CASE REPORT

The potential for antimicrobials to adversely affect mental state

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SUMMARY

This is a case report highlighting the influence that antimicrobials (clarithromycin in particular) can have on one's mental state. We discuss the case of a middle-aged woman who presented to an acute admissions unit under Irish Mental Health Act for involuntary admission because of concerns expressed by her family and general practitioner regarding a recent change in behaviour and onset of irritable mood. This lady was diagnosed with an episode of mania that was thought to be precipitated by a combination of psychosocial stressors, recent discontinuation of psychotropic medication and complicated by a recent course of clarithromycin.

BACKGROUND

Antimicrobial-induced mania is a rare but important side effect of some antibiotics. It should be considered as a risk for patients with and without known mood disorders who develop episodes of mania.

Clarithromycin and ciprofloxacin are thought to be the two most frequently associated with development of mania.¹ This case reports aims to highlight the potential for the antibiotic clarithromycin to negatively affect mental state. At the point of admission it is necessary to enquire about all medications that a patient may be taking, including non-psychotropics. This case report hopes to remind readers of this essential element of history taking. In this case the patient had recently completed a course of clarithromycin therapy although this did not come to light at the point of admission. It is also important to keep in mind the possibility of an organic or non-psychiatric cause to atypical presentations. It is hoped that this case report highlights one such unusual presentation and that the reader may be reminded of some basic history taking skills and the need to compile a comprehensive list of differential diagnoses.

CASE PRESENTATION

This is the case of 57-year-old mother of three who presented to an acute psychiatric unit for involuntary admission after the family voicing concerns to general practitioner (GP) regarding sudden onset of erratic behaviour, irritable mood and disinhibition.

History revealed that the patient had not been sleeping well in the previous 5 days and reported not feeling able to relax. She reported having excess energy and decreased concentration. Collateral history revealed that she had appeared confused and preoccupied at times and was hostile and verbally aggressive towards family.

Precipitating factors included the sudden death of the patient's elderly mother 3 weeks previously as well as the patient feeling concerned about her daughter's ill health. Also the patient had been on duloxetine 60 mg once per day but her prescription had run out 4 days prior to admission. She had also been prescribed a course of clarithromycin 500 mg three times per day for a lower respiratory tract infection (LRTI) by her general practitioner (GP) which was completed 1 week prior to her presentation to the psychiatry department.

Psychiatric history included having had a short admission (3 days) in 2008 for a mild-moderate depressive episode and also a 6 week admission in 1999 for a steroid-induced psychosis in another mental health service. She had been treated with duloxetine for the previous 24 months by her GP for the treatment of neuropathic pain.

This woman was living at home with her husband and three adult children. She had been in full-time employment until approx 1 week prior to admission. She is a non-smoker and non-drinker.

Regarding medical history, she was being treated for chronic back pain, hypertension and recurrent respiratory tract infections. Medications prescribed at the time of admission included only duloxetine 60 mg once daily although she was not taking this medication in the preceding 4 days.

There was no known family history of mental health problems.

Mental state examination at the time of admission revealed a well-groomed woman who appeared agitated and restless. Her speech was pressured and there was evidence of flight of ideas. She was easily distractible with poor concentration. Her mood was notably labile. There were no psychotic symptoms elicited and no evidence of perceptual abnormalities. She denied suicidal ideation.

She was offered a combination of stat dose of 5 mg haloperidol and 2 mg lorazepam to help manage her level of distress at the time of admission. She was started on high-risk observations (15 min checks) and 4 hourly BP, O₂ saturation, HR and temperature checks.

INVESTIGATIONS

- ▶ Mini Mental State Examination 30/30
- ▶ Physical exam
- ▶ Blood tests—full blood count (FBC), urea & electrolytes (U&E), liver function tests (LFTs), thyroid function tests (TFTs)
- ▶ Urine drug screen

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All blood test results were within normal limits and physical exam was unremarkable. Urine drug screen was negative.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses at the time of admission included:

- ▶ F30.1 Mania without psychotic symptoms
- ▶ F30.9 Manic episode, unspecified
- ▶ F31.8 133 Bipolar affective disorder (BPAD), current episode mania without psychotic symptoms
- ▶ F38.0 Other mood disorder—mixed affective episode
- ▶ F39.0 Unspecified mood disorder
- ▶ F06.3 Organic manic disorder

TREATMENT

The patient was reviewed by the consultant the following day who found her mood to be elated with possible delusions of reference. She appeared perplexed with circumstantial speech. An admission order under the Mental Health Act 2001 was completed. She was started on olanzapine 5 mg two times a day and clonazepam 0.5 mg three times a day.

