Treatment resistant catatonia secondary to clozapine withdrawal

Yasmine Nasr MBChB, Ramanathan Ganapathy MBBS, MRCPsych, Pg Cert (Mental Health Law)

Catatonia has a wide range of psychiatric and organic causes. It has been less commonly associated with withdrawal of clozapine. The authors describe the case of a male with paranoid schizophrenia presenting with catatonia following abrupt cessation of clozapine, which showed little improvement with benzodiazepines or electroconvulsive therapy (ECT).

Case report
We present the case of a 53-year-old male, well known to psychiatric services with a diagnosis of paranoid schizophrenia having been stable on clozapine 100mg OM and 350mg ON for over 15 years. He was reviewed by his community consultant for a routine six-monthly follow-up appointment and was reported to be doing well and stable in mental state. Two days later he collected his medication from the day hospital, and other than not ing that there had been some weight loss, the patient interacted appropriately and again seemed stable from a mental health point of view.

Seven days following this, his support worker contacted the community mental health team urgently with concerns regarding the patient’s limited oral intake, continued weight loss, minimal speech and interaction and psychomotor retardation (he described him as taking 45 minutes to open the front door). His support worker had also found unopened clozapine strips by his bedside (a number greater than he would have collected from the day hospital a week earlier). He was urgently assessed by the community duty worker who...
described him as grimacing and twitching, putting himself on the floor, staring at staff and remaining mute for most of the review. He was referred urgently to the home treatment team and subsequently admitted to a mental health ward.

A collateral history from the patient’s sister later revealed that two friends of the patient, who were also tenants at the same supported accommodation, had, of their own volition, decided to reduce the dose of their psychotropic medications without informing healthcare professionals. It was felt that our patient had been influenced by these friends, but had also taken things a step further and stopped his medication completely. Other possible precipitating factors to his deterioration included the anniversary of his mother’s death (to whom our patient had been a carer to for many years), anxieties around forming of a rash he had developed in his groin (this was diagnosed as a mild fungal infection), as well as anxieties around forms he had been requested to complete regarding his benefits.

Following his admission, our patient’s mental state quickly deteriorated over the course of the subsequent three days, and he was noted to be mute, staring, have minimal oral intake, with evidence of negativism and posturing and he was subsequently diagnosed with catatonia. Furthermore, he was noted to be acting bizarrely at times, for example, urinating on the floor in his room, or lying in the middle of the ward corridor.

Having initially been seen by the medical registrar and advised to continue management on the psychiatric ward, he was later transferred to the medical team due to pyrexia and the development of a new rash. The initial working diagnosis was that of viral encephalitis. However, his investigations, including baseline blood tests, creatine kinase, CT head and lumbar puncture (bacterial and viral studies) were all within normal limits. He was subsequently transferred back to the mental health ward where he underwent further investigations including an autoimmune screen, NMDA antibodies and an MRI head, all of which were normal and it was felt that this was likely a case of catatonic schizophrenia.

He was initiated on lorazepam with gradual increases in the dose, reaching 6mg in 24 hours, however, further increases were limited by hypotension. He was also initiated on aripiprazole, which required intramuscular administration due to his poor oral intake. There seemed to be little improvement with these medications and he was subsequently referred for ECT. Although there was evidence of some improvement after the initial three to four sessions in the form of alertness, improved oral intake and non-verbal communication, this improvement quickly plateaued despite continuing to complete a course of 12 ECT sessions. During this time he also required further transfer to a medical ward for nutritional support in the form of nasogastric feeding, having lost over 35% of his body weight.

Once a consistent oral intake could be established, our patient was re-initiated on clozapine. This seemed to bring about the most marked improvement. Having been catatonic for nearly seven weeks, within just eight days of re-initiating clozapine and reaching a dose of 50mg OM and 75mg ON, there was evidence of spontaneous speech, eating full meals and engagement with exercises with the physiotherapy team. Due to lability of his heart rate and blood pressure, the dose of clozapine had to be increased more cautiously than we would have preferred, however, he was established on his usual dose of 450mg daily within six weeks. By this time our patient was mobilising independently, engaging in simple ward activities and enjoying escorted leave with his family.

As our patient became more spontaneous in his speech he described experiencing auditory hallucinations as well as feeling low in mood. This raised the question of the underlying diagnosis: whether catatonia was purely due to clozapine withdrawal or whether there may have been an underlying psychotic or affective condition also contributing to this. He was subsequently started on sertraline and was transferred to a non-acute inpatient ward for further rehabilitation.

Discussion
Catatonia poses many challenges for the treating clinician. With numerous aetiologies to be considered and minimal or no history available from the patient, identifying the underlying cause often poses a diagnostic challenge. Nearly all systems of the body have the potential to be affected in catatonia and such patients require close and careful monitoring of their physical health. In particular one must protect against the risks of malnutrition, re-feeding syndrome, venous thromboembolism, joint contractures and pulmonary aspiration.4,7

Clozapine withdrawal catatonia appears to occur as a separate entity from other psychiatric aetiologies. Although benzodiazepines and ECT have long been considered the mainstay of treatment, it is becoming more
apparent that not all cases will respond to this, posing the question of whether the neurochemical imbalances in such patients are different or whether other mechanisms come into play.

Since abrupt withdrawal of clozapine can result in catatonia, this should be taken into consideration when clozapine is stopped suddenly for reasons such as agranulocytosis. It is important to consider initiating clozapine as soon as possible in similar cases as this may aid earlier recovery.

Dr Nasr is CT2 Psychiatry at Parkview Clinic, Birmingham, and Dr Ganapathy is a Consultant Psychiatrist at Bruce Burns Unit, Solihull Hospital.

References

Diagnosing dependence in rhyme

Diagnosing dependence is what I aim to teach to you today And I hope to do so in a fun and memorable way. This syndrome is so undoubtedly ubiquitous That to not know about it is completely iniquitous. ‘Dependence’ is the word which has replaced ‘addiction’ And alcohol dependence is the commonest affliction. For diagnosing alcohol and drug problems, this poem is intended
But I see no reason why to other things, the criteria can’t be extended.

The ICD-10 lists six criteria, of which three are required (Though to confirm the diagnosis, all six are desired). In dependence, like any disease, the time course must be clear: Symptoms must be present for three months of the past year.

Compulsion is the first symptom you must lodge in your head ‘I feel I just have to,’ is what you’ll often hear said. That is, the patient feels a strong desire to use It can be for drugs but most commonly it’s for booze.

Your patient might say that the substance governs their life And that this is something which is a source of great strife. What the patient means is that they have a loss of control So you see, the list of symptoms continues to unroll.

Symptom number three is a tricky one to find. Your questions and interpretation must be very well refined. If they continue to use their substance, despite causing harm

Then they should have just triggered your symptom alarm. If because of their substances other activities are neglected Then a preoccupation is what you’ve just detected. However, because a lot of dependent patients also have depression You’ll have to use your diagnosing discretion.

The body can adapt and get used to a substance being present So more substance has to be used to keep the patient feeling pleasant. Tolerance is the name that we give to this event And you should eagerly aim to explore its extent.

Substances cause a high followed by some sort of low (Of course, in between, there may be a plateau). Suffering withdrawal symptoms in the low gives your history lots of ticks As that is the final criterion, bringing the total to six! Withdrawal symptoms are specific to the substance being used So from detailing them all in this poem, I hope to be excused.

I hope that my poem has helped cover a topic not-so-explored And that it may help you in your clinic or on your ward. Hopefully while reading the above you’ve had good attendance And now feel more confident in diagnosing dependence.

Dr Gregory Schey, FY2 doctor, Wales 2014