Electroconvulsive therapy in a case of catatonia with severe somatic complications

Trattamento con terapia elettroconvulsivante di un caso di catatonia complicato da gravi manifestazioni somatiche

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Summary

Background

Catatonia is a neuropsychiatric syndrome that may occur in association with mental, neurological and medical disorders. A delay in diagnosis and treatment of catatonic symptoms is related to a high risk of medical complications such as dehydration, malnutrition, pressure ulcers, thrombotic events, aspiration pneumonia and infections.

Objectives

The authors present the case of a bipolar patient, admitted to the Psychiatric Clinic of the Azienda Ospedaliero-Universitaria Pisana for catatonic syndrome, complicated by weight loss, deep vein thrombosis (DVT), pressure ulcers and systemic infection.

Results

Supportive therapy, including hydration, electrolytic restoration and antibiotics was adopted to stabilize the patient's general conditions. Treatment with low molecular weight heparin was given for DVT and to prevent pulmonary embolism. Catatonic symptoms were initially treated with intravenous administration of delorazepam, with some improvement in catalepsy and waxy flexibility. As treatment with benzodiazepines was not completely effective, electroconvulsive therapy (ECT) was used in combination with delorazepam, which led to progressive resolution of catatonic symptoms.

Conclusions

The existence of medical complications requires a multidisciplinary therapeutic strategy, with the intervention of different specialists. Our experience confirms the efficacy and safety of ECT in catatonia, even in the presence of serious complications such as DVT. In these cases, combination of ECT and benzodiazepines should be considered elective treatment to achieve quick resolution of symptoms and reduce morbidity and mortality.

Key words

Catatonia • Bipolar disorder • Electroconvulsive therapy • Benzodiazepines

Introduction

Catatonia is a complex neuropsychiatric syndrome characterized by onset of psychomotor manifestations (negativism, mutism, mannerisms, stereotypies, immobility, rigidity) in association with a number of pathologies, not only psychiatric, but also physical such as neurologic, toxicologic, endocrinologic or infective. Despite the original description of catatonia by Kalbahum [1], who highlighted some clinical characteristics such as cyclic course, interepisode remission and frequent association with affective symptoms shared with mood disorders, for many years, influenced by the studies of Kraepelin and Bleuler [2 3], catatonia has been classified as a subtype of schizophrenia. In recent years, several clinical and epidemiological studies [4-6] have shown that catatonia is not only underdiagnosed, but that patients with bipolar disorder have a higher prevalence of catatonic symptoms than patients with schizophrenia. Thus, both clinicians and researchers have acknowledged the need for better classification and diagnosis. Other authors, such as Taylor and Fink [7], have proposed that the next edition of the DSM should classify catatonia as a separate diagnostic entity, while still others have stressed the need to reformulate diagnostic criteria, noting the currently inadequate psychopathologic description and the lack of evaluation criteria on severity and duration [8 9].

The main epidemiological studies [10], even if conducted in apparently homogenous patient populations, such as psychiatric in-patients, report a prevalence of catatonia that varies widely, from 7% to 31%. Clinical expression of catatonia, in fact, includes a large and variable spectrum of motor, behavioural, affective and cognitive manifestations (Table I) that consider the complexity of presentation and diagnostic difficulties. Mutism, negativism and catalepsy are classic symptoms that are

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TABLE I.
Main clinical features of catatonia (from Fink and Taylor) [6]. *Principali caratteristiche cliniche della catatonia (da Fink e Taylor)* [6].

