Nonresponse to Electroconvulsive Therapy (ECT) in a Patient with Depression, Substance Abuse and Personality Disorder

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Abstract: The authors report the case of a patient with a history of episodic, severe clinical depression who demonstrated an apparent absence of response to ECT. His illness was complicated by substance abuse and personality disorder. The vicissitudes of his course of treatment are described and the literature on ECT in depressed patients with substance abuse and personality disorder is reviewed. The heterogeneity of depression, and its relation to the ECT consultation process, is briefly discussed.

Keywords: Non-response to ECT, ECT and substance abuse, ECT and personality disorder, heterogeneity of depression, ECT consultation.

INTRODUCTION

Classic major depressive episodes have long been known to demonstrate a very high response rate to ECT [1-3]. However the factors that characterize the minority of depressed patients who do not respond to ECT are less clear. An earlier generation of ECT researchers sought specific clinical correlates of response and non-response to ECT [2, 4]. Contemporary research has generally focused on the issue of treatment of depression with comorbid substance abuse and/or personality disorder, both of which are commonly associated with diminished response to ECT [5, 6]. Clarification of the correlates of nonresponse to ECT- and ultimately an understanding of the reasons for such non-response - would likely inform the ECT consultation process [7].

We report the case of a patient with a history of episodic, severe clinical depression and possible hypomania who demonstrated an apparent absence of response to ECT. His illness was complicated by substance abuse and personality disorder, and his ECT treatment was complicated by Ocular Myasthenia Gravis (OMG). The literature on ECT in depressed patients with personality disorder and with substance abuse is briefly reviewed.

CASE REPORT

The patient is a 37 year old man who was referred to Beth Israel Hospital for severe, medication-refractory depression. He reported a 20-year history of fluctuating depression; a variety of prior mood disorder diagnoses, including Bipolar II disorder; three prior psychiatric hospitalizations; a self-interrupted suicide attempt at age 21; agoraphobia; alcoholism since age 17 with abstinence for the previous four months (since the diagnosis of OMG was made); and sporadic use of marijuana and cocaine. He reported a family history of substance abuse and no other family history of psychiatric illness. He had been depressed since his last hospital discharge one year earlier, and depressive symptoms had become increasingly severe over the preceding several months. Over the prior ten months he had been irregularly attending an addictions group, and meeting monthly with a psychopharmacologist. He had been previously treated with multiple antidepressants and mood stabilizers without response. He was currently receiving fluoxetine 80 mg daily, valproic acid 1000 mg daily, prednisone 20 mg daily, and pyridostigmine 120 mg three times daily.

The patient's social history included several semesters in college, extensive world travel, sporadic jobs in marketing and journalism, five years of disability on the basis of Bipolar Disorder, and minimal contact with his parents and siblings. For the past year he had been living intermittently with a girlfriend.

Psychological testing suggested feelings of loneliness and emotional deprivation, strong dependency needs, expectations that others will fail to meet his needs, and hostility. A diagnosis of Personality Disorder NOS with borderline and dependent features was made.

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Although scheduled for ECT, the patient grew impatient and signed out of hospital against medical advice. Mood was modestly less depressed, and he denied suicidal ideas.

He was readmitted to our hospital one month later complaining of depressed and anxious mood, frequent crying spells, profound loss of interest, anorexia, hypersomnia, social withdrawal, hopelessness, and a wish to die but without suicidal plans or intent. He was treated with valproic acid 1000 mg daily, fluoxetine 80 mg daily, and pyridostigmine 120 mg three times a day, and was scheduled for ECT. This medication regimen was continued throughout the course of ECT.

The first ECT treatment was administered in the operating room in the event that intubation and prolonged ventilator assistance might be necessary [8]. A Mecta spECTrum 5000Q ECT device was utilized, with bifrontal electrode placement and stimulus parameters based on clinical experience and judgment of 1 millisecond, 60 herz, and 3 seconds (288 millicoulombs). Anesthesia and muscle relaxation were achieved with propofol 70 mg (.66mg/kg) and succinylcholine chloride (SCC) 65 mg (.6 mg/kg). A grand mal seizure lasting 35 seconds was obtained. Ventilatory efforts resumed four minutes after SCC injection.

