

A Case Report of Double Incontinence Associated With Clozapine

Sir: Clozapine is known to be an effective agent in the treatment of refractory psychotic disorders. Although clozapine causes minimal extrapyramidal symptoms, adverse effects such as agranulocytosis, weight gain, hypersalivation, seizures, and urinary incontinence form obstacles to patients' compliance. Clozapine-induced urinary incontinence is a frequently reported side effect¹; however, the literature is sparse about the combination of urinary and fecal incontinence.

Here, we present a male adult patient who had transient double incontinence during clozapine treatment.

Case report. Mr. A, a 35-year-old man with a 16-year history of DSM-IV schizophrenia, paranoid type, was admitted to the inpatient unit in September 2005 with psychotic symptoms after 1-month cessation of his medication (200 mg/day of clozapine). We decided to restart clozapine with a titration of 25 mg every 2 days in addition to flupenthixol depot once every 2 weeks. After 5 weeks of hospitalization, Mr. A was discharged on treatment with 350 mg/day of clozapine in combination with flupenthixol depot once every 2 weeks.

On his first outpatient visit after 3 weeks, his father reported development of double incontinence once every 2 days for the previous 2 weeks. His medical history and physical examination results were normal, so we decided to wait for his second outpatient visit in another 3 weeks and informed him that it might be a time-limited side effect and resolve spontaneously. On his second visit, it was noted that the double incontinence had remitted. Four months after Mr. A's discharge, the depot antipsychotic treatment has been stopped, and for the last 3 months he has been on treatment with clozapine 350 mg/day and has not experienced these side effects again.

Although the prevalence of clozapine-induced urinary incontinence is reported to range from 2.4% to 42%,² double incontinence has never been reported. It has been documented that patients with chronic psychotic disorders have high rates of urinary incontinence, but it is still not well understood whether the urinary incontinence is due to the severity of the mental illness or to the medication.³ Our patient had been suffering from schizophrenia for 16 years and had been on clozapine treatment for the last 2 years at a maximum dose of 200 mg/day without reporting such symptoms.

It is impossible to directly link our patient's double incontinence to clozapine, as he was receiving 2 neuroleptics; however, he did not develop such side effects when he was on treatment with flupenthixol depot and clozapine titration doses of less than 350 mg/day.

Clozapine-induced urinary incontinence has been shown to be dose dependent.³ Previous treatment with clozapine doses lower than 350 mg/day did not result in incontinence in our patient, which supports that double incontinence might also be dose related.

The adrenergic blockade effect of clozapine is suggested to be the cause of fecal and urinary incontinence by decreasing the tonus of the internal anal sphincter⁴ and internal bladder sphincter,³ respectively. As the incontinence may be time-limited and resolve spontaneously,³ waiting

and monitoring may be an option before starting any adjunct medication or switching to another antipsychotic.

Urinary incontinence alone is an embarrassing side effect for patients to report to staff, and double incontinence would certainly be underreported, with more negative effects on patients' compliance to treatment. Thus, clinicians should consider these facts more thoroughly during their daily practice.

The authors report no financial or other relationship relevant to the subject of this letter.

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Aripiprazole as the Causative Agent of Neuroleptic Malignant Syndrome: A Case Report

Sir: Neuroleptic malignant syndrome (NMS) is a rare and potentially life-threatening neurologic emergency commonly associated with the use of antipsychotic medications. As a class, atypical antipsychotic agents have lower associated rates of extrapyramidal symptoms and are less likely to induce NMS as compared to conventional antipsychotics. One of the newest agents in the atypical antipsychotic class is aripiprazole. We report the case of a 71-year-old woman with paranoid schizophrenia, who presented with NMS while on single-agent therapy with aripiprazole. In our review of the literature, this is the first reported case of NMS induced by aripiprazole as the single causative agent in an elderly patient.

