Medical Certification of Pilots With Pituitary Microadenoma

Case Report, by Michael Penny

Pituitary adenomas have an estimated incidence in the population of approximately 16.7%. The natural history of these tumors varies with the cell type, hormonal activity, and rate of tumor growth. Pituitary microadenomas are defined as being less than 10mm in size. This case report presents a pilot with a first-class certification who was diagnosed with pituitary microadenoma and reviews pituitary adenomas and associated issues related to aeromedical suitability (1).

History

A 3mm pituitary microadenoma was discovered by MRI in this 47-year-old male first-class pilot during work-up for hypogonadism in 2007. Subsequently, he was evaluated by neurosurgical and neuroendocrine specialists. Due to the tiny size (3mm), lack of hormonal hypersecretion on laboratory testing, and normal neurological examinations, it was thought that surgical and pharmacological interventions were currently unnecessary. The airman was started on testosterone (AndroGel) 5 grams once daily and growth hormone replacement therapy because of low free and total testosterone levels and a low insulin-like growth factor 1 level. These hormone deficiencies were thought to be unrelated to the pituitary adenoma. During this work-up and all follow-up visits, the airman was noted to be asymptomatic, specifically denying headache or visual problems.

Between 2007 and 2010, surveillance of the airman's pituitary adenoma by annual MRIs showed no change in tumor size. Aside from noting hyperlipidemia and slightly elevated hemoglobin, the airman's remaining laboratory tests (including his thyroid function test) were within normal limits during this interval. Patient notes from the attending neurosurgeon in 2009, as well as the attending endocrinologist in 2009, both state that the tumor was small, stable, non-functioning, and was unlikely to progress or cause neurological symptoms. A 1-year follow-up interval with MRI and annual vision testing was suggested, and both specialists recommended that the airman be cleared for flight duties.

In March 2011, the airman's annual MRI failed to demonstrate evidence of pituitary adenoma, and the airman's neurosurgeon recommended that no additional surveillance was needed. The endocrinologist concurred, stating that the patient had been asymptomatic since initial diagnosis; the pituitary microadenoma was stable, very small, and most likely an incidental finding requiring no intervention. Additionally, because his growth hormone and testosterone levels normalized, the airman was directed to wean off of his testosterone and growth hormone medications. It was noted that the prolactin level was slightly elevated at 17.7. The airman was directed to return in 4 months to have this test repeated.

Aeromedical Issues

The clinical decision-making process in aerospace medicine requires the aviation medical examiner to focus on the safety-of-flight factors surrounding an airman's medical condition. Frequently, this special focus drives a more thorough and more expensive surveillance and treatment of the disease process. In the case of a commercial pilot, the additional aeromedical evaluation is deemed necessary, as subsequent decisions regarding the airman's flight status affects public safety as well. According to Title 14 Code of Federal Regulations Part 67, intracranial tumors should be deferred to the FAA for medical certification decisions (2).

Pituitary microadenomas are frequently asymptomatic and discovered incidental to imaging for other neurological issues. The potentially deleterious effects they can produce are related to rapid growth or hormonal activity. Initial work-up should therefore include an MRI, as well as prolactin levels, thyroid panel, insulin-like growth factor levels, dexamethasone suppression test, and luteinizing hormone and follicle-stimulating hormone levels (3). A 12-month period of stability after initial diagnosis is generally required for follow-up. The annual work-up must include an MRI to document the tumor size and the appropriate lab work to document normal hormone levels. A study of pituitary adenoma surveillance methods, which compared quality of life measures and effectiveness, concluded that annual prolactin levels were the most cost-effective method of surveillance in the general population. In light of the aeromedical goal of ensuring public safety, it is suggested here that this conservative approach falls short (4).

