Successful Electroconvulsive Therapy for a 74-year-old Female with Major Depressive Disorder and Tardive Tremor: A Case Report and Literature Review

Jia-Yin Yeh, Nien-Mu Chiu, Yung-Yee Chang, Pao-Yen Lin, Yu Lee

Departments of Psychiatry and Neurology, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Kaohsiung, Taiwan

Tardive tremor is an infrequently form of tardive syndrome that is developed from prolonged treatment with dopamine receptor blocking agents. This condition presents as a prominent tremor that may cause significant distress but currently lacks effective treatment. Electroconvulsive therapy (ECT) has been applied to treat tardive syndrome. In this study, we report a 74-year-old female patient with major depressive disorder, whose tardive tremor and depressive symptoms showed remarkable improvement after receiving 10 sessions of ECT treatment.

KEY WORDS: Depression; Electroconvulsive therapy; Tremor.

INTRODUCTION

Tardive syndrome (TS) is a movement disorder that presents with abnormal, involuntary movement after taking dopamine receptor blocking agents for over three months [1]. Tardive tremor (TT) is one of subtypes of TS that was infrequently documented [2]. Patients with TT have a high-amplitude, 4 to 8 Hz rest and postural tremors after being chronically treated with dopamine receptor blocking agents [3]. Electroconvulsive therapy (ECT) has been applied to treat TS in the past [1]. However, to the best of our knowledge, no studies have studied the improvement of TT after using ECT. In this study, we present a patient with major depressive disorder whose TT showed remarkable improvement after receiving ECT treatment.

CASE

A 74-year-old female has been treated for major depressive disorder that manifested with depressed mood, loss of interest, fatigue, psychomotor retardation, insomnia, poor appetite, negative thoughts, and suicidal ideation since the age of 59 years in 2002. From 2002 to August 2016, her physicians have treated her with several antidepressants, including paroxetine (20 mg/day), venlafaxine (300 mg/day), duloxetine (90 mg/day), escitalopram (20 mg/day), mirtazapine (45 mg/day), agomelatine (50 mg/day), and bupropion (450 mg/day). In this period, her pharmacological treatments have even been augmented with several antipsychotics and other agents, including quetiapine (50 mg/day), aripiprazole (5 mg/day), lithium carbonate (600 mg/day), and thyroxine sodium (0.1 mg/day). We did not observe any extrapyramidal symptom. And her depressive symptoms were unremitted.

In September 2016, she began to receive treatment of mirtazapine 30 mg/day and aripiprazole 5 mg/day. Three months later, tremors over the mandible, lips, tongue, and both hands were detected. No vivid bradykinesia, rigidity
of limbs, or loss of balance was observed. To relieve the involuntary movement, we changed her medication to quetiapine 25 mg/day, bupropion 150 mg/day, and agomelatine 25 mg/day but observed no improvement. Then, we discontinued all antidepressants and antipsychotics in January 2017. Nevertheless, the tremor symptoms did not improve, and her depressive symptoms were worsened. Her routine blood tests, electrolytes, renal and hepatic functions, thyroid and cortisol hormones, homocysteine, rapid plasma reagin test, autoimmune disorder-related blood examinations, and brain magnetic resonance imaging all revealed no significant abnormalities. The tremography reported a 6 Hz postural tremor in both hands. We prescribed piracetam 2,400 mg/day, vitamin B6 400 mg/day, and propranolol 10 mg/day, but the movement symptoms did not improve.

