

Short report

Keywords: Catatonia; Aripiprazole; Second generation antipsychotics; ECT; Bipolar disorder.

Successful treatment of catatonic syndrome in bipolar I disorder adding aripiprazole to ECT: A case report

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ABSTRACT – Background and Objectives: Catatonic syndrome is a condition presenting in multiple ways, sharing many of them with the neuroleptic malignant syndrome and other diseases. This diagnostic challenge is the main cause of keep treating catatonic syndromes without neuroleptics.

Methods: Review of the literature and a case report.

Results: We present the case of a 19 years old bipolar I patient with a severe catatonic syndrome, with a torpid clinical evolution, partial response to benzodiazepines and ECT, which successfully resolved with intramuscular aripiprazole. We found through a systematic review (PubMed 2005-2010) that there are few but significant case reports of catatonic syndromes treated with new second generation antipsychotics for different reasons with good outcomes as ours. The pharmacological profile of aripiprazole and the low incidence of NMS reported make it a suitable option in treating this syndrome.

Conclusions: We think that this case report could contribute to add more evidence for aripiprazole to be considered a good third-line option in the treatment of catatonic syndrome. However, this would require randomized controlled trials to confirm its effectiveness and safety.

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Introduction

Catatonic syndrome is a life threatening condition, classically described in schizophrenia but could be the expression of many psychiatric and non-psychiatric (infectious, metabolic, neurological, and toxic) diseases. Its presentation is always polymorph with a wide range of signs and symptoms, which make it sometimes difficult to differentiate from other diseases^{1,2}. It is probably produced by a complex imbalance of dopamine, serotonergic, noradrenergic and cholinergic systems at basal ganglia and prefrontal cortex, although the exact mechanism remains unknown^{1,3,4}. Catatonic syndrome treatment should be fast, safe and effective. Even though benzodiazepines resolve most of the cases, there are still some of them that are even resistant to electroconvulsive therapy (ECT)^{5,6}. The use of first generation antipsychotics showed an important incidence of catatonia worsening and inducing of neurological malignant syndrome (NMS)^{1,7}. Nevertheless, the experience with some second generation antipsychotics showed a lower number of cases and even possible beneficial effects in brain function and on the catatonic symptoms⁸. In the last years we found few reported cases which responded to the treatment with aripiprazole when benzodiazepines and ECT failed or when the last was not available⁹⁻¹³ (Table 1). Aripiprazole is a second generation antipsychotic with a mechanism of action ($D_2/5-HT1_A$ partial agonist and $5-HT1_{2A}$ antagonist) that seems suitable for the treatment imbalance neurochemistry that probably produces the catatonic syndrome. Since some theories points that the catatonic syndromes could be explained by a prefrontal hypodopaminergic state, the partial agonism of aripiprazole and rise in dopamine levels in these regions could explain its therapeutic

Table 1
Systematic review of published cases of catatonic syndrome treated with aripiprazole (PubMed 2005-2010)

Authors	Year	Gender	Age	Previous diagnosis Psychiatry or Non-psychiatric	BFCRS	Initial catatonia treatment	Aripiprazole* Dose	Time to improvement
Huffman <i>et al.</i> ¹¹	2005	Male	37	Hepatitis B - HIV	N/A	Lorazepam 1 mg IV /day, lorazepam 2 mg PO /day	15 mg PO/day	3 days
Strawn <i>et al.</i> ⁹	2007	Female	15	Pervasive developmental disorder	N/A	Clonazepam 1 mg PO/day	30 mg IM initial, 10 mg to 15 mg IM/day	Hours
Bastiampillai <i>et al.</i> ⁸	2008	Female	36	Catatonic Schizophrenia	N/A	Flupenthixol, lorazepam, risperidone and clozapine	20 mg PO/day	2 weeks
Voros <i>et al.</i> ⁷ (Case 1)	2009	Male	61	Undifferentiated Schizophrenia	52	None	30 mg IM/day	3 days
Voros <i>et al.</i> ⁷ (Case 2)	2009	Male	58	None	41	Clonazepam 6mg PO/day	30 mg IM/day	2 days
Voros <i>et al.</i> ⁷ (Case 3)	2009	Male	35	None	45	None	30 mg IM/day	1 day

* None of the cases reported concomitant ECT treatment.

benefits. However, there is not enough evidence that demonstrates its clinical effectiveness (9). We present in this report the case of a bipolar I patient with a severe catatonic syndrome, with a torpid clinical evolution, partial response to benzodiazepines and ECT, which successfully resolved with intramuscular aripiprazole.

Methods: Review of the literature and a case report.

