Surgical Therapy of Pituitary Adenomas

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In a series of approximately 1,000 patients with pituitary adenoma who were operated on at our institution from 1970 to 1994, 932 were operated on for the first time. Most microadenomas were corticotropin (ACTH)-secreting, whereas all nonfunctioning adenomas were macroadenomas, reflecting internal surgical policy. Only 48 of 932 patients (5.1%) had transcranial surgery. Using stringent criteria for the definition of a cure, we obtained remission of disease in 54.9%, 87.3%, 66.7%, and 46.2% of all patients with growth hormone (GH)-, ACTH-, thyrotropin (TSH)-, and prolactin (PRL)-secreting adenomas, respectively. The good result in patients with Cushing's disease is related to the higher percentage of microadenomas (≅80%) in this group. Unfavorable prognostic characteristics for all adenomas are increasing tumor size, invasiveness, infiltration, and high serum levels of the hypersecreted hormone. The absence of a reliable tumor marker makes it difficult to assess the results of surgery in patients with nonfunctioning pituitary adenoma, but normalization or improvement of visual defects occurred in 72.4% of patients. Permanent worsening of vision was detected in 2.2%, mostly operated on through the transcranial approach, but they had large tumors and so were at greater risk. Accordingly, there was a higher death rate in patients who received the transcranial operation (two of 48; 4.2%) than in patients operated on through the trans-sphenoidal route (seven of 884; 0.8%). However, between 1970 and 1980, the mortality rate was 1.6% (six of 367 patients), while between 1981 and 1994, it was 0.5% (three of 565 patients), stressing the importance of surgical experience and perioperative medical management in improving the safety of pituitary surgery.

PITUITARY ADENOMAS can be treated by surgery, radiation, medical therapy, and a combination of these. The choice of one form of therapy over the other depends on several factors, such as age of the patient, his or her medical condition, the type of pituitary tumor, history of previous treatment, and availability of effective medical therapies. Refinements in the neuroradiological diagnostic and in perioperative management have considerably improved both the safety and efficacy of surgical treatment of pituitary adenomas, making it the treatment of first choice in most patients. It is now generally accepted that surgery is the preferred therapy for all pituitary adenomas, except for prolactin (PRL)-secreting adenomas, since they are usually responsive to dopaminergic drugs.[1]

Aims of surgery depend mainly on the stage of tumor development. Thus, remission of hormone hypersecretion in small adenomas should be achieved without damage to the normal pituitary gland, whereas resolution of neurological and/or visual defects and control of tumor growth become increasingly important in large tumors. Surgery achieves remission of hormone hypersecretion in approximately 70% to 90% of all types of hypersecreting microadenomas.[2] Outcome of surgery becomes less favorable as tumor size increases. Extrasellar extension of the tumor drastically reduces the probability of cure to 10% to 30%. Preservation of normal pituitary function depends on the ability of the neurosurgeon to distinguish normal tissue from the tumor and leave it undamaged. However, it must be stressed that selective removal of the pituitary adenoma is commonly not able to restore normal pituitary function if the tumor had already caused hypopituitarism by destroying the normal gland.

TYPE OF SURGERY

Surgical management approaches pituitary adenomas by the trans-sphenoidal or the transcranial route (in some cases a transmaxillar-ethmoid-sphenoidal approach has also been used). Indications for one over the other of the two principal approaches are still cause for some controversy. There is consensus that all microadenomas, intrasellar macroadenomas, extrasellar macroadenomas with slight suprasellar extension, and extrasellar macroadenomas with significant downward extension into the sphenoid sinus, should be operated through the trans-sphenoidal route. On the other hand, extrasellar adenomas with a large suprasellar component, especially if irregular in shape, are best approached through the transcranial route. The choice in the case of extrasellar macroadenomas with moderate suprasellar extension is more subject to the personal preference of the neurosurgeon. Because of the lesser risk of side effects with the trans-sphenoidal operation compared with the transcranial approach, the former is increasingly preferred in most centers with expertise in pituitary surgery.