It came to light during consultant review that she had been on antibiotic therapy for a chest infection prior to admission. The patient had been treated by her GP with a 7 day course of clarithromycin 500 mg three times a day which finished 1 week prior to psychiatric review.

OUTCOME AND FOLLOW-UP

The patient's condition improved very quickly and she was regarded to voluntary status 4 days later and had a period of two nights leave with her family which went well. Her mental state was fully improved by day 4 with no signs of elation or hypomania. She was then discharged and was followed up in the community. Duloxetine was restarted as it was helpful for her back pain. Olanzapine 5 mg at night was prescribed on discharge. Clonazepam was reduced to 0.5 mg at night. She was cautioned about the potential adverse effects of clarithromycin on her mood.

She was seen in outpatient clinic 2 weeks later and was noted to be very well. She was feeling quite tired so it was decided that olanzapine be reduced to 2.5 mg at night and clonazepam was discontinued. There were no concerns expressed by family regarding her mental state.

She continues to be followed up in clinic on a regular basis.

DISCUSSION

Clarithromycin is an antibiotic commonly used in the treatment of respiratory tract infections, local infections and in the treatment of *Helicobacter pylori* infection. Common side effects include nausea, vomiting and diarrhoea. More unusual and rare side effects include anxiety, dizziness, disorientation, mania, hallucinations and insomnia.² The first description in the published literature of clarithromycin-induced mania was in 1995 where two patients were receiving treatment for *Mycobacterium avium* infection.³ In 1996 a further case was described where a patient developed mania after clarithromycin treatment for a soft tissue infection.⁴ Other cases were described from 1998 to 2004 where the antibiotic was prescribed for treatment of sinusitis infection and in another case for the treatment of *H pylori* infection.^{5–8}

The mechanism of action for antibiotic-induced mania is thought to possibly involve central nervous system penetration and possible interaction with neurotransmitters although the exact mode of action remains unknown.⁹

It is recognised that clarithromycin has excellent cerebrospinal spinal fluid penetration.¹

Treatment of antibiotic-induced mania generally involves discontinuing the offending agent and symptoms improve. However, if symptoms do not resolve quickly or the patient's level of functioning is impaired then it may be necessary to add a psychotropic medication, for example, antipsychotic with or without benzodiazepine.

We cannot say for certain the exact cause of the short-lived manic episode in our patient but it was important to consider Clarithromycin as a potential causative or contributory agent. It is important to bear in mind that any patient on certain antibiotic medication may be at increased risk of developing mania. Cases documented in the literature report the occurrence of the symptoms of mania approximately 1 week after initiation of clarithromycin. In our case the symptoms occurred approximately 1 day after discontinuation of the antibiotic. The symptoms tend to resolve very rapidly in 24–36 h although in our case it was closer to 48 h post admission.¹⁰ We acknowledge that it is unusual that symptoms worsened rather than improved after discontinuation of the antibiotic. However, it is important to keep in mind that there were other factors affecting this patient's mental state including the stress caused by the death of her mother and the anxiety about her daughter's ill health.

Another important consideration in this case is the role played by duloxetine. The medication was being taken by the patient for many years for the treatment of neuropathic pain. Two to 3 days after the discontinuation of clarithromycin and while the manic symptoms were beginning this medication was stopped by the patient herself as she failed to have her prescription filled. As we know duloxetine can be associated with inducing mania although in this case with discontinuation of duloxetine symptoms did not abate, they in fact worsened further necessitating admission.

Clarithromycin-induced mania is a rare phenomenon that should be considered in the differential diagnosis of an episode of mania, particularly when it is acute in onset, atypical and/or where there is no known underlying major mood disorder.⁸

Learning points

- ▶ It is essential to enquire about all current and recent medication, both psychotropic and non-psychotropic being taken by a patient at the point of admission.
- ▶ It is important to take a detailed medical history.
- ▶ It is imperative to ask about drug allergies or interactions as the patient or family may be able to recall an incident where an antibiotic or other medication had an adverse effect on mental state.
- ▶ It is good practise to bear in mind a possible organic cause, for example, medication related, for symptoms of mania especially when the onset is extremely acute.
- ▶ If an antibiotic-induced mania is suspected, it is extremely important that this information is communicated to the patient's general practitioner or medical physician at the point of discharge in order to help prevent this from occurring in the future.

Competing interests None.

Patient consent Obtained.

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