CASE REPORT

Catatonic schizophrenia: therapeutic challenges and potentially a new role for electroconvulsive therapy?

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Dr Deirdre Philbin,
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A 36-year-old man with known schizophrenia, presented with increasingly bizarre behaviour. The development of catatonia and subsequent neuroleptic malignant syndrome in itself posed numerous therapeutic challenges. However, following resolution of neuroleptic malignant syndrome, the reintroduction of antipsychotics was not tolerated. This case report proposes a novel use for electroconvulsive therapy as a treatment of mental state, following resolution of neuroleptic malignant syndrome, to facilitate successful reintroduction of antipsychotics.

BACKGROUND

This case highlights the therapeutic challenges encountered during the management of catatonic schizophrenia and the subsequent development of neuroleptic malignant syndrome (NMS).

There is a lack of definitive guidelines regarding the reintroduction of antipsychotics post-NMS and little evidence addressing options when initial rechallenge is not tolerated.

This case report proposes a novel use for electroconvulsive therapy (ECT) as a treatment of mental state, following resolution of NMS to facilitate successful reintroduction of antipsychotics.

CASE PRESENTATION

The patient was previously known to psychiatric services, having initially presented 5 years ago with an acute psychotic episode. Schizophrenia was subsequently diagnosed and he responded well to aripiprazole.

The patient presented to the outpatient clinic exhibiting dissociative behaviour, with poor sleep and the return of auditory hallucinations. A recent family bereavement was noted. He was started on haloperidol 2.5 mg twice daily. He was monitored daily in the community but continued to deteriorate, becoming more anxious and developing neologisms. Olanzapine 2.5 mg twice daily was started. Two days after initial presentation, a home visit revealed an agitated, dishevelled appearance with tearful, uncooperative behaviour. Urinary incontinence was evident. His speech was non-spontaneous with occasional echolalia. Mood was objectively perplexed with a restricted affect. It was difficult to assess further but he was visibly responding to auditory hallucinations. Collateral history from his father later revealed that he had gone up into the attic with a dog-lead, the patient confirmed intermittent suicidal ideation.

INVESTIGATIONS

Physical examination revealed a mild tachycardia (pulse rate: 100 bpm) but the remainder of his vital signs were within normal parameters. Neurological examination was grossly normal. The patient was, however, noted to walk backwards and occasionally, turned on the spot in a circular motion. Features such as gegenhalten, waxy flexibility and posturing were not evident.

The new onset of these stereotyped behaviours and echolalia, together with deterioration in mobility and speech, in a patient with known schizophrenia was strongly suggestive of catatonic schizophrenia and our patient was referred for voluntary admission. Olanzapine was increased to 20 mg at night and diazepam 5 mg twice daily was started. Two stat doses of haloperidol were administered for agitation.

Over the following 2 days, the patient continued to deteriorate. A fixed stare and oneiroid state were evident. His vital signs demonstrated hyperthermia (temperature 39.9°C) with diaphoresis, tachypnoea (respiratory rate=25 breaths/min), tachycardia (pulse rate=132 bpm) and hypertension (blood pressure=152/99 mm Hg). Rigidity of all four limbs was now present. His creatine kinase (CK) level was 2199 IU/L. The patient met criteria for the diagnosis of NMS and was subsequently transferred for medical admission.

TREATMENT

Full supportive measures were undertaken for medical management of NMS. Intensive care unit admission was not required. All antipsychotic medication was discontinued. Vital signs and CK levels were monitored closely. The development of urinary retention required short-term catheterisation.

Over the following days, the patient's observations improved. He remained tachycardic but his temperature and respiratory rate normalised. Lability of blood pressure was not present. His rigidity gradually improved. His CK levels returned to the normal range. Four days later, he was medically stable and transferred back to psychiatric services. His physical improvement however was accompanied by a further deterioration in his mental state.

