BROMOCRIPTINE-INDUCED SCHIZOPHRENIA

Sebastian A. Peter, MD, Arthur Autz, MD, and Marie Louise Jean-Simon, RPA
Brooklyn, New York

A 53-year-old male, without any prior history of psychosis, developed schizophrenia 4 days after starting low-dose bromocriptine therapy for a macroprolactinoma. Five days after discontinuation of this medication his mental status returned to normal. This case is reported in support of the dopamine hypothesis for the etiology of schizophrenia. (*J Natl Med Assoc.* 1993;86:700-701.)

Key words • bromocriptine • schizophrenia

Prolactin-producing cells in the pituitary are under inhibitory control from the hypothalamus. Dopamine is believed to be the putative prolactin-inhibitory factor.[1] Bromocriptine, a semisynthetic ergot alkaloid, acts as a dopamine receptor agonist in the hypothalamus, anterior pituitary, and the mesolimbic system. As a result of this activity, bromocriptine is used in the management of prolactinomas and Parkinson's disease, and for suppression of postpartum lactation.[2] There is a high recurrence rate of prolactinomas treated with transsphenoidal surgery, and as a result bromocriptine is now the therapy of choice for prolactinomas.[3] Bromocriptine-induced psychosis has been reported in patients receiving high doses (15 mg to 20 mg) and those with a history or family history of psychosis.[4-6] This article reports a case of a 53-year-old male who became psychotic on low-dose bromocriptine therapy.

CASE REPORT

A 53-year-old male came to the emergency room at St. Mary's Hospital on August 25, 1992 with complaints of progressive weakness and headaches. He gave a history of hypertension. The significant findings on physical examination were pale mucous membranes and a blood pressure of 96/60 mm Hg. The initial laboratory evaluation confirmed anemia with a hemoglobin of 8.1 g. The patient's sodium level was 125 mmol/L (136-148), and his potassium level was 4.9 mmol/L (3.5-5.0). Investigation of the anemia confirmed the diagnosis of anemia of chronic disease.

Evaluation of the hyponatremia showed that the patient had secondary hypothyroidism, thyroid-stimulating hormone 3.11 uiu/mL (0.46-3.59), triiodothyronine uptake 27% (33-47), thyroxine 5.0% μg (5.3-13.7), and secondary hypoadrenalism. The cosyntropin test revealed a baseline cortisol of 3.2% μg. Cortisol at 30 minutes and cortisol at 60 minutes were, respectively, 7.7% μg and 11.0% μg (and normal cortisol was 5.0 to 25.0). Adrenocorticotrphin hormone was 7 pg/mL (9-52). The diagnosis of a pituitary tumor was considered and the prolactin level was found to be 933 ng/mL (0-23). Magnetic resonance imaging of the brain confirmed a pituitary macroadenoma with a diameter of 2 cm.

The patient was started on bromocriptine 2.5 mg before bedtime on September 25, 1992. On September 29, 1992, he began exhibiting abnormal behavior with auditory hallucinations and a fear of being killed by ingestion of poison. He refused to eat or take medications. He was evaluated by a psychiatrist who made a diagnosis of paranoid schizophrenia. On October 5, 1992, the patient's mental status became normal. He was reevaluated by the same psychiatrist on October 8, 1992 and was diagnosed as having a completely normal mental status. The patient was transferred to another institution for pituitary surgery.

DISCUSSION

The time course on bromocriptine therapy and withdrawal is compelling evidence that the psychosis exhibited by this patient was induced by bromocriptine. Our patient differs from the reported cases in that he

From the Department of Medicine, St Mary's Hospital of Brooklyn, Brooklyn, New York. Requests for reprints should be addressed to Dr S.A. Peter, Dept of Medicine, 170 Buffalo Ave, Brooklyn, NY 11213.

became psychotic after 4 days of therapy with bromocriptine and recovered normal mentation 5 days after the medication was discontinued. He denied any past history of psychosis or any family history of psychosis. The "dopamine hypothesis" initially proposed that schizophrenia is a manifestation of a hyperdopaminergic state. However, it has become evident that such a state of excessive dopamine activity in all regions of the brain in schizophrenic patients is an untenable hypothesis. Recent evidence suggests that a hyperdopaminergic state in the mesolimbic system is a more likely etiological factor in schizophrenia.[7,8] Our case report supports this "modified dopamine hypothesis."

Physicians caring for patients on bromocriptine therapy should be alert for the complication of psychosis. Also, those patients who develop bromocriptine-induced psychosis should be monitored closely during periods of extreme stress for the manifestation of overt psychosis.

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