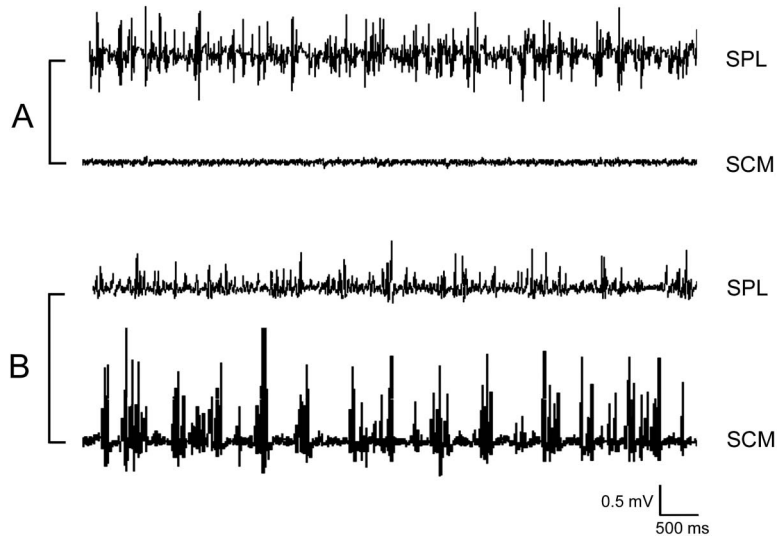
Figure EMG by needle concentric electrode



Co-recorded from right splenius capitis (SPL) and sternocleidomastoid (SCM) muscles in case 2 when the head was kept straight (A) and during sudden anteroflexion movements of the head (B). In A, tonic EMG activity is recorded on SPL, whereas simultaneous EMG bursts of variable length (>300 ms) occurred on SCM and SPL during the head drops. In both cases, EMG was also recorded from semispinalis capitis and upper trapezius (data not shown), in which variable EMG activity from antagonist muscles was recorded during head drops.

of observation, whereas case 1 was being treated only with a low dose of pimozide.

Our cases widen the spectrum of diseases associated with sudden head and trunk drops and illustrate that this sign might not be pathognomonic of a distinct pathologic condition but rather might represent a phenomenologic manifestation of chorea.

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PROPOFOL-RELATED INFUSION SYNDROME HERALDING A MITOCHONDRIAL DISEASE: CASE REPORT

Propofol-related infusion syndrome (PRIS) is a rare but catastrophic complication of propofol use. It is clinically characterized by metabolic acidosis, rhabdomyolysis, arrhythmias, myocardial failure, renal failure, and hepatomegaly, and may lead to death.[1] Some risk factors are associated with PRIS, namely young age, critical illness, high fat intake, catecholamine or steroid use, inborn error of fatty acid oxidation, propofol doses exceeding 4–5 mg/kg/hour, and duration of use exceeding 48 hours.[1] Some evidence also suggests that PRIS is related to a mitochondrial toxicity of propofol.[2,3]

Recessive mutations in the *POLG1* gene result in an aberrant replication and an impaired maintenance of mtDNA, leading to organ dysfunction.[4] Numerous overlapping phenotypes have been described, including Alpers syndrome, progressive external ophthalmoplegia, and epilepsy.[4] This report contains an observation about a patient with PRIS associated with a genetically proven mitochondrial disease, which has only been reported once before.[5]

Case report. A 27-year-old French Canadian woman known for focal nocturnal motor epilepsy, 1 month postpartum, presented to the emergency room in status epilepticus (SE) that proved to be refractory to lorazepam and phenytoin. Predominant abnormal activity on EEG was located in the posterior area of the right hemisphere. Following endotracheal intubation, a propofol infusion was initiated with doses requiring to be increased to as high as 10.7 mg/kg/hour to adequately control the seizures, vasopressors being required. The initial MRI was unremarkable. Levetiracetam and clobazam were then added to the therapy.

On day 3, cardiac monitoring showed an increased QTc of 685 ms, in combination with an abnormal arterial blood gas revealing a metabolic acidosis (pH 7.28, pCO_2 33 mm Hg, pO_2 133 mm Hg, HCO_{3-} 15.5 mEq/L). Arterial lactate increased to 3.7 mmol/L (normal < 1.6) and creatine kinase increased to 3,037 U/L (normal 35–170). A diagnosis of PRIS was made. The propofol was thus discontinued after a 69-hour infusion and midazolam was initiated, as well as hemofiltration. At this point, the combination of refractory SE with posterior focus led the medical team to suspect that a mitochondrial disorder may be underlying the patient's clinical condition and *POLG* genetic testing was ordered. The PRIS resolved the next day, but the SE was found to be less responsive to midazolam and required dosages up to 100 mg/hour.

The SE was still not fully controlled on subsequent days and ketamine was added to the drug regimen on day 12. From that point to day 68, numerous approaches were used to control the refractory SE, namely topiramate, valproic acid, lacosamide, magnesium sulfate, dexamethasone, and electroconvulsive therapy. Pentobarbital and ketamine were the only drugs successfully controlling the SE. On day 30, the result of the *POLG1* gene test result was obtained, leading to the discovery of 2 previously reported pathologic mutations (c.1880 g-a and c.3287 g-a). Valproic acid was stopped at this point.

On day 68, an ultimate trial with isoflurane was proved ineffective once again at drug weaning. Considering the duration of the SE, its highly resistant nature, and the fact that the patient carried a genetic disease associated with high mortality and morbidity, the medical team and the family decided to end the life-sustaining therapies. The patient died 75 days following admission.

Discussion. Studies on animals models[2,3] suggested that propofol may disrupt electron flow through the mitochondrial respiratory electron transport chain. A reduction in cytochrome *c* oxidase activity has been described previously, in a child with PRIS following a muscle biopsy.[6] Moreover, abnormalities in the carnitine profile of a patient with PRIS, consistent with an impaired entry of long-chain acylcarnitine in the mitochondria and failure of the respiratory chain at complex 11, have also been observed.[7] These observations support the hypothesis that a mitochondrial defect may predispose to PRIS. A similar case was recently reported in a blind patient experiencing PRIS and found postmortem to be carrying a mutation associated with Leber hereditary optic neuropathy.[5]

The case we presented had some known risk factors for developing PRIS in addition to the mitochondrial disease. Therefore, at this point, it is not possible to rule out the possibility of a coincidence. However, given the low prevalence/incidence of these 2 clinical conditions (mitochondrial disease and PRIS) and the observation that the vast majority of patients with similar propofol exposure will not develop PRIS, the clinical association is important in this case and cannot be ignored. Thus, clinicians should promptly screen patients experiencing PRIS for mitochondrial diseases. Our observations support the recommendation to avoid using propofol in patients with known mitochondrial diseases.

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