Outcome

This case was reviewed by the Aerospace Medical Certification Division of the Civil Aerospace Medical Institute, and specific concerns were raised in regards to hormone secretion and growth of the adenoma. As previously stated, the airman remained asymptomatic, and the most recent MRI indicated that the microadenoma had resolved. He had no evidence of hormone hypersecretion, but instead had transient growth hormone and testosterone deficiencies that normalized and no longer required hormone replacement. From 2008-2010, he was given first-class, time-limited certification. The decision to re-issue a first-class certification with a warning for pituitary adenoma revolved around resolution of the adenoma on the current MRI and normalization of the hormone levels.

References

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Pituitary Microadenomas and Incidentalomas

Pituitary adenomas are the most common central nervous system tumors, accounting for 10% of all intracerebral tumors and are common in the general population with an incidence of 16.7%, based on a combination of imaging studies and post-mortem examination (5). Formerly classified by size (tumors > 10mm as macroadenomas and tumors < 10mm as microadenomas), immunohistochemical methods now allow determination of cell type predominance and hormonal activity. Prolactin-secreting cells are the predominant cell type, occurring in 25-41% of pituitary adenomas (1).

Clinical detection of symptomatic pituitary adenomas typically occurs due to mass effect or hyper secretion of hormones from the anterior pituitary axis. The mass effect is most common in pituitary macroadenomas and results in headaches, visual deficit due to pressure on the optic chiasm, or (rarely) cavernous sinus thrombosis. Pituitary apoplexy is a rare complication caused by hemorrhagic infarction of macroadenomas. It presents with sudden onset of headache, nausea, vomiting, vision loss, and cranial nerve deficits. The risk of this complication in pituitary macroadenomas is 0.4 to 7% over 2-6 years of follow-up (3).

Hypersecretion, or hyposecretion of hormones in the anterior pituitary gland, may occur in micro- or macroadenomas. The most common hypersecretion syndrome is prolactinemia, which produces weight gain, infertility, galactorrhea, hypogonadism, decreased libido, and eventual osteopenia. In women, it also causes amenorrhea (6). Pituitary adenomas account for 80% of Cushing's syndrome cases due to hypersecretion of ACTH. Hypersecretion of growth hormone causing acromegaly, and thyrotropin leading to hyperthyroidism, are other less common complications of anterior pituitary hypersecretion. It is noteworthy that surveillance for these complications is relatively straightforward, involving periodic lab tests that are readily accessible in the United States (3).

Asymptomatic pituitary adenomas are frequently discovered incidental to imaging studies for other medical workups. Frequently referred to as *incidentalomas*, they have a low complication rate. In one small study, visual field deficits were found in 4.2% and prolactin secretion in 11.9% of incidentalomas. Progression in size was seen in 3.2% of microadenomas versus 26.3% of macroadenomas (7). In a recent metaanalysis by the Mayo Clinic in 2011, microadenoma growth occurred in 3.3 per 100 patient years versus 12.5 per 100 patient years in macroadenomas. The overall incidence of new endocrine dysfunction was 2.4 per 100 patient years (8).

Treatment and surveillance in pituitary adenomas vary according to the size, growth, and hormone production of the tumor. Surgical excision via the transphenoidal route is the most common method of intervention in symptomatic or rapidly growing pituitary adenomas. Other modalities include radiotherapy or medications specific to the cell type. Bromocriptine, for example, is a dopamine agonist used for medical treatment in prolactin-secreting tumors (3).

In the case of non-secreting, asymptomatic, stable pituitary microadenomas, conservative treatment is standard. Initial workup includes a comprehensive history and physical exam focusing on neurological, ophthalmological, and potential stigmata of pituitary hypersecretion. Laboratory studies should be obtained to include CBC, electrolytes, kidney and liver functions, thyroid panel, urine cortisol, prolactin level, insulin-like growth factor, follicle stimulating hormone, and luteinizing hormone. Imaging by MRI (if not already performed) is used to assess adenoma size and to look for impending mass effect (3).

Follow-up in a conservatively managed patient typically occurs every 12 months. Education of the patient with respect to possible symptoms from a progressing pituitary adenoma is key to this approach. Presence of symptoms warrants timely follow-up. Annual MRIs are indicated to assess potential tumor growth (9).