ECT in Delusional Depression With Multiple Sclerosis

TO THE EDITOR: ECT has been used effectively to treat major depression associated with multiple sclerosis (1, 2). However, concerns remain that ECT might exacerbate multiple sclerosis by increasing the size and number of plaques and/or periplaque edema (1, 2).

Ms. A, a 51-year-old woman, had her first multiple sclerosis symptoms 7 years ago. A magnetic resonance imaging (MRI) proton-density-weighted axial brain scan performed 1 year later at a specialized center for multiple sclerosis showed ventricular enlargement and several multiple white matter lesions in the right part of the brainstem and bilaterally in the periventricular and subcortical areas.

Five years after the onset of multiple sclerosis, Ms. A was first hospitalized in the psychiatric ward for major depression and responded well to sertraline, 100 mg/day. One year later, a significant deterioration required hospitalization in the neurology ward followed by hospitalization in the psychiatric ward for severe catatonic delusional major depression (DSM-IV-TR) necessitating tube feeding.

ECT was required to obtain rapid improvement in this life-threatening situation. A pre-ECT brain computerized tomography scan showed moderate cortical and subcortical atrophy. ECT stimuli were delivered bilaterally by a Thymatron Tm, DG-100%=504 microcoulomb (brief-pulse) device. Anesthesia was induced with intravenous methohexital (1 mg/kg) followed by intravenous succinylcholine (1 mg/kg) and oxygenation with 100% oxygen. Improvement was seen after the third session and persisted during the subsequent 11 consolidation ECT pulse sessions. Ms. A's total score on the 17-Item Hamilton Depression Rating Scale was 26 before ECT and 10 after ECT. Haloperidol (15 mg/day) was also prescribed.

Neither significant confusion nor memory impairment suggesting the encephalopathic effect of ECT was observed, and there was neither clinical evidence of exacerbation nor remission of neurological multiple sclerosis symptoms. Brain MRI after ECT showed no change compared to the first MRI performed before ECT. Three months later, Ms. A was still in remission while being treated with venlafaxine, 100 mg/day, and haloperidol, 5 mg/day.

This case report shows rapid significant improvement after ECT for severe life-threatening catatonic delusional major depression in a patient with multiple sclerosis. No neurological deterioration was shown after ECT.

To our knowledge, only four case reports have been published regarding patients with multiple sclerosis treated with ECT for depression and with MRIs before and after ECT. Three reports, one with six right unilateral pulse (1), a second with nine right unilateral pulse, and a third with 10 bilateral pulse (2), reported efficacy without any neurological adverse effects, while one (six with a right unilateral pulse) (2) reported significant neurological deterioration.

In conclusion, a high bilateral ECT pulse rate was not found to be associated with a greater risk of neurological deterioration in the treatment of major depression with multiple sclerosis when it is well tolerated by the patient.

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Excretion of Quetiapine in Breast Milk

TO THE EDITOR: To our knowledge, there is no published report regarding the excretion of the antipsychotic agent quetiapine into breast milk. In this case report, we describe what we think is the first account of measuring quetiapine levels in breast milk.

Ms. A, a 36-year-old woman (92.5 kg, gravida one, para one), contacted our program after the birth of a full-term male infant. She was taking 200 mg/day of quetiapine throughout pregnancy and wished to continue treatment and to breast-feed her infant. Because no previous measurements on the excretion of quetiapine in breast milk existed in the published literature, Ms. A and her physician decided to feed the infant formula until breast-milk measurements were available. Written informed consent was obtained from Mr. A after the procedures had been fully explained.

Manually expressed breast-milk samples were collected over a 6-hour period at 3 weeks postpartum. Samples were obtained just before quetiapine dosing and again at 1, 2, 4, and 6 hours postdose. Samples were kept frozen at –20°C until analysis. The breast-milk samples were centrifuged at 8,000 rpm. The infranatant was extracted with heptane/isoamyl alcohol (98.5/1.5) at alkaline pH. The solvent extract was dried off and reconstituted with phosphate buffer (pH=2.5), and the solution was washed twice with heptane. High-performance liquid chromatography analysis was performed by using 150 mm of C18 column Kromasil (Chromomatography Sciences Company, Inc., Montreal). The mobile phase consisted of a phosphate buffer (pH=2.5) containing acetonitrile (25% vol/vol) and methanol (19% vol/vol). Quetiapine was measured by using photodiode array detection, and the linear calibration curve ranged from 2–500 μg/liter.

The area under the curve of quetiapine in breast milk from time 0 to 6 hours was calculated by using the trapezoidal method. The elimination half-life of quetiapine in breast milk was calculated by using the log-linear elimination phase of the drug. The daily amount of quetiapine ingested by a nursing infant was calculated by assuming that an infant ingests 150 ml/kg/day of breast milk and by using the average milk concentration of quetiapine over 6 hours. The maximum amount an infant will ingest was calculated based on the highest milk concentration.