Feature	Description
Mutism	Verbal unresponsiveness, not always associated with immobility
Stupor	Unresponsiveness, hypoactivity, and reduced or altered arousal during which the patient fails to respond to queries; when severe, the patient is mute, immobile and does not withdraw from painful stimuli
Negativism	Patient resists examiner's manipulations, whether light or vigorous, with strength equal to that applied, as if bound to the stimulus of the examiner's actions
Catalepsy	Maintains postures for long periods. Includes facial postures, such as grimacing or Schmauzkrampf (lips in an exaggerated pucker). Body postures, such as psychological pillow (patient lying in bed with his head elevated as if on a pillow), lying in a jackknifed position, sitting with upper and lower portions of body twisted at right angles, holding arms above the head or raised in prayer-like manner and holding fingers and hands in odd positions
Waxy flexibility	Offers initial resistance to an induced movement before gradually allowing himself to be postured, similar to bending a candle
Stereotypy	Non-goal-directed. Repetitive motor behaviour. The repetition of phrases and sentences in an automatic fashion, similar to a scratched record, termed verbigeration, is a verbal stereotypy). The neurologic term for similar behaviour is palilalia, during which the patient repeats the sentence just used, usually with increasing speed
Automatic obedience	Despite instructions to the contrary, the patient permits the examiner's light pressure to move his limbs into a new position (posture), which may then be maintained by the patient despite instructions to the contrary
Ambitendency	The patient appears 'stuck' in an indecisive, hesitant moment, resulting from the examiner verbally contradicting his own strong non-verbal signal, such as offering his hand as if to shake hands while stating, "Don't shake my hand, I don't want you to shake it"
Manierisms	Odd, purposeful movements, such as holding hands as if they were handguns, saluting passersby, or exaggerations or stilted caricatures of mundane movements
Echophenomena	Includes echolalia, in which the patient repeats the examiner's utterances, and echopraxia, in which the patient spontaneously copies the examiner's movements or is unable to refrain from copying the examiner's test movements, despite instruction to the contrary

highly suggestive of diagnosis, but are not consistent or exclusive, and have no pathognomonic relevance. Psychomotor investigations are often needed as these signs may not be immediately recognized due to their overlap with prominent affective and/or cognitive symptoms. Frequent alterations in symptoms, with the possibility of dramatic changes, requires clinical observation that is lengthy and/or repetitive [11 12].

There is general agreement that benzodiazepines and electroconvulsive (ECT) are the most effective treatment for [10 13]. Parenteral administration of lorazepam (IM or IV) at an initial dose of 2-6 mg/day, which can be increased up to 12-16 mg/day, is the most commonly used therapy, while ECT is generally used as second-line therapy in patients with partial or no response to lorazepam [12 13]. The appearance of hyperthermia or other signs of instability of the autonomic nervous system, indicative of evolution to a malignant form, impose immediate use of ECT, which can often resolve these forms[12,13]. Some recent data, even if preliminary, suggest that antiepileptics and NMDA antagonists may have a role in treatment of catatonia [14 18]. Two case reports have also described the use of repeated transcranial magnetic stimulation (TMS) [19 20], while the role of atypical antipsychotics is still under investigation even if they appear to be limited to forms of catatonia associated with schizophrenic psychosis [9 10].

Clinical case

D. is a 43-year-old woman, divorced, with a 24-year-old daughter. She had been previously followed by Psychiatric Services at a hospital near her home for bipolar type I disorder with psychotic features, and was admitted to our Psychiatric Clinic following the appearance of catatonic manifestations. Clinical history, with the help of family members, revealed the onset of psychiatric symptoms following puerperium, with a depressive episode having both mood-incongruent and mood-congruent psychotic features. In later years, the patient presented numerous recurrences with the same symptoms that needed hospi-

tal admission, and maintained a low level of social and work functioning with residual psychotic symptomology characterized by persecutory delusions, self-harm and auditory hallucinations with mixed content.

About 3 months prior to coming under our observation, the patient showed gradual sitophobia (she suspected poisoning) that led to progressive, severe weight loss (about 35 kg in 3 months), with hospitalization at a local psychiatric clinic. Despite a number of therapies, mostly typical and atypical antipsychotics (haloperidol, olanzapine, risperidone, clozapine) and benzodiazepines (delorazepam), there was no improvement in clinical symptoms, and catatonic manifestations began to develop (psychomotor arrest, mutism, negativism, rigidity with catalepsy, sitophobia, oppositivity). The patient was transferred to our clinic, which is a level III regional reference centre for severe and complex pathologies, and is licensed to perform ECT.

