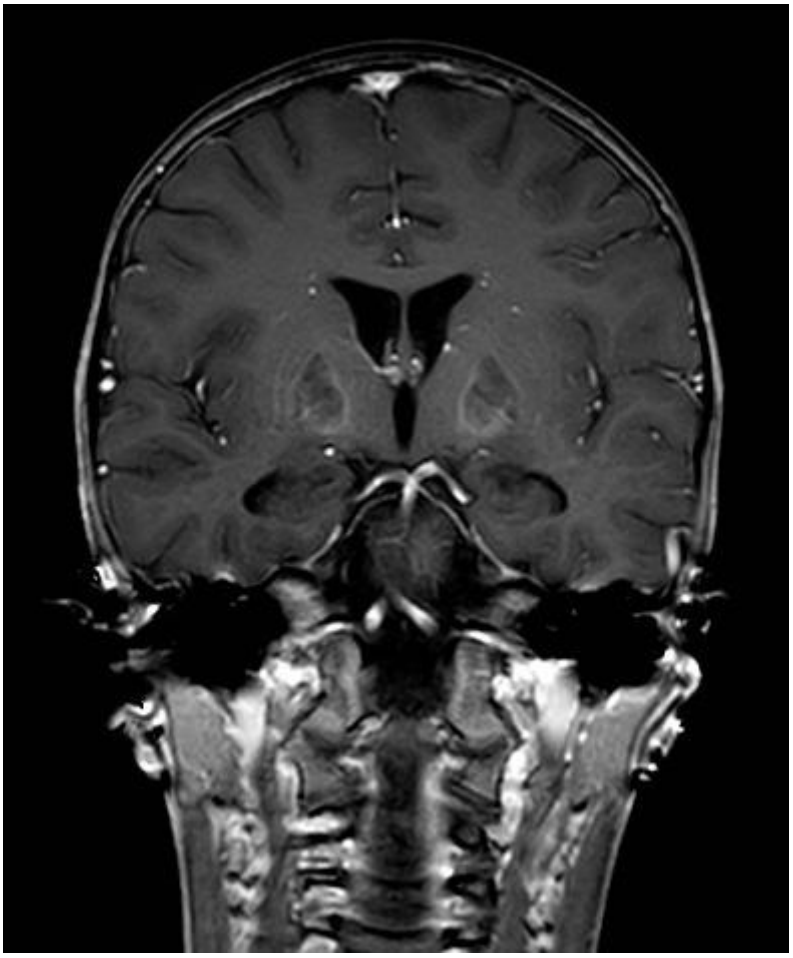
Figure 3

a



Description: Axial gadolinium-enhanced T1-weighted image showing mild peripheral enhancement of the lentiform nuclei. **Origin:** Papageorgiou Hospital, Department of Radiology, Thessaloniki, Greece

