Unusual association of diseases/symptoms

Repeated activation of mania by atypical antipsychotics in a patient

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Summary

A 50-year-old, white female patient was diagnosed with schizophrenia in her teens. Her illness did not respond adequately to treatment until she was placed on a combination of fluoxetine and conventional antipsychotics. She discontinued the conventional antipsychotics on a number of occasions, which caused her to become psychotic, but not manic. On two separate occasions she was placed on atypical antipsychotics that were associated with the occurrence of manic symptoms. Once the patient was restarted on conventional antipsychotics, she remained stable.

BACKGROUND

Given the widespread use of atypical antipsychotics for the treatment of psychosis, there is a rare likelihood that they could be associated with the activation of mania in some patients. When evaluating these patients, it is important to recognise that another atypical antipsychotic may have the same effect.

This is the first case report of a repeated occurrence of mania by atypical antipsychotics in the same patient.

CASE PRESENTATION

A 50-year-old, white, female patient was diagnosed with schizophrenia in her teens. When the patient first presented, she had marked psychomotor retardation, blunt affect and auditory hallucinations. She also experienced repetitive, intrusive thoughts and delusions of reference concerning her previous psychiatrist.

Her maternal grandfather was reportedly institutionalised in a psychiatric hospital with an unknown diagnosis and her first cousin's nephew was diagnosed with schizophrenia.

Prior to her being seen at the age of 29, she had been treated with a number of conventional antipsychotics, including thioridazine, chlorpromazine and haloperidol. This time she was placed on loxapine 100 mg once daily and fluoxetine 20 mg once daily. The latter was gradually increased to 60 mg once daily. She improved dramatically under this treatment, though she complained of sedation with the loxapine and would stop it occasionally. She did not present any manic symptoms while on fluoxetine alone.

Three years later, in 1995, she was placed on risperidone 2 mg in addition to the loxapine 100 mg and fluoxetine 60 mg daily. She stopped the risperidone after 1 week due to marked attention and concentration difficulties. These difficulties were not due to akathisia.

At 2 years later, in 1997, in order to improve her negative symptoms, the patient was additionally placed on olanzapine 5 mg every bedtime for 4 days and 10 mg thereafter. The loxapine was gradually reduced from 100 to 25 mg and discontinued after 1 month.

She continued the 60 mg of fluoxetine and 10 mg of olanzapine. Two months later, she felt she had special, God-given powers to heal the sick and read minds. She was hospitalised with pressure of speech, pressure of activity and flight of ideas. The olanzapine was increased to 30 mg, but the mania persisted. At this time it was suspected that the olanzapine was responsible for the mania and so was discontinued. She was restarted on loxapine 100 mg in addition to the 60 mg of fluoxetine and her mania subsided.

Due to her tendency to stop taking loxapine, she was placed on pipotiazine palmitate 100 mg intramuscularly every 4 weeks while continuing the daily fluoxetine 60 mg and loxapine 100 mg. On at least six occasions, she discontinued the loxapine, which caused her psychosis to return, but not the mania.

At 3 years later, in 2010, again to alleviate her negative symptoms, the patient was started on 2 mg of aripiprazole daily, which was gradually increased to 20 mg over 3 weeks. Simultaneously, the loxapine dosage was reduced from 100 to 25 mg daily. Within 2 weeks of her achieving these dosages, her mood became elated, her libido increased and she began to have delusions of reference and grandiosity. She had pressured speech and flight of ideas. As a result, she was hospitalised and the aripiprazole was discontinued and the loxapine reinstated at a dose of 100 mg daily. Throughout this episode, she continued taking the 60 mg fluoxetine daily and pipotiazine palmitate 100 mg intramuscularly every 4 weeks.

Since 2010, the patient has remained stable on loxapine 100 mg daily, fluoxetine 40 mg daily and pipotiazine palmitate 100 mg intramuscularly every 4 weeks.

INVESTIGATIONS

Urine toxicology was always negative for illegal substances and there was no alcohol abuse or use of herbal medications. Her thyroid function tests were within normal limits. All other routine investigations were normal.

OUTCOME AND FOLLOW-UP

At present, the patient's illness remains well-controlled on loxapine 100 mg daily, fluoxetine 40 mg daily and pipotiazine palmitate 100 mg intramuscularly every 4 weeks. She has not needed any antiparkinsonian drugs throughout the course of her illness and she has not had any further episodes of mania.

DISCUSSION

There have been a number of reports of atypical antipsychotics causing mania in patients who have previously exhibited no manic symptoms. Most of the atypical antipsychotics have been implicated.^{1 2}

During her manic episodes the patient had been taking fluoxetine 60 mg daily and this could have contributed to her manic symptoms. However, she had not previously had any episodes of mania while taking fluoxetine alone.

It is believed that the combined antagonism of 5-HT_{1A} and partial agonism of D₂ receptors could cause frontal dopamine release, contributing to manic symptoms.³ Lane *et al* suggested a ratio of 5-HT₂/D₂ receptors occupied at low doses of an atypical antipsychotic resulted in higher 5-HT₂ activity⁴ though there are still not enough data to support this finding.⁵

Although there are many hypotheses, the true mechanism of action of antipsychotic-induced mania remains unknown.

Competing interests None.

Patient consent Obtained.

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Learning points

- Some patients on atypical antipsychotics for the treatment of psychosis though rare, could have activation of mania while on them.
- It is important to recognise that in a patient with previous activation of mania by one atypical antipsychotic, there is a possibility that this can recur with a different atypical antipsychotic too.
- It is important to consider all causes of mania in a patient.

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