Increasingly, family physicians find themselves as the primary providers for patients with mental health needs. In the case of patients taking antipsychotic medications for any in a broad array of psychiatric diagnoses, recognizing adverse therapeutic reactions is extremely important. Neuroleptic malignant syndrome, although rare, is a well-documented life-threatening condition that has been associated with antipsychotic or neuroleptic medications. The reported incidence rate of NMS ranges from 0.02% to 3% in patients who take neuroleptic agents.¹ Neuroleptic malignant syndrome is typically characterized by high fever, muscular rigidity, and mental status changes, along with characteristic laboratory findings including creatinine phosphokinase (CPK) elevation and often leukocytosis. NMS has been observed in every class of neuroleptic medi-

Table 1. Stages in Severity of Neuroleptic-Induced Catatonia–Neuroleptic Malignant Syndrome Spectrum^a

Score	Muscle Rigidity	Autonomic Nervous System Instability (2 of the 3 listed)	Mental Status	CPK (U/L)
0	Mild, with cogwheel rigidity	Temperature < 38°C Pulse < 100 bpm Blood pressure < 140/80 mm Hg	Baseline—some agitation	< 200
1	Moderate, with cogwheel rigidity	Temperature 38–39°C Pulse 90–110 bpm Blood pressure 130/80–150/90 mm Hg	Agitation-confusion	200–1500
2	Moderate–severe, lead-pipe rigidity	Temperature > 39°C Pulse > 110 bpm Blood pressure > 140/100 mm Hg	Delirium-coma	> 1500

^aReprinted with permission from Hynes and Vickar.¹¹
Abbreviation: CPK = creatinine phosphokinase.

cation, but has been reported most often in high-potency agents like haloperidol.² It is less often associated with low-potency agents like chlorpromazine and the newer neuroleptics such as risperidone and olanzapine.³ The antiemetic medications metoclopramide and promethazine have also been implicated as causative agents of NMS.

Atypical antipsychotics have proven useful in the treatment of a wide spectrum of psychiatric conditions including dementia, delirium, psychosis, agitation, and affective disorders.^{4,5} When compared to the first-generation “conventional” antipsychotic drugs, atypical antipsychotic drugs demonstrate enhanced efficacy and safety owing to their pharmacologic differences.⁶ The conventional antipsychotic drugs are high-affinity antagonists of dopamine D₂ receptors, resulting in effective management of psychotic symptoms but high rates of neurologic side effects such as extrapyramidal symptoms and tardive dyskinesia.⁷ In contrast, the atypical agents have lower affinity for dopamine D₂ receptors and greater affinities for other neuroreceptors, including those for serotonin and norepinephrine.⁷ Despite the lower rates of extrapyramidal symptoms relative to conventional antipsychotics, cardiovascular side effects, NMS, weight gain, hyperprolactinemia, diabetes, and hyperlipidemia have been reported with atypical antipsychotics.⁸

Aripiprazole represents one of the most recent additions to the atypical antipsychotic class. In comparison to the other atypicals, it possesses a unique mechanism of action that may limit the development of hypodopaminergic states. Aripiprazole is a dopamine D₂-receptor partial agonist with partial agonist activity at serotonin 5-HT_{1A} receptors and antagonist activity at 5-HT_{2A} receptors. At clinically used doses, aripiprazole results in an almost complete saturation of D₂-like dopamine receptors, yet the incidence of extrapyramidal side effects is no higher than with placebo; it is felt that the most likely explanation for this is the weak partial agonism of the drug at D₂-like dopamine receptors.⁹

Case report. Ms. A, a 71-year-old white woman with a history of pre-hypertension and paranoid schizophrenia, presented to the hospital in March 2006 with an abrupt change in her baseline mental status, noted skin flushing, and worsening tardive dyskinesia consisting of grimacing, tongue protrusion, lip sucking, and upper extremity choreiform movements. For the past 9 months, the patient had been taking aripiprazole at a dose of 15 mg daily, having only a subtle escalation of abnormal buccal-oral muscle movements and upper arm athetosis in the 4 weeks preceding presentation. Eight days prior to her emergency department presentation, the patient’s aripiprazole dose was decreased to 10 mg daily, and she was given a 1-week course of

benztropine at 1 mg daily for these extrapyramidal reactions. A review of the patient’s medication list revealed no other medications or supplements.

On examination, Ms. A’s rectal temperature was 106.5°F, her pulse was 137 beats per minute, her respiratory rate was 22 breaths per minute, and her blood pressure ranged from 99/54 mm Hg to 147/100 mm Hg. The patient was uncomfortable and in moderate distress. She exhibited marked muscle rigidity in addition to her obvious choreoathetoid movements. Her speech was initially slurred, but she became mute as her evaluation continued. There was a mild rise in her CPK level, which was initially 78 U/L and then increased to 103 U/L 8 hours later. Further studies revealed no leukocytosis, a normal complete metabolic panel, normal urine analysis, and brain computed tomography demonstrating only atrophic changes consistent with the patient’s age.