In March 2017, the patient was hospitalized with aggravated depressed mood, hopelessness, and helplessness. A course of ECT was administered due to her severe depressive and distressing tremor symptoms. Intravenous thiamylal sodium 90 to 210 mg was used for the anesthesia. The patient received bitemporal ECT by a Thymatron® system IV machine (Somatics, LLC., Venice, FL, USA) every other day. According to system IV instruction manual, we selected the preset LOW 0.5 program (fixed 0.5 ms pulsewidth, varies frequency to maximize duration) with a pulse width of 0.5 milliseconds, a frequency of 60 Hz, a duration of 2 seconds, and a current of 0.9 mA because it provided a broadly effective stimulus that was in the physiological range for most patients. To avoid excessive initial treatment stimuli [4], we did not use most applicable “half-age method” for the bilateral ECT (set PERCENT ENERGY dial to approximately one-half the patient’s age, e.g., 35% for a 70-year-old patient) [5]. We used simple and practical “stimulus titration method” for bitemporal ECT with an initial setting of “PERCENT ENERGY dial” at 10% ENERGY, followed by re-stimulations at 5% ENERGY increments until a seizure occurs. If no seizure activity results, the PERCENT ENERGY setting should be increased step by step to 100% and the patient re-stimulated within 30 to 60 seconds to maximize the likelihood of obtaining a therapeutically satisfactory seizure at the first treatment session. Once the seizure threshold is determined for a specific PERCENT ENERGY setting, the subsequent treatments should be administered at recommended doses approximately 2 times this threshold (e.g., 20% ENERGY for a patient with 10% ENERGY seizure threshold). According to motor activity measurement, her seizure duration ranged from 25 to 35 seconds.

Upon completing 10 ECT sessions, both the TT and the depressive symptoms showed significant improvement. The patient’s scores on the Extrapyramidal Symptoms Rating Scale decreased from 31 to 15 and from 22 to 10 on the Hamilton Depression Rating Scale-17 items. Retrograde amnesia occurred, but it was temporary and related to the period of impairment immediately following ECT, thus we considered it was the adverse effect of ECT. She was discharged after one month of hospitalization. The tremor symptoms did not recur in the six months after discontinuing all antidepressants and antipsychotics.

This study was approved by the Human Research Ethics Committee of Chang Gung Memorial Hospital (2018 00084B0), and the informed consent was obtained from the subject.

**DISCUSSION**

TT was first described by Stacy and Jankovic [2]. This symptom has been reported in less than 3% of neuroleptic-treated patients [6]. The underlying mechanism of TT is still unknown. One possible explanation is dopamine receptor upregulation in the basal ganglia caused by therapy with chronic dopamine receptor blocking agents, which may also cause disinhibition of the brain stem and cerebellar or thalamic oscillators, and is ultimately expressed as tremors [2].

Few effective treatment options are available for TT. Some studies reported that tetrabenazine may be a possible treatment option [2,7]. However, tetrabenazine is known to have a risk of depression in high doses. Furthermore, its tolerability is also problematic, primarily due to its side effects [7].

In our case, the patient exhibited prominent tremors over the mandible, lips, tongue, and 6 Hz postural tremors on both hands after having undergone prolonged treatment with dopamine receptor blocking agents. The symptoms persisted even after these drugs were discontinued. We were able to rule out tardive parkinsonism as we observed no vivid bradykinesia, rigidity of limbs, or loss of balance; tremor was the only symptom. A diag-
Table 1. Reports of electroconvulsive therapy (ECT) for patients with tardive syndrome

