

Case report

Olanzapine and ECT combined therapy in a refractory catatonic subtype schizophrenia patient with previous neuroleptic malignant syndrome episodes

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INTRODUCTION

This is an objective clinical report carried out with information obtained with the patient's family and registered in the patient's record. The study comprises the patient's clinical history and the treatment provided to an adult male patient with catatonic schizophrenia refractory to typical neuroleptic drugs (haloperidol and chlorpromazine) and to another typical agent (risperidone) with two antecedents of neuroleptic malignant syndrome (NMS). The authors' treatment of choice was electroconvulsive therapy (ECT) and olanzapine (7.5 mg), which brought considerable benefits to the patient. The association between ECT and an antipsychotic in the control of refractory schizophrenia is reported in the literature. Our goal is to share an effective and safe therapeutic experience in a case that had a high risk for NMS development.

CASE REPORT

Patient: A 35-year-old single male patient, Caucasian, natural from Presidente Prudente (a town in the state of São Paulo, Brazil), follower of the evangelical church.

History of current disease: The patient was referred to the *Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo* after going to a secondary hospital in his town. He presented with a catatonic status for 15 days characterized by an intense negativism, refusal to eat and mutism, as well as brief episodes of sudden psychomotor agitation and accelerated and uninterrupted speech, when he was hostile to his family and care givers.

Previous hospital and drug therapy history His first hospital stay was in 1992, when he was 23 years-old, and suffered with alcohol dependence. He escaped from hospital after 4 days. He was hospitalized five times in a period between 1996 and 2002 for heteroaggressiveness and alcohol dependence. He had NMS after taking oral haloperidol in 2002, when his axillary temperature reached 41 °C and the creatine phosphokinase enzyme (CPK) was 4,303 u/L. He was discharged from hospital after 32 days with a stable psychotic status, persistent abulia and socially withdrawn. In 2003 he arrived at the hospital again, escorted by policemen. He was wearing superman clothes

and was extremely aggressive and agitated. As reported by physicians, he talked to himself, had visual, auditory and persecutory delusions that alternated with delusions of grandness. He was administered an ampoule of intramuscular chlorpromazine, carbamazepine 600 mg/day, risperidone 1 mg/day and diazepam 20 mg/day due to the hypothesis of paranoid schizophrenia. The patient developed malignant hyperthermia and extrapyramidal symptoms, requiring a 2-week intensive therapy. He was discharged after 53 days in good clinical conditions except for motor sequelae (forearm and hand extensor deficits) that persist until today. He presented delusive and delirium symptoms refractory to several psychopharmacons administered in therapeutic doses and adequate time, such as haloperidol, levomepromazine, risperidone, valproic acid and phenobarbital. Drugs were administered by the legal responsible (brother) and nurses, therefore, non-compliance was discharged.

Personal antecedents and habits: He was born from normal delivery at term, with satisfactory neuropsychomotor development. He studied up to class 6 with many difficulties, after repeating 2 years. He had a few friends and no girlfriend during childhood and adolescence. He said he had some occasional heterosexual relationships. At the age of 18 he started to work as a bricklayer but he was never financially independent. At that time he dressed in a punk style and started to drink alcohol and smoke tobacco frequently. During his adolescence he sporadically tried marijuana, cocaine and “mushroom tea”.

Family history: There is history of alcoholism, depression and mental retardation in first-degree relatives.

Psychic examination on admission (May 2004): Mutism; passive negativism; blunt mood, hypomodulant; hypokinesia and serum flexibility.

Clinical and neurological examination: Muscle atrophy and both upper limb extensors deficit. Other aspects were within the boundaries of normal behavior.

Lab tests: No relevant findings.

Imaging examinations: Magnetic resonance imaging of the brain (axial sequential techniques T1, T2, FLAIR, sagittal T1 and postgadolinium) showed sulci between the cortical gyri of the frontal lobe and the sylvian brain fissures compliant to a chronic degenerative process.

Diagnostic hypothesis: 1) Paranoid/catatonic refractory schizophrenia; 2) Catatonic syndrome; 3) Smoking; 4) Alcohol dependence (for 8 years); 5) Development of dementia process (alcoholic?); 6) History of NMS (two episodes with motor sequelae).