The decision was then taken to cautiously restart antipsychotics—quetiapine 25 mg at night in combination with regular diazepam. Quetiapine was chosen due to its short half-life and weak D2 antagonistic activity. The patient did not, however, tolerate a further increase in quetiapine to 50 mg and redeveloped urinary incontinence. His temperature

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rose to 37.9°C and his CK started to rise again. Antipsychotics were again discontinued.

The patient continued to deteriorate. He became mute, mild movements of his lips were observed but no sound. He appeared frightened and seemed to be responding to auditory hallucinations. He remained incontinent of urine.

The possibility of using ECT for treatment of the patient's mental state was addressed. Unlike previous literature, the use of ECT in this case was being considered, not for treatment of NMS, but for treatment of mental state prior to reintroduction of antipsychotics.

As the patient did not have capacity to give consent for treatment, he was discharged and readmitted involuntarily. Following assessment by a second independent consultant psychiatrist, the decision was taken to proceed with ECT.

Four sessions of ECT were administered. Refrigerated intravenous fluids were given throughout and temperature was monitored immediately preprocedure and postprocedure. Dantrolene was prepared in case urgent administration was required. On each occasion, a mild temperature spike was noted approximately 6–8 h postprocedure. This responded well to tepid sponging, regular paracetamol and lorazepam 2 mg three times a day.

A significant improvement was noted following the four sessions of ECT. The patient's mood improved, he became more spontaneous and he denied hallucinations. The regime for reintroduction of antipsychotics is not well documented. Quetiapine was reintroduced slowly (initially 25 mg once daily and gradually increased in 25 mg increments every 3–5 days) with close monitoring of temperature. Lorazepam was increased to 3 mg four times a day.

At a dose of quetiapine 50 mg in the morning, 100 mg at night, he remained without fever. However, the effects of electroconvulsive therapy were reducing and therapeutic levels of quetiapine had not yet been reached. The patient's mental state again began to deteriorate. His mood was depressed and, for the first time, suicidal ideation was expressed. He became perplexed with mood congruent delusions. Venlafaxine XL 75 mg was started and subsequently increased to 150 mg in the morning. Vitals signs, physical examination and CK levels were all normal.

Following further discussion, the decision was taken for further ECT. Again, the aim was to improve his mental state while therapeutic levels of antipsychotics were being achieved.

Six further sessions of ECT were undertaken using the same precautions as above. During this time, a therapeutic level of quetiapine was reached and was well tolerated. The patient was then switched to the slow release formulation—quetiapine XR 300 mg once daily.

OUTCOME AND FOLLOW-UP

His mood continued to improve and he became more spontaneous. Lorazepam was gradually tapered down. There was no evidence of psychosis. His family reported that he 'was back to normal'. He was discharged home on quetiapine XR 300 mg once daily and Venlafaxine 150 mg—euthymic and without any memory problems. He is reviewed regularly but remains well.

DISCUSSION

This case posed numerous therapeutic challenges:

1. The development of NMS while on maintenance aripiprazole.

Aripiprazole is deemed to be a valuable therapeutic option in the management of patients with schizophrenia.¹ It is a quinolone derivative with a high affinity for dopamine D2 and D3

receptors, and serotonin 5-HT1A, 5-HT2A and 5-HT2B receptors. The mechanism of action of aripiprazole is not yet known, but evidence suggests that its efficacy in the treatment of the positive and negative symptoms of schizophrenia and its lower propensity for extrapyramidal symptoms may be attributable to aripiprazole's partial agonist activity at dopamine D2 receptors. At serotonin 5-HT1A receptors, in vitro studies have shown that aripiprazole acts as a partial agonist whereas at serotonin 5-HT2A receptors aripiprazole is an antagonist.

Literature review revealed one documented case of treatment resistant schizophrenia who developed NMS following the start of aripiprazole.²

The case of our patient, however, was complicated by the administration of haloperidol (selective antagonism of dopamine D2 receptors), which in addition to aripiprazole may have contributed to the development of NMS. Theoretically, the abrupt discontinuation of aripiprazole could also have contributed.

