Acromegaly—The Place of the Neurosurgeon

R. Fahlbusch, J. Honegger, and M. Buchfelder

Over 12 years, we performed 498 operations for growth hormone (GH)-secreting pituitary adenomas (489 in acromegaly and nine