Given the patient’s medical history and presentation, the diagnosis of NMS was made. Ms. A received intravenous hydration, cooling blankets, and ice packs applied to her axilla and groin. She was also given bromocriptine 2.5 mg every 8 hours, in addition to benztropine 1 mg daily. Aripiprazole treatment was stopped, and she was placed on treatment with lorazepam 1 to 2 mg as needed for the remainder of her hospitalization.

The patient remained in the intensive care unit for 2 days awaiting stabilization of her autonomic lability and downward trend in CPK. She was then relocated to the medical ward, where, aside from mild tardive dyskinesia, she continued an uneventful recovery. Five days after her admission, the patient was transferred to a psychiatric hospital under the care of her psychiatrist.

Neuroleptic agents have been shown to be highly effective and in general, safe, obtaining widespread use in medicine. However, it is imperative to note that all antipsychotics have been reported as having the ability to induce NMS, including rare reports of NMS caused by clozapine, olanzapine, and risperidone.¹⁰ This case presents a unique occurrence of one of the newest atypical antipsychotics, aripiprazole, causing NMS in an elderly patient.

It is clear that, given this patient’s medication history and clinical presentation, she would be classified as having moderate to severe NMS according to the neuroleptic-induced catatonia–neuroleptic malignant syndrome (NIC-NMS) scoring system proposed by Hynes and Vickar,¹¹ shown in Table 1. In keeping with the concept of NIC-NMS as a single spectrum disorder, this patient would have scored 6, indicating moderate to severe NMS. Additionally, the NIC-NMS scoring system attributes additional severity based on CPK levels greater than

200 U/L. Although this patient's CPK peaked below this level, a likely explanation was the timely recognition of NMS. Her CPK levels would most likely have increased had there not been an abrupt discontinuation of aripiprazole in conjunction with early administration of bromocriptine to restore lost dopaminergic tone. It should also be noted that the use of serum CPK level as a major criterion for the diagnosis of NMS has been brought into question due to its lack of specificity.¹²⁻¹⁴ Nonetheless, assessing the patient for the presence of rhabdomyolysis, for which CPK is the most sensitive test, is an invaluable component in the assessment of NMS and its comorbidities.^{15,16}

NMS can be ambiguous in its presentation. It has been suggested that extreme temperature elevations and extrapyramidal symptoms occur less frequently in NMS attributed to atypical antipsychotics compared to conventional antipsychotics.¹⁰ Although infrequent, this case and 2 previously published cases of NMS in which pyrexia was absent illustrate that NMS can occur with aripiprazole.^{17,18} Further investigation is warranted to determine if the incidence of aripiprazole-induced NMS is greater than that of other atypical antipsychotics. Nonetheless, the roles of vigilance and patient education for those taking antipsychotic medications, whether typical or atypical, remain the key in averting the life-threatening complications of NMS. With the shortage of mental health services, the management of these patients is falling in the hands of primary care providers.¹⁹ It is vital that these providers be able to recognize NMS along with its causative agents and implement appropriate care.

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Psychotic Symptoms 10 Years After a Single Episode of Childhood Sexual Abuse

Sir: Can a single episode of sexual abuse in childhood cause psychiatric problems at a later point in life? Childhood sexual abuse is one of the major risk factors for psychiatric conditions and for numerous physical symptoms in adolescence and adulthood.¹ In most cases, symptoms occur within the first several months after childhood sexual abuse and last for a long time.² Recently, we encountered a girl who developed acute psychotic symptoms more than 10 years after a single episode of childhood sexual abuse.

Case report. A 16-year-old girl was hospitalized in February 2005 for psychotic symptoms. Seven days before the hospitalization, she witnessed some violent actions: as a prank, a few male seniors tore off her sister's skirt during a junior high school graduation ceremony. From that time, she suffered from insomnia, anorexia, anxiety, agitation, and hypersensitivity to sex-related scenes or words. Four days before the hospitalization, a man from her neighborhood visited her father, and after the neighbor's visit, new symptoms developed, including auditory hallucinations, referential ideas, persecutory delusion, and fear of men. She was even afraid of her own father. Sometimes she did not recognize her family and thought that they were villains disguised as her family who would sell her to a brothel.

During a psychiatric interview, she revealed that the man from the neighborhood had abused her sexually once when she was 5 years old. The man touched her external genitalia through her underwear at his house. At that time, there was no immediate reaction from her and therefore nobody recognized the episode.