Despite lack of supporting evidence for this theory in patients with schizophrenia, studies reviewing malignant features occurring in patients with Parkinson's disease clearly identify the immediate triggering event as discontinuation or reduction of antiparkinsonian drugs.³

Further studies of aripiprazole are therefore required, given its relatively beneficial therapeutic profile described in the literature to date.

2. The development of catatonic schizophrenia and subsequent diagnosis of NMS.

Opinions are clearly divided concerning the existence of a link between these two conditions. One hypothesis is that catatonia and NMS are two entities on the same spectrum.⁴ This postulated link clearly has implications for the use of antipsychotic medications.

In the case of our patient, development of catatonic schizophrenia was closely followed by the development of NMS. We would suggest that the presence of catatonic symptoms should raise clinical suspicion for the development of NMS. Vital signs and CK levels should be monitored closely to ensure early diagnosis.

Furthermore, the presence or absence of known risk factors should be used to assess risk of developing NMS.

Although not an exhaustive list, known risk factors include those with concurrent infection, organic brain disease or sympathoadrenal hyperactivity,⁵ postpartum women⁶ and those with low serum iron.⁷

Other documented risk factors include chronic ingestion of neuroleptic agents, rapid neuroleptisation, a long history of polysubstance abuse and combination usage of haloperidol and lithium.⁸

Male gender in itself has not been reported as a definitive risk factor. Although NMS has been reported to be more common in men, this is thought, however, to be most likely due to increased use of neuroleptics in men.⁹ Young adult men in particular predominate among reported cases of NMS.¹⁰

We would suggest that, particularly in the context of catatonic symptoms, individual risk factors should be identified and used as a tool to assist in predicting likelihood of developing NMS.

3. Lack of definitive guidelines regarding reintroduction of antipsychotics post-NMS.

The treatment of NMS is well documented. However, a literature review did not reveal clear guidelines regarding the reintroduction of antipsychotics following resolution of NMS. In the case of our patient, quetiapine was chosen due to its short half-life and weak D2 antagonistic activity.

One study recommended reintroducing neuroleptics within few days of recovery, using low potency neuroleptics and

starting with low doses which should be gradually increased. Using this method, in none of the four cases examined, did the patients experience partial or complete recurrence of NMS.¹¹

There is a need for further studies to identify and develop definitive guidelines for the reintroduction of antipsychotics postresolution of NMS.

4. The use of ECT to improve mental state while reintroducing antipsychotics

The use of ECT in the treatment of NMS is well documented. A review of the literature suggests that ECT is effective in many individuals with NMS, even when drug therapy has failed.¹²

Several case reports identify ECT as the preferred treatment in severe NMS, cases where the underlying psychiatric diagnosis is psychotic depression or catatonia.

This case report, however, proposes a novel use of ECT as a treatment of mental state, following resolution of NMS, as antipsychotics are gradually being introduced.

While the patient remained floridly psychotic, he could not tolerate initial re-challenge with antipsychotics and developed fever.

However, treatment with ECT reduced one of the known risk factors for NMS, that is, active mental illness and we propose that this led to subsequent successful reintroduction of antipsychotics.

To our knowledge, there is no evidence to date which examines the use of ECT for this purpose.

Learning points

- ▶ In the context of catatonic symptoms, individual risk factors should be identified and used as a tool to predict likelihood of developing neuroleptic malignant syndrome.
- ▶ There is a need to develop definitive guidelines for the reintroduction of antipsychotics postresolution of neuroleptic malignant syndrome.
- ▶ Following resolution of neuroleptic malignant syndrome, we propose that treatment with electroconvulsive therapy can be used to improve mental state (and thus reduce one of the risk factors for neuroleptic malignant syndrome), which can then lead to the subsequent successful reintroduction of antipsychotics.

Contributors All authors contributed to this work. DP wrote the paper and together with DM, completed the literature search. MOG supervised and edited the case report.

Competing interests None.

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