Case presentation

The case is about a 19 years old Caucasian man, with a well-documented history of type I bipolar disorder by the DSM-IV criteria treated with lithium carbonate and risperidone presenting to the emergency room with grossly disorganized behaviour, disinhibition, agitation and stereotyped movements which required physical restraint and haloperidol 5 mg IM. The family reported a week of expansivity; altered sleep pattern and probable medication drop out, scoring at admission a Young Mania Rating Scale (YMRS) of 56. A couple of hours after admission the patient progressed to mutism, motor rigidity, stupor and fever of 38.9°C, together with a leukocytosis (14300/mm³) and elevated CPK (2121 U/L) totalizing a Bush-Francis Catatonia Rating Scale (BFCRS) of 36. The urine and the rest of blood tests did not show any other abnormal values. He was started on increasing doses of flunitrazepam IM up to 3 mg/day (since parenteral lorazepam is not available in our market and the patient was unable to tolerate oral administration), acetaminophen 1g qid, IV fluid therapy and re-started lithium carbonate PO 1200 mg/day. A chest x-ray did not demonstrate any considerable abnormalities and a brain magnetic resonance ex-

ploration showed no brain lesions. The clinical picture of the patient became an interesting diagnostic challenge between catatonia, neuroleptic malignant syndrome (NMS), antipsychotic-induced rhabdomyolysis (RML) or an acute infectious disease. After stopping neuroleptics and adding empiric antibiotic coverage, the fever persisted, CPK increased (7408 U/L), and also the rigidity. In front of the clinical situation ECT every other day was indicated, with poor results after the first 4 sessions. The adverse clinical course obligated us to consider other options; we decided to add aripiprazole 15 mg IM/day to the treatment along with ECT at the same parameters and benzodiazepines also at same doses. In the following days the patient showed a continuum clinical progress without fever peaks, being able of doing autonomous basic tasks in 4 days (BFCRS: 16; 44.4% improvement) and progressive normalization of laboratory values (Leukocytes and CPK). The patient was discharged from our hospital almost 1 month after the admission with IM aripiprazol for two weeks rotated after to PO aripiprazol 30 mg/day for other two weeks along with decreasing doses of flunitrazepam and totalizing 16 ECT sessions showing a full clinical recovery.

Discussion

Catatonic syndrome could be a challenging diagnosis when it present with severe signs and symptoms as our case¹. This and the fact that the patient had a history of using antipsychotic medication at home and also the one administered in the emergency room, made things even more difficult to differentiate from an incipient NMS, iatrogenic catatonia, RML or catatonia due to mania. Even though antipsychotics are fre-

quently associated with rhabdomyolysis, we discard the diagnosis because there were no muscular signs nor myoglobinuria in urine test and normal creatinine-BUN levels in blood tests¹⁴. At the same time, there was a history of progressive symptoms the previous days that made us think of a catatonia due to mania or induced by the risperidone. Although the acute exacerbation of symptoms and signs along with the elevation of CPK after the administration of IM Haloperidol inclined us to suspect an incipient NMS or an iatrogenic catatonia. There is still an on-going debate if NMS is a subtype of catatonia or not, what we know for sure is that catatonia is a risk factor for NMS. It is also obvious that both share symptomatology and probably neurochemical mechanisms⁴. We consider here the condition as a syndrome as it was impossible to differentiate a specific type or cause. There is a good rate of effectiveness in catatonic patients with benzodiazepines (aprox.70%), most of them improve in the first four days⁶. ECT usually resolves catatonic syndromes in approximately 90% of cases, most of them with a substantial improvement within the first two to five sessions¹⁵. After 6 days of treatment with benzodiazepines and 4 ECT sessions, the patient condition did not seem to improve. The use of second generation antipsychotics in this setting seemed an option, considering the low incidence of adverse effects and the good response in some reported cases⁹⁻¹³. Among them, we decided to introduce aripiprazole because it's pharmacological profile and also the low incidence of NMS reported with its use in mania^{16,17} along with the suitable mechanism of action mentioned. Even though we think that benzodiazepines and ECT contributed to the improvement, there was a favourable inflection point in the clinical course with the introduction of aripiprazole.

Conclusion

Catatonic syndrome is a condition presenting in multiple ways, sharing many of them with the neuroleptic malignant syndrome and other diseases. This diagnostic challenge is the main cause of keep treating catatonic syndromes without neuroleptics. There are few but significant case reports of catatonic syndromes treated with new second generation antipsychotics for different reasons with good outcomes as ours. This fact and taking into account the low risk of NMS reported of these new antipsychotics, may make aripiprazole a good third-line option to be considered in the treatment of catatonic syndrome. However, this would require randomized controlled trials to confirm its effectiveness and safety.

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