After hospitalization, the patient was treated with risperidone syrup 0.4 mg t.i.d. for 3 days. At that point, her symptoms ameliorated, and the dose was decreased to 0.5 mg per day for 7 days. She was hospitalized for a total of 10 days. At the time of discharge, she showed no symptoms.

It cannot be proven that the patient's psychotic symptoms were related to her past sexual abuse episode. However, since she started having psychotic symptoms after she witnessed an action (her sister's skirt being torn off) that had sexual content,

and then met the man who abused her, we can assume that these events were related to the development of her symptoms and worked as a catalyst that reminded her of the past trauma.

As far as we know, there are no reports of psychotic symptoms more than 10 years after a single episode of childhood sexual abuse. We found that a child who had experienced a single episode of sexual abuse with no immediate psychiatric symptoms might develop psychotic symptoms later. Therefore, we should recognize that even a single sexual abuse episode in early childhood might later lead to psychiatric symptoms even if it does not affect the child immediately. Further research is indicated.

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A Protracted Case of Psychosis, Motor Abnormalities, and Agitation

Sir: Somatization is a psychological process whereby psychological distress is expressed in the form of somatic symptoms.¹ Conversion disorder is a type of somatization that presents with signs and symptoms limited to the central nervous system.² Despite the substantial literature, the exact etiology of conversion disorder is still controversial. Two important DSM-IV criteria for the diagnosis of conversion disorder include association of psychological factors with either initiation or exacerbation of symptoms and inability to explain the symptoms due to any general medical condition. Some earlier studies have postulated that the prognosis of this disorder varies with symptoms; for example, seizures and tremors would have worse prognosis as compared to weakness and sensory disturbance.³ We present an interesting case by its complicated course and sudden improvement of what we believe is conversion disorder.

Case report. Mr. A, a 30-year-old male Honduran native, was brought to the emergency department by his family secondary to fainting, questionable seizures, fever, recent right arm numbness, and agitated behavior. The history was obtained from the patient's sister as Mr. A was unable to answer questions reliably and did not speak English. The sister reported that his symptoms began approximately 2 weeks earlier, when he experienced an episode of twitching and foaming at the mouth consistent with a seizure. He was seen by a medical doctor at another hospital at that time and was discharged home; however, 2 days later he experienced a second seizure with the same symptoms. Mr. A was again taken to the hospital, where he was admitted and discharged home 2 days later.

At that time, Mr. A was started on phenytoin 100 mg t.i.d. He was also started on risperidone 1 mg nightly and diazepam 5 mg

p.r.n for agitation. Since then, the patient markedly deteriorated in terms of thought organization. Initially he was more forgetful and subsequently became grandiose, believing he was god and trying to stop traffic, reasoning that, as god, he would not get hurt. He also began having visual and auditory hallucinations that his father, who passed away several months ago, was speaking to him through the television.

The patient's family reported a possible seizure episode with similar symptoms approximately 7 years ago. The family stated that the patient was typically a pleasant, well-mannered gentleman without any alcohol problems or illicit drug use.

Mr. A was admitted to the university hospital floor at this time and initiated on vancomycin, acyclovir, ceftriaxone, and thiamine as empiric therapy for meningitis. His phenytoin level was 3.0 µg/mL in the emergency department. A lumbar puncture was performed, and cerebrospinal fluid was negative for infection and malignancy. Urine and blood culture findings were negative as well. Magnetic resonance imaging of the brain showed borderline low inferior cerebellar tonsils, but findings were otherwise normal.

He also complained of some psychotic symptoms, seeing horns on the television, ideas of reference, and grandiosity. Risperidone was raised to 2 mg nightly with 1 mg every 8 hours p.r.n., and lorazepam 5 mg p.r.n. was given for agitation, and diazepam treatment was stopped; however, he continued to have agitation throughout his hospital stay. Ceftriaxone, vancomycin, and acyclovir were discontinued as cultures remained negative, and polymerase chain reaction assay for herpes simplex virus was also negative. His phenytoin therapy was continued. After a 2-day hospital stay, he was transferred to an inpatient psychiatric hospital for further care with a DSM-IV diagnosis of bipolar disorder with psychotic features and seizure disorder.

