RECURRENT SELF-LIMITED HYPERTHERMIA FOLLOWING ELECTROCONVULSIVE THERAPY

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To the editor,

Electroconvulsive therapy (ECT) is an effective and safe treatment for severe mental disorders, when it is implemented under an adequate surveillance. Its most frequently described side effects are anterograde amnesia, mania, post-ictal confusion, nausea, headache, myalgia, oral lacerations and dental injuries. Moreover, cardiac and respiratory complications can occur which are usually mild and they correlate with patient's age and previous comorbidities[1]. Fever has not formally been described as a side effect of ECT so far. However, some rare cases of transient hyperthermia after ECT have been previously reported[2,3,4]. Therefore, we consider of interest the case-description of a patient recently treated in our ward who presented two episodes of transient, recurrent and self-limited hyperthermia, after receiving ECT sessions.

Case report

This is a 42 years-old male diagnosed of type I bipolar disorder at the age of 15, and previously admitted to hospital for a delusional-hallucinatory episode with exalted mood. During the course of his illness, he had suffered depressive and hypomanic episodes with no need for further hospitalizations. Lithium was removed years before due to the patient's intake refusal, maintaining clinical stability under the treatment with aripiprazole 10 mg/day. At the time present, our patient was being treated with such dose of aripiprazol. Besides his major psychiatric illness, he was diagnosed of acute lymphoblastic leukemia (ALL) bcr/abl negative, almost 3 years prior to the recent hospitalization.

The actual hospital admission was motivated by a new manic episode with severe psychotic symptoms. Treatment with aripiprazole was maintained with a dose increase of up to 25 mg/day for three weeks and treatment with olanzapine was started at a dose of up to 20 mg/day for two weeks. However, there was still persistence of prominent delusional, hallucinatory and manic symptomatology. He did not tolerate risperidone at a dose of 3 mg/day due to extrapyramidal symptoms. Furthermore, during hospitalization, he was receiving maintenance treatment for ALL with methotrexate 20 mg/, ursodeoxycholic acid 450 mg/day and mercaptopurine 50 mg/day. Due to torpid course in terms of psychopathological symptoms, we decided to prescribe electroconvulsive therapy.

In the first ECT session (MECTA SPECTRUM 5000Q stimulator) a charge of 96 mC was administered in the bifrontotemporal position and the patient convulsed for 101 seconds. In order to achieve sedation and muscle relaxation, the anesthesiology team administered 16 mg of etomidate and 75 mg of succinylcholine. During the first 4 hours after the administration of ECT session, the patient presented an episode of fever (38.9ºC, 101.66 ºF), accompanied by shivering, sweating and tachycardia. In terms of blood analysis, he did not display either leucocytosis or elevation of CK. Fever ceased in less than 12 hours under treatment with 1gr of acetaminophen. Neither the clinical examination nor the complementary tests evidenced any abnormalities that suggested an infectious etiology of the episode. A second ECT session was applied three days later, in which a charge of 86.4 mC was administered in the bifrontotemporal position, leading to a convulsion of 87 seconds. The anesthesiology team administered 22 mg of etomidate and 80 mg of succinylcholine. The patient presented another episode of hyperthermia post-ECT session (38.7ºC, 101.66 ºF) of similar characteristics to the previously described.

The Internal Medicine department carried out an extensive study in search of the hyperthermia etiology that included a physical exam and several complementary tests: blood analysis (hemogram, biochemistry, coagulation exams), microbiology test (blood and urine cultures) and a chest

x-ray. None of them showed any abnormalities. Moreover, the neurology department discarded any concomitant neurological pathology after an exhausted physical exam, a lumbar puncture and both a CT-scan (computed tomography scan) and a MRI (magnetic resonance imaging). Finally, the Haematology department dismissed a ALL (acute lymphoblastic leukemia) recurrence or any other haematologic conditions taking into account the previously described complementary test.

After the second ECT session, our patient suffered a remarkable psychopathological improvement. Therefore, after an exhaustive case-review, we decided to finalize the administration of ECT and we started treatment with lithium 800 mg/day associated with olanzapine 20 mg/day, He experienced excellent therapeutic response during the follow-up visit and he did not present any other episode of hyperthermia during hospitalization.

