Surgical experience with chromophobe adenomas of the pituitary gland

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Between 1950 and 1969, 165 operations were performed on 146 patients for the treatment of chromophobe adenoma of the pituitary gland unassociated with either acromegaly or Cushing's syndrome. The over-all operative mortality was 1.2%, and no deaths occurred in 138 cases operated on for the first time. In 106 of the patients who had not received prior treatment, vision was improved in 80% of cases and returned to normal in 50%. In the group of patients whose initial treatment was surgery, postoperative radiation therapy was administered in one-half of the cases. The rate of recurrence was 8% in those who received radiation and 22% in those who did not. Recurrence of symptoms within less than 1 year often was due to a hemorrhagic cyst which could be treated better by reoperation than by radiation therapy.

Key Words: pituitary tumor • chromophobe • surgery • radiation therapy • vision • hormone

The pituitary gland in both its normal and pathological states continues to challenge our complete understanding. A revival of interest in the gland has been in progress for nearly 20 years, and neurosurgeons concerned principally with therapeutic measures have added substantially to a growing body of information about its structure and function.

Since so many are occupied with a variety of therapeutic techniques, differences of opinion about the proper management of pituitary neoplasms have arisen from time to time and deserve to be aired. This report deals with our surgical experience with the common chromophobe tumor but excludes consideration of similar-appearing tumors found in acromegaly and Cushing's disease. The surgical treatment of tumors that secrete trophic pituitary hormones differs sufficiently to require separate consideration.

Clinical Material

In 1961 we reported 63 cases of chromophobe tumor in a general discourse of surgical treatment of pituitary tumors, and to this number we have added 83, enlarging the series to 146 patients in whom 165 operations have been performed. These are consecutive cases over a period of 19 years from 1950 to 1969 in which a nearly uniform surgical technique was employed. Although a majority of the operations were performed by one of us, the series includes operations by four other members of the senior staff and by 10 residents. During the same period this staff of surgeons had a much larger experience in the performance of surgical hypophysectomy as palliative treatment for cancer and diabetic retinopathy, which provided a useful familiarity with the surgery of the sellar region and with the postoperative management of patients.
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Males comprised 60% of patients in our series. Most patients were between 30 and 70 years of age at the time of operation, but eight were less than 20 and six were over 70 years of age. The initial symptoms were usually either visual disturbance or hypopituitary states, in about equal numbers. By the time the patients came to operation almost all had significant loss of vision and 75% had some measurable endocrine dysfunction (Table 1). All too often, unexplained amenorrhea, impotence, and even hypoadrenalism were treated endocrinologically, and visual complaints went unexplained for long intervals before the possibility of a pituitary tumor was explored. Five patients in the series developed the dramatically acute illness from hemorrhage into the tumor ("pituitary apoplexy"), and in two of these it was the first symptom of pituitary disease.

Of the 146 patients, 22% had received prior radiation therapy (mostly at other institutions) and came to operation because of progressive loss of vision during treatment or thereafter. Eight others had undergone surgery for pituitary tumor elsewhere and were referred with symptoms of recurrent tumor; five of these had also received radiation therapy; two had already had two operations, and one had had three.

Surgical Management

Including 19 secondary operations for recurrent symptoms, 165 operations were performed on the 146 patients of this series. Operations in recent years often were preceded by air encephalography and less frequently by angiography. With few exceptions the operations were all intracranial, transfrontal on the right side in their approach. Exceptions were made when studies indicated extension behind the chiasm or into the temporal fossa, when a more lateral approach along the sphenoid ridge was suitable. Di-ethyl ether by endotracheal administration was the preferred anesthetic.

A coronal scalp incision was used to avoid an unsightly scar, and a relatively small bone plate was removed in the right frontal region. The size and location of the frontal sinus was not allowed to compromise the cranial opening low in the brow, which extended from above the lateral canthus to the margin of the sagittal sinus. Care was taken to avoid damage to the dura, which was opened with a transverse incision. Great attention was given to avoiding undue traction on the brain in exposing and dealing with the tumor. In lifting the frontal lobe, the retractor was angled inward from the outer end of the brow in order to preserve the olfactory nerve but was shifted to a position near the midline if a more direct exposure of the tumor proved necessary. To facilitate retraction, 100 cc or more of cerebrospinal fluid were removed through previously placed spinal needles, and often an osmotic diuretic was given to shrink the brain. Trimethaphan sometimes was employed to reduce nuisance bleeding, and venous bleeding from the cavity of the sella was controlled by temporary tamponade of the cavity or by elevation of the head of the table.

When the tumor was confined to the sella beneath the thinned bulging diaphragma, which often is alluded to erroneously as the "capsule of the tumor," its removal was fairly simple and was accomplished through an opening in the diaphragma by the use of sharp and dull ring curettes, pituitary scoops, and suction. Tougher fragments of tumor were removed more laboriously by small rongeurs and sharp dissection. At a first operation the diaphragma usually fell away or could be gently separated from the nerves and chiasm. Adhesions between the diaphragma, nerves, and chiasm were not disturbed for fear of increasing the visual

<table>
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<tr>
<th>Type of Symptom</th>
<th>Initial Symptom (%)</th>
<th>Eventual Symptom (%)</th>
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<tbody>
<tr>
<td>gonadal dysfunction</td>
<td>31</td>
<td>51</td>
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<tr>
<td>other endocrine dysfunction</td>
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<td>22</td>
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<tr>
<td>pituitary apoplexy</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>extraocular palsy</td>
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<td>4</td>
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<tr>
<td>diabetes insipidus</td>
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<td>hemiparesis</td>
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deficit, but every attention was given to insuring removal of fragments of tumor that might distort these structures.

