Primary pituitary aspergillosis responding to transsphenoidal surgery and combined therapy with amphotericin-B and 5-fluorocytosine

Case report

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Pituitary abscess is an unusual cause of sella turcica enlargement. Because its presentation closely mimics that of a pituitary tumor, the condition is seldom recognized preoperatively. Most cases have been of bacterial etiology; however, a single patient with a primary mycotic pituitary abscess secondary to *Aspergillus* species has been reported. That patient died of diffuse *Aspergillus* meningoencephalitis following a transfrontal craniotomy. In the present case, a woman with primary pituitary aspergillosis survived her infection with virtually intact pituitary function following a transsphenoidal approach which avoided contamination of cerebrospinal fluid. Postoperative amphotericin-B and 5-fluorocytosine therapy probably contributed greatly to her survival. Factors that should alert the clinician to the presence of a pituitary abscess in a patient with sella turcica enlargement are prior episodes of meningitis, sinusitis, or cerebrospinal fluid abnormalities, including pleocytosis, depressed glucose, and elevated protein.

**KEY WORDS**
- pituitary abscess
- *Aspergillus* infection
- amphotericin-B
- 5-fluorocytosine
- transsphenoidal surgery

Previous cases of pituitary abscess have been almost exclusively bacterial in origin. A single case of primary mycotic pituitary abscess has been reported which was secondary to *Aspergillus* infection. That patient died of diffuse *Aspergillus* meningoencephalitis. We are reporting a patient who also had primary pituitary aspergillosis, but she survived her infection with virtually intact pituitary function. We discuss features important in recognizing this infection and the factors that appeared essential for our patient’s recovery.

**Case Report**

This 54-year-old woman was admitted to the hospital in February, 1975, for evaluation and management of an enlarged sella turcica. She first experienced occasional headaches with retro-orbital and supraorbital pressure in 1966, which became more severe and frequent by October, 1974. At that time, sinus films demonstrated normal sinus cavities, but the sella turcica was enlarged.

On physical examination her temperature was 37°C, her pulse 86/min, and blood pressure 114/62 mm Hg. There was an abdominal scar from a previous appendectomy and total abdominal hysterec-toomy and bilateral salpingo-oophorectomy. Testing of ears, nose, nasopharynx, and eyes (including visual fields by Goldman perimetry) was normal, as was the rest of the examination.

Her complete blood count, fasting blood sugars, and routine biochemical profile were normal. Chest x-ray films were unremarkable. Skull x-ray films and sella laminogram revealed a greatly enlarged sella turcica with erosion and thinning of the floor. Serum thyroxine (T4) was 7.1 µg/dl (normal, 5 to 12 µg/dl), and triiodothyronine (T3) resin uptake was 32% (normal, 25% to 35%). The urinary 17-hydroxycorticosteroids, in response to standard metyrapone testing, increased from 15 to 25 mg/24 hours. Bilateral
carotid angiography was normal. Pneumoencephalography demonstrated a mass with slight suprasellar extension. The cerebrospinal fluid (CSF) was clear without cells. The protein content was elevated to 55 mg/dl and the glucose concentration was low at 29 mg/dl.

In March, 1975, the patient underwent a transsphenoidal exploration of her sella turcica for a presumed pituitary tumor; however, only purulent, necrotic material was found. Histopathology demonstrated findings typical of aspergillosis (Fig. 1). Culture of the material was unfortunately not performed. There were normal pituitary cells, but there was no evidence of pituitary tumor. Sphenoid sinus linings were normal. The postoperative period was characterized by transient diabetes insipidus. There was no temperature elevation greater than 37.5°C. A careful search for other foci of aspergillosis was unrevealing. A 2-month course of 1 gm of amphotericin-B and 5-fluorocytosine (2.5 gm every 8 hours) was given. The patient was discharged receiving cortisol acetate, 25 mg in the morning.