Upon admission, the patient was under treatment with risperidone (1.5 mg/day), delorazepam (2 mg/day) and enoxaparin sodium (4000 IU/day, s.c.), was immobile, stuporous, with waxy flexibility. She was mute, negativist and oppositive and refused both food and therapy. Severe malnutrition was present (BMI = 15 kg/m^2), with marked diffuse muscular hypotrophy and dehydration. Objective examination revealed a deep vein thrombosis (DVT) at the popliteal region of the left leg, grade IV pressure ulcer at the sacral level and modest fever (37.8°C). Arterial pressure, cardiac frequency and ECG were within normal limits. Laboratory investigations showed no relevant alterations with the exception of modest hypoalbuminaemia (3.14 mg/dl) and high levels of D-dimer (0.67 mg/dl). An emergency encephalic CT was carried out with negative results, while objective neurological examination revealed waxy flexibility in all four limbs that was more predominant in the arms, an a distal tremor at resting in the left arm, which could be attributed to iatrogenic damage subsequent to neuroleptic therapy. Therapy with delorazepam (8 mg/day i.v.) and systemic antibiotics were initiated (levofloxacin and teicoplanin i.v.) for pressure ulcers at the sacral level. A urinary catheter and a nasogastric tube for parenteral nutrition enteral were inserted after placing a peripherally inserted central catheter (PICC). Antiplatelet therapy with enoxaparin was administered, and it was also decided to start topical therapy for the pressure ulcers with collagenase and polyurethane film.

On the first day after admission, the patient initiated diagnostic work-up for ECT. Cardiac and respiratory pathologies that would contraindicate ECT were excluded by echocardiography and thoracic radiography. Echo colour Doppler revealed the presence of endoluminal thrombotic material involving the left superficial vein, popliteal vein and several of the homolateral subpopliteal veins. To avoid pulmonary embolism, in anticipation of ECT, antiplatelet therapy was substituted with dalteparin sodium 10,000 IU/day.

In the following days, while the psychopathological picture was substantially unvaried, except for the loss of waxy flexibility, the general conditions of the patient began to worsen with an increase in febrile episodes (> 38°C) until reaching a state of constant hyperpyrexia (with the appearance of frequent bigeminal ventricular extrasystoles by ECG), in spite of a change in antimycotic i.v. therapy (tigecycline, fluconazole) based on the results of the antibiogram of cultures from the pressure ulcer (*S. haemoliticus*, *E. coli*, *C. albicans*). Haemoculture was positive for *Pseudomonas aeruginosa*. Considering this, at 14 days after admission, the patient was transferred to the Internal Medicine department, and three days later, to the Intensive Care Unit due to loss of ventilatory capacity. In the ICU, vital functions were stabilized and after a negative cerebrospinal fluid test, with consent of her legal guardian, began a cycle of ECT. Four applications of ECT were performed during the first week in the ICU. Therapy with dalteparin sodium was effective in prevention of pulmonary embolism: vital signs remained stable, peaks of fever were reduced in both frequency and entity (< 38°C), although anaemia was revealed (Hb 8 g/dl), which was likely not identified at admission due to haemoconcentration. The psychopathological state was not substantially modified, and catatonic manifestations continued. On day 28 after admission, considering the improvement in general somatic conditions, it was decided to transfer the patient back the Psychiatric Clinic. Enteral nutrition was supplemented with parenteral nutrition, and system antibiotic treatment was continued (meropenem, amphotericin B), as well as antithrombotic therapy with dalteparin sodium s.c. in addition to i.v. delorazepam. At 32 days, a fifth application of ECT was administered, and the patient began to show signs of reawakening: she asked who the doctors were, where she was and why she was in hospital. She responded adequately to questions, and showed preservation of memory of past events, even if there was some amnesia about events in recent months. The patient was disorientated from a spatial-temporal standpoint, but recognized people and familial objects. Passive mobility to all four limbs was normalized, while active mobility was present but limited to severe and diffuse muscular hypotrophy. Upon interview, neither delusional thinking nor dysperceptions were present, while assessment of the affective domain showed a mild depressive symptoms that were partly due to pain from the pressure ulcer. The next day the patient began to feed herself, and enteral and parenteral nutrition were substituted with a semi-liquid diet integrated with protein and potassium.

