Febrile Reaction With Elevated CPK After a Single Electroconvulsive Therapy (ECT) in an Adolescent Patient With Severe Bipolar Disorder

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Abstract: This report describes the electroconvulsive therapy (ECT) course of a 15-year-old male with severe bipolar disorder unresponsive to medical management. After his first treatment, the patient exhibited fever, elevated creatine phosphokinase levels, and leukocytosis. Treatment was halted although the patient reported an improvement in symptoms, which was not maintained with pharmacotherapy alone. Subsequent treatments were completed without adverse reactions, and the patient entered remission. We discuss the possible causes of this reaction and remind the reader that a single adverse event does not always require the abandonment of a treatment modality.

Key Words: ECT, adolescent, bipolar disorder, fever, CPK, creatine phosphokinase, leukocytosis

(*J ECT* 2012;28: 70–71)

Dear Editor:

The literature on pediatric and adolescent patients consists primarily of case reports, and there are few data regarding complication rates or the development of untoward reactions to ECT. In one report, an adolescent patient developed an elevated creatine phosphokinase (CPK), with signs and symptoms suggesting neuroleptic malignant syndrome after her first ECT session; and the decision was made to abandon further treatment with ECT.[1] We report the development of a febrile reaction with leucocytosis and elevated CPK values after a single ECT session in an adolescent patient with severe bipolar disorder who subsequently completed an acute course of ECT without further complication, suggesting that a single adverse event does not always require the abandonment of a treatment modality.

In this case, a 15-year-old 50-kg male with a history of severe bipolar disorder since age 12 was referred for electroconvulsive therapy (ECT) after failure to control his symptoms with numerous medications and hospitalizations over a 3-year period. The initial ECT treatment was performed at another institution. The patient was premedicated with glycopyrrolate, and general anesthesia was induced with etomidate followed by succinylcholine for muscle relaxation. Immediately after the procedure, he developed fever, cough, headache, chills, and rigors. Total white blood cell count (WBC) at that time was 19.9, and CPK was 1100. Because the initial treatment was performed at a freestanding clinic, the patient was taken to the emergency department of a children's hospital where he was admitted for observation. At that time, the chest x-ray was clear; and symptoms had completely resolved by 24 hours. For approximately 1 week after the initial treatment, the patient's parents reported significant psychiatric improvement, suggesting that the ECT treatment was helpful.

Despite the family's desire for their son to continue with this treatment, the clinic where ECT had been performed refused to do so. Despite resumption of medical therapy, the patient continued to have severe mood swings alternating between manic behavior and depression, with each phase lasting for hours or days. Subsequently, he was referred to our institution for evaluation and continuation of ECT. Four months after his initial treatment and after extensive review of his case by our institution's ethics committee and the departments of psychiatry and anesthesiology, the patient received his second ECT treatment in what would go on to be an immediate course of 21 treatments administered over a period of 2 months.

The patient received no premedication before the first ECT treatment at our institution. General anesthesia was induced with propofol, and muscle relaxation was achieved with succinylcholine. Pretreatment WBC count and CPK value were $8.3 \times 10^3/\mu L$ and 124 U/L; posttreatment WBC count and CPK value were $7.6 \times 10^3/\mu L$ and 110 U/L. The patient did not experience any febrile reaction or require any medical treatment for hypotension or hypertension but did develop significant postprocedural nausea. For all subsequent treatments, the patient was premedicated with ondansetron; these 20 additional ECTs were uneventful and well tolerated. At the end of the course, the patient was substantially improved, with markedly better control of mood symptoms than had been achieved in the previous 2 years.

Several etiologies for our patient's initial presentation of fever, leukocytosis, and elevated CPK values after the initial ECT session are possible. Although neuroleptic malignant syndrome and malignant hyperthermia were both initially considered, he did not exhibit any other signs or symptoms suggestive of either reaction. Consultants at both the children's hospital and our institution felt that the observed elevation in CPK was likely due to the ECT and not a reaction to the depolarizing muscle-relaxing agent. Because he received a higher dose of succinylcholine on all of his subsequent treatments (during which a satisfactory neuromuscular block and no subsequent elevation in CPK was noted), it is possible that the elevation in CPK noted in the initial treatment resulted from a less-than-adequate muscle relaxation. Etomidate can also cause transient skeletal muscle movements in approximately 30% of patients, primarily myoclonic movements, which could explain the elevation in CPK, which was not observed when propofol was used to induce general anesthesia for all subsequent treatments. Whereas aspiration could explain the transient fever and leukocytosis, negative physical signs and an unremarkable course coupled with a negative chest x-ray suggest that this is not likely.

The enzyme CPK is found in myocardium, skeletal muscle, brain, and the gastrointestinal tract. Elevated serum measurements of CPK isoenzymes due to release from damaged tissue can be

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The authors have no conflict of interest to declare. Support was provided solely from institutional and departmental sources.

DOI: 10.1097/YCT.0b013e31823dfeb0

used as a marker for specific events such as brain injury (CPK-BB)[2] or myocardial infarction (CPK-MB),[3] and have also been reported in convulsive disorders and after ECT.[4] In the case of serum elevations of CPK after ECT, it is the total CPK that is elevated. Elevations of isoenzymes specific for myocardial infarction are typically not observed during ECT without concurrent damage to the myocardium, even in patients with documented coronary artery disease and prior infarction.[5] Brain-type CPK (CPK BB) is also not released into the circulation in appreciable quantities during ECT, suggesting that ECT does not cause actual injury to the brain or alterations in the blood-brain barrier.[2]

Despite recommendations from the American Psychiatric Association Task Force on Electroconvulsive Therapy that ECT is an acceptable procedure for use in adolescents with severe psychiatric disorders, most of the treatments administered each year involve adult patients. Historically, the use of ECT in patients younger than 18 years has been limited by lack of experience with pediatric patients. The existence of legislative prohibitions on using the procedure in patients younger a certain age in some states and an unsubstantiated fear of causing damage to the developing brain may have played a role in the decision to refuse further treatment to this patient after his unexpected response to the initial session. After careful consideration of the alternatives, and after a rigorous informed consent process, the patient and his family decided to continue treatment with ECT. This led to a safe resolution of his symptoms.

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