Case Report

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Antibiomania: Clarithromycin-Induced Mania?

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Abstract

The authors present a case of antibiomania in a 55-year-old woman with a previous history of borderline personality disorder, anorexia nervosa, and long-lasting anxious and depressive symptomatology associated with her husband´s serious illness.

The switch to mania occured after two 500mg doses of clarithromycin – the third antibiotic she had been administered in four months. Manic symptoms were so severe that involuntary hospitalization was required. Signs of mania disappeared within a week in the psychiatric ward.

The authors submit the hypothesis that the pathogenetic pathway of this sudden reversal into mania may have been triggered by clarithromycin-induced dysmicrobia of the intestinal flora, which crossed into the CNS through either a leaky gut or by direct stimulation of the nervus vagus.

Keywords: Antibiomania; Mania; Clarithromycin; Gut microbiota; Dysmicrobia

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Introduction

Antibiomania is the name for any mania induced by antibiotics. It is a rare, but important side effect of clarithromycin and other antibiotics even in persons with no previous history of bipolar affective disorder. In 2002 Abouesh et al. reviewed reported cases of antibiotic-induced manic episodes and among them 29 implicated clarithromycin [1]. We found seven other cases of clarithromycin-induced mania in PubMed [2-8].

Case Report

The patient was a 55-year-old married woman with inborn spastic cerebral palsy, borderline personality disorder, and anorexia nervosa in early adolescence. A former teacher, she is now a handicapped retiree. For the last three years, she attended psychiatric outpatient clinic for anxious and depressive symptoms connected with her husband´s serious illness.

Depressive episodes were mild or medium in intensity; episodes of mania or hypomania neither were nor recorded during outpatient care or in the patient's medical history. History taken from her daughter and husband confirmed that the patient had never had any previous manic psychiatric symptoms or complaints. Also family history was negative.

Past emotional lability as described by the patient fit the diagnosis of personality disorder [9]. The patient´s main complaint was insomnia which was caused partly by delayed sleep-phase syndrome and partly by her peculiar habits. These habits were also responsible for her critical nutritional status (BMI ~ 18) and were more a result of manipulative behavior than a manifestation of the disease. Depressive episodes were mostly related to any worsening of her husband´s health status, and fullfilled all kriteria for ICD-10. However, she was more anxious than depressed most of time.

Therapy consisted of supportive psychotherapy (including the use of e-mail to make a connection in case of emergency) and pharmacotherapy. At the start of treatment the patient was prescribed benzodiazepines, but due to patient's misuse and even abuse of these, they were replaced by low doses of antipsychotics and the basis of pharmacotherapy were antidepressants (mirtazapine, trazodone).

The patient was given two full courses of ciprofloxacin treatment for acute bronchitis in the last four months. Eventually, two days before admission, she was given clarithromycin (Klacid®) for the resistant respiratory tract infection. After the second dose of perorally administered 500 mg clarithromycin, she gradually became active, irritable, agitated, reduced her sleeping hours, had a subjective sensation of increased energy, grandiosity and enormously increased mental capacity (she was able to "grasp the whole of mathematics," to "perfectly understand,

speak and write English," and so on). She had a partial insight into the morbidity of her condition, and at 1:30 a.m. she wrote psychiatrist: *My current physical troubles are crap compared to what has been going on with me since midnight Friday. I am in terrible trouble! I couldn't care less that you have 22+ patients tomorrow -- please, it is absolutely necessary (!!!) that I talk to you tomorrow!!!* Next morning she came to outpatient clinic with her husband who told that during the night his wife " ... it was like she came to life, had new powers, energy -- she was flying around the apartment talking incessantly." She was talkative, uninterruptible, irritated, petulant. Finally she accepted a prescription for olanzapine 2 x 10 mg and lithium 3 x 300 mg and promised to stay in e-mail contact with psychiatrist. The next night was sleepless too and as the manic symptomatology progressed, the patient refused to take the prescribed medication and had serious conflicts with her husband such that admission to our ward in the psychiatric hospital was accepted as the best measure.

The patient agreed with no objections, but once in the admissions office became aggressive and violent including attacking staff with her crutches. It was necessary to apply an IM injection of olanzapine and place her in a special observation ward. She was able to sleep well and long enough that she could be transferred the next day to a specialized department for bipolar disorders. Even though she was still hypomanic, she was able to view her previous behaviour critically.

During the following week she calmed down with olanzapine 10 mg, valproate 1000 mg and clozapine 2 mg per day and on the ninth day after admission she was released in a stable state of mood. Follow-up after six months: normophoric mood, normal psychomotor speed. Medication: mirtazapine 15 mg, olanzapine 5 mg which we will gradually discontinue.

Discussion

When an adult female patient with a history of personality disorder and anorexia nervosa presents with a sudden episode of mania, it is of course necessary to carefully examine and eliminate whether this emotionally unstable psychopathology was hiding a bipolar disorder [10]. We were able to exclude this alternative with utmost certainty.

The manic episode was triggered directly by clarithromycin as in the other cases described in the literature. There are lot of hypotheses dealing with the possible influence of macrolide antibiotics – especially clarithromycin – on CNS dysfunction. We are presenting a new one: the application of clarithromycin may lead to intestinal dysmicrobia with pathologic consequences in metabolism of any neurotransmitter through either a leaky gut or direct stimulation of the nervus vagus [11, 12].

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