DOI: 10.5455/bcp.20120731051540

Clozapine Withdrawal Catatonia Refractory to ECT: A Case Report

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ÖZET:

Klozapin çekilmesine bağlı ortaya çıkan katatoni: Bir olgu sunumu

Katatoni şizofreninin bir alt tipi olmakla beraber katatonik tablolar bir çok farklı tıbbi durumda da karşımıza çıkabilmektedir. Klozapin çekilmesine bağlı ortaya çıkan katatoni tablosuyla ilgili az sayıda vaka bildirimi mevcuttur. Bu çalışmada klozapin kullanımını bıraktıktan beş gün sonra katatoni tablosuyla hastaneye başvuran 46 yaşında bir erkek hasta sunulmuştur. Hastanın 30 yıllık bilinen şizofreni tanısı olup rezidüel şizofreni tanısıyla 10 yıldır düzenli şekilde klozapin kullanmaktaydı. Onbir seans EKT uygulamasından fayda görmeyen hastaya klozapin başlanmasından sonra hızlı bir iyileşme gözlendi. Şizofreni hastalarında başka sebeplere bağlı olarak ortaya çıkan katatonik tablolar tanı karmaşasına ve dolayısıyla tedavide aksamalara yol açabileceğinden bu tip klinik durumların tanınması önemlidir.

Anahtar sözcükler: Klozapin, klozapin çekilmesi, katatoni, EKT'ye dirençli katatoni

Klinik Psikofarmakoloji Bülteni 2012;22(3):275-7

ABSTRACT:

Clozapine withdrawal catatonia refractory to ECT: a case report

Although catatonia is defined as a subtype of schizophrenia it may occur due to various medical conditions. Catatonic states associated with clozapine withdrawal have been described in a few cases. In this case report, a 46 year old man admitted to hospital in a catatonic state five days after discontinuing clozapine is presented. The patient has been diagnosed with residual schizophrenia for 30 years and he has been well maintained on clozapine for 10 years. The catatonia did not respond to ECT after 11 sessions but improved rapidly with the administration of clozapine. Catatonic states due to other etiological causes may present diagnostic and therapeutic difficulties in patients with schizophrenia. The importance of identifying such clinical conditions is underlined.

Key words: Clozapine, clozapine withdrawal, catatonia, ECT-refractory catatonia

Bulletin of Clinical Psychopharmacology 2012;22(3):275-7

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Gönderme tarihi / Date of submission: 21 Aralık 2011 / December 21, 2011

Kabul tarihi / Date of acceptance: 31 Temmuz 2012 / July 21, 2012

Bağıntı beyanı:
C.C., B.T., E.A., E.S.: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

Declaration of interest:
C.C., B.T., E.A., E.S.: The authors reported no conflict of interest related to this article.

INTRODUCTION

Catatonia is a neuropsychiatric syndrome characterized by mutism, stupor, refusal to eat or drink, posturing, and excitement or hypokinesis (1).

Although it is defined as a subtype of schizophrenia, psychotic and severe mood disorders, neurological disorders (e.g. nonconvulsive status epilecticus, brain neoplasms, head traumas), infections (e.g., encephalitis), metabolic disturbances (e.g. hepatic encephalopathy, hyponatremia, hypercalcemia), and medications (e.g. corticosteroids, immunosuppressive and antipsychotic agents) may cause catatonia(2). Catatonic symptoms may also be seen in extreme forms of neuroleptic induced parkinsonism or neuroleptic malignant syndrome (2).

Clozapine is the first atypical antipsychotic agent which treats both the negative and positive symptoms of schizophrenia while causing a minimum of extrapyramidal adverse effects. The significant pharmacological actions of clozapine appear to be due to the antagonism of dopamine and seratonin receptors (3). Clozapine is the "gold standard" of treatment for schizophrenic patients who are resistant to antipsychotics. Its use is limited due to the well-known agranulocytosis risk (4). Clozapine also has been reported to induce various withdrawal signs. Nausea, vomiting, diarrhea, headache, agitation, and rapid-onset psychosis (supersensitivity psychosis) are some of the adverse events associated with withdrawal of

clozapine (5).

Catatonic features associated with discontinuing clozapine have been described in several cases (6-13). Although the mechanism of development remains unclear, catatonia is thought to be caused by cholinergic and serotonergic rebound hyperactivity due to clozapine withdrawal (8).Symptom resolution with cyproheptadine is described by Zesiewicz et al. (14) which supports the serotonergic-rebound hypothesis. Also the γ-aminobutyric acid (GABA) system has been suggested to have a role on the etiology of catatonia (9).

In this case report, we present the clinical features and treatment course of a patient who has been diagnosed with residual schizophrenic for 30 years and was admitted to hospital in a catatonic state.

