Incidental pituitary adenomas

ANDREW D. PARENT, M.D., JOSE BEBIN, M.D., AND ROBERT R. SMITH, M.D.
Departments of Neurosurgery and Pathology, University of Mississippi, Jackson, Mississippi

Pituitary glands from 500 consecutive autopsies were reviewed and the findings correlated with clinical symptomatology. Occult pituitary adenomas were identified in 42 pituitary glands (8.5%). In only one case was a pituitary lesion clinically questioned, but specific hypophyseal function studies were not performed. These tumors occurred most frequently in the sixth and seventh decade of life, without obvious sex predominance. Of these patients, 48% were obese, 57% were hypertensive, and diabetes mellitus was noted in 34%. Of the 17 cases in which skull x-ray films had been taken, suspicious or abnormal areas were found in 11. The tumor size ranged from 1 to 15 mm, but was greater than 1 cm in only one case. In 34 cases, the tumor was located along the periphery of the gland. Even though the etiological and functional significance of these tumors is unclear, the clinical course appears to be relatively benign.

KEY WORDS • pituitary tumor • pituitary gland • adenoma • sella turcica • endocrine system

In the past decade, it has been recognized that pituitary adenomas too small to cause mass effect are capable of causing endocrinopathy. These microadenomas are frequently found at postmortem examinations in apparently asymptomatic patients. The actual incidence and natural history of these small tumors remain unknown, and in the asymptomatic patient, the significance to the visual or endocrine system has not been ascertained.

In a study of microadenomas, we have reviewed the pituitary glands of 500 consecutive autopsies performed between 1973 and 1979 at the University of Mississippi School of Medicine. In most cases, the pathologist had routinely made three sagittal sections of the pituitary at 3-mm intervals. These were examined by conventional histological methods under light microscopy. The medical records of these tumor patients were carefully studied. Skull films, if available, were reviewed.

Summary of Findings

Occult pituitary adenomas were identified in 42 pituitary glands, for a prevalence of 8.5%. Tumors were found in 26 males and 16 females. The patients' ages varied from 6 to 85 years, with a mean of 59 years (Fig. 1). The cause of death in most of the cases was related to disease of middle life.

Radiological Evaluation

Skull x-ray films were performed in 17 cases, but the requests for radiography did not indicate a special interest in sella abnormalities. Careful review of these films indicated that the sella turcica was considered suspicious or abnormal in 11 of 17 cases (65%). However, in none of these cases had polytomography been performed. In almost all cases, the sella appeared to be asymmetrical or focally eroded. In only one case was the sella volumetrically enlarged, and in this case two intrasellar adenomas were identified, both placed laterally.

Progression of focal anterior sella asymmetry was noted in a patient who had skull films taken 6 years apart. Clinically, no symptomatology had developed, and at postmortem examination a 5-mm adenoma was found anterolaterally.

Pathological Findings

The tumors were located in the periphery of the pituitary in 34 cases (Fig. 2 left). The largest tumor was 1.5 cm in size and demonstrated a lobular pattern with fibrous trabeculation (Fig. 2 right). All of the other tumors were less than 1 cm in diameter. There were three glands in which multiple adenomas were found.

When stained with hematoxylin and eosin, these
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adenomas were shown to be mainly of the chromophobe type. The tumor margins were readily identified from the normal ascinar pituitary pattern, despite the absence of a capsule. In many of these tumors, degenerative changes were noted, with variable staining characteristics and cellular morphology. Cystic formation, hypophyseal hemorrhage, and cell clumping were specifically excluded as not demonstrating a definite adenoma.

Medical Records

The medical records were available for review for 35 cases. Hypertension, obesity, and diabetes mellitus were specifically searched for in these records as being suggestive of a hormonal problem. Hypertension (defined as a diastolic reading of greater than 100 mm Hg on repeated measurements, or a history of treated hypertension) was identified in 20 patients (57%). In a controlled group of autopsied patients without adenomas, matched for age and sex, only eight cases had hypertension. Although this was statistically significant (p < 0.01), it should be noted that 16 of these patients were blacks, in whom hypertension is prevalent in at least 30% of the population.

Twelve of 35 patients (34%) had diabetes mellitus. Again, in matched-pairs analysis for age and sex, only three of the control group had diabetes mellitus. This was statistically significant (p < 0.05).

Seventeen of 35 patients (48%) were noted to be moderately or markedly obese, defined as at least 20 lb over the ideal weight for height. By matched-pairs analysis, this was not considered to be statistically significant.

There were no recorded cases of visual field deficits. Headaches, sexual dysfunctions, and psychological problems were also rarely noted, except in three cases of organic brain syndrome of the elderly. There were no consistent electrolyte abnormalities that would have suggested a hormonal problem. Specific endocrine tests were noted in only two charts.

