QTc Prolongation and Torsades de Pointes in an Elderly Woman Taking Fluoxetine

TO THE EDITOR: We describe an 83-year-old woman who experienced multiple episodes of torsades de pointes, probably because she was taking fluoxetine.

Transient unexplained loss of conscience in Ms. A led to her admission. Routine physical and laboratory examinations revealed no abnormalities (e.g., ischemia, electrolyte disturbances) besides a left bundle branch block and a prolonged QTc interval (478 msec, corrected for QRS interval widening because of the left bundle branch block; reference <450 msec). Her medications at admission were acetylsalicylic acid, 30 mg/day, and fluoxetine, 20 mg/day (serum levels at admission: fluoxetine, 204 μg/liter; norfluoxetine, 138 μg/liter); fluoxetine had been started 6 months earlier. During the night, continuous ECG recordings revealed recurrent short episodes of torsades de pointes. Multiple syncopal episodes occurred before admission, each time resolving spontaneously, which had never been observed before the initiation of fluoxetine.

Ms. A started having symptoms after the initiation of fluoxetine treatment and the documented pause-dependent polymorphic ventricular tachycardia characteristic of drug-induced QTc prolongation (1), which render fluoxetine use the most likely cause. Therefore, fluoxetine was discontinued. ECG recordings 2 and 8 months after fluoxetine discontinuation were normal apart from the left bundle branch block (QTc interval, 421 msec and 408 msec, respectively, corrected for the widening of the QRS interval). No further episodes of syncope or tachyarrhythmias were seen.

ECG recordings in fluoxetine preregistration trials (N=312) showed no heart-block-inducing ECG conductance disturbances. However, four case reports implicating fluoxetine in QTc prolongation (2, 3) or torsades de pointes (4, 5) have been published. One involved intentional overdose (5), and one involved concomitant verapamil treatment (3). Because of fluoxetine's widespread use, the absence of cardiac conductance disturbances in the limited relatively healthy population in the preregistration phase is not very informative. However, at postregistration, thousands of ECG recordings in patients taking fluoxetine have been performed; in two studies focused on those with heart disease, no conduction disturbances were recorded. In our patient, there was a suggestive temporal relationship between the use of fluoxetine and the occurrence of QT prolongation and repeated episodes of torsades de pointes. After withdrawal of fluoxetine, the QTc interval returned to normal. In the absence of other plausible explanations, we conclude that the use of fluoxetine was the probable cause of the development of recurrent torsades de pointes. Older age, preexistent left bundle branch block, and female gender were likely additional risk factors (1).

Prescribers should be aware of the potential capacity of fluoxetine to prolong the QTc interval. Although it is probably extremely rare, it can have serious consequences for the patients involved.

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Pisa Syndrome in a Patient in a Wheelchair Taking Valproic Acid

TO THE EDITOR: Pisa syndrome (pleurothotonus) is a condition characterized by sustained flexion of the body with the head to one side, creating a "Leaning Tower" posture. It was first described by Ekbom et al. in 1972 (1). General incidence rates are not well established, although it appears to be more common in older patients; an 8% incidence was found in one series of newly admitted geropsychiatric patients (2). Most authors have described Pisa syndrome as a side effect of prolonged exposure to conventional neuroleptics (3). More recently, other agents, including atypical antipsychotics, cholinesterase inhibitors, antiemetics, and tricyclic antidepressants, have been implicated (4). Although treatment with anticholinergic agents has been proposed, definitive therapy remains the discontinuation of the offending agent (5). We report a case of suspected Pisa syndrome in a 65-year-old patient in a wheelchair receiving valproic acid.

Mr. A was a 65-year-old nursing home resident being treated for schizoaffective disorder. He was in a wheelchair secondary to severe arthritis. His medications were 750 mg b.i.d. of valproic acid, 200 mg b.i.d. of carbamazepine, and 3 mg b.i.d. of risperidone—a regimen that had been stable and unchanged over several months. His valproic acid and carbamazepine levels were monitored routinely and were never above the therapeutic range.