Progression during hospital stay: Carbamazepine 800 mg/day prescribed in the service of origin was suspended, and lorazepam 12 mg/day was administered instead, in order to promote muscular relaxation and relief of catatonic symptoms. The patient was administered twelve ECT applications three times a week, under anesthesia, muscular relaxation and under the relative's consent. After the third ECT application, the patient negativism remitted, and he started to present psychomotor elation and delusions of grandness. After completing the 12 applications, the positive symptoms of schizophrenia still persisted and we opted for the gradual and careful introduction of olanzapine. The patient was submitted to other five applications of ECT (total of 17). He then presented total remission of positive symptoms with olanzapine 7.5 mg/day associated to ECT. Cognitive impairment still persisted (attention and fixation memory), decrease of pragmatism and poverty ideation (previously reported in intercritical periods). There were no alterations in CPK, renal or liver functions and glycemia/lipids laboratory examinations. The patient was discharged and referred to the service of ECT for treatment maintenance using olanzapine 7.5 mg, and remained under relatives' care.

DISCUSSION

The reported patient was referred to our ECT service for three basic reasons: 1) catatonic symptoms; 2) risk of being administered powerful high doses of neuroleptic drugs (possibility of NMS recurrence); and 3) clinical refractoriness to antipsychotic drugs,

Karl Ludwig Kahlbaum firstly described catatonia in 1874 in a monograph entitled *Die Katatonie oder Spannungsirresein*. Originally considered an independent disease characterized by deep mental and motor changes, catatonia was later considered a sub-type of schizophrenia, as described in the DSM-IV and IDC-10.¹ Notwithstanding, it is known that catatonia symptoms do not occur specifically in schizophrenic patients, but in a range of psychiatric diseases, such as mood disorders and conversive disorders.¹ Wernicke-Kleist-Leonhard created independent concepts, based on the accurate differences of motor disorders: episodic and systematic or even hyperkinetic and akinetic.² Catatonia is a clinical condition that requires prompt treatment, because dehydration and stupor are important complications that can be fatal.³ Before any psychiatric intervention is performed, a detailed clinical evaluation is indicated in order to avoid electrolytic and metabolic unbalance.³ The ECT has a fundamental role in the resolution of catatonic symptoms.⁴

NMS is a neurotoxic state that may be fatal. It occurs in about 0.2% of patients managed with neuroleptic drugs. The ideal approach to NMS includes treatment in ICUs.⁵ Known risk factors are: agitation, dehydration and high doses of powerful neuroleptic drugs.⁵ Hyperthermia, disautonomy, mental confusion and stiffness are diagnostic patterns.⁵ CPK enzyme elevation is a lab data that helps in the diagnosis. Recurrence of NMS is very frequent, therefore it is advisable to administer safe drugs and perform careful titration.⁵ The ECT becomes an important strategy in these cases.⁵ Refractoriness to antipsychotic agents (absence of satisfactory clinical response to more than two distinct classes of neuroleptics, administered with proper time and dose)⁶ is not rare in the psychiatric practice, and such conditions were found in the case we are reporting.

The three situations presented – 1) catatonic syndrome; 2) NMS; and 3) refractoriness to antipsychotics – are accurate indications for the ECT application, which resulted a satisfactory clinic response and a few side effects already expected (headache and transient amnesia). After the 12 ECT applications, the catatonic symptoms remitted but the delusions of grandness and residual persecutory delusions persisted. The association between ECT and an antipsychotic has been showing positive results in the control of positive symptoms of treatment-refractory

schizophrenia.^{7,8} We opted for the gradual and careful introduction of olanzapine, because the patient had already presented NMS with the use of typical neuroleptics (haloperidol and chlorpromazine) and poor clinical response to another atypical agent (risperidone). The literature^{9,10} reports on cases of NMS triggered by atypical antipsychotic agents, among them there is olanzapine. This is the reason why the dose administered was carefully increased, always considering the least effective dose. Submitted to additional applications of ECT (total of 17) and in use of olanzapine 7.5 mg/day he presented total remission of positive symptoms. The patient continued with the negative symptoms such as cognitive deficits, hypobulia, affective stupor and poor ideations, which were already expected, once the combination of a psychopharmacological with ECT was shown to have a low impact on the control of negative symptoms.⁸ The literature¹¹ points out the efficacy of maintenance ECT to decrease the psychotic symptoms relapse and the number of hospitalizations of psychiatric patients. It has been providing excellent outcomes in our service.

The association between neuroleptics and ECT has been successfully employed. Although there are reports of NMS triggered by atypical agents, the association between olanzapine (7.5 mg) and ECT has been a safe choice in cases of refractory catatonic subtype schizophrenia with high risk for NMS development.

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ABSTRACT

This article describes the clinical history and management of an adult male patient with refractory catatonic schizophrenia to two typically used neuroleptic medications (haloperidol and chlorpromazine) and to another atypical agent (risperidone). The patient had also presented two neuroleptic malignant syndrome episodes due to typical neuroleptic agents. The authors combined ECT and olanzapine (7.5 mg) as treatment, and a considerable clinical improvement was obtained.

Keywords: *ECT, olanzapine, catatonia.*

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