| Study                        | Patient (n, sex) | Concurrent psychiatric diseases                                                                 | Concurrent medication use                                                                 | Number of ECT sessions | Results                                                                 | AIMS score |
|------------------------------|------------------|-------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|------------------------|-------------------------------------------------------------------------|------------|
| Tardive dyskinesia           |                  |                                                                                                |                                           |                        |                                                                        |            |
| Asnis and Leopold (1978)     | 4, F             | 1 with bipolar disorder, depressive type 1 with schizoaffective disorder 1 with organic brain syndrome 1 with paranoid schizophrenia | No medication 3 weeks before ECT                                                      | 6−13<sup>b</sup>        | 3 without change 1 (paranoid schizophrenia) with worsening result         | Unclear    |
| Price and Levin (1978)       | 1, F             | 1 with depression                                                                              | Unclear                                                                                 | 7<sup>b</sup>           | 1 with improvement                                                       | Unclear    |
| Rosenbaum et al. (1980)      | 1, F             | 1 with depression and agitation                                                                | Unclear                                                                                 | 8<sup>b</sup>           | 1 with improvement                                                       | R (19→7)  |
| Chacko and Root (1983)       | 2                | 1 with major depressive disorder 1 with chronic schizophrenia                                  | 1 with amitriptyline, 100 mg/day 1 with fluphenazine decanoate, 75 mg IM/vwk; diphenhydramine, 200 mg/day; trihexyphenidyl 15 mg/day; haloperidol, 70 mg/day | Unclear                | 2 with improvement                                                       | Unclear    |
| Holcomb et al. (1983)        | 1, F             | 1 with delusion depression and Parkinson disease                                               | No medication                                                                          | Unclear                | 1 with worsening result                                                   | Unclear    |
| Flaherty et al. (1984)       | 3, M             | 3 with depression (previous diagnosis: schizoaffective disorder or schizophrenia)             | No medication                                                                          | 4−6<sup>b</sup>         | 3 with emergent dyskinetic movements after ECT, later with improvement   | Unclear    |
| Gosek and Weller (1988)      | 1, F             | 1 with bipolar affective disorder                                                              | Lithium, 900 mg/day; diazepam, 30 mg/day; trazodone, 150 mg/day                          | 9<sup>b</sup>           | 1 with improvement                                                       | R (41→10) |
| Malek-Ahmadi and Weddige (1988) | 1, F         | 1 with depression with psychotic features                                                      | Unclear                                                                                | 5<sup>b</sup>           | 1 with improvement                                                       | Unclear    |
| Roth et al. (1988)           | 1, M             | 1 with mania and parkinsonism                                                                  | Unclear                                                                                | 10 right unilateral     | 1 with improvement                                                       | Unclear    |
| Hay et al. (1990)            | 3 (2, F; 1, M)   | 3 with depression                                                                               | Unclear                                                                                | 6                      | 3 with improvement                                                       | Unclear    |
| Salama and England (1990)    | 1, M             | 1 with schizophrenia                                                                           | No change or little neuroleptics                                                       | 20 unilateral           | 1 with improvement                                                       | Unclear    |
| Yassa et al. (1990)          | 9 (5, F; 4, M)   | 5 with bipolar depression 2 with depression 2 with schizophrenia                              | 4 with haloperidol 15−40 mg/day + TCA 8−10<sup>b</sup>                                  | 1 with improvement     | 8 with unchanged                                                        | IR (14→4) |
| Besson and Palin (1991)      | 1, F             | 1 with psychotic depression                                                                    | Unclear                                                                                | 8<sup>b</sup>           | 1 with improvement                                                       | PR (22→16) |
| Uçok and Uçok (1996)         | 1, M             | 1 with catatonic schizophrenia                                                                  | No medication                                                                         | Maintenance ECT         | 1 with improvement                                                       | Unclear    |
| Nobuhara et al. (2004)       | 1, M             | 1 with depression                                                                               | Unclear                                                                                | 8<sup>b</sup>           | 1 with improvement                                                       | R (16→4)  |
### Table 1. Continued

| Study                       | Patient (n, sex) | Concurrent psychiatric diseases | Concurrent medication use | Number of ECT sessions | Results        | AIMS score |
|-----------------------------|-----------------|---------------------------------|---------------------------|------------------------|----------------|------------|
| **Tardive dystonia**        |                 |                                  |                           |                        |                |            |
| Kwentus et al. (1984)       | 1, F            | 1 with catatonia (ever diagnosed with schizophrenia and manic-depressive illness) | Lithium carbonate         | 9 unilateral ECT       | 1 with improvement | Unclear    |
| Adityanjee et al. (1990)    | 1, M            | 1 with schizophrenia            |                           |                        | 1 with improvement | Unclear    |
| Kaplan et al. (1991)        | 1               | Unclear                         |                           |                        | 3 with 10b       | Unclear    |
| Postolache et al. (1995)    | 1               | Unclear                         |                           |                        | 1 with improvement | Unclear    |
| Sienaert and Peuskens (2005)| 1, M            | 1 with paranoid schizophrenia  | Amitriptyline 175 mg, valproate 1,000 mg, and clozapine 700 mg | Continuation-ECTb (total of 43 treatments during a 1-year period) | 1 with improvement | R (15→5)    |
| Manteghi et al. (2009)      | 1, M            | 1 with paranoid schizophrenia  |                           |                        | 6               | Unclear    |
| Yasui-Furukori et al. (2014)| 10 (5, F; 5, M) | 1 with depression 9 with schizophrenia | 2 with no medication 1 with olanzapine 10 mg/day 4 with risperidone 1–3 mg/day 3 with aripiprazole 3 mg/day | 1 with 6b 1 with 9b 5 with 10b 1 with 12b 2 with 15b | 10 with improvement | 3 with R 7 with PR |