When the tumor was found to have broken through the confining diaphragma or perhaps escaped through one that was congenitally deficient, it usually had a thin membranous capsule and still lent itself to systematic excision. Those tumors that had become adherent to nerves or blood vessels or were invading adjacent structures were dealt with as well as the situation permitted, but with the purpose of at least providing decompression of the optic nerves.

Some neurosurgeons may consider it a matter of choice whether a tumor confined to the sella and with limited upward extension beneath an intact diaphragm should be dealt with by an intracranial or transsphenoidal operation, but tumors that have extended beyond these confines do not lend themselves readily to other than the intracranial approach.

In a primary operation a subtotal excision of the tumor was practiced in an effort to leave functioning gland. The exact location of the gland in relation to the tumor was constant, but the pituitary stalk often served as a useful guide for finding it. Removal of the tumor by gentle suction usually can be counted on to preserve the normal pituitary tissue. On the other hand, in operations for recurrent tumor we came more and more to disregard the importance of preserving any remaining gland and have attempted to enterate the sella in the hope of avoiding further recurrence.

Results

Mortality and Complications

Two patients died within 1 month after operation, resulting in an operative mortality of 1.2%. Each of the deaths occurred in patients seriously ill with recurrent tumor following previous surgery and radiation therapy. No deaths occurred among 138 patients operated on for the first time. Important complications in the postoperative period, comprised principally of superficial infection, cerebrospinal fluid leak, and intracranial clots, occurred in 18 patients.

Vision

The principal reason for operation in most cases was to restore loss of vision or to preserve existing vision and avoid further loss. The effects of surgery were assessed in 106 patients after an initial operation without prior radiation therapy. Significant improvement in vision occurred in 80% of the patients, and in approximately 50% normal vision was restored; 18% had no change in vision, and only two patients suffered some measurable loss of vision. The record was less good following operations for recurrent tumor, in that over one-half of this group failed to experience improvements.

Endocrine Function

Although pituitary insufficiency present before operation often persisted, endocrine function measurably improved in a substantial number of patients. This was best demonstrated among the women, 46 of whom had amenorrhea at the time of operation; normal menstruation was restored in eight. Of four women who were under 40 years of age and in the childbearing period, two subsequently bore children.

Many today are interested in restoring ovulation in women with hypopituitarism so that they can become pregnant. None of our female patients has resorted to this, but one young man with complete loss of pituitary function after pituitary apoplexy was treated with menopausal gonadotropins to induce spermatogenesis and chorionic gonadotropins to restore ejaculation: he subsequently sired a healthy child.

Some comment is in order about the unjustified and sometimes promiscuous use of substitution therapy, particularly cortisone, following operation. Steroids commonly are administered during and after the operation to fortify adrenal function. Patients then are discharged on a tapering dose but for one reason or another the medication is continued in undue amounts and for undue periods of time. Sometimes a permanent dependence results when initially the pituitary had the capacity to produce an adequate amount of adrenotropic hormone. We need only recall that prior to the advent of substitution therapy many patients survived the operation and lived comfortably thereafter without the aid of steroids.

Although diabetes insipidus has been observed in about one-half of our patients sub-
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mitted to hypophysectomy for breast cancer, it was an infrequent and usually transitory consequence of surgery in the present series. Probably the fact that radical removal was not attempted in most cases but instead an effort made to preserve the normal gland accounts for the difference.

Radiation Therapy

Recurrent growth of the tumor following its subtotal removal by surgery is of special concern. In our report of 9 years ago we were unable to relate the incidence of recurrence to the lack of postoperative radiation therapy. Radiation therapy was withheld in approximately one-half of our patients; in 106 whose initial treatment was surgery in our institution, the rate of recurrence was 8% in those who received postoperative radiation and 22% in those who did not. This lends support to physicians who recommend postoperative radiation, but the numbers in this study are small, the study retrospective, radiation not without risk, and therefore treatment justifiably might be reserved until recurrence became evident or for those with an invasive tumor at the first operation.

Symptoms recurred within 1 year of operation in five patients, and in three the lesion proved to be a hemorrhagic cyst, which was rarely the case when symptoms recurred later. As a cyst might be expected to respond poorly to irradiation, recurrences soon after surgery probably should be treated by reoperation. All but two recurrences occurred within 5 years, which supports the notion that this is the period when follow-up examinations should be most diligent.

The question as to which patients should be given an initial trial of radiation therapy and which should be subjected immediately to operation is one that cannot be settled in a few words. The trial use of radiation therapy has its place, but all too often surgery is delayed unjustifiably because of the presumed high risk that the operation will worsen vision or cause death. Among those patients in the present series who were treated for the first time by surgery, vision improved in 80% and became normal in 50%, and there were no operative deaths. The results suggest that if surgery is not to be the primary treatment for chromophobe adenoma, it should not be delayed too long if vision fails during radiation therapy.

Reference


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