Discussion

Pituitary adenomas that have existed without recognized clinical symptoms are rather commonly found at autopsy (Table 1). In 1909, Erdheim and Stumme noted 10 adenohypophyseal adenomas in 118 post-mortem examinations. Their study was only directed toward the changes of the anterior lobe of the pituitary in pregnancy. Kraus, in 1914, described 25 adenomas in an autopsy series of 300 pituitary glands. Multiple adenomas were identified in three cases, and there were 13 cases of hyperplasia. In 1932, Susman was able to identify 23 adenomas in 260 pituitary glands at

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TABLE 1  
Reported incidence of pituitary adenomas in autopsy series

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Autopsies</th>
<th>No. of Adenomas</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erdheim &amp; Stumme, 1909</td>
<td>118</td>
<td>10</td>
<td>8.4</td>
</tr>
<tr>
<td>Kraus, 1914</td>
<td>300</td>
<td>25</td>
<td>8.3</td>
</tr>
<tr>
<td>Susman, 1933</td>
<td>260</td>
<td>23</td>
<td>8.4</td>
</tr>
<tr>
<td>Close, 1934</td>
<td>130</td>
<td>39</td>
<td>22.3</td>
</tr>
<tr>
<td>Costello, 1936</td>
<td>1000</td>
<td>225</td>
<td>22.5</td>
</tr>
<tr>
<td>Hardy, 1969</td>
<td>1000</td>
<td>27</td>
<td>2.7</td>
</tr>
<tr>
<td>McCormick &amp; Halmi, 1971</td>
<td>1600</td>
<td>145</td>
<td>9</td>
</tr>
<tr>
<td>Kovacs, et al., 1980</td>
<td>152</td>
<td>20</td>
<td>13</td>
</tr>
<tr>
<td>Parent, et al., 1981</td>
<td>500</td>
<td>42</td>
<td>8.5</td>
</tr>
</tbody>
</table>

In 1934, in collaboration with Dr. Dorothy Russell, Close initially sectioned 200 pituitaries with the single-cut technique. An adenoma was found in 18 intact glands, for an incidence of 9%. It was their observation that those adenomas tended to occur in patients who were older than 45 years of age and who had additional tumor growths in some other part of their body. Each pituitary gland was studied with 60 to 120 serial sections, 7 μm thick. In a group of 50 autopsy cases in which no growths had been found elsewhere, only five had pituitary adenomas, for an incidence of 10%. However, in patients with tumor growth in some other part of their body, 34 of 80 sectioned glands had adenomas, for an incidence of 42.5%. Of the 130 glands studied by Close, 39 (22.3%) had adenomas.

In 1936, Costello, in a diligent study of 1000 consecutive autopsied pituitary glands, recognized 225 adenomatous growths, for an incidence of 22.5%. He did stress that the true adenoma formation was difficult to differentiate from unusual structural variations such as hyperplasia, cell clumping, and cyst formation. He was unable to find any clinical features in the history of these cases which would have suggested the presence of pituitary dysfunction. Although the specific measurement of tumor size was not recorded, he did note that the smallest tumor was larger than 1.5 mm, and the largest tumor had completely destroyed the gland. His criteria for true tumor formation included degeneration, necrosis, and vacuole formation as well as the nodular formation of homogeneous cells.

Hardy, in 1969, in a similar number of autopsied pituitary glands, was able to identify only 27 adenomas, for an incidence of 2.7%. He used a single-section technique to study these glands, and therefore this method most likely resulted in missing many of the smaller adenomas. In 1971, McCormick and Halmi found 145 pituitary adenomas in 1600 consecutive autopsies.

In 1980, Kovacs, et al., reported on a series of 152 unselected autopsies of patients aged 80 years and older. Twenty adenomatous glands were identified. In nine out of 17 cases so tested, the immunoperoxidase technique was positive for the presence of prolactin. This finding suggested that these glands were actively producing prolactin, and that approximately 6% of the population over 80 years of age might harbor a pituitary prolactinoma.

With the advent of transsphenoidal microsurgery, it became possible to selectively remove a microadenoma while preserving the normal pituitary. Refined hormonal assay has permitted the biochemical detection of these microadenomas in many cases before mass effect or severe endocrinopathy has occurred. The syndrome of hyperprolactinemia with amenorrhea or galactorrhea, due to pituitary microadenomas, has been recognized in almost 30% of these patients. Based on the presence of infarcts and cystic changes proximal to some pituitary adenomas, and the resolution of neuroendocrinopathy, presumably some of these tumors regress spontaneously. Whether the occult adenomas described in this study and others are nonfunctional, or whether they cause some yet undefined endocrinopathy, cannot be resolved on the basis of present histochemical techniques. Perhaps immunocytochemical studies not applicable to our initial study will be more fruitful.

As noted by previous authors, these tumors tend to occur with greater frequency in the sixth and seventh decade of life, without obvious sex predominance. In our series, about 50% of these patients were obese, 10 patients weighing more than 200 lb. The presence of diabetes mellitus in 34% also suggests some hormonal aberration. In only one case was a pituitary lesion questioned and elevated serum cortisol documented, but specific hypothalamic function studies were not performed.

The radiological findings in our series corroborate those of several other studies, in which at least 80% of patients with pituitary microadenomas showed enlargement or asymmetry of the sella floor, especially when polytomography was performed.

Our studies would lead to the conclusion that occult primary adenomas produce a relatively benign course, and occur in 8% to 9% of autopsy cases.

Acknowledgments

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References

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Address reprint requests to: Andrew D. Parent, M.D., Department of Neurosurgery, University of Mississippi Medical Center, 2500 North State Street, Jackson, Mississippi 39216.