CASE REPORT

The patient was a 46 year old man who has been diagnosed as suffering from residual schizophrenia for 30 years. Hehas been well maintained on clozapine 200mg/day for 10 years. Two months before admission he stopped taking his pills. By the 5th day of clozapine withdrawal, he refused oral intake, became uncommunicative and unable to move and speak. He was admitted to a psychiatric hospital, diagnosed with catotonic schizophrenia and received electroconvulsive therapy (ECT). His symptoms did not resolve after 11 sessions of ECT. Because of his clinical deterioration and decubitus ulcers he was transferred to a general medical hospital.

On our first mental examination, the patient was cachectic, mute and his only response to verbal stimulus was eye contact; he responded to questions by closing his eyes. He was reluctant to communicate and his affect was restricted. No rigidity was observed. He scored 13 points on the Bush-Francis Catatonia Scale. No abnormalities were seen in the EEG. The 12-panel blood chemistry was normal including liver, thyroid and renal function tests. His CPK level was 56 U/L. A temperature of 38.2°C and tachycardia (90-100/min) were noted on the first day of admission. Leucocyte count (White Blood Cell (WBC): 17,500 cell/mm^3; segmentation 87.7%) was elevated. Blood and urine cultures were done. Pseudomonas aeruginosa grew on urine culture and antibiotic therapy was started. On follow up after 3 days, his fever had decreased to 36.8°C and his WBC count had decreased to 7,500 cell/mm^3. The patient had no oral intake thus he required supportive treatment including parenteral nutrition for the first 4 days and then he was started on nasogastric feeding.

On day 2, clozapine 100 mg/day was administered. Two days later, the patient started to respond to questions with one word replies. Lorazepam 1 mg/day was added to the regimen when he experienced sleeplessness on day 4. By the 6th day, he could get out of bed and take a few steps with support. At the end of the first week, he was answering questions with a few words. His nasogastric feeding was stopped and he started to take nutrition orally. He could walk with no support. Persecutory delusions and visual and auditory hallucinations were noted . Clozapine was gradually raised to 200 mg/day at day 7 and to 250 mg/day at day 21. After the 20th day of admission, his medical condition improved significantly, he was able to eat and drink. His delusions and hallucinations were resolved. Improvement in social cohesion was observed. He was discharged from the hospital after 30 days.

DISCUSSION

In this case, the fact that catatonia occured soon after discontinuing clozapine and recovered dramatically after clozapine resumption indicates that it was related to the withdrawal of clozapine. NMS was ruled out because of the lack of rigidity and because his CPK was within the normal limits. The leucocytosis and fever were decreased soon after antibiotic treatment which supports that these symptoms were due to an urinary infection rather than NMS.Cranial MR imaging was planned after the first week of admission but we decided not to do it because of the rapid improvement in clinical findings after clozapine administration.

Benzodiazepines and ECT have been the mainstay of treatment of catatonia(1). Nevertheless Hung et al. have mentioned that catatonia had very minimal response to BZD or ECT and the appearance of catatonia in that case was related to clozapine withdrawal (12). As far as we know, this is the first case report of clozapine withdrawal catatonia totally unresponsive to ECT. Two case reports mentioned an improvement with ECT (9,10). Both stated a response after the fourth session. Most of the case reports mentioned that clozapine administration has dramatically improved catatonia due to clozapine withdrawal (6,8,12,13).

In this case, the catatonic state improved shortly after clozapine resumption therefore we raised the dose of clozapine instead of lorazepam. The treatment during the first admission should be discussed in this case. We think that clozapine and/or lorazepam should have been administered earlier instead of continuing ECT. The patient's history of schizophrenia might have caused the other possible reasons for catatonia not to be noticed.Thus we highlight the importance of considering the etiological cause in the treatment of catatonic states. Catatonic states in schizophrenia may not be related only with the course of illness, but also can emerge for different medical reasons such as the withdrawal of antipsychotic agents.

The mechanism of catatonia due to clozapine withdrawal is unclear. Yeh et al. reported a patient with a catatonic stuporous state following abrupt discontinuation of clozapine, associated with features of cholinergic and serotonergic hyperactivity. They suggested that serotonergic hyperactivity was involved accompanied by cholinergic rebound in the pathogenesis of clozapine withdrawal catatonia (8). Wadekar et al. have suggested that the clinical presentation indicates serotonergic hyperactivity, with cholinergic overdrive, and heightened D2-receptor sensitivity (6) .

It is notable that the catatonia was refractory to ECT in this case despite the known effectiveness of ECT in catatonic states. We think that the differences in the etiopathogenesis of catatonia might be associated with the irresponsiveness to ECT.Thus we comment that other etiological causes of catatonia should be investigated in cases of ECT-refractory catatonia.

Catatonic symptoms may appear due to various medical conditions such as neurological disorders, infections, medications, neuroleptic induced parkinsonism, and neuroleptic malign syndrome. Thus differential diagnosis might be difficult. As a limitation of this case report, we have to consider the lack of diagnostic examinations such as cranial imaging.

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