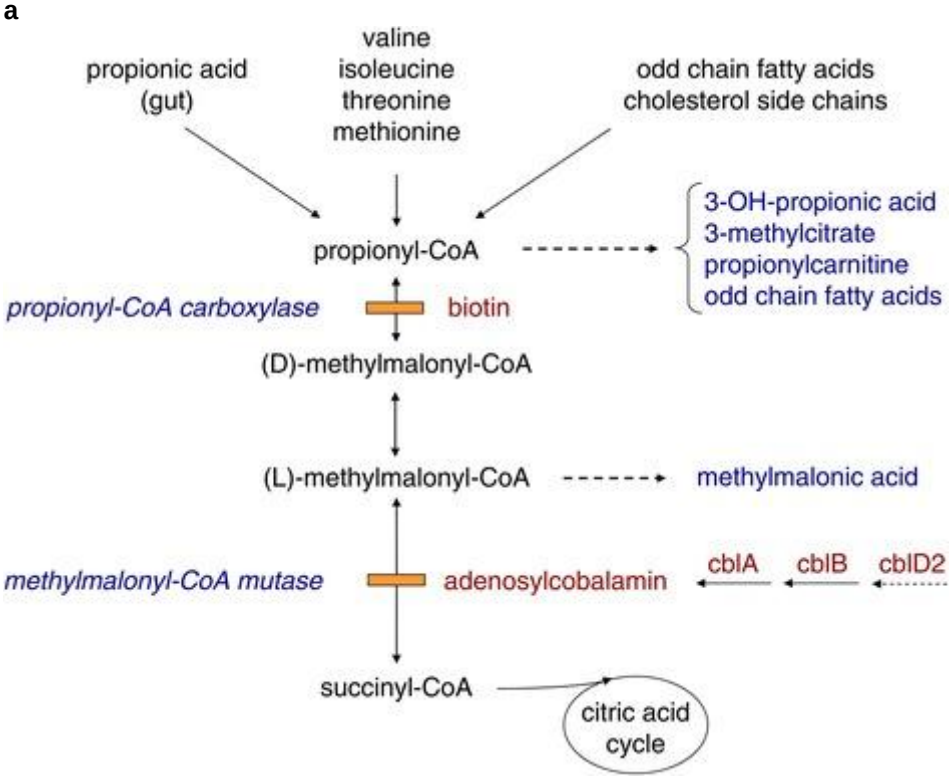
b



Description: Coronal gadolinium-enhanced T1-weighted image showing peripheral enhancement of the lentiform nuclei. **Origin:** Papageorgiou Hospital, Department of Radiology, Thessaloniki, Greece

Figure 4

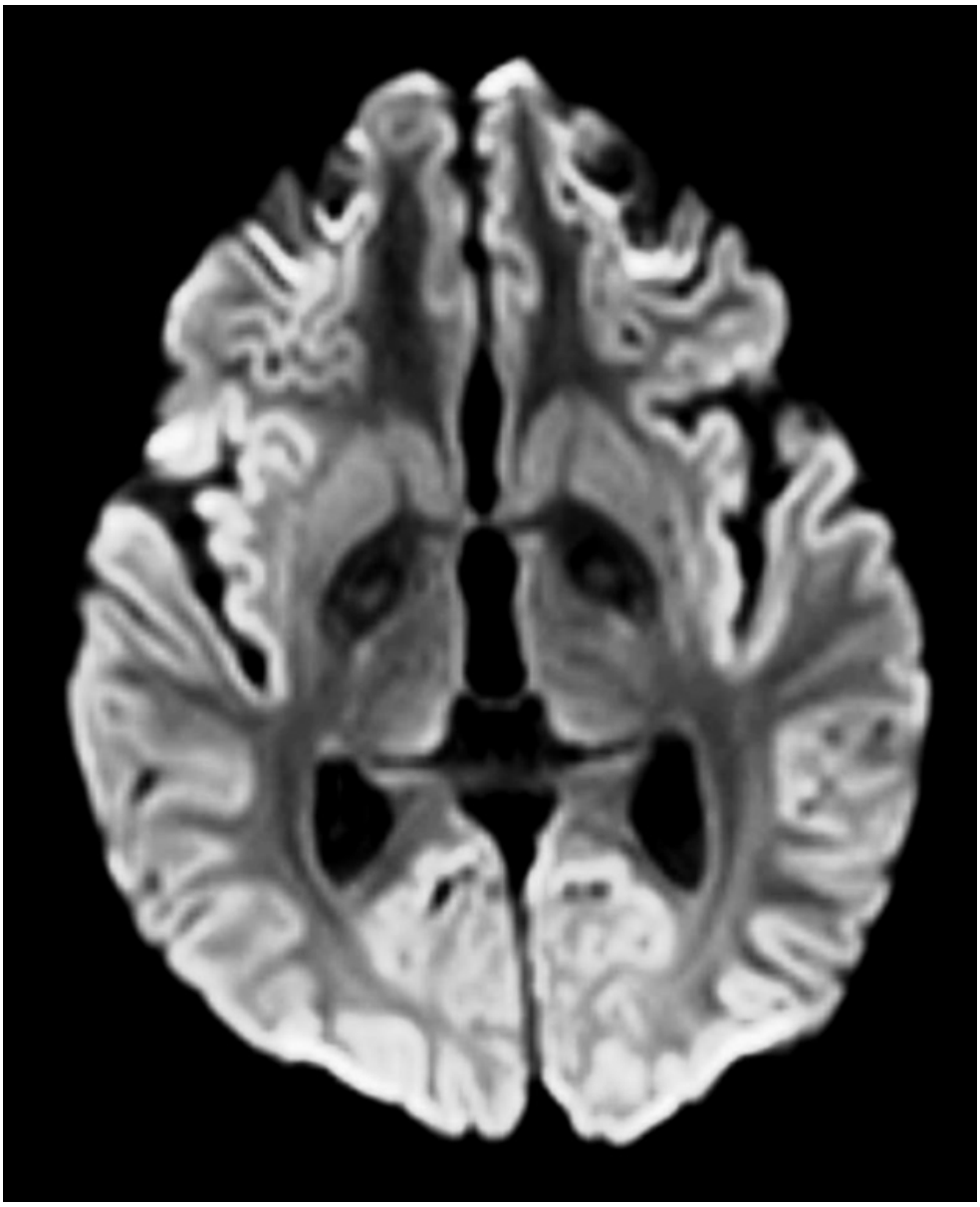
a



Description: An image explaining pathophysiology of MMA. **Origin:** Papageorgiou Hospital, Department of Radiology, Thessaloniki, Greece