RESULTS OF SURGERY

Several surgical series have now been reported, with almost all demonstrating the efficacy and safety of pituitary surgery in experienced hands.[3-6] Our personal series consists of more than 1,000 patients with pituitary adenoma who were operated on at our institution from 1970 to 1994. Roughly 100 patients underwent a repeat operation for persisting or recurrent adenoma. Of 932 patients operated on for the first time, 267 (28.6%) had a growth hormone (GH)-secreting adenoma, 222 (23.8%) a PRL-secreting adenoma, 126 (13.5%) a corticotropin (ACTH)-secreting adenoma, 18 (1.9%) a thyrotropin (TSH)-secreting adenoma, and 299 (32.2%) a nonfunctioning adenoma. Considering tumor size, 258 patients (27.7%) had a microadenoma, 221 (23.7%) had an intrasellar macroadenoma, and the remaining 453 (48.6%) had an extrasellar macroad-

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enoma. Most microadenomas were ACTH-secreting, whereas all nonfunctioning adenomas were macroadenomas, reflecting our policy not to operate on small nonfunctioning adenomas that are discovered incidentally. Only 48 patients (5.1%) received their first operation through the transcranial approach, since we prefer the less traumatic trans-sphenoidal approach whenever it is technically possible.

Careful definition of the criteria for cure is crucial in assessing and comparing the success rate of the different treatments for pituitary adenomas.[6,7] In the case of hypersecreting adenomas, we used rather stringent criteria. Suppression of GH levels below 2 μg/L during oral glucose load and/or normalization of elevated insulin-like growth factor-1 (IGF-1) levels were required for a successful outcome in patients with a GH-secreting adenoma. Patients with Cushing's disease were considered cured when urinary steroids were low or normal and when the serum cortisol level was suppressed after administration of a low dose of dexamethasone. Patients with TSH-secreting adenoma were considered cured when free thyroid hormone levels returned to within the normal range or, if patients had been previously thyroidectomized, when TSH levels could normally be suppressed after oral administration of 80 μg tri-iodothyronine for 10 days. In the case of PRL-secreting adenomas, we relied on normalization of elevated PRL levels only, because dynamic testing of PRL secretion is not useful in the postoperative evaluation of patients with PRL-secreting adenoma. Using these criteria, we obtained remission of disease in 54.9%, 87.3%, 66.7%, and 46.2% of all patients with GH-, ACTH-, TSH-, and PRL-secreting adenomas, respectively. The good result in patients with Cushing's disease is related to the higher percentage of microadenomas (≅80%) in this group, as compared with that in both GH- and PRL-secreting adenomas. In fact, the success rate in acromegalic patients with microadenoma and patients with microprolactinoma is approximately 80%. On the other hand, unfavorable prognostic characteristics for all adenomas are: increasing tumor size; invasiveness into the surrounding structures; infiltration of the normal gland, dura, or bone; and high serum levels of the hypersecreted hormone.

The absence of a reliable tumor marker makes it difficult to assess the results of surgery in patients with nonfunctioning pituitary adenoma. Because of the high frequency of visual disturbances in patients with nonfunctioning adenoma, amelioration of the visual field or visual acuity can be regarded as an important objective of surgical treatment. Normalization or improvement of visual defects occurred in 72.4% of patients, whereas permanent worsening of vision was detected in 2.2% of cases. With only one exception, this complication occurred in patients operated on through the transcranial approach.

COMPLICATIONS OF SURGERY

Trans-sphenoidal surgery is a safe procedure, with a mortality rate of less than 1% and a risk of major morbidity not higher than 3% to 5% in most surgical series, while the transcranial route is associated with a higher risk of mortality and major morbidity. However, it must be remembered that the latter approach is usually reserved for patients with large tumors and these are intrinsically more prone to surgical complications. Our own experience is in line with these results. In our series, there were two deaths among 48 patients who received the transcranial operation (4.2%) and seven deaths (0.8%) among 884 patients operated on through the trans-sphenoidal route (two due to hypothalamic injury, one to cavernous sinus injury, three to CSF leak complicated by meningitis, and one to pulmonary embolism). However, further analysis of the mortality data revealed that in the period 1970 to 1980, the mortality rate was 1.6% (six of 367 patients), while in the period 1981 to 1994, it was 0.5% (three of 565 patients), stressing the importance of surgical experience and perioperative medical management in improving the safety of pituitary surgery.

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