Letters to the Editor

Mirtazapine-Associated Withdrawal Symptoms: A Case Report

Sir: Discontinuation symptoms associated with abrupt cessation of antidepressant medications including tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), and selective serotonin reuptake inhibitors (SSRIs) are widely reported in the literature.[1] To date, there is only one published report of withdrawal symptoms associated with mirtazapine.[2] A case is presented herein of a patient who experienced withdrawal symptoms associated with the sudden discontinuation of mirtazapine.

Case report. Ms. A, a 25-year-old woman, was diagnosed with a major depressive episode, moderate and panic disorder without agoraphobia according to DSM-IV. She was taking mirtazapine, 60 mg/day, as well as clonazepam, 0.5 mg b.i.d. She was doing well until she had to go out of town unexpectedly due to a family emergency. Toward the end of her stay, she ran out of mirtazapine and within 48 hours began to notice anxiety, restlessness, irritability, nausea, vomiting, and insomnia. She continued taking clonazepam and did not experience any panic attacks. Upon her return, Ms. A was evaluated and restarted on mirtazapine therapy at her usual dose. Her symptoms completely resolved within 24 hours. At 3 months, she remains stable.

Sudden withdrawal from antidepressants can cause a variety of somatic and psychological symptoms.[3] Although the exact mechanism is not fully known, a state of serotonin dysregulation may play a role.[4] Schatzberg et al.[5] postulate that other neurotransmitters such as dopamine, norepinephrine, and γ-aminobutyric acid (GABA) may be involved, as well as cholinergic rebound. A state of dysregulation of both the serotonin and noradrenergic systems may have been involved in this particular case, given the pharmacologic profile of mirtazapine of enhancing both serotonergic and noradrenergic transmission.[6] Because sudden or abrupt cessation of antidepressant therapy can lead to a withdrawal or discontinuation syndrome, clinicians need to be aware of this possibility. Although the syndrome is time-limited, the symptoms can be troublesome to patients as well as contribute to decreased compliance, leading to unnecessary visits.

Conclusions and opinions expressed are those of the author and do not necessarily reflect the position or policy of the U.S. Government, Department of Defense, Department of the Army, or the U.S. Army Medical Command.

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Timothy R. Berigan, D.D.S., M.D.
William Beaumont Army Medical Center
El Paso, Texas

Dysphagia and Chronic Mental Illness: Looking Beyond Hysteria and Broadening the Psychiatric Differential Diagnosis

Sir: Over the past 30 years, the deinstitutionalization of individuals with severe and persistent mental illness has led primary care clinicians and psychiatrists to collaborate in the long-term medical management of these individuals. No longer is treatment confined to institutions and staff working there; community-based physicians have assumed primary responsibility for the care of individuals with serious mental illness. This care includes treatment of complications due to long-term exposure to antipsychotic medications as well as treatment of illnesses that, having long been present in the general population, are now increasingly comorbid with serious mental illness in the community. The need for close coordination is heightened by the knowledge that individuals with serious mental illness have increased mortality rates,[1] dying up to 9 years earlier than individuals without serious mental illness.[2]

Soon after the introduction of antipsychotic medications in the 1950s, disorders of swallowing and their association with the presence and treatment of psychotic disorders were observed. Associations have been reported between dysphagia and tardive dyskinesia,[3–6] extrapyramidal side effects of medications,[6,7] a decreased swallowing reflex,[5] psychogenic factors,[8,9] xerostomia secondary to antipsychotic and coadministered anticholinergic medications,[5] and botulinum toxin injections.[10] The diagnosis of psychogenic dysphagia, also known as hysterical dysphagia or globus hystericus, is rarely an adequate explanation for dysphagia. A review by Ravich and colleagues[8] of patients previously diagnosed with psychogenic dysphagia showed that a medical etiology was found in two thirds of the cases, illustrating that the pursuit of a complete differential diagnosis is always indicated.

To elucidate the importance of close coordination in the diagnosis and management of dysphagia, we report the following case.

Case report. Mr. A, a 54-year-old man with a 30-year history of schizoaffective disorder, bipolar type (DSM-IV criteria), and tardive dyskinesia with spasmodic torticollis, presented to his primary care physician with the complaint of weight loss and an acute onset of an inability to swallow solids. He associated the difficulty swallowing with having recently choked while eating. He had also recently experienced the death of his long-time companion. At the time of the onset of dysphagia, Mr. A was taking risperidone, 8 mg/day; loxapine, 60 mg/day; carbamazepine, 1000 mg/day; botulinum toxin injections; trihexyphenidyl, 30 mg/day; levothyroxine, 100 µg/day; and atenolol, 50 mg/day. He did not smoke or drink alcohol or caffeine.

Physical examination at the time of presentation was unremarkable; a neurologic examination showed no abnormalities, a gag reflex was present, and he showed no signs of respiratory impairment. The spasmodic torticollis showed no evidence of worsening. A psychiatric examination 2 days later revealed minimal anxiety in the absence of manic or psychotic symptoms. A diagnostic evaluation coordinated by Mr. A's primary care physician included chest x-ray that showed no abnormalities, barium swallow, and esophagogastroduodenoscopy that showed only the presence of hiatal hernia. The treating psychiatrist decreased and then stopped loxapine and began a course of clonazepam, 1.5 mg/day.

The symptoms of dysphagia resolved over a 3-week period, and psychiatrically Mr. A has remained stable, benefiting from psychotherapy to resolve significant symptoms of grief. Lacking other objective evidence, the likelihood is that Mr. A developed a transient dysphagia secondary to a recent botulinum toxin injection.

The treatment of psychotic disorders carries several risk factors for dysphagia. Antipsychotic drugs decrease esophageal propulsion through impairment of both striated and smooth muscle function.[5] Xerostomia, or dry mouth, also frequently arises from the use of antipsychotic medications and the frequently coadministered anticholinergic agents such as benztropine. Decreased saliva leads to a dryness of the bolus to be swallowed and removes the acid neutralization that saliva enhances; both of the effects can lead to difficulty in swallowing.[5,11]

Tardive dyskinesia, a dysfunction of the voluntary muscles that arises in 20% of patients taking antipsychotic medications over a prolonged period, is also associated with impaired swallowing[3–6] and can be exacerbated by the use of anticholinergic agents, which can combine with tardive dyskinesia to decrease the gag reflex in affected individuals. In addition, tardive dyskinesia can interfere with the normal mechanism for chewing and swallowing through the development of involuntary buccolingual movements.

Extrapyramidal side effects arising from the use of antipsychotic medications can also contribute to dysphagia. Parkinsonian symptoms of bradykinesia, rigidity, or tremor can interfere with the normal process of mastication and swallowing.[6,7] Rapid and rhythmic oral movements may disrupt the process, as can hypokinetic pharyngeal movements. Finally, up to one third of patients receiving botulinum toxin injections for spasmodic torticollis secondary to tardive dyskinesia develop dysphagia during the course of their treatment.[10]

Several behaviors that contribute to esophageal disease and dysphagia coexist with psychotic disorders. Rates of alcohol, caffeine, and nicotine use are high in individuals with psychotic disorders,[12,13] and their use is associated with a decrease in lower esophageal sphincter pressure and resulting gastroesophageal reflux disease.

This case represents a convergence of these factors that can lead to problems swallowing for an individual with chronic mental illness and highlights the importance of a close working relationship between primary care physicians and psychiatrists in treating these individuals.

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Jeffrey G. Stovall, M.D.
Lisa S. Gussak, M.D.
University of Massachusetts Medical School
Worcester, Massachusetts