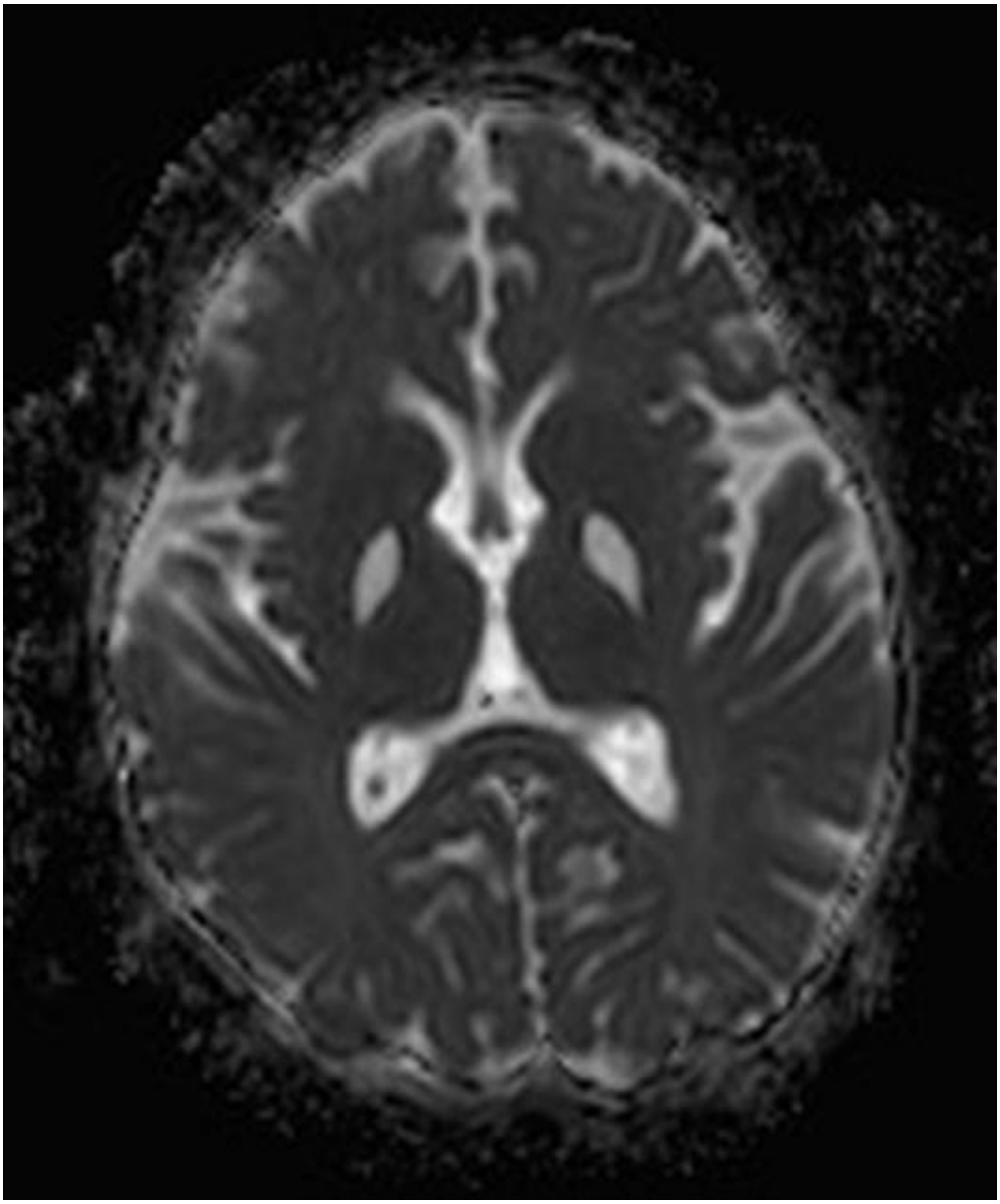
Figure 5

a



Description: Isotropic Diffusion (b value=1000) showing no restriction of diffusion since the lesions are not acute. **Origin:** Papageorgiou General Hospital, Department of Radiology. Thessaloniki, Greece.

b



Description: ADC map showing hyperintense lesions in globus pallidi, sign of chronicity. **Origin:** Papageorgiou General Hospital, Department of Radiology. Thessaloniki, Greece.