Ketamine: An effective and safe treatment for patients with MELAS and refractory status epilepticus

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Abstract

We present a case of a 10 year-old boy with history of mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) who presented with refractory status epilepticus (RSE). SE was resistant to multiple antiseizure medications and responded favorably to ketamine.

This case demonstrates the importance of continuous video EEG in patients with MELAS, for early recognition of electrographic seizures or status epilepticus as well as administration of ketamine as an effective and safe treatment option in this patient population.

Background

Epilepsy is very common in MELAS(71-96%). Although the mechanism of the epilepsy associated with MELAS is not fully understood, current widely accepted mechanisms include oxidative stress damage, ion mechanisms, energy mechanisms and neurotransmitter mechanisms. Both focal and generalized seizures can be seen in the context of metabolic stroke. Seizures may evolve into non-convulsive or convulsive status epilepticus, which seriously affects prognosis. Most episodes with status epilepticus are refractory to treatment, thus it persists despite administration of anti seizure medications.

Effective seizure management is crucial in patients with MELAS to reduce metabolic distress.

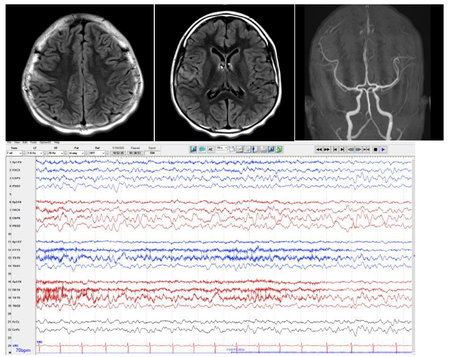

Figure1: FLAIR images reveal moderate edema involving the cortex and subcortical white matter of right postcentral gyrus. MRA is normal. No diffusion restriction seen in ADC map. EEG: Slow disorganized background which is more prominent over the right posterior quadrant.

Case Summary

- Patient presented the first time at 8 years of age, with lethargy, left hemiparesis and left focal motor status epilepticus controlled with antiseizure medications. His MRI showed a right frontal stroke (figure 1)
- Genetic testing revealed pathogenic variant in the mitochondrial MT-TL1 gene, m.3243A>G at approximately 75%heteroplasmy and confirmed MELAS diagnosis.
- Past medical history: Born full term, without any complications during pregnancy and delivery. Diagnosed with speech delay at 2. noted to have alternating exotropia, amblyopia, poor visual acuity at age 5. lost to follow up until age 8. Diagnosed with intellectual disability, gross motor, fine motor and speech delays at age 8.
- At 9 years of age, he presented with a similar picture. His long-term video EEG (LTM) showed abundant right parietal electrographic seizures (seizure burden up to 21 minutes/hour), concordant with new stroke in this region. (figure 2)
- Seizures were refractory to levetiracetam, lacosamide, phenobarbital and midazolam drip. Finally, ketamine resulted in complete seizure control.
- Two months later, he presented with encephalopathy and frequent right motor seizures associated with a new left parietal stroke.
- His LTM showed left parietal electrographic seizures with a seizure burden of 23 minutes/hour, refractory to fosphenytoin, phenobarbital and levetiracetam.
- Seizures were immediately controlled after ketamine 1mg/kg intravenous bolus administration. He was started on 0.5 mg/kg/h iv ketamine infusion and received for 24 hours. Seizures did not recur during ketamine infusion weaning.
- Discharged from hospital with two oral anti seizure medications (levetiracteama and lacosamide).

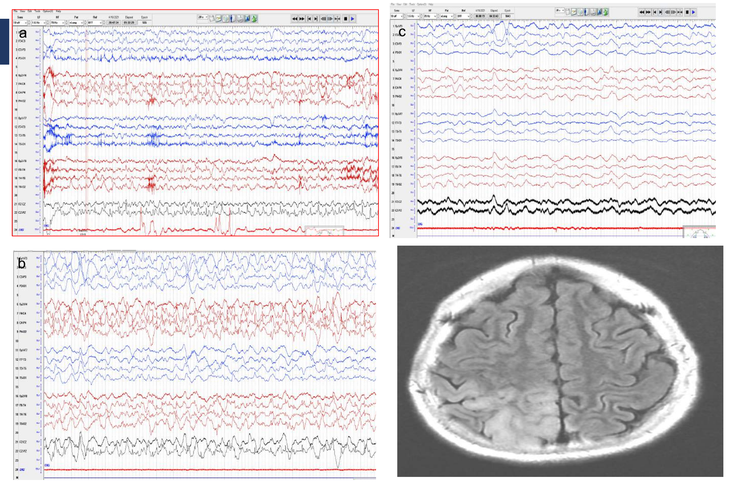

Figure2: a-b: Frequent focal seizures involving the right parietal region were captured both awake and sleep. Seizure burden was 21 minutes/hour. Figure 2c: Complete seizure resolution after ketamin 1 mg/kg administration. MRI –T2 images revealed right parietal metabolic stroke with moderate edema.

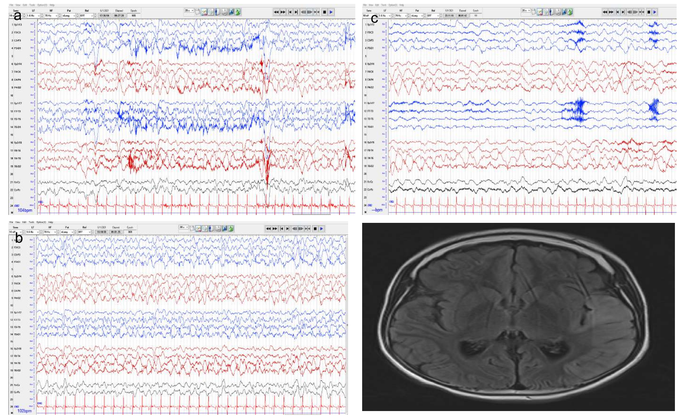

Figure3: a-b: EEG revealed frequrent left occipital and parietal seizures during sleep and wakefulness. Figure3c:Complete seizure resolution after ketamine administration. MRI-FLAIR images revealed new ischemic changes and moderate edema over the left posterior temporal and parietal cortex.

Discussion

We present a favorable experience with ketamine in the treatment of a patient with two different presentations of non convulsive status epilepticus (SE) in the context of MELAS and new metabolic strokes.

It is important to capture seizures with video EEG in patient with MELAS and new onset encephalopathy.There is no standardized treatment modality in terms of treatment of SE in MELAS and it is usually resistant to anti seizure treatment . As many anti seizure medications including benzodiazepines, phenobarbital, propofol, and valproate can lead to worsening of seizures and increase the metabolic distress and multi-system damage.

In our case, SE was confirmed by EEG and SE cessation was established by EEG resolution of the ictal activity. A combination of several anti seizure medications was used to treat refractory SE. In both presentations, seizure freedom was achieved immediately following iv ketamine administration.

During prolonged seizures, the numbers and activities of GABA receptors decrease, and glutamergic NMDA receptors increase. Therefore, a non competitive NMDA antagonist, Ketamine, may be an effective option in SE associated with MELAS syndrome. Rapid onset of action, neuroprotective profile, less respiratory and cardiovascular depression side effects makes ketamine a relatively safe medication for children with SE in the setting of MELAS.

References

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