

Benign Recurrent Febrile Reactions Induced by Electroconvulsive Therapy in an Adolescent Chinese with Catatonic Schizophrenia: A Case Report

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Abstract

Electroconvulsive therapy is a widely practiced, safe and effective treatment for severe mental illness. A febrile reaction induced by electroconvulsive therapy is rarely reported as an adverse effect. We present a 15-year old Chinese girl with first episode catatonic schizophrenia who developed recurrent febrile reactions after electroconvulsive therapy. Vigilant clinical monitoring and laboratory tests are necessary in the management of these cases. The natural course of fever, clinical characteristics and suspected risk factors of this case were discussed.

Keywords: Electroconvulsive therapy; Catatonic schizophrenia; Cerebral palsy; Febrile reactions

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Introduction

Electroconvulsive therapy (ECT) has been used for decades for the treatment of psychiatric disorders. Despite controversies on the potential risks incurred, as well as stigmatisation associated with negative depictions of the procedure in the mass media, ECT remains the recommended [1] and one of the most effective treatments for severe depressive illness, prolonged or severe episodes of mania, and catatonia. The procedure has been demonstrated to be equally effective and safe in children as much as in adults [2]. Common side effects of ECT include headache, memory problems, confusion and muscle aches [3]. Febrile reactions after ECT has rarely been reported in the literature. To date, there have only been a few case reports on fever after ECT for the treatment of bipolar disorder [4-6] and depression [7]. Among them, two cases were associated with organic brain conditions, namely cerebral palsy [4] and learning disability [6]. We report a case of recurrent febrile reactions after ECT for the treatment of catatonic schizophrenia in an adolescent girl with history of cerebral palsy.

Case report

The patient was a 15 year-old Chinese girl who suffered from

first-episode catatonic schizophrenia. At the age of six, she was diagnosed with cerebral palsy which resulted in persistent contraction of the tibialis anterior muscle and pes planus. At that time, magnetic resonance imaging (MRI) scan showed normal brain structures. Her IQ had not been assessed, but there was no reported developmental delay. She had no other medical illness. She had no past or current history of alcohol or substance abuse.

On presentation, the patient had auditory hallucinations, referential and persecutory delusions, and complained of being stared at by a pair of green eyes. She was prescribed with risperidone 0.5mg daily. However, she developed catatonic symptoms within two weeks, including mutism, waxy flexibility (pillow sign), anxiety, perplexity and poor oral intake. As a result, she was admitted to a regional psychiatric hospital.

Investigations including complete blood picture, liver and renal function tests, electrocardiogram (ECG), chest x-ray (CXR) and electroencephalogram (EEG) showed normal findings. Urine toxicology was negative for illicit substances. The dosage of risperidone was increased gradually to 4mg daily. Lorazepam 3mg daily was given with limited effect.

In view of the persistence of catatonic symptoms, ECT was started after 20 days of admission. Prior to the ECT, the patient had been afebrile since admission. The ECT was carried out by a psychiatrist, an anaesthesiologist and psychiatric nurses in a well-equipped ECT suite. ECT was delivered with general anaesthesia and muscle relaxant twice weekly. We used 0.3 ms ultra-brief pulse width with bitemporal placement. Table 1 shows the details of the treatment parameters of all the ECT sessions.

In the first session of ECT (Day 1), we used the dose titration method to estimate the patient's seizure threshold. Propofol was used as the induction agent for all ECT sessions. Atracurium was given as the muscle relaxant for the first session. Five hours after the first session of ECT, the patient developed high fever with a tympanic temperature of 38.9 degree Celsius. There were no localising signs or symptoms of infection, but laboratory findings revealed an elevated white blood cell count of 14.6 (reference range 3.9-10.7 $10^9/L$), neutrophil count of 13.0 (2.1-7.8 $10^9/L$), and serum bilirubin level of 18 (2-12 $\mu\text{mol/L}$). The assays for amylase, creatinine phosphokinase (CPK), and troponin-I were within normal range. Urine culture found no growth of bacteria. Computer tomography (CT) scan of the brain performed on Day 2 showed no intracranial lesions and CXR showed no signs of infection. We empirically prescribed amoxicillin/clavulanic acid 375mg three times daily for five days (from Day 2 to Day 7) and she took paracetamol from Day 1 to Day 4. The second session of ECT, originally scheduled on Day 4, was suspended pending workup for the fever. The fever subsided completely on Day 5.