All subsequent ECT treatments were administered in the regular ECT suite without intubation or other extraordinary precautions. Stimulus duration was progressively increased to 6 seconds (576 millicoulombs) and the dosage of SCC was reduced to 40 mg. Etomidate 15-20 mg was substituted for propofol following a short seizure during the 4th ECT treatment, and successive treatments each lasted more than 20 seconds.

Following the 9th ECT treatment, the patient reported no significant improvement in mood, energy or interest. However suicidal ideas were no longer present, and nurses' notes indicated some modest decrease in sadness. He was discharged to home, referred to the mental health clinic for psychotherapy and pharmacotherapy, and scheduled for outpatient ECT (OPECT).

Upon his return for the initial OPECT (ECT#10), the patient reported depressed mood and memory difficulty. Three days later, when seen for OPECT #2 (ECT#11), he was more severely depressed. He acknowledged drinking "4 or 5" drinks a day since his last ECT treatment, and reported the return of suicidal ideas ("I don't want to live anymore"). Following the ECT treatment he reluctantly agreed to be readmitted to hospital. His girlfriend reported that he had begun to decompensate shortly after discharge, with increasing alcohol intake, depressed and irritable mood and social withdrawal.

Over the ensuing nine hospital days, in the absence of additional ECT treatment, the patient's mood gradually improved, and suicidal ideas remitted. The following morning, prior to the resumption of inpatient ECT treatment (ECT #12), he reported feeling well, with normal sleep and appetite, and increased energy and interest. His girlfriend and he had decided to move in together, and had made plans to visit her parents in Arizona. In view of this improvement - which had not occurred in following the prior detoxifications our hospital – we proposed two OPECT treatments following discharge and, if stable, a subsequent course of continuation and maintenance ECT (CMECT).

Two days later, when the patient appeared for OPECT (ECT#13), he was mildly anxious and subdued, and reported being pleased to be home. He acknowledged having had "one glass of wine with lunch yesterday."

The final OPECT (ECT #14) was administered three days later. On this occasion the patient was again very depressed. He denied drinking over the preceding several days except for "one glass of wine with lunch yesterday." The treatment was unremarkable. However in view of the generally unsatisfactory response to ECT, the uncertain role of alcohol abuse, and the deterioration of mood, he was again referred to the emergency room for readmission, mood stabilization and consideration of more extended alcohol rehabilitation and psychotherapeutic treatment.

DISCUSSION

Our patient's unsatisfactory response to an extended course of ECT is most likely explained by his comorbid substance abuse and personality disorder. However the possibilities that he was a true ECT nonresponder (despite symptoms of melancholic depression), or that a more extended course of ECT might have been more effective, cannot be excluded.

Approximately one-third of patients with Major Depressive Disorder present with some type of recent substance abuse disorder. This comorbidity is associated with younger age of onset, male sex, greater depressive symptomatology, a higher risk of suicide, and greater social, personal and occupational impairment [9]. As Davis *et al.* note, differential treatment effects of depression with and without substance abuse (alcohol and/or drug) comorbidity have been

understudied because most patients with such comorbidity are typically excluded from treatment studies [10]. Nonetheless, it is clear that patients with co-occurring mood and substance abuse disorders have a more severe and difficult to treat illness, that both the depression and substance abuse require treatment, and that evidence for best-practice recommendations is lacking [5]. Uncertainty about whether the substance abuse reflects an effort to treat an underlying depression, or the depression is a result of the substance abuse and its impact, suggests that antidepressant treatment be withheld until abstinence has been accomplished, and initiated only if significant depressive symptoms persist [11]. According to American Psychiatric Association guidelines, early use of somatic treatment for comorbid substance abuse and mood disorders is recommended when severe symptoms show no sign of remission after 2 or 3 days, history clearly indicates symptoms of depression preceding substance abuse, or patient has a strong family history of depression [12]. Moreover delaying treatment of a mood disorder in a patient with substance abuse can result in the patient becoming suicidal, manic, paranoid or hopeless about recovery [5].

