Psychosis Induced by Cefuroxime and Metronidazole

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SUMMARY

We report a case 35-year-old lady who developed acute psychosis following administration of cefuroxime and metronidazole. Earliest mood changes occurred on the second day of antibiotics therapy. She developed hallucinations, delusions and bizarre behavior 1 day after the completion of the antibiotic therapy. All the relevant investigations including CT brain were normal. The psychosis resolved completely within 5 days of antipsychotic treatment.

KEY WORDS:
Psychosis, mood, metronidazole, cefuroxime

INTRODUCTION

Metronidazole and cefuroxime are widely used antibiotics in the past four to five decades. Both are broad spectrum antibiotics and can cross the blood brain barrier. Although rare, psychosis has been associated with the use of metronidazole [1,2] or cefuroxime [3]. Central nervous system toxicity was thought to be the cause in which renal impairment played an important role [3]. Inhibition of gamma-amino butyric acid (GABA) binding to receptors in the brain by cephalosprins has convulsant effect [4] and has been postulated to cause panic attacks [5]. Here, we report a case of acute psychosis following therapy with metronidazole and cefuroxime, which resolved completely within 2 weeks after discontinuation of the antibiotics.

CASE REPORT

A 35-year-old married lady with no prior history of psychiatric illness presented with bizarre behaviour for a duration of 9 days. Seventeen days prior to presentation, the patient had fever (38° Celsius) along with spotting per vagina after two weeks delay in menstruation. Thinking that she might be pregnant, the patient went to a local hospital, where the urine pregnancy test was negative. She was admitted for 6 days and treated as a case of pelvic inflammatory disease. As the fever did not abate after 3 doses of intravenous ampicillin (500 mg thrice daily), the antibiotic treatment was switched to metronidazole (500 mg thrice daily) and cefuroxime (750 mg thrice daily) for 5 days. On the second day of the new antibiotics she felt different from her usual self. She became irritable and felt that the husband did not love her, which she brushed off. She was discharged after completion of the antibiotics course.

On the second day of coming home, the patient went into a fit of rage at her son for slamming the door, and started beating and pinching him, which was totally uncharacteristic of her. Following that the patient cried inconsolably asking for forgiveness, claiming that she was a bad person and should be buried along with her dead child. Now that she was deluded it was an abortion although she was earlier told it was not. She slept only 2-3 hours at night associated with sadness, guilt feeling and loss of appetite. She started experiencing auditory hallucination saying she was a bad person and that she should die. She was deluded that a snake was inside her abdomen, which scared her immensely. On several occasion, she acted bizarrely whereby she laid on the bathroom floor dragging her chin. At other time, she covered herself with a blanket and acted like an old woman, talking in a strange voice.

She was brought to the hospital after 9 days of the symptoms and she had to be sedated as she was screaming and trying to get off the stretcher. On admission, the patient covered her head with blanket and kept patting her face for hours. She was oriented to time, place and person. Neurological examination was normal. Plain computer tomography (CT) of the brain and ultrasound of the abdomen did not show any pathological findings. Her full blood count, differential count, ESR, bleeding and clotting profile, liver profile, renal profile and thyroid function test (free T4 25.8 pmol/l, TSH 0.2 mIU/L) were all within normal limits. She was negative for rheumatoid factor, ANA, CRP and her C3, C4 were within normal limits. Urine drug and beta HCG test were negative as well.

She was treated with olanzapine 5 mg nocte. On the second day of admission, she started taking care of her own activities of daily living. Her mental status examination was normal except for feeling scared of the delusion of snake, but it was already shakable by the third day. She was discharged well after 5 days of admission with olanzapine 5 mg nocte. She came for follow up after 2 weeks of discharge and did not have any psychotic or mood symptoms and has returned to her prior functioning at home and planned to start work the next week. The olanzapine was stopped and the patient did not have further psychotic or mood symptoms.

DISCUSSION

The psychosis developed shortly after the treatment with metronidazole and cefuroxime and abated totally within 2 weeks after the treatment, suggesting a causal relationship.

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Encephalopathy or toxic psychosis was unlikely in this case as the patient was well orientated and able to recall the psychotic experiences. In addition to that the CT brain was normal.

We suspect the psychosis was induced by cefuroxime and metronidazole. The mechanism by which cefuroxime induces psychosis is unclear [3]. Administration of cephalosporin antibiotics have been shown to induce convulsive activity in rats through suppression of inhibitory postsynaptic responses, mainly mediated by γ-amino butyric acid $(GABA)_A$-receptors [4]. The resulting activation of limbic areas may give rise to mood and psychotic symptoms.

Traditionally, brief reactive psychosis should also be considered whenever psychosis develops shortly after a markedly stressful event. It can be argued that this patient might be stressed by her erroneous belief that she had an abortion. However, the fact that she did not plan to have another child and negative findings to suggest pregnancy made this diagnosis unlikely.

CONCLUSION

In conclusion, although it is rare, antibiotic-induced psychosis should be considered in the differential diagnosis in any patient presenting with brief psychosis after the more common causes have been excluded.

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