DISCUSSION

Hyperthermia is not a commonly described side effect of electroconvulsive therapy and, consequently, its presence raised some questions about its different possible etiologies. At first, we needed to exclude an infectious etiology, such as aspiration pneumonia during the administration of ECT. However, the self-limitation of the episode and the absence of abnormal results in the different complementary tests made the infection an unlikely hypothesis. Reviewing scientific literature, we overcame old case reports of fever after convulsions[5]. Nevertheless, to our knowledge, no other episodes of fever after administration of ECT were reported until the last decade[2,3,4]. That is the reason why we carried out an extensive differential diagnosis and we consider the hypothesis of neurogenic fever induced by ECT.

In order to carry out such differential diagnosis, we had to exclude the possibility of malignant hyperthermia after the administration of ECT[6]. During every ECT session, drugs such as etomidate (16 mg) and succinylcholine (75 mg) were used, the latter being described as an anesthetic drug that participates in the etiopathogenesis of such syndrome. However, the absence of temperature above 40ºC, muscular stiffness and myoglobinuria, besides normal values of CPK, made such diagnosis highly unlikely[7]. Moreover, fever itself has not been described as a side effect of neither of the drugs mentioned above[8,9].

As another possible etiology of hyperthermia after ECT administration, we consider the neuroleptic malignant syndrome. The absence of extrapyramidal syndrome, elevation of CK, dysautonomia or changes in the level of consciousness, as well as the absence of any similar previous medical history, made it highly unlikely[10].

Due to the fact that the fever could be caused by a relapse of his haematological disease, we consulted to haematology department. After reviewing the case, they dismissed the possibility that the fever could be caused by an ALL relapse or any other haematological condition. Moreover, in order to prevent an immunosuppressive condition in a patient that was being studied by a febrile episode, they decided to withdraw the treatment with methotrexate y 6-mercaptopurine, since the patient was only lacking one month in order to finalize the complete treatment and since he had experienced a completed remission of ALL. Likewise, our patient was studied by the neurology department, which carried out different complementary imaging tests (CT scan, MRI). Such tests did not show any abnormalities that could justify neither the psychopathological course nor the patient's fever.

After having excluded all the different etiologies described above, and according to the evident temporary relation between the administration of ECT and the fever episodes, we consider the possibility that ECT could induce such episodes. Until the present time, the mechanism by which ECT could cause hyperthermia has been poorly studied. After the review of the previously described cases, we acknowledged the interruption of the hypothalamic thermoregulation centre by the electric currents generated during ECT, as a possible explanation of the febrile episodes[3]. The thermoregulation centre resides in the anterior hypothalamus, more specifically in the pre-optic hypothalamic region. Such region avoids temperature elevations. There is evidence that ECT administration modulates the hypothalamus and the autonomic nervous system (ANS). ECT firstly leads to an activation of the parasympathetic system for 10-15 seconds, followed by a sympathetic discharge of 5-7 minutes duration. It is known that a sympathetic discharge could lead to a transient temperature rise[11], which could explain a transient episode of fever. However, in our case, the fever episode extended for hours (<12 hours). This prolonged episode could be explained if we assume that during the administration of ECT we can produce small lesions in the pre-optic hypothalamic region, which could prevent our brain from being able to correctly thermo-regulate the temperature rise mentioned above. This hypothesis is also reflected in several case-reports similar to ours[3,4].

Likewise, it could be of interest to underline that recent multicentric studies with a great sample size have published anatomic alterations in such cerebral area in patients diagnosed with bypolar disorder[12]. Although a correlation between such alterations and the development of hyperthermia after ECT sessions has not been published, we would like to remark that some clinical cases similar to ours have been described in the scientific literature. Furthermore,

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it is possible that similar clinical manifestations have been occurring to patients under ECT treatment that are not being reported to the scientific community. Therefore, it could be convenient to evaluate the risk of such clinical manifestations in patients with bypolar disorder that are being treated with electroconvulsive therapy.

CONCLUSION

In summary, fever is not a frequently described side effect of electroconvulsive therapy. However, some episodes of fever have been reported after the administration of ECT. Therefore, our experience may suggest that ECT could rarely lead to transient hyperthermia episodes without severe impact on the patient. Nevertheless, prior to assuming ECT as the cause of the fever episodes, it would be advisable to discard other potentially life-threatening conditions for the patient. In the presence of hyperthermia, we should exclude infections, central conditions such as malignant hyperthermia, neuroleptic malignant syndrome and other intercurrent diseases, such as a relapse of our patient's ALL. Taking this into account, it is highly important to individualize the study of the patient and the decision of continuing or discontinuing ECT.

Conflicts of interest

The authors declare that they have no conflicts of interest in relation to this manuscript.

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