During the next 10 days, the patient received another 5 ECT sessions, with consolidation of previous results. Dur-

ing this time, transfusion of red blood cell concentrate was given for chronic anaemia, with improvement of haemoglobin values (from 7.5 to 10.7 g/dl), and i.v. potassium was also administered (with an increase in serum values from 2.6 to 4.4 mEq/l). At 39 days after admission, the dose of delorazepam was reduced (from 8 mg/day i.v. to 4 mg/day oral) and antidepressant therapy with mirtazapine was introduced at an initial dose of 15 mg/day, which was progressively increased over 2 weeks to 30 mg/day along with olanzapine at 5 mg/day. A new echo colour Doppler exam of the lower limbs showed resolution of DVT (dalteparin sodium was reduced from 10,000 to 5000 IU s.c.), and the pressure ulcers showed improvement (from grade 4 to grade 3) with the aid of vacuum assisted closure therapy (VAC).

Over the following weeks, the patient gradually recovered both spatiotemporal orientation and long-term memory. Nonetheless, mild depression was present with feelings of anguish and abandonment, associated with psychotic symptoms characterized by persecutory delusions, partially accessible to criticism, in the absence of visual and auditory dysperceptions. Based on this, the dose of olanzapine was increased to 7.5 mg/day. Oral iron, folates and vitamin B12 were administered orally for anaemia. Considering the inadequate response in psychotic symptoms, olanzapine was substituted with clozapine after 15 days at an initial dose of 25 mg/day, and increased to 50 mg/day over a 2-week period.

At one month after the first cycle, 6 new ECT sessions were administered over a 4-week period for depressive and psychotic symptoms and to reinforce the improvement in catatonic symptoms. After this new cycle of ECT, the patient experienced partial remission of psychotic symptoms (residual delusions of reference) and gradual improvement in the affective domain, with recovery of energy levels, diminution of feelings of anguish and despair, with sleep and feeding patterns that were substantially normal. The patient underwent physiotherapy with recovery of sphincter control and autonomous ambulatory capacity in about 5 weeks. The patient also experienced modest weight gain (BMI = 17 kg/m^2).

After 105 days of admission, the patient was discharged in good overall condition (except for moderate anaemia and pressure ulcers, which were both showing improvement) with stable psychopathologic conditions (good memory capacity, substantial euthymia with residual psychotic symptoms). At discharge, the patient was on clozapine 50 mg/day, mirtazapine 45 mg/day and delorazepam 3 mg/day.

Discussion

Here, we present a case of a patient with bipolar I disorder, with post-partum onset at the age of 20 years, accompanied by a depressive psychotic episode. In the following years, the disorder was characterized by recurrent affective episodes of prevalent mixed/psychotic polarity, with partial recovery and persistence of psychotic symptoms in the intervals between episodes. The last episode, occurring 3 months before the patient came under our observation, needed recovery at a psychiatric clinic near the patient's home for severe weight loss due to sitophobia, sustained by fear of poisoning. The successive worsening of clinical conditions, with the appearance of catatonic manifestations such as mutism, negativism and rigidity, led to her transfer to our clinic.

Correct diagnosis required identification of the pathology at the basis of her condition, together with the recognition of catatonic symptoms. Even in the presence of a positive psychiatric anamnesis, such as in the present case, it is necessary to exclude that catatonic symptoms have a somatic origin, taking particular attention to acute, life-threatening pathologies such as infective, neurological or toxicological (meningoencephalitis, stroke, cerebral haematoma, brain tumour) [12]. Thus, in the first instance, objective psychiatric assessment must be integrated with accurate general and neurological examination; based on these findings, additional laboratory and instrumental investigations can be carried out.

