The Effect of Aripiprazole on Psychosis in the Presence of a Dopamine Agonist

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The patient, Mrs. M, is a 48-year-old, white female with a history of anxiety disorder not otherwise specified and alcohol dependence with physiologic dependence in sustained full remission for 20 years.

Mrs. M had previously followed up with a psychiatrist with partial compliance, only attending two sessions. She was prescribed quetiapine 100 mg orally at bedtime for insomnia and maintained compliance despite neglecting further follow-up with her psychiatrist.

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Mrs. M presented to the emergency department (ED) with anxiety as well as worsening persecutory delusions that reportedly began 6 months earlier, coinciding with a formal diagnosis of a prolactinoma and subsequent treatment with the dopamine agonist cabergoline. The content of these delusions included a belief that her husband was bugging her room

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and poisoning her food, subsequently resulting in a 15-pound weight loss over the past month. The week prior to presenting to the ED, these delusions intensified, resulting in Mrs. M's belief that her husband was trying to kill her.

No further psychotic or mood symptoms were reported. Additionally, no manic or anxiety symptoms, suicidal ideation, or homicidal ideation were reported. No current substance use was reported.

Mrs. M was admitted to our facility for stabilization with the following regimen: 10 mg daily of aripiprazole for the treatment of psychosis, and 0.5 mg of clonazepam orally twice daily was prescribed for anxiety. Cabergoline was held to avoid exacerbation of psychotic symptoms.

Six months prior to this presentation, Mrs. M presented with bilateral galactorrhea. Upon follow-up with an endocrinologist, her laboratory results showed an isolated elevation of prolactin level at 66 ng/mL. All other laboratory results were within normal limits, including complete blood count and thyroid function and kidney function tests. Mrs. M denied any further associated symptoms, such as visual field changes, amenorrhea, or decreased libido.

An MRI of the brain revealed a lesion in the intrasellar area of the pituitary gland, measuring 0.9 cm × 1.9 cm × 1.6 cm. A preliminary diagnosis of pituitary microadenoma was made and Mrs. M began treatment with a dopamine agonist, cabergoline 0.5 mg orally two times per week. After 18 days of treatment, prolactin levels improved and decreased to 6.9 ng/mL, a level within normal limits. Mrs. M continued maintenance treatment with cabergoline.

During her hospital course, a full laboratory work-up was obtained, including a complete blood count with differential and comprehensive metabolic panel (CMP-14). All results were within normal limits. Prolactin and thyroid function tests

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results were also within normal range: prolactin level was 8.5 ng/mL (normal range for a nonpregnant female is 3.0 ng/mL to 30.0 ng/mL); thyroid-stimulating hormone (TSH) level was 1.33 (normal range is 0.34- 4.82); and T4 level was 0.84 (normal range is 0.59-1.61). At that time, no associated symptoms were reported, including galactorrhea, nipple discharge, or abnormal menses. Additionally, Mrs. M reported no abnormalities in her last four menstrual periods, with each cycle lasting 28 days, with low flow of 5 days in duration.

Mrs. M maintained treatment with aripiprazole, and clonazepam was titrated to discontinuation after her symptoms of anxiety had subsided. Neurology and medical liaison consultations were employed for further care of Mrs. M's comorbid prolactinoma. As a result, cabergoline was resumed, because discontinuation of it prior to a 3- to 5-year surveillance period may provoke a resurgence of the benign prolactinoma, as exhibited by the mild elevation in prolactin levels in 1 day from 8.5 ng/mL to 10.1 ng/mL.

No visual field changes or rise in prolactin levels were noted. However, additional close monitoring of prolactin level or tumor size with an endocrinologist was recommended, as well as a follow-up MRI within 6 to 12 months.

After 7 days of compliance with aripiprazole, Mrs. M exhibited moderate relief of psychotic symptoms with marked improvement in insight. This was exemplified by the increase in her food intake, with a subsequent 9-lb increase.

After evidence of improvement, aripiprazole was titrated further to a final dose of 15 mg orally once daily to further reduce Mrs. M's psychotic symptoms. Upon discharge, Mrs. M made plans to continue therapy and follow up with an outpatient psychiatrist the following week.

DIAGNOSIS

Hyperprolactinemia, Caused by a Pituitary Microadenoma

Prolactinomas are the most common type of benign pituitary tumors. They secrete a hormone called prolactin. Dopamine agonists have an inhibitory effect on this tumor, resulting in decreased prolactin secretion and tumor size, making these tumors more susceptible to medical treatment rather than surgical dissection. Dopamine agonists are the primary treatment of a prolactinoma, with cabergoline being the drug of choice due to its lower adverse effect profile com-

pared with bromocriptine. However, the use of dopamine agonists in patients with hyperprolactinemia may lead to the development of new-onset psychosis. This creates an oppositional treatment profile for patients suffering with a prolactinoma and psychosis.

Aripiprazole has become the drug of choice in these patients due to its unique mechanism of action as a partial agonist at dopamine D2 receptors. This allows psychotic symptoms to be minimized while simultaneously lowering prolactin levels.

For patients with a prolactinoma, a 3-year maintenance treatment on a dopamine agonist is recommended for adequate surveillance of the prolactinoma's invasive properties. Therefore, when patients present with psychosis in this setting, the dilemma remains as to how to minimize the psychosis while patients are maintained on dopamine agonists. Our goal is to demonstrate that aripiprazole is an effective and appropriate treatment of choice when psychosis and prolactinoma coexist.

Hyperprolactinemia, caused by a pituitary microadenoma, may be treated pharmacologically with a dopamine agonist. Dopamine's inhibitory effect on prolactin is beneficial for patients with hyperprolactinoma because it reduces prolactin levels and tumor size. It is recommended that patients remain on a dopamine agonist for a minimum of 3 years to maintain normal prolactin levels and prevent tumor regrowth. A consequence of long-term dopamine therapy, however, is the development of new-onset psychosis. The addition of antipsychotic medications can help to minimize psychotic symptoms. Aripiprazole, a partial dopamine agonist, may help to minimize psychosis while concurrently inhibiting prolactin levels.

Aripiprazole is the best treatment for the patient presented in this case due to its unique mechanism of action.

Mrs. M presented with late-onset psychosis, which is atypical for most psychotic disorders. Additionally, her psychotic symptoms presented shortly after she was diagnosed with and subsequently treated for a prolactinoma with cabergoline. In review, and by exclusion, Mrs. M's delusions were most likely a result of her pharmacologic treatment with cabergoline for the pituitary tumor. It should also be noted that Mrs. M's thyroid levels remained within normal limits, which would rule out the possibility of psychosis secondary to hypothyroidism. Hypothyroidism may also result from pituitary adenomas, more specifically, those that are non-hormone secreting. As a result of treatment with the low-potency dopamine antagonist aripiprazole, and despite reinstatement of cabergoline, Mrs. M's symptoms improved. Future treatment recommendations must take into account this reinstatement of a dopamine agonist (cabergoline). Therefore, in addition to regular follow-up visits with an endocrinologist, regular follow-ups with a psychiatrist are advised in order to monitor for psychotic symptoms.

CONCLUSION

Aripiprazole is the best treatment for the patient presented in this case due to its unique mechanism of action, being a partial dopamine D2 and 5-HT1 agonist and an antagonist at the dopamine and 5-HT2 locus. The partial D2 receptor agonism provides decreased liability for extrapyramidal symptoms and hyperprolactinemia.

REFERENCE

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