Clinical Parkinsonism & Related Disorders 4 (2021) 100090

Contents lists available at ScienceDirect

Clinical Parkinsonism & Related Disorders

journal homepage: www.elsevier.com/locate/prdoa

Electroconvulsive therapy for mania associated with Wilson disease: Improvement in psychiatric and motor symptoms

Mood disorders are the most common psychiatric manifestation of Wilson disease (WD) [1]. Furthermore, there is an association between bipolar disorder (BD) and WD [2]. Electroconvulsive therapy (ECT) has been shown in a few case reports to be effective for WD catatonia and depression [3]. To date, there have been no reports of WD mania treated with ECT, and no reported association between psychiatric and neurological improvements in WD following ECT. We describe a case with WD and BD mania who was safely treated with ECT, with a remarkable improvement in their psychiatric and motor symptoms. To evaluate the severity of the mania and the motor changes, the Young Mania Rating Scale (YMRS) and the Global Assessment Scale for Wilson's Disease (GAS-WD) were administered to the patient the day after every fourth treatment by the same rater (LAB). GAS-WD Tier 2 – Neurological Assessment (GAS-N) – was used to assess the motor changes, since it has a high convergent validity with the Unified Parkinson's Disease Rating Scale Part III (motor examination) [4]. This study was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from the subject. A 29-year-old man was referred to our inpatient ward due to symptoms of refractory mania. The patient's baseline YMRS was 33 points, the GAS-WD was 29, and the GAS-N was 19. Neurological examination at admission revealed symptoms and signs of parkinsonism (bradykinesia, cogwheel rigidity and postural instability) in addition to a symmetrical postural tremor, action tremor, and motor stereotypy (right arm flapping). In addition, his speech was slightly slurred but easily intelligible, and he had difficulty swallowing, resulting in frequent choking episodes. The aforementioned neurological symptoms had appeared fifteen months and were investigated as soon as they manifested, leading to the diagnosis of Wilson Disease, based on the patient's serum ceruloplasmin of 13 mg/dL (normal range: 22–58), serum copper of 67 ng/dL (70–140), 24 h urinary copper of 304 mcg (15–60 mcg/24 h), the presence of Kayser-Fleischer rings on slit-lamp examination of his eyes, and cranial magnetic resonance imaging showed low signal intensity in the basal ganglia on T2-weighted images. According to his parents, the mania episodes had begun eight months ago and were accompanied by persecutory ideas. During these months, his behavior became increasingly disruptive towards his parents and siblings, resulting in recurrent verbal and physical aggression episodes. As a consequence, he was admitted to inpatient care facilities in other psychiatric hospitals three times. During previous hospitalizations, he underwent different treatments, including lithium (at the therapeutic range, for more than 24 weeks) proposed as a preferred option in WD mania [5], olanzapine (10 mg/day, for more than 12 weeks), valproic acid (1000 mg/day, for more than 12 weeks), and lurasidone (dosage/length not known) with minimal response. Relapse ensued a few weeks later, leading to multiple hospital admissions.

At admission in our hospital, the clinical presentation was characterized by expansive and irritable mood associated with inflated self-esteem, distractibility, talkativeness, hyperactivity, a diminished need for sleep, increased sexual desire and social disinhibition. Past history revealed that he exhibited hypomania symptoms in the last two years, which remitted with lithium but were followed by a depressive episode, presenting a persistent feeling of sadness, loss of interest in activities, pessimism, suicidal thoughts, and trouble making decisions. This episode lasted until the current manic states arose.

Given the poor control of his psychiatric manifestations by medications, and the risk of worsening parkinsonism on antipsychotics, it was decided to start ECT. A course of 18 bitemporal ECT sessions was administered three times weekly on alternate days. For the ECT procedure, the spECTrum 5000Q (Mecta Corporation, Tualatin, OR, USA) device parameters were set using a pulse width of 0.5 ms, 80 Hz, train duration 5 s, and current at 800 mA with a resulting charge of 320 mC. No post-ECT complications were observed. Regarding medication, clozapine was initiated before the ECT, and valproic acid was titrated to 500 mg twice daily. During hospitalization, the patient's neurological and affective symptoms fluctuated together. Nevertheless, a thorough evaluation indicated improvement of both neurological and psychiatric symptoms during hospitalization (see Fig. 1). Based on all the clinical evidence, we hypothesized that, in addition to the mania symptoms, the improvement in acute motor symptoms could be associated with the ECT treatment. During ECT, the YMRS score declined from 33 before the first ECT to 7. The GAS-WD score declined