Although some controversy persists, most studies have reported a decreased response rate in depression with comorbid personality disorder regardless of modality of treatment – medication, psychotherapy, combination treatment and ECT. A retrospective review of 107 inpatients with major depression found that a clinical diagnosis of personality disorder (PD), especially a cluster B PD (borderline, narcissistic, histrionic, antisocial), predicted both a relatively unfavorable acute treatment response and a higher relapse rate in treatment responders during the first year post-ECT [13]. A review of 13 studies of ECT response in patients with comorbid borderline personality disorder concluded, while noting significant methodological weaknesses in available studies, that comorbid personality disorder patients may have poorer outcomes on some measures [14]. A meta-analysis of 32 studies reported a doubling of the risk of poor outcome in depressed patients with comorbid personality disorder [6].

Nonetheless, most studies emphasize that such comorbidity does not indicate that patients with depression and personality disorder should not be treated with ECT. The Sareen *et al.* study [13] reported a response rate of 89% in depressed patients without a PD compared to a 56% response rate in those with a comorbid PD diagnosis, and concluded that many patients with comorbid PD may need more prolonged treatment and/or more broadly based treatment for depression to optimize outcome.

The DeBattista and Mueller review [14] concluded that while depressed patients with comorbid PD may have a poorer outcome on some measures, available data suggest that depression in such patients can be effectively treated with ECT. Similarly, the Newton-Howes *et al.* review [6] concluded that comorbid PD is not necessarily a poor prognostic indicator, and may indicate the necessity of treating both the depression and the personality disorder.

Although our patient's reported lack of a family history of mood disorder contributed to diagnostic uncertainty [15], his history of a severe, episodic mood disorder and a prior suicide attempt, the severity and danger of his current depressive symptoms and of his suffering, and his failure to respond to prolonged and aggressive pharmacologic treatment, rendered a trial of ECT indicated despite the reduced likelihood of response [16, 17]. Simultaneous treatment of mood disorder, substance abuse and character pathology was likely necessary. In such patients, a candid discussion of these facts with patient and family prior to initiating a course of ECT is recommended.

What accounts for our patient's transient improvement during his last readmission and detoxification? He had been detoxified with only very modest improvement during each of his two prior hospital admissions, and had shown minimal response to 11 inpatient ECT treatments. On the other hand, following each discharge his resumption of drinking was associated with acute and severe exacerbation of depression. While the absence of alcohol did not necessarily alleviate depression, its resumption presumably contributed to its worsening. Presumably too, non-specific aspects of hospitalization –including a supportive milieu–contributed to his improvement [18]. Whether life circumstances –the enhanced mutual commitment with his girlfriend – were the cause or result of the transient improvement is unclear but likely plays a role. The possible unreliability of some of the patient's reports – both positive and negative – and other and unknown factors contribute to our uncertainty.

Kraepelin [19] emphasized the heterogeneity of Manic Depressive Illness, and undoubtedly the term "clinical depression" represents a wide variety of conditions which differ in genotype, heritability, pathophysiology, natural course, symptom pattern and responsiveness to treatment. Differences in temperament, life experience, character pathology,

comorbidity, substance abuse and contemporary life stresses likely contribute to differences in treatment responsiveness. Our inability to clearly distinguish mild, moderate and severe mood states, and to ascribe relative importance to the multiple contributing factors in any individual case, confound research and treatment [17, 20-22].

Accordingly, each case of clinical depression may be unique despite considerable overlap of symptoms [23-25]. Genome scans may ultimately allow a distinction between diagnostic categories which respond to our current somatic treatments and those which do not. Meanwhile treatment decisions must be based on a flexible combination of literature guidelines, clinical experience and judgment, and tolerance of the uncertainty which is part of everyday clinical practice [17].

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