Tourette's Symptoms Provoked by Lamotrigine in a Bipolar Patient

TO THE EDITOR: Lamotrigine is a modern anticonvulsant with established antiepileptic and mood-stabilizing properties. We present the first case, to our knowledge, of an adult bipolar patient who developed multiple motor and vocal tics during treatment with lamotrigine.

Ms. A, a 55-year-old woman, was referred to our bipolar outpatient center by her general practitioner for frequent recurrent depressive episodes. Laboratory measures, including a CSF level, a magnetic resonance imaging scan, and an EEG, revealed no hint of an organic cause of her depressive symptoms. Because her history also revealed a manic episode, she was diagnosed as having bipolar I disorder with a rapid-cycling course. Lamotrigine monotherapy was initiated for mood stabilization and was titrated up to 200 mg/day (a blood level of 4.6 μg/ml).

For 3 months, Ms. A's mood remained stable, but she began to develop tics of increasing extent and complexity. She started to produce motor tics, such as shrugging her right shoulder, wagging her hips, and pawing her feet on the ground. Moreover, she was picking at her clothes and blinking her eyes. In due course, she developed vocal tics for the first time in her life. Thus, she then had repetitive throat clearing, single expiratory grunts, and mental coprolalia.

At her follow-up visit, Ms. A reported a history of rare left shoulder shrugging and head nodding for 2 years before referral to our clinic. No previous vocal tics were reported. During childhood she suffered from mild orofacial motor tics that disappeared spontaneously after 6 months at the age of 7. At that time, no diagnosis was made. Thus, Ms. A had only two episodes of slight motor tics.

Suspecting an exacerbation of Tourette's syndrome due to lamotrigine, we began to taper her lamotrigine dosage. With the reduction of lamotrigine to 100 mg/day, most of her symptoms faded and disappeared completely 2 weeks after total withdrawal.

Our literature search identified eight case reports describing the induction of tics in children with epilepsy treated with lamotrigine but none in adult nonepileptic patients (1, 2). In line with these case reports, most of Ms. A's symptoms disappeared after dose reduction, indicating a dose-dependent side effect. An explanation for the exacerbation of Tourette's syndrome during lamotrigine treatment remains speculative.

Inhibition of excitatory amino acid release can alter dopamine uptake in the striatum (3). In addition, the potent inhibitory effect of lamotrigine on the presynaptic release of excitatory amino acids might also modify striatal dopamine uptake (4) and lead to the occurrence of Tourette's syndrome.

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FLORIAN SEEMÜLLER, M.D.
SANDRA DEHNING, M.D.
HEINZ GRUNZE, M.D.
NORBERT MÜLLER, M.D., PH.D.
Munich, Germany

Adjunctive Lamotrigine as a Possible Mania Inducer in Bipolar Patients

TO THE EDITOR: Lamotrigine is currently being used to treat bipolar and unipolar mood disorders. We report three cases in which lamotrigine acted as a possible hypomania/mania inducer, although it was used in addition to other mood stabilizers. These are probably the first such reported cases besides one report of hypomania induced by adjunctive lamotrigine in antidepressant treatment (1).

Ms. A, a 41-year-old woman, suffered from bipolar I affective disorder. She was stabilized with 1700 mg/day of valproic acid. She then began to develop depressive symptoms. Lamotrigine was added to valproic acid as a mood stabilizer, with an elevating effect (2). After 2 days of 50 mg/day of lamotrigine, Ms. A reported an improvement in her mood. This made her decide to increase her dosage to 100 mg/day. Within 1 week of lamotrigine treatment, she became hyperactive and agitated, needed no sleep, and spent money without judgment. The lamotrigine was stopped, resulting in rapid remission within 2–3 days of Ms. A's iatrogenic mania.

Mr. B, a 32-year-old man, had bipolar I disorder. He was stabilized with 750 mg/day of carbamazepine, along with 600 mg/day of quetiapine. He then began having episodes of rapid mood changes from euphoria to depression, with grandeur delusions and suicidal ideation. There was no improvement when quetiapine was increased to 800 mg/day. Lamotrigine was then added, 25 mg at bedtime, and elevated to 200 mg at bedtime within a week because of Mr. B's serious condition; he continued treatment with carbamazepine and quetiapine. A typical manic episode developed within 48 hours. A decrease in his lamotrigine dosage to 50 mg/day resulted in abatement of his mania symptoms within 1 week.

Mr. C, a 29-year-old man, had been diagnosed with schizoaffective disorder at the age of 16. For years, he had been stabilized with 1500 mg/day of lithium. However, he started to develop hypomanic symptoms. Quetiapine, 400 mg/day, was added to the lithium. This resulted in amelioration of his hypomanic signs but a propensity toward depression. It was thought that lamotrigine added to lithium and quetiapine would stabilize him without a manic explosion. Lamotrigine was gradually elevated to 200 mg/day over 3 weeks; Mr. C manifested manic symptoms toward the end of the fourth week. A gradual reduction of his lamotrigine dosage until cessation over 3 weeks resulted in parallel disappearance of his manic symptoms.