Three weeks later, he was readmitted to the psychiatric hospital for increasing seizure activity, reportedly 2 to 3 episodes daily for 3 or 4 days. Psychiatric hospital staff also reported that Mr. A had become less responsive and less cooperative with hospital personnel. He would not bathe himself nor go to the bathroom and had refused to eat or drink for the previous 2 or 3 days. In the same time period, the patient also appeared to be having more hallucinations. At the time of admission, Mr. A was very agitated and speech was nonexistent. Quetiapine and lithium were started to help him with his agitation. Quetiapine was titrated up to 450 mg q.a.m. and 450 mg q.h.s., and lithium was titrated up to 300 mg b.i.d. An electroencephalogram showed no seizure activity. There was increased muscle tone and muscle rigidity in both arms and legs. The remaining findings of the examination were within normal limits.

At admission, Mr. A was started on intravenous (IV) fluids. He was loaded on divalproex 1000 mg and was started on a valproate dose of 500 mg t.i.d. IV. Due to the patient's psychosis, the dose of risperidone was adjusted to 3 mg nightly and 1 mg every 4 hours p.r.n. The patient's creatine kinase (CPK) was 2124 U/L. Risperidone was switched to olanzapine 5 mg daily due to a concern of neuroleptic malignant syndrome, which was later ruled out. The patient continued to be agitated during his hospital course; however, no seizure activity was observed. Eventually, the patient was switched to oral valproate. The patient's CPK levels fluctuated throughout his hospital course, which may have been due to the patient's being restrained. The patient was in 4-point restraints because of his physical aggression.

The patient then began to eat a majority of meals and was able to urinate and have bowel movements. He had no seizures throughout the hospitalization. After a week of hospitalization,

the patient was again discharged from the inpatient psychiatry hospital.

He continued to have refractory psychotic symptoms and subsequently began electroconvulsive therapy (ECT) treatment. Following his third ECT episode, Mr. A had onset of status epilepticus and was transferred back to the university hospital. The patient was admitted to the intensive care unit (ICU) for intubation for airway protection; loaded with fosphenytoin, phenytoin, and midazolam; and placed on a ventilator. Lithium and quetiapine were discontinued. In the ICU, he continued to have waning levels of consciousness and responsiveness, occasional seizure activity, right facial twitching, and lip smacking. He had some minor seizure activities, but remained stable and was subsequently transferred out of the ICU. On the general hospital ward, Mr. A continued seizure free for weeks.

Later one day, his family arrived, and, to our surprise, Mr. A started talking with them. We requested his family to visit with him more frequently. In response to increased visitation, we noticed that the patient started to get more responsive and eventually became more alert and oriented. His condition remained stable, and after a 1-month hospital stay, Mr. A was diagnosed with DSM-IV conversion disorder and transferred to a hospital at his home in Honduras per the family's request.

This appears to be an unusual case of what we believe to be conversion disorder. Although this patient might have an underlying bipolar disorder with psychotic features, the sudden resolution of symptoms associated with the visitation from his family clues us toward a diagnosis of conversion disorder.

Conversion disorder is a challenging psychiatric illness that represents a somatic defense against threats to mental instability.¹ The rate of misdiagnosis of conversion disorder has significantly dropped from 29% in 1950s to 17% in 1960s to 4% in 1990s, an outcome that has partly been associated with improvement in the diagnostic methods.⁴ The management of this disorder should be focused on developing a therapeutic alliance with the patient and to further explore the areas of the patient's life beyond the presenting symptoms, to develop a treatment plan centered around reduction of distress, and to address other comorbid illnesses.⁵ Close attention should be paid to the physiologic needs of the patient including mobility, skin care, disuse atrophy, and contractures to prevent troublesome injury.⁶

Contrary to earlier beliefs, it has now been suggested that the presence of an occult neurologic disorder is not responsible for the symptom production, and the chances of missing a neurologic disorder are low.⁵ In one study, it has been reported that 20% of 50 documented cases of conversion disorder had a coexisting neurologic disorder.⁷ Some studies are conflicting in that they argue the presence of organic brain disorders in their early stages when they are most difficult to detect.⁸

While dealing with this interesting case, we also kept in mind a differential diagnosis of neuroleptic malignant syndrome, malingering, and factitious disorder. Neuroleptic malignant syndrome was ruled out due to the absence of fever, rigidity, and other autonomic instability. A trial of intramuscular lorazepam was also given with no benefits. Despite the extensive workup, an underlying occult neurologic or medical illness could not be completely ruled out, but the sudden change in the symptomatology demonstrated by this patient upon visits by his close family members favored a diagnosis of conversion disorder.

