Reversible dementia due to macroprolactinoma

Case report

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SubfrONTAL tumors are an infrequent cause of dementia. Most of those that do cause dementia are meningiomas, and the symptoms may recede when the tumor is resected. A patient with a huge prolactinoma who came to medical attention because of dementia is described. The tumor shrank dramatically after bromocriptine therapy and the patient's mental status returned to normal.

KEY WORDS • prolactinoma • reversible dementia • bromocriptine

Patients with pituitary tumors usually present with symptoms related to hypersecretion or deficiency of pituitary hormones, visual field impairment, or headaches. Prolactinomas in men are likely to be larger than those in women and are associated with symptoms of mass effect, primarily visual impairment. Upon further investigation, impotence and decreased libido are often found as well. In women, however, prolactinomas are commonly detected earlier because of amenorrhea or galactorrhea.

Current reviews point out that it is conceivable for a patient with a pituitary tumor to present with personality changes or dementia if tumor growth extends as far as the deep subfrontal region; however, such cases are not enumerated, suggesting that these presentations rarely occur. We report a patient with a pituitary macroprolactinoma who presented with dementia; this is the first published case of dementia reversed by bromocriptine therapy.

Case Report

This 46-year-old left-handed man who was employed as a television director presented in April, 1989, with a 1-year history of what had been diagnosed as depression. For about 8 months, his wife had noted a marked personality change. He lost his sense of humor and his behavior became inappropriate and uninhibited; at times he displayed excessive friendliness to strangers. Psychiatric consultations and trials of antidepressant and hypnotic agents (trazodone, fluoxetine, and flurazepam) were of no benefit. Gradually, the patient became less motivated, spending most of his day in bed. He would forget recent events and repeat himself frequently. His libido had been reduced for at least 3 years, and he was impotent. Two months prior to presentation, he had scraped his car on the left side as he steered into a parking space.

Examination. On examination, the patient was alert and oriented, and recalled correctly the names of the three previous presidents, but could recall none of three objects after 5 minutes. Olfactory sense was decreased in the right nostril and absent in the left. There was no papilledema or optic atrophy, and visual fields appeared to be normal at bedside examination. There was a mild left facial paresis and a mild left-arm drift. The toe response was extensor on the left and equivocal on the right. There was a positive snout reflex. There was no gynecomastia or galactorrhea.

A magnetic resonance (MR) image of the head revealed an 8 x 6.5-cm tumor at the base of the skull (Fig. 1). Endocrine evaluation included the following levels: thyroxine 6.0 µg/dl (normal 4.5-12.0 µg/dl); triiodothyronine 1.10 µg/dl (normal 0.84-1.31 µg/dl); thyroid-stimulating hormone 0.5 µIU/ml (normal 0.2-5.9 µIU/ml); testosterone 192 ng/dl (normal 240-960 ng/dl); luteinizing hormone (LH) 3.55 mIU/ml (normal 3-12 mIU/ml); follicle-stimulating hormone (FSH) 1.05 mIU/ml (normal 4-20 mIU/ml); and prolactin greater than 100,000 ng/ml (normal 0-20 ng/ml).
Treatment and Course. The patient was treated with bromocriptine (2.5 mg three times a day) starting on May 5, 1989. Ten days later he reported a dramatic improvement in memory and behavior, and 25 days later both the patient and his wife thought his condition had almost returned to normal, although emotional lability persisted. On June 15, 1989, the endocrine levels were as follows: testosterone 271 ng/dl; LH 2.25 mIU/ml; FSH 2.25 mIU/ml; and growth hormone less than 0.5 ng/ml (normal 0–5 ng/ml). On July 11, 1989, the bromocriptine dose was raised to 2.5 mg four times a day. Examination on August 1, 1989, revealed that the patient had a normal mental status and scored 100% on the Modified Mini-Mental Status examination; however, he reported difficulty in finding a job, which he believed was due to his outspokenness and inability to control his temper. Serial prolactin levels and MR images showed a significant reduction in both serum prolactin levels and tumor size (Table 1 and Fig 2). On May 10, 1990, the patient was normal neurologically and was employed selling automobiles, leading his dealership in sales.

Discussion

Dementia is a global impairment of higher mental functioning significant enough to interfere with work or usual social interactions, and not occurring solely during periods of altered consciousness. Of those patients who are truly demented, only a small number harbor a brain tumor as the cause: 0% to 2.5% in various series. Between 10% and 30% of dementias may be partially or totally reversible. Cummings, et al., lists 65 causes of reversible dementia, three of which are due to mass effect on the brain, caused by a meningioma, a subdural hematoma, and hydrocephalus.

Pituitary tumors may extend outside the sella in all
Reversible dementia from macroadenoma

TABLE 1

Prolactin levels in a patient with a large macroadenoma treated with bromocriptine

<table>
<thead>
<tr>
<th>Date</th>
<th>Prolactin Level* (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>before treatment</td>
<td>&gt; 100,000</td>
</tr>
<tr>
<td>4/21/89</td>
<td>4700</td>
</tr>
<tr>
<td>6/15/89</td>
<td>130</td>
</tr>
<tr>
<td>5/10/90</td>
<td>94</td>
</tr>
</tbody>
</table>

* Normal prolactin level: 0-20 ng/ml.

possible directions, producing a variety of different syndromes. There are, however, only a few cases in the literature in which a pituitary tumor has been noted to cause significant deterioration in higher mental function. 8,17

Surgical management of giant pituitary adenomas is not without risk; in one series the mortality rate was 6%. 18 Even when surgery is without complications, prolactin levels are often not restored to normal, particularly if the preoperative prolactin level was very high. Improved management is now available for these tumors, in large part because of the development of microneurosurgical technique but also due to the use of dopamine agonist therapy.

The dopamine agonist bromocriptine shrinks prolactinomas and lowers serum prolactin levels; it may also restore other pituitary hormones to normal levels. 16 Bromocriptine can relieve visual symptoms produced by large prolactinomas within 2 to 3 days. 17,18 Reports of bromocriptine treatment for 19 prolactinomas with suprasellar extension 19 and for two giant prolactinomas showed marked reduction in both prolactin level and tumor size. The reduction in prolactin level was usually more dramatic than tumor regression, with prolactin levels often returning to normal. Our patient also had a greater percentage decrease in prolactin level than in tumor size.

Bromocriptine is not tumoricidal; patients in whom bromocriptine therapy is discontinued can show a rapid regrowth of the macroadenoma, a rise in prolactin levels, and a return of symptoms. 16,18 Furthermore, bromocriptine is not always effective in shrinking prolactinomas. These bromocriptine-resistant tumors have been shown to lack the high density of D2 dopamine receptors found on the surfaces of most prolactinoma cells. 7

Surgery and radiotherapy may be effective in reducing the size of giant prolactinomas but each carries a risk, including substantial surgical morbidity and mortality and late cognitive and endocrine effects of radiotherapy. In our patient, medical therapy with bromocriptine was both safe and effective, but it is not known whether it will provide indefinite suppression of tumor growth and hyperprolactinemia. In rare instances, giant macroadeninomas cause dementia, which is reversible with medical therapy of the tumor.

References


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