MANAGEMENT OF INTRACTABLE PSYCHOSIS IN A PATIENT WITH HEREDITARY ACERULOPLASMINEMIA-ASSOCIATED NEURODEGENERATION: THE ROLE OF ELECTROCONVULSIVE THERAPY

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BACKGROUND

Hereditary Aceruloplasminemia (HA) is a rare autosomal recessive disorder of iron metabolism that arises due to loss-of-function mutations in the ceruloplasmin gene, leading to systemic iron overload including cerebral and liver parenchyma (Lobbes et al., 2020). Affected individuals often present with late-onset (6th decade) degenerative brain changes with neurologic and psychiatric sequelae, as well as laboratory studies demonstrating microcytic anemia, elevated serum ferritin, and a complete absence of serum ceruloplasmin ferroxidase activity (Nittis et al., 2002). Neurologic and psychiatric manifestations include abnormal movements, ataxia, cognitive impairment, extrapyramidal symptoms, and psychiatric-like symptoms, many of which lead to disabilities. While magnetic resonance imaging reveals iron accumulation within the basal ganglia, diagnosis is based on transferrin saturation and hepatic iron content evaluated by magnetic resonance imaging of the liver (Lobbes et al., 2020). The usual therapeutic approach is based on iron chelators that are effective in reducing systemic iron overload. However, they have demonstrated poor efficacy in counteracting the progression of neurologic manifestations while also often exacerbating anemia (Piperno et al., 2018). We highlight the presentation of a patient with HA and describe our management approach with ECT.

CASE DESCRIPTION

Our patient is a 59-year-old woman with a history of HA, who was psychiatrically admitted due to a 6-month history of progressively worsening paranoia and anxiety (crippling fear of being beheaded or shot to death by "marines"). Notably, she had suffered risperidone-induced parkinsonism in the outpatient setting, leading to a switch to quetiapine (100 mg total daily dose). Other home medications were valproic acid (VPA), sertraline, mirtazapine and deferiprone.

Upon admission, her quetiapine was titrated over 8 days to a total daily dose of 600 mg with no other medication changes. On day 9, she developed high fever, elevated CPK, mild rigidity, and altered mental status (concerning for neuroleptic malignant syndrome). All psychotropic medications were discontinued, and the patient was medically admitted for further workup. No evidence was found of infection or metabolic derangements. MRI-brain in February 2023 showed susceptibility artifacts in the basal ganglia, thalamus, brainstem, as well a diffusely throughout the brain (Figure 1). The patient's fever and delirium resolved over 24-48 hours with supportive management.

Subsequently, the patient's psychiatric symptoms continued, limiting her participation in physical therapy with resultant deconditioning. Olanzapine was cautiously introduced, with no noticeable benefit (up-titration limited by increased rigidity). Clozapine was considered but deemed inappropriate due to the patient's pancytopenia. The patient was then referred for ECT, which was well tolerated. The patient had her first ECT treatment (LOW 0.5, bilateral) on 03/07/2023. After 6 ECT treatments, a marked improvement was noticed in her psychotic symptoms (50% reduction of PANSS score). Her rigidity and parkinsonian gait also improved. The rest of her ECT course and improvements are shown in Figure 2.

FIGURES

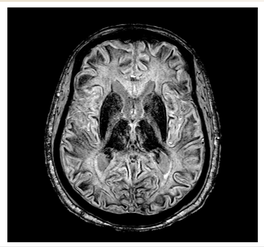

Figure 1. SWI MRI Brain without contrast

Date -- 02/12/2023

Impression -- extensive susceptibility artifact throughout the white matter, cerebral cortex, basal ganglia, thalami, midbrain structures, dentate nuclei, and along the surface of the brainstem — consistent with patient's known history of hereditary aceruloplasminemia. No acute infarct or intracranial hemorrhage.

FIGURES

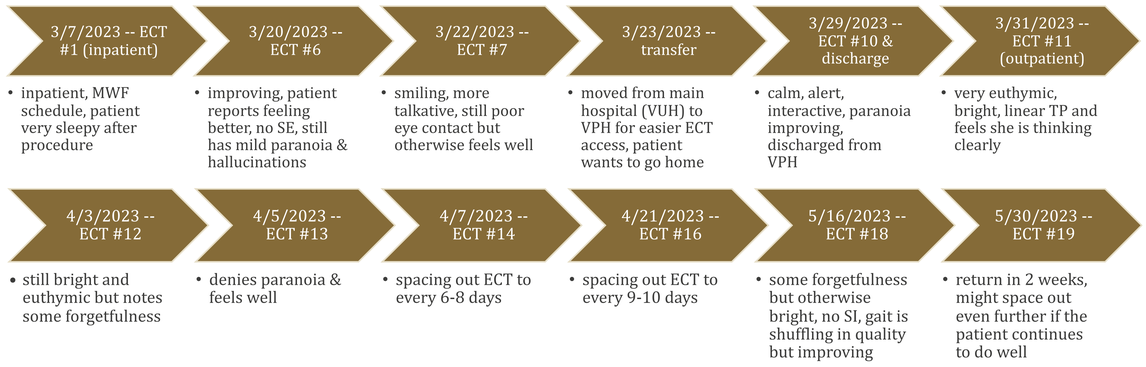

Figure 2. Timeline of Patient's ECT Treatments and Improvement

DISCUSSION

Our case highlights the presentation of a patient with florid psychotic symptoms in the context of HA-associated Neurodegeneration with Brain Iron Accumulation (NBIA). Treatment of psychosis in this population is complicated by their inherent neuroleptic hypersensitivity, as well as proneness to blood dyscrasias, which limits the use of antipsychotics (including clozapine). There is high-quality evidence that ECT is effective for both the neuropsychiatric and motor symptoms of idiopathic Parkinson's Disease (Takamiya et al., 2021). However, there is scarce evidence supporting the use of ECT in patients with HA. To our knowledge, we report the first case that demonstrates a clear benefit from ECT in this patient population.

CONCLUSION

While the pathophysiology of HA involves defects in iron homeostasis, iron chelators have not been found to be effective for its neuropsychiatric manifestations. While the initiation of iron chelation therapy (ICT) may prevent or slow down neurodegeneration, its clinical efficacy remains uncertain after the onset of symptoms (Lobbes et al., 2020). Given the known efficacy and tolerability of ECT for neuropsychiatric and motor symptoms exhibited by patients with neurodegenerative diseases affecting the basal ganglia such as Parkinson's Disease, ECT should be similarly considered in patients with rarer diseases such as HA who develop similar neuropsychiatric symptoms.

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