In the case described, laboratory exams and encephalic CT upon admission excluded a somatic cause, and confirmed a clinical diagnosis of a mixed episode of bipolar type I disorder with catatonic manifestations. In anticipation of ECT, the patient underwent additional diagnostic work-up that included cardiologic, neurologic and other investigations (encephalic CT, ECG, thoracic radiography) to exclude contraindications for ECT. The prolonged immobility and malnutrition led to the appearance of severe complications including weight loss, diffuse muscular hypotrophy, dehydrations, DVT in the popliteal region and grade 4 pressure ulcers at the sacral level. Thus, a urinary catheter was promptly inserted along with a nasogastric tube for enteral nutrition, later integrated with parenteral nutrition following the placement of a PICC. The early administration of antibiotic prophylaxis (pulmonary, urinary, pressure ulcers) did not prevent progression of infection for which the patient was transferred first to Internal Medicine and then to the ICU. The patient's recovery in the ICU was decisive for resolution of sepsis and stabilization of vital signs. Our experience also confirms the crucial role of an early and integrated multidisciplinary approach to a catatonic patient involving psychiatrists, internists, infectologists, anaesthesiologists and physiotherapy specialists. In expectation of ECT, particular attention was paid to the risk of pulmonary embolism associated with DVT at the popliteal area of the left leg.

In the literature, pulmonary embolism is one of the most feared complications that an untreated catatonic patient

can encounter [21 22]. The increased risk for thromboembolic events is mostly related to immobility, although the concomitant presence of pre-existing cardiovascular comorbidities or other complications such as dehydration are also factors for increased risk [22]. Further information is needed, however, on the association between ECT and the risk of thromboembolic events as only rare cases of pulmonary embolism have been described in the literature in patients subjected to ECT [23 24]. In reality, a direct cause-effect relationship between ECT and thromboembolic events has not been demonstrated, although the efficacious use of ECT in catatonic patients with a recent history of pulmonary embolism and anticoagulant treatment has been described [24 25]. For prophylaxis of thromboembolic events, our patient was administered enoxaparin (4000 IU/day s.c.) which was substituted with dalteparin sodium (10,000 IU/day s.c.). This strategy was effective even during ECT, confirming the validity of indications in the literature regarding the use of low molecular weight heparin formulations for prevention of thromboembolic events in catatonic patients [23-25].

On the basis of literature data, treatment of catatonia with parenteral administration of benzodiazepines and ECT should be considered elective [10-13]. Lorazepam is the most frequently used drug, with a reported remission rate of catatonic symptoms between 70% and 80% [12]. In Italy at present, lorazepam is not available in a liquid formulation, which is a serious limitation in management of catatonic patients; in the case described, we administered a drug with a high efficacy, namely delorazepam (8 mg/day i.v.). Considering the reported synergism between ECT and benzodiazepines [26], some authors have suggested that combined treatment with ECT and lorazepam should be initiated immediately, especially when the critical conditions of the patient require rapid resolution of catatonic symptoms [27].

In the present case, initial treatment with i.v. delorazepam led to only a slight improvement in neurologic symptoms; therefore, once vital signs were stabilized, a first cycle of 10 sessions of ECT over 2 weeks was initiated, which led to a progressive improvement in both affective and motor symptoms. In literature, it is reported that, especially in severe cases of malignant catatonia at initial management phase, several applications of ECT should be administered over short intervals, sometimes with daily sessions [6 28].

After remission of catatonic symptoms in our patient, depressive symptoms with psychotic features appeared, which was resistant to initial treatment with mirtazapine and olanzapine. It was therefore decided to initiate a second cycle of 6 sessions of ECT over a longer time interval of one month. This led to significant improvement of depressive symptoms and reinforcement in the improvement of catatonic symptoms. The patient was discharged in good clinical conditions with the ability to feed herself and walk autonomously, despite of the difficulties due to muscular hypotrophy, and in a stable psychopathological state, characterized by residual psychotic symptoms such as self-reference and interpretive schemes.

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