These cases highlight the possibility of lamotrigine acting as a quick antidepressant, even when added to other mood stabilizers. Our clinical impression is that the provocation of mania is related to the titration rate and dosage. Thus, special caution should be taken when prescribing lamotrigine to-

gether with valproate because the latter decreases the clearance of lamotrigine.

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SERGEY RASKIN, M.D.
ALEXANDER TEITELBAUM, M.D.
JOSEF ZISLIN, M.D.
RIMONA DURST, M.D.
Jerusalem, Israel

Electric Sensations: Neglected Symptom of Escitalopram Discontinuation

TO THE EDITOR: We make reference here to a patient who experienced electric sensations after discontinuing escitalopram treatment.

Ms. A was first referred to our clinic by her family doctor for depressive symptoms (asthenia, insomnia) in the context of a psychosocial stress situation. Treatment with citalopram, 20 mg/day, was initiated, which was soon replaced by escitalopram, 10 mg/day, the enantiomer of citalopram. Because she was responding well, Ms. A reduced her dose to 5 mg/day and, 3 weeks later, stopped treatment altogether. About a week later, she began to experience electric shock-like sensations or visual flashes lasting for about 1 second each. This was followed by a phase of spatial disorientation that lasted for about 30 seconds and was experienced as highly unpleasant and frightening. The sensations were only felt when Ms. A was in an upright position; she had no history of loss of tonicity. These episodes occurred up to three times a day over a period of 2 weeks. Prodromal symptoms or specific triggers were not reported. While Ms. A was taking citalopram/escitalopram, no side effects were observed. Interactions with other substances could be eliminated because this was her only medication.

Ms. A's depressive symptoms soon returned, resulting in more therapy with escitalopram (10 mg/day). She began to feel better and thus decided to reduce her medication, although it was well tolerated, to 5 mg/day and, after 4 weeks, again ceased taking it. One week later, the electric shocks reappeared, although they were now less intense. Ms. A's family doctor continued to urge pharmacological intervention to treat her depression. However, she refused to cooperate out of fear of becoming addicted to antidepressants because of the sensations that she interpreted as withdrawal symptoms. An EEG as well as a detailed neurological examination revealed no abnormalities.

There is not much relevant literature on the subject of electric sensations as a discontinuation symptom of selective serotonin reuptake inhibitors and nothing at all in connection with citalopram or escitalopram, although comparable symptoms have been described as occurring after treatment with paroxetine and sertraline (1). The pathophysiology is not clear; the down-regulation of serotonin 5-HT_2 receptors and the desensitization of both the 5-HT_2 receptor transmembrane signaling system and the 5-HT autoreceptors seem to be of particular concern (2). There are two therapeutic options: resuming the medication and tapering it off even more slowly (2) or allowing the syndrome to run its course. However, the patient would need to be reassured that the symptoms are likely to disappear within 2–8 weeks without serious consequences. None has been reported so far (3).

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NADIA FETH, M.D.
KATJA CATTAPAN-LUDEWIG, M.D.
Berne, Switzerland
EVELINE JAQUENOUD SIROT, M.SC.
Brugg, Switzerland

Aripiprazole-Induced Movement Disorder

TO THE EDITOR: Aripiprazole is a dopamine D_2 partial receptor agonist (1). Trials have shown rates of extrapyramidal side effects similar to those of placebo administration, as seen with other atypical antipsychotic agents (1). Some case reports have found that atypical antipsychotics may even be helpful in treating tardive dyskinesia (2, 3). Although the occurrence of extrapyramidal symptoms seems to be less frequent with atypical antipsychotics, it is important to note that these effects can still occur. To our knowledge, only one case of aripiprazole-associated dyskinesia has been reported (4). We report a case of pseudoparkinsonism and rabbit syndrome that occurred in an antipsychotic-naive patient during treatment with aripiprazole.

Ms. A was a 27-year-old woman diagnosed with bipolar I disorder. Before she received care through our clinic, her condition was maintained with 150 mg/day of extended-release bupropion, 100 mg/day of lamotrigine, and 75 mg/day of extended-release venlafaxine. She had an emergence of manic symptoms and was administered aripiprazole, 10 mg/day. Ms. A had never been treated with an antipsychotic in the past. One month later, her dose of aripiprazole was increased to 20 mg/day. During the course of the next month, she was tapered from lamotrigine and venlafaxine to consolidate her drug regimen. She was seen for follow-up, where she complained of muscle stiffness and tongue movements that had grown increasingly worse over the last 2 months. She was observed by her outpatient psychiatrist to have muscle rigidity, a masked face, a shuffling gait, and orofacial movements consistent with rabbit syndrome.

It was decided to taper the aripiprazole and start ziprasidone, 60 mg b.i.d., along with benztropine, 1 mg b.i.d. Ms. A was seen 5 days later with a marked improvement in symptoms. She had no orofacial movements, decreased muscle rigidity, and only a slight tremor. At this visit, aripiprazole was completely stopped, and ziprasidone was increased to 80 mg b.i.d. Two weeks later, Ms. A was seen with no muscle rigidity or orofacial movements. Benztropine was discontinued, and her condition was maintained with ziprasidone without any reemergence of symptoms. When we evaluated these events with the