The authors report no financial or other affiliation relevant to the subject of this letter.

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"Bipolar Family": Useful Mnemonic to Differentiate Bipolar From Unipolar Depression

Sir: When depression is preceded by a history of manic, mixed, or hypomanic episode, classifying it as bipolar depression rather than unipolar depression becomes straightforward. However, when there is no access to such history and the initial presentation is from the depressive end of the pole, correctly classifying the disorder as bipolar rather than unipolar then becomes difficult. Being able to correctly classify depression as bipolar rather than unipolar is crucial due to the ramifications of the diagnosis in terms of management. For example, it has been recommended that the depressive period of uncomplicated bipolar disorder should be treated for shorter periods than that for unipolar depression.¹ Whereas in unipolar depression antidepressant monotherapy may be appropriate, in bipolar depression, without coupling it with a mood stabilizer, it may precipitate a "manic switch" and create a state of chronic irritable dysphoria and possibly a long-term rapid-cycling course.

Due to symptomatic similarity between the 2 diagnostic entities, no particular symptom invariably distinguishes between the 2 disorders. However, if residents, psychiatrists, and family physicians can maintain a high index of suspicion, then certain factors from the past or present history would indicate that the depressive episode is more likely to be bipolar rather than unipolar. We describe the mnemonic "Bipolar Family" to remind clinicians of factors or symptom clusters that would make a depressive episode more likely to be bipolar rather than unipolar (Table 1).

In view of the significant difference in treatment³ and despite the similarity in presentation, we hope that residents, psychiatrists, and primary care clinicians will utilize this mnemonic as a screening tool when faced with a patient who primarily presents with a depressive episode.

The authors report no financial or other affiliation relevant to the subject of this letter.

Table 1. "Bipolar Family": Factors That Make a Depressive Episode More Likely To Be Bipolar Rather Than Unipolar^a

B	Brevity of episodes
I	Impulsivity
P	Premorbid hyperthymic personality; polarity switch in response to antidepressant monotherapy
O	Overeating and oversleeping
L	Lability of mood
A	Anxiety disorders ² and substance use disorders are usually comorbid
R	Relatively resistant to treatment
F	Family history of schizophrenia or bipolar disorder
A	Abrupt onset, agitation, and behavioral abnormalities
M	Mixed episodes
I	Instability of job and marriage
L	Lamotrigine or lithium is recommended first-line treatment ³
Y	Young age

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A Case Report of Photosensitivity to Amisulpride

Sir: Amisulpride is a second-generation antipsychotic approved as monotherapy for treatment of refractory schizophrenia.¹ It acts with a unique pharmacologic profile that has preferential affinity for D₂/D₃ receptors and specificity for limbic rather than striatal structures. Very few side effects of amisulpride therapy, and none with a dermatologic nature, have been reported.²

We hereby report the following case of photosensitivity to amisulpride in a patient with chronic schizophrenia.

Case report. Ms. A is a 38-year-old white woman with a 15-year history of paranoid schizophrenia (DSM-IV³). During her previous hospitalization for an acute exacerbation of her mental disorder with bizarre paranoid delusions and auditory hallucina-

tions, she was treated with clozapine 300 mg/day for 2 months, but this medication was discontinued in June 2005 because of a weight gain, strong sedation, and persistence of auditory hallucinations.

After clozapine treatment was stopped, Ms. A was treated with amisulpride. Six days after the initiation of this therapy at a dose of 400 mg/day, she experienced a photosensitivity dermatitis, as evidenced by erythema over exposed areas of the body (face, hands, posterior aspect of the neck); covered skin was spared. Ms. A denied the recent use of new soaps, new creams, or different foods and also denied more exposure to sunlight than usual.

With the exception of this dermatitis, the patient tolerated amisulpride well and had a good clinical response, i.e., decrease in auditory hallucinations. A dermatologic consultation confirmed the diagnosis of a photoallergic reaction. A medical history and physical examination revealed no somatic disorder. Results of a blood test were normal (no inflammatory or autoimmune factors were detected), and there was no remaining clozapine in the patient's system. No other prescribed medications were changed during the 2 weeks of amisulpride treatment.

Amisulpride treatment was interrupted, and Ms. A was instructed to apply sunscreen to the affected areas 3 times daily. The degree of erythema diminished over the next 10 days. Dermatitis continued to remain quiescent with the daily application of sunscreen.

