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A case of clarithromycin psychosis

A 19-year-old woman developed an immediate psychotic reaction following intravenous administration of clarithromycin. She responded to atypical antipsychotic drugs but needed psychiatric hospitalisation. She recovered after a year and is now symptom-free without any medication. This is a rare side-effect, but needs to be recognised.

A 19-year-old woman presented to her general practitioner in June 2002 with a sore throat. A course of penicillin was prescribed but had to be discontinued because she developed a rash. Difficulty in swallowing and a continuing sore throat led to the patient being admitted to the medical ward of a general hospital. Following confirmation of the diagnosis of acute tonsillitis, a course of intravenous clarithromycin was prescribed.

Following the second dose of intravenous clarithromycin the next day, the patient became psychotic and agitated with visual and auditory hallucinations, and believed that she was in heaven: she could see the angels, she was walking on clouds. She became disoriented for time, place and person and expressed feelings of derealisation and depersonalisation. Antibiotic therapy was stopped and immediately replaced by intravenous haloperidol and lorazepam; on the third day the patient developed a dystonic reaction, which responded to benzotropine. The patient was examined by the liaison psychiatrist who continued the prescription of haloperidol, but her psychotic state persisted. All her physical investigations were normal on assessment by the general medical consultant physician and her tonsillitis had improved. On her fifth day in hospital the psychotic symptoms were still present, and now the patient felt that she was possessed and was the cause of other people's deaths, and could not be treated in a medical unit. This acute psychiatric reaction could have been secondary to her acute physical illness, coincidental or a reaction to the clarithromycin.

The patient was transferred to the psychiatric department at Ennis General Hospital for further treatment of her acute psychotic state. In the unit, she remained paranoid and perplexed, and admitted to auditory hallucinations in the third person. She also smiled and laughed inappropriately. Haloperidol administration was immediately stopped and atypical antipsychotic therapy with risperidone (2 mg) was commenced.

The patient responded slowly and during her stay the psychotic symptoms persisted, but with a gradual improvement noted every few days by the nursing staff and the patient's family. All routine blood investigations were normal when repeated in the psychiatric unit and no cerebral abnormality was detected by computed tomography. A lumbar puncture was not done. The patient was discharged home after a month of treatment in the acute psychiatric unit with a diagnosis of acute psychosis secondary to an unusual reaction to clarithromycin, even though her illness was schizophreniform in type. Her medication on discharge was risperidone 3 mg at night.

Medical history

There was no family history of psychiatric illness, and the patient did not have any premorbid symptoms of schizophrenia or of any psychiatric illness; she was a bubbly, extroverted college student who never misused drugs or alcohol.

Out-patient treatment

The young woman and her family were reviewed every few weeks in the clinic. Her family were informed of all our views and participated in all clinical decisions. As the patient returned to normal life and community living, her risperidone dosage was gradually reduced over a period of 6 months. She returned to college but noted a problem with memory for names, places and events, especially of her time in the general hospital and the early days in the psychiatric unit. This memory problem was confirmed by psychological testing but has gradually resolved, except for memories of the time of the acute onset of her psychosis.

Present time

The young woman is now able to continue with her academic studies, and is able to complete her

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assignments and projects. She is mixing socially with fellow students, and her personality has returned. Her family are pleased with her progress. Her risperidone therapy has been stopped for 7 months (August 2003) and no adverse reaction has been reported. She continues to be reviewed as an out-patient.

Other cases

Psychosis secondary to clarithromycin is a rare event and has been reported in the medical literature. Adverse events have been reported in 4–30% of patients, but worse effects on the nervous system have occurred in 3% of patients including dizziness, anxiety, insomnia, bad dreams, confusion, disorientation and hallucinations (Beers & Berkow, 1999; Dukes & Aronson, 2000). To confirm that this was a case of sensitivity to clarithromycin would require another challenge, but this would be dangerous to both patient and medical staff and would be merely an academic exercise.

Examples

A young patient with advanced AIDS experienced acute psychosis shortly after taking clarithromycin. The psychosis was resolved on withdrawal but recurred on a second challenge.

A 77-year-old man developed mania 6 days into treatment with clarithromycin for a soft-tissue infection. His mania resolved on withdrawal.

A 56-year-old man with chronic renal insufficiency and underlying aluminium intoxication maintained on peritoneal dialysis developed visual hallucinations. These developed 24 h after the start of clarithromycin administration for chest infection and resolved completely 3 days after withdrawal of the drug. There is no clear evidence that neuropsychiatric complications of clarithromycin develop more readily in uraemic patients, but several factors may predispose towards these adverse effects, such as reduced drug clearance, altered plasma protein binding, different penetration of drug across the blood–brain barrier or an increased propensity for drug interaction.

A 53-year-old man taking long-term fluoxetine and nitrazepam developed a frank psychosis 1–3 days after starting to take clarithromycin for a chest infection. His symptoms resolved on withdrawal of all three drugs and did not recur with erythromycin or when fluoxetine and nitrazepam were restarted in the absence of antibiotics. The symptoms might have been due to a direct effect of clarithromycin or else inhibition of hepatic cytochrome P450 metabolism leading to fluoxetine toxicity. There are also two incidents reported of patients who were being treated with clarithromycin for a *Helicobacter pylori* infection.

The UK pharmacovigilance group the Committee on Safety of Medicines has had 17 reports since 1991 of paranoid delusional psychosis in relation to this drug. There is speculation that these reactions may be under-reported. To date the Irish Medicines Board has three reported cases of a similar kind.

Conclusion

A 19-year-old woman reacted to clarithromycin with the development of an acute psychotic reaction, which responded to risperidone; she has now resumed a normal life. The family were alarmed that their daughter entered a general hospital as a normal young person and was discharged with a psychotic illness 5 days later. It frightens the family to think that their child could react in this way to antibiotics and that a similar reaction might develop with other antibiotics or if clarithromycin was prescribed again. The patient too is frightened of a recurrence of the psychosis, and medically one wonders whether she may now be prone to further psychotic episodes.

This case illustrates the importance of being vigilant before making a diagnosis of schizophrenia, and the close relationship between general medicine and psychiatry.

This is a rare event.

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