**Tardive tremor**

| Current report              | 1, F            | 1 with depression              | Propranolol 10 mg/day     | 10b                    | 1 with improvement | R (ESRS 31→15) |

AIMS, Abnormal Involuntary Movement Scale; F, female; M, male; IM, intramuscular; TCA, tricyclic antidepressant; ESRS, Extrapyramidal Symptom Rating Scale.

*A response (R) was defined as a 50% improvement relative to the baseline, and a partial response (PR) was defined as a 25% improvement relative to the baseline.*  
*Bilateral frontotemporal ECT.*
nosis of TT was determined after excluding other possible organic etiologies, e.g. infections, stroke, electrolyte imbalance, thyroid dysfunction, and structural brain lesion. After ECT without taking any antidepressant or antipsychotic medications, she showed marked improvement in both depression and TT symptoms. This result suggests that ECT is a treatment option with satisfactory efficacy for TT patients.

ECT has been reported to be a treatment option for tardive dystonia and tardive dyskinesia with mild to moderate efficacy [8]. Several studies have indicated that it has success in relieving both extrapyramidal symptoms and depressive features of certain patients suffering from concurrent Parkinsonism and depression [9-12]. Currently, no literature has addressed using ECT as a treatment for TT. The possible mechanism associated with ECT in tardive dyskinesia was that ECT may increase striatal GABA concentrations and prevent supersensitization of postsynaptic dopamine receptors, which then allows it to improve dyskinetic symptoms [13]. This effect may also explain its efficacy in resolving TT symptoms.

Here, we review the literatures that documented about the patients with TS, including tardive dyskinesia, tardive dystonia, and tardive tremor, treated by ECT (Table 1). There are 57 patients recruited. Among 40 patients with tardive dyskinesia, after ECT, 27 of the patients had improvement [6,8,9,14-25], 11 patients remained no change [23,26] and 2 patients presented worsening symptoms [26,27]. Among 16 patients with tardive dystonia, all of them showed improvement after ECT [8,28-33]. As for TT, our case was the only report and presented with improvement after ECT. Overall, about three fourths of the patients with TS showed improvement after treated with ECT.

However, the influence from the confounding effects of psychiatric diagnosis, concurrent physical illness, previous medications, and the setting and number of sessions of ECT remains unclear [18]. Besides, the adverse cognitive effect throughout the ECT course is also an important issue. Despite these factors, this result suggests that ECT may offer potential treatment for TS. Further larger-scale studies are warranted to clarify the efficacy.

TT is a rare subtype of TS that can be disabling and may not respond to conventional anti-tremor therapy [2]. The patient in our case showed marked improvement in both depressive symptoms and TT after receiving ECT treatment. This result indicates that ECT is a viable treatment option for patients suffering from both depression and TT.

**Conflicts of Interest**

No potential conflict of interest relevant to this article was reported.

**Author Contributions**

Conceptualization: Jia-Yin Yeh, Yu Lee. Original draft: Jia-Yin Yeh. Critical revision: Nien-Mu Chiu, Yung-Yee Chang, Pao-Yen Lin, Yu Lee. Supervision: Pao-Yen Lin, Yu Lee.

**ORCID**

Jia-Yin Yeh https://orcid.org/0000-0002-2008-8463
Nien-Mu Chiu https://orcid.org/0000-0002-1839-463X
Yung-Yee Chang https://orcid.org/0000-0001-6840-8537
Pao-Yen Lin https://orcid.org/0000-0002-1394-4567
Yu Lee https://orcid.org/0000-0001-7322-8936

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