The patient reported that she was prescribed amisulpride 4 years ago, during a previous hospitalization, with the same side effect, and the treatment was stopped 2 weeks after introduction.

This is the first reported case of photosensitivity to amisulpride. While other neuroleptics are well known to cause photosensitivity,⁴ there is no report of a dermatologic side effect with amisulpride.

Those individuals who are known to be photosensitive and are started on a regimen of amisulpride should be monitored carefully to minimize their unprotected exposure to the sun. Further studies are needed to understand the precise mechanisms involved. This research is particularly important because atypical antipsychotics are now commonly prescribed over conventional neuroleptics.

The authors report no financial or other relationship relevant to the subject of this letter.

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Possible New Causes for False-Positive Diagnosis of Pheochromocytoma: Lamotrigine, Aripiprazole, or the Combination

Sir: Pheochromocytomas are rare neuroendocrine tumors diagnosed by elevated plasma and/or urine catecholamines or their metabolites.^{1,2} Medications reported to cause false-positive serum or urine studies include acetaminophen, phenoxybenzamine, amitriptyline, labetalol, haloperidol, levodopa, tamsulosin, venlafaxine, hydrochlorothiazide, and buspirone.^{2,3} We report a case in which lamotrigine, aripiprazole, or both caused symptoms and biochemical evidence suggesting pheochromocytoma that resolved when the drugs were discontinued. There are no previous reports of lamotrigine or aripiprazole associated with false-positive biochemical testing for pheochromocytoma.

Case report. Mr. A, a 60-year-old white man, presented in May 2005 with anxiety, palpitations, and panic attacks starting 3 months prior to evaluation, immediately after he underwent cardiac bypass surgery. He had no medical complications perioperatively and initially attributed his symptoms to the stress of surgery. He was seen by Psychiatry and diagnosed with depression, attention-deficit/hyperactivity disorder, and bipolar disorder and placed on treatment with aripiprazole, lamotrigine, and venlafaxine.

Mr. A's attacks became more frequent, and he felt incapacitated. On examination, he appeared anxious. His blood pressure was 141/96 mm Hg, and his pulse was 97 bpm. The remainder of his examination was unremarkable. Additional medical history of the patient included hypothyroidism, hypertension, and obstructive sleep apnea. At initial presentation to the Division of Diabetes, Endocrinology and Metabolism, 3 months after his first evaluation by Psychiatry, his medications were lamotrigine, venlafaxine, and aripiprazole in addition to tamsulosin, aspirin, levothyroxine, amlodipine, benazepril, and rosuvastatin. He was taken off tamsulosin and venlafaxine to undergo biochemical testing for pheochromocytoma. Laboratory tests showed elevated urine and plasma normetanephrines (Table 1). Abdominal computed tomography scan and metaiodobenzylguanidine (MIBG) scan findings were normal.

We discontinued lamotrigine and aripiprazole treatment and repeated plasma and urine studies 3 weeks later, at which time results of Mr. A's plasma and urine studies had normalized, and his symptoms had resolved (Table 1).

Lamotrigine is an antiepileptic medication, and aripiprazole is a new atypical antipsychotic; both are used in the treatment of bipolar disorder. Lamotrigine prolongs the refractory phase of voltage-gated sodium channels.⁴ Aripiprazole is a partial D₂ agonist and acts differently from the existing atypical antipsychotics.⁵ Neither drug has an obvious mechanism for raising catecholamines or its metabolites. Given the severity of our patient's symptoms, both drugs were stopped simultaneously. His laboratory values returned to normal, and his symptoms resolved completely. He is unwilling to reintroduce each medication separately to determine if the effect observed was an individual drug effect or a synergistic occurrence. Additional reports are needed to evaluate this further. Given this case, we recommend considering lamotrigine and aripiprazole as 2 additional medications that could cause a false-positive biochemical result when evaluating for pheochromocytoma.

Dr. Goldner has received honoraria from Abbott and Takeda and has been a member of the speakers/advisory board for Takeda.

Table 1. Biochemical Workup for Pheochromocytoma

Test	March 2005 ^a	May 2005 ^b	Reference Range
Urine free normetanephrines, $\mu\text{g}/24\text{ h}$	2100	713	138–900
Urine total metanephrines, $\mu\text{g}/24\text{ h}$	2202	804	233–1300
Plasma free normetanephrines, nmol/L	1.46	0.63	< 0.9

^aLaboratory tests done at baseline during treatment with aripiprazole and lamotrigine.