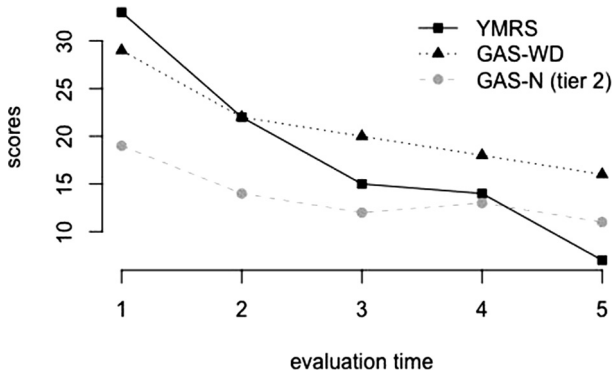

Fig. 1. Overall improvement in the Young Mania Rating Scale (YMRS), Global Assessment Scale for Wilson's Disease (GAS-WD), and GAS-Neurological Assessment (Tier 2) scales during the course of the electroconvulsive therapy (ECT). Axis (T) 1 represents the baseline score, before the first ECT session, and (T) 5 represents the last evaluation after the 18th ECT session.

https://doi.org/10.1016/j.prdoa.2021.100090

from 29 to 16, and the GAS-N score declined from 19 to 11, mainly due to motor improvement. The patient was discharged seven weeks later. At the time, the patient's clinical presentation was characterized by a slight expansive mood associated with hyperactivity and increased sexual desire. On the other hand, talkativeness and distractibility were no longer present, and his self-esteem was not inflated.

In relation to his neurological symptoms, the parkinsonism improved considerably; although he still experienced episodes of postural instability and freezing of gait, the resulting impact on his activities was diminished. His speech remained slurred but easily intelligible. The rest, postural, and action tremors that the patient was experiencing ceased, and he obtained better control over the arm-flapping stereotypy. While the mechanism of action of ECT on the motor symptoms of neuropsychiatric disorders remains unclear, there is preliminary evidence from a few controlled trials and case reports that ECT is effective in Parkinson's disease (PD), epilepsy, and NMS [6]. We hypothesized that ECT might have influenced the improvement in motor symptoms experienced by our patient with WD. To the best of our knowledge, this is the first description of mania in WD that was not only successfully treated with ECT, but was also associated with a marked improvement in motor symptoms at the same time.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] A. Czlonkowska, T. Litwin, P. Dusek, et al, Wilson disease, Nat. Rev. Dis. Primers 4 (1) (2018) 21.
[2] M.G. Carta, O. Sorbello, M.F. Moro, et al, Bipolar disorders and Wilson's disease, BMC Psychiatry 12 (2012) 52.
[3] C.M. Braga, I.F. Pina, A. Cantilino, L. Machado, Catatonia - not only a schizophrenia subtype: a case report of Wilson's disease, Braz. J. Psychiatry 41 (5) (2019) 460–462.
[4] A. Aggarwal, N. Aggarwal, A. Nagral, G. Jankharia, M. Bhatt, A novel global assessment scale for Wilson's disease (GAS for WD), Mov. Disord. 24 (4) (2009) 509–518.
[5] T. Litwin, P. Dusek, T. Szafrański, K. Dzieżyc, A. Członkowska, J.K. Rybakowski, Psychiatric manifestations in Wilson's disease: possibilities and difficulties for treatment, Therapeut. Adv. Psychopharmacol. (July 2018) 199–211. doi:10.1177/2045125318759461
[6] W.M. McDonald, B.D. Greenberg, Electroconvulsive therapy in the treatment of neuropsychiatric conditions and transcranial magnetic stimulation as a pathophysiological probe in neuropsychiatry, Depress Anxiety 12 (3) (2000) 135–143.

Luis Antonio Bozutti [a]
Jose Gallucci-Neto [a,b,*]
Renato Luiz Marchetti [a]
[a] *Neuropsychiatry Program, Institute and Department of Psychiatry, University of Sao Paulo, Sao Paulo, Brazil*
[b] *ECT Service, Institute of Psychiatry, University of Sao Paulo, Sao Paulo, Brazil*
* Corresponding author at: Director of ECT Service, University of Sao Paulo, Institute and Department of Psychiatry, Rua Ovídeo Pires de Campos 785, Sao Paulo, Brazil.
E-mail address: jose.gallucci@hc.fm.usp.br (J. Gallucci-Neto)
Received 19 October 2020
Revised 22 November 2020
Accepted 13 February 2021

Available online 20 February 2021