The average milk concentration of quetiapine over the 6 hours was 13 μg/liter, with a maximum concentration of 62 μg/liter at 1 hour. Levels of quetiapine rapidly fell to almost predose levels by 2 hours. Therefore, an exclusively breast-fed infant would ingest only 0.09% of the weight-

adjusted maternal dose. At maximum, the infant would ingest 0.43% of the weight-adjusted maternal dose.

Upon receiving the results of levels in the breast milk, the woman began breast-feeding exclusively at 8 weeks after delivery. Follow-up of the infant at 4.5 months indicated that the infant was developing well, and no adverse effects of quetiapine were reported.

Although more studies are required to confirm our findings, the level of infant exposure to quetiapine in breast milk appears to be too small for significant pharmacological effects.

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Neuroacanthocytosis

To the Editor: Neuroacanthocytosis, also known as choreoacanthocytosis, denotes a heterogeneous group of diseases that are characterized by CNS abnormalities in association with blood dyscrasia (1, 2).

Neuroacanthocytosis is a rare movement disorder marked by progressive muscle weakness and atrophy, progressive cognitive loss, chorea, and acanthocytosis (spiked RBCs). Other symptoms may include facial and vocal tics, uncontrolled muscle movement, progressive gait instability, seizures, self-injury of the tongue and lips, and changes in personality (3). It is associated with atrophy and neuronal loss within substructures of the basal ganglia, particularly within the caudate nuclei, the putamen, and the globus pallidus (4, 5).

The disorder may be confirmed by tests demonstrating over 15% of RBCs with acanthocytes or abnormal circulating RBCs that have thorny projections. In addition to RBC acanthocytes, creatine phosphokinase and serum transaminases can be markedly elevated (6).

This disease has been reported in several ethnic groups, but epidemiological data are insufficient to report prevalences. This neurodegenerative disorder is usually inherited as an autosomal recessive trait linked to chromosome 9q21 (7). Symptoms typically become apparent between the ages of 25 to 45 years. Disease progression is poorly understood, and no cure exists. Reported causes of death include the following: emaciation due to progressive weakness, dysphagia, and tracheobronchial aspiration (8).

Ms. A was a 33-year-old woman who was admitted to the general medical hospital for rhabdomyolysis. She had been diagnosed with neuroacanthocytosis 4 years earlier in a university setting. She had continuous, uncontrolled, and rapid involuntary movements; a heart rate of 132 bpm; a WBC count of 13.1/mm^3; and a creatine phosphokinase level of 35673 U/liter. She arrived at the hospital taking 5 mg t.i.d. of diazepam, 0.5 mg t.i.d. of benztropine mesylate, and 0.5 mg of haloperidol, as needed for agitation.

We recommended that she be placed into an intensive care unit and intubated. Molindone hydrochloride, 50 mg t.i.d., was introduced; diazepam, benztropine mesylate, and haloperidol were discontinued. After 5 days of taking propofol and with ventilator support, Ms. A's creatine phosphokinase level had fallen to 911 U/liter. Ms. A was extubated on day 8 when her creatine phosphokinase level was 876 U/liter. On day 9, the molindone hydrochloride was titrated to 100 mg t.i.d. On day 11, divalproex sodium, 250 mg t.i.d., was introduced. Upon discharge on day 14, Ms. A's creatine phosphokinase level was 794 U/liter.

The combination of molindone and divalproex was effective in reducing her extreme involuntary movements. Ms. A was calm, alert, aware, conversant, and oriented to the clinical setting, her age, the month, and the year. She regained some level of independent function in her upper extremities and was able to ambulate on a treadmill for brief periods. Upon discharge, her parents took her to their home.

Treatment for this disorder is symptomatic and supportive. Maintenance of proper nutrition is a challenge. A feeding tube may be needed for some patients as the disorder progresses. Antipsychotic drugs can provide stage-dependent relief from chorea and tics. Benzodiazepines may be used to reduce anxiety and diminish the intensity of movement disorders.

Neuroacanthocytosis is a progressive disease. It is usually fatal, the result of symptoms that contribute to pneumonia, cardiomyopathy, and nutritional deficiencies. Life expectancy following the onset of moderate symptoms is typically 5–10 years. However, the life span may be near normal for patients with no prominent neurological or cardiac complications (9).

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Modafinil Augmentation of Phenelzine for Residual Fatigue in Dysthymia

To the Editor: Monoamine oxidase inhibitors (MAOIs) are sometimes required to treat refractory depressive disorders (1). Although effective, they require careful attention to concomitant medicines and foods to avoid a hypertensive crisis or other severe reactions (2, pp. 2557–2559). Modafinil is an agent used to promote wakefulness in patients suffering from excessive daytime somnolence (2, pp. 1160–1162). Most patients with depression complain of fatigue even after antide-