During her follow-up period, there was no recurrence of any symptoms. Her biochemical profile remained normal. Reevaluation of her endocrine status was performed in May, 1980, using insulin-induced hypoglycemia and thyrotropin-releasing hormone. With the blood glucose nadir of 36 mg/dl, the plasma cortisol increased from 9 to 27 μg/dl (normal response is an increase to 20 μg/dl or greater), and the prolactin increased from 5 to 33 ng/ml (normal response is an absolute increase of at least 15 ng/ml). Growth hormone, however, demonstrated a blunted response increasing from undetectable levels to 2.2 ng/ml (normal response is an increase to 7 ng/ml or greater). Follicle-stimulating hormone was 100 mIU/ml (normal 4 to 20 mIU/ml) and luteinizing hormone was 52.5 mIU/ml (normal 4 to 20 mIU/ml). These postmenopausal levels indicate normal gonadotropin secretory capability. With 500 μg of thyrotropin-releasing hormone, the thyrotropin-stimulating hormone (TSH) increased from 2 to 22 μU/ml (normal response is an absolute increase of 7 μU/ml). Peripheral levels of thyroid hormone were normal with a T4 of 7.1 μg/dl, a T3 of 146 ng/dl (normal, 80 to 220 ng/dl), and a T3 resin uptake of 30%.

Discussion

The patient harboring a pituitary abscess presents the physician with a vexing problem. Infection is uncommon; therefore, it is rarely considered. In addi-
Primary pituitary aspergillosis

Aspergillus glucose concentration occur in patients with pituitary tumors, and the abscess usually does not elicit a febrile response or cause an elevated blood leukocyte count. Radiographically, a pituitary abscess mimics a pituitary tumor by causing sellar enlargement and destruction. Thus, it is not surprising that most pituitary abscesses are diagnosed intraoperatively when the surgeon finds pus rather than tumor. In some cases, the surgeon has found both an abscess and a tumor.

Unfortunately, no preoperative diagnostic maneuvers are specific for pituitary abscess; however, knowledge of several features can suggest its presence. Several patients have experienced one or more episodes of meningitis or generalized sepsis. Others have had purulent sinusitis, which extended to the pituitary gland, causing abscess formation. Secondary pituitary aspergillosis has developed in three patients following transsphenoidal implantation of yttrium-90. Cerebrospinal fluid abnormalities consisting of pleocytosis, elevated protein content, or depressed glucose concentration occur in patients with pituitary abscess, although these findings are not invariably present. In our patient, the CSF protein was high and the glucose concentration was low. Culture of CSF is rarely accomplished prior to operation in patients with pituitary abscess; however, in the few patients in which it was, no organism was identified. Although our patient had no evidence of sinus infection, the ubiquity and thermostability of the Aspergillus spores are probably important in the pathogenesis of the infection.

Suspicion of an abscess before surgery is critical, since this could lower the high mortality associated with this disorder. This assumes even greater importance in the case of Aspergillus since cerebral aspergillosis is known to be a particularly lethal infection. A transfrontal approach to the pituitary greatly increases the risk of spilling the contents of the abscess into the CSF, which can cause subsequent development of meningoencephalitis. This complication occurred in the only other case of primary pituitary mycotic abscesses (which was presumed to be a pituitary tumor) and caused the patient’s death 4 days after transfrontal craniotomy. In contrast, a transsphenoidal operation minimizes the likelihood of CSF contamination.

The combined amphotericin-B and 5-fluorocytosine therapy has shown in vivo evidence of synergism against Aspergillus species. Two patients were particularly noteworthy. Flucytosine without amphotericin-B was used with success for their aspergillosis. Furthermore, Yu, et al. by in vitro susceptibility testing showed that the Aspergillus fumigatus isolated from a patient with sino-orbital aspergillosis was susceptible to 5-fluorocytosine and resistant to rifampin and amphotericin-B. Although there has been no correlation in man of clinical response and results of in vitro susceptibility tests, our case and those cited in the literature suggest that 5-fluorocytosine had a significant activity against Aspergillus species. It is likely that the transsphenoidal approach taken to evacuate our patient’s pituitary abscess, coupled with postoperative amphotericin-B and 5-fluorocytosine therapy, were critical for her complete recovery.

References

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