^bLaboratory tests done 3 weeks after discontinuation of aripiprazole and lamotrigine.

Drs. Shivaswamy and Erwin report no financial or other relationship relevant to the subject of this letter.

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Association of Psychosis and Hyperthyroid Goiter: A Case Report

Sir: Psychiatric symptoms have been reported, not infrequently, with disorders of the thyroid gland,¹ most commonly with hypothyroidism. Additionally, psychosis is quite a rare occurrence,^{2,3} with hyperthyroxinemia being considered a potential cause.⁴ We present a case of a young man with preceding symptoms of hyperthyroidism and an acute psychotic state.

Case report. Mr. A, a 31-year-old married man, was brought to the psychiatry outpatient clinic by his family in March 2003. Around January 2003, he had started reporting subtle complaints in the form of gradually increasing appetite and thirst, loss of weight, mild tremors, and occasional nervousness without any apparent reason. Around February 2003, he started remaining tense, preoccupied, irritable, and restless, complaining of lack of confidence with poor concentration. Subsequent worsening led to additional features of irrelevant speech, inappropriate affect, paranoid ideas, and auditory hallucinations.

Mr. A was premorbidly well-adjusted, with no significant medical or surgical history or any history of substance abuse. There was family history of hypothyroidism in the mother and bipolar affective disorder in the father.

Physical examination showed moist palms, fine tremors of fingers, and exaggerated deep tendon reflexes in all the limbs. Mr. A had a soft, diffusely enlarged thyroid gland.

Investigations found high triiodothyronine/thyroxine levels, low thyroid-stimulating hormone levels, and high radioactive iodine uptake at 4 hours that became low at both 24 and 48 hours. Ultrasound of the thyroid revealed bilateral symmetrical enlargement of both lobes and isthmus, with multiple tiny nodules. Test for thyroid microsomal antibody was positive. The endocrinologist made a diagnosis of diffuse toxic goiter and advised nonsurgical treatment.

Initially, Mr. A was treated with risperidone, clonazepam, and trihexiphenidyl as an outpatient. However, due to nonresponse he had to be managed as an inpatient.

Olanzapine (10–20 mg/day), lorazepam (4–8 mg/day intravenously/oral), and zolpidem (10 mg nocte) were used for treating psychosis, with carbimazole (40 mg daily) and atenolol (50 mg daily) for hyperthyroidism. Mr. A showed improvement in all the symptoms over the next 7 to 10 days, and the symptoms were negligible after around 4 weeks, except for occasional apprehension regarding his office work.

Mr. A was discharged in a stable condition with recommendations to visit psychiatric and endocrinology outpatient clinics and to continue with medicines. His diagnosis at that time was organic delusional (schizophrenia-like) disorder (ICD-10 criteria).⁵

After discharge, Mr. A maintained euthyroid status (with medication). He was followed up in the psychiatry outpatient clinic. There was no emergence of psychosis; his antipsychotic was tapered and stopped after 6 months. Mr. A was asymptomatic at last follow-up (8 months post-discharge).

Patients with elevated thyroid hormonal levels frequently have psychological symptoms and sometimes have well-defined psychotic syndromes, as described above in our index patient. The pattern and association of onset and resolution of symptoms with treatment response in our patient point to the likelihood that the psychosis was secondary to the hyperthyroid state.

Case reports refer to certain manifestations, i.e., thyrotoxic psychosis,² organic schizophreniform disorder in autoimmune thyroiditis,⁶ and psychosis following acute alteration of thyroid status.⁷ It is important to distinguish these cases from the transient hyperthyroxinemia that may accompany acute exacerbations of certain psychiatric disorders,⁸ as the distinction can

have important implications for management. As in our index case, most people with a psychotic illness induced by hyperthyroxinemia may respond well to a combination of short-term antipsychotic treatment and management of the underlying thyroid illness.^{3,9}

Other researchers have put forward a case for studying neuropsychiatric aspects of thyroid disorders.^{3,9} We affirm this suggestion, highlighting the need for a close liaison between psychiatrists and endocrinologists.

Dr. Gupta has received honoraria/lecture fees from AstraZeneca and education-related fees for attending conferences from Eli Lilly, Janssen, Wyeth, and Lundbeck. Dr. Singh reports no financial or other relationship relevant to the subject of this letter.

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