The second session of ECT was conducted on Day 8. Mivacurium was used as the muscle relaxant in this session. The stimulus dosage was stepped up to 1.5 times of the seizure threshold determined at the last session. Seven hours after the ECT, the patient developed recurrent fever with a tympanic temperature of 38.9 degree Celsius. She also complained of cough and sore-throat. Throat swab was negative for bacterial growth. We repeated a CXR and found no signs of aspiration pneumonia. We empirically prescribed another antibiotic, clarithromycin 250mg twice daily for seven days (from Day 8 and Day 15). She took paracetamol 500mg on Day 8 and Day 10. Her fever subsided on Day 11.

The third session of ECT was conducted on Day 11 with the same stimulus dosage as the second session. Suxamethonium was used as the muscle relaxant. The patient remained afebrile after this session.

The fourth session of ECT was conducted on Day 15 with the same stimulus dosage and the same muscle relaxant. She developed recurrent fever with a tympanic temperature of 38.8 degree Celsius. Laboratory findings showed a raised white blood cell count of 17.5 (3.9-10.7 $10^9/L$) and a neutrophil count of 15.4 (2.1-7.8 $10^9/L$). C-reactive protein was mildly elevated at 5.8 (<5mg/L). Liver and renal function tests and lactate dehydrogenase (LDH) levels were normal. Two doses of paracetamol 500mg were given. The fever subsided on Day 16. **Figure 1** summarises the pattern of fever, administration of ECT and the use of antipsychotics and antibiotics.

Further ECT treatment was stopped after the fourth session since there was complete resolution of catatonic symptoms and reduction in auditory hallucination. There had been no recurrence of fever. The patient was discharged from hospital on Day 19. She was maintained on olanzapine 10mg daily, propranolol 20mg daily and benzhexol 4mg daily.

Discussion

The differential diagnoses for patients with catatonic schizophrenia presenting with fever include (i) concomitant infection; (ii) catatonic symptoms ranging from mild temperature fluctuation to lethal catatonia; (iii) neuroleptic malignant syndrome (NMS); and (iv) benign fever induced by antipsychotic agents, particularly clozapine. However, these possible causes are unlikely to account for the occurrence of recurrent fever in our patient, in view of the absence of localising signs of infection, negative findings in CXR, urine and swab culture, normal CPK and LDH, and the absence of other essential features suggesting lethal catatonia or NMS. Olanzapine-induced fever could be a rare adverse effect but compared with clozapine, olanzapine has much lower immunomodulatory potency on interleukin-6, which is raised in patients with clozapine-induced fever [8].

More interestingly, there appears to be a temporal relationship between the delivery of ECT and the occurrence of fever in our patient. There are a few case reports of ECT-induced fever in the literature. The common characteristics in most of these reports involve patients who were adolescents or young adults, and two of them had organic brain conditions, namely cerebral palsy and intellectual disability [4, 6], which is compatible with our patient's profile. In all of these cases, ECT could be continued without any physical complications. It has even been suggested that ECT-

Table 1 Treatment Parameters and Fever Characteristics.

Treatment No.	Stimulus Power (mC)	Propofol (mg)	Atrophine (mg)	Neostigmine (mg)	Atracurium (mg)	Mivacurium (mg)	Suxamethonium (mg)	Peripheral Seizure Duration (s)	Fever (Degree of celsius)	Onset of Fever (Hour After ECT)	Duration of Fever (Hours)
1	9.6 then 19.2	60	0.96	2	10	-	-	0/33	38.9	5	72
2	48.0	60	-	-	-	3	-	43	38.9	7	24
3	48.0	60	-	-	-	-	20	17	36.4	-	-
4	48.0	60	-	-	-	-	20	45	38.8	7	4

ECT Machine: MECTA Spectrum 5000Q Stimulator with ULTRABRIEF 0.3ms Pulse Width Option (Mecta Corp., Lake Oswego, OR)

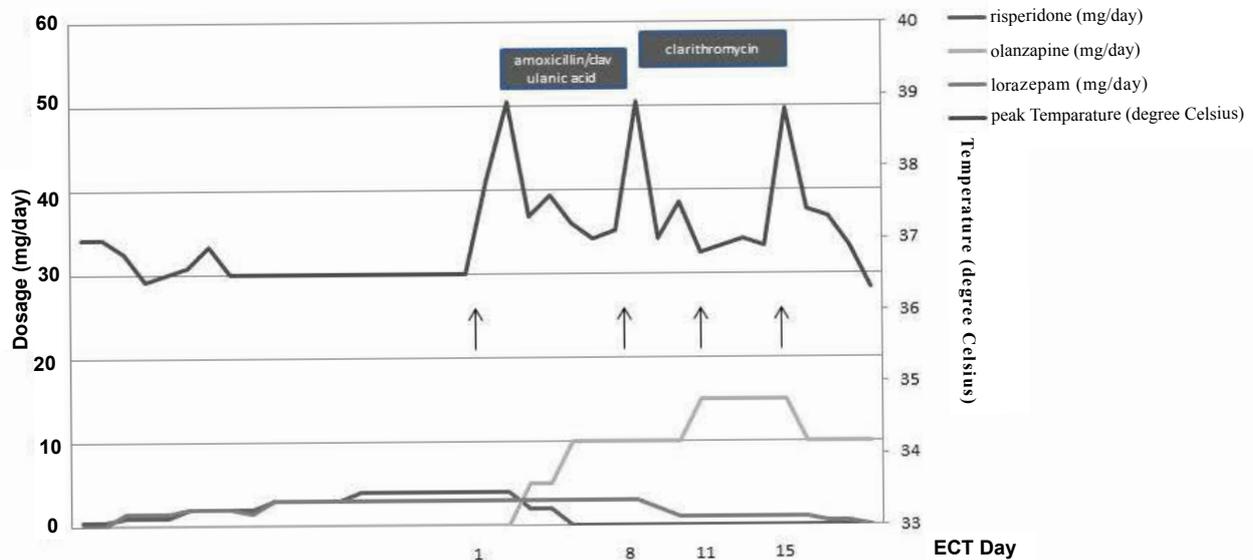


Figure 1 Change in body temperature during ECT and medication titration.

induced fever could be associated with symptom improvement [7].

The exact mechanism of how ECT induces febrile reactions is unclear. Complications associated with the use of general anaesthesia have to be considered. It is possible that anaesthetic agents may induce febrile reactions. Propofol had been used in our patient for each session of ECT as the induction agent. There have been reports of fever associated with the use of propofol [9]. Bacterial contamination [10] has been proposed but is considered unlikely in this case, because other patients who received the same anaesthetic agents for ECT in the same session as our patient did not develop any febrile reactions. Malignant hyperthermia triggered by other anaesthetic agents, suxamethonium in particular, is also possible. However, associated features such as muscle rigidity, rhabdomyolysis or elevated CPK were absent in our patient. Besides, our patient developed two febrile episodes even before suxamethonium was used. Other common causes of post-anaesthetic fever, including aspiration pneumonia, intravenous access site infection, or deep vein thrombosis had been ruled out in our patient.

It has been postulated that electrical stimulation of the brain could induce febrile reactions. However, the pathophysiology remains unclear. One postulation is derived from reports of febrile

reactions after spontaneous seizures [11, 12], which may be explained by ictal involvement of the hypothalamus [13], where the thermoregulatory centre is located. Innate immune reaction with production of pyrogens [14] after electrical stimulation could result in febrile reactions. We speculate that subtle brain lesions in the periventricular area may have been present in our patient leading to diplegic cerebral palsy. The existing brain insult might have promoted seizure progression or enhanced the sensitivity of the hypothalamus. This postulation is consistent with the two previous case reports [4, 6] on patients with organic brain conditions who developed post-ECT fever.

In summary, our case report illustrates a rare but important adverse effect of ECT. Although we do not consider cerebral palsy or other organic brain conditions as contraindications to ECT, we recommend vigilant monitoring of clinical and vital signs after ECT in this subgroup of patients. We believe that ECT remains one of the most effective treatment modalities for psychosis, in particular for those with catatonia. For cases with suspected benign recurrent fever induced by ECT, thorough investigations should be carried out to rule out other causes of fever. Neurochemical changes in the thermoregulatory centre associated with electrical stimulation may be a possible mechanism for fever associated with ECT.

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