Over a few weeks, the staff noticed that Mr. A had begun leaning to one side, a change that progressed to the point at which he was tilted at a 30° angle throughout the day. He seemed unaware of and unconcerned by this change. He showed no other signs or symptoms suggestive of an extrapyramidal syndrome. The only medication change to which Mr. A consented was a trial discontinuation of valproic acid. Immediately upon discontinuation, his posture returned to a stable, upright position.

Pisa syndrome has not been reported in association with valproic acid, but our patient's dramatic improvement with its discontinuation strongly suggests a medication-related effect, either solely due to valproic acid or perhaps secondary to a pharmacodynamic interaction between valproic acid and risperidone. We believe that this patient's wheelchair state contributed to a delay in recognizing this condition and hope

this report will heighten awareness to the fact that this syndrome can occur in nonambulatory patients.

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Comorbidity of Anxiety With Eating Disorders and OCD

TO THE EDITOR: The article by Walter H. Kaye, M.D., et al. (1) on comorbid anxiety disorders in eating disorders is a considerable contribution to this research area. However, other studies on this topic (2–4) were not referred to. Important information for several points of discussion is raised by these unmentioned studies.

We (2) found that 71% of 271 current subjects with eating disorders had lifetime comorbidity with at least one anxiety disorder (64% for Dr. Kaye et al.). The proportion of generalized anxiety disorder that was reported by Dr. Kaye et al. (10%) appears lower than our findings (anorexia nervosa: 45.6%, bulimia nervosa: 31.4%; all current). Converse to their finding, the eating disorders in our study group were all current, which may have affected the comorbidity rates. Given that subjects with a lifetime eating disorder (who are not currently ill) have a ratio of having no anxiety disorder to having an anxiety disorder significantly higher than for people who are currently ill (1), we wonder whether this discrepancy reflects a diagnostic bias instead of a bias of recall or a weak association with recovery. Indeed, high levels of anxiety and depressive symptoms (due to denutrition [5] or other factors, such as duration of illness, social disability, or preexisting trait anxiety) could lead to excessive current diagnoses of anxiety disorder.

Obsessive-compulsive disorders (OCDs) were nearly twice as frequent in the study of Dr. Kaye et al. (41%) as in our study (anorexia nervosa: 24.1%) and that of Iwasaki et al. (3). Although we did not use a symptomatic scale and thus may have missed some cases, the study by Iwasaki et al. suggests that it may rather be because the participants in the study by Dr. Kaye et al. "came from enriched pedigrees," leading to higher rates of comorbidity than in the community (1) or in other eating disorders groups.

Dr. Kaye et al. found that 66% of their comorbid cases and 42% of their entire study group had an onset of at least one anxiety disorder before the onset of an eating disorder. Our rates were, respectively, 50% and 33% (2). Although OCD and generalized anxiety disorder usually preceded the onset of an eating disorder in the study by Dr. Kaye et al., we observed the inverse pattern (2). This discrepancy could be due to some memory bias (i.e., people who have durably been characterized by obsessive-compulsive traits may have difficulties in remembering the exact time of the onset of OCD) or to a selection bias. Knowing that unusually precocious age at the onset of OCD is a risk factor for the development of eating disorders (6) and that the group selection of Dr. Kaye et al. was specific, we wonder whether the rate of early-onset OCD in their group of "enriched pedigrees" might have been unusually high.

Dr. Kaye et al. reported no differences in the rates of OCD between the patients with anorexia nervosa and those with bulimia nervosa, converse to another of their studies (4) in which they observed higher rates of OCD in patients with anorexia nervosa than in those with bulimia nervosa. In another of our studies (7), current diagnoses of agoraphobia and OCD were significantly more frequent in patients with anorexia nervosa than in those with bulimia nervosa. These contradictory results stress the need for developing further research on the comorbidity between eating disorders and anxiety disorders.

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TO THE EDITOR: We read with interest the report by Dr. Kaye et al. on the rates of comorbid anxiety disorders in individuals with eating disorders. The suggestion that child/adolescent-onset anxiety disorders may be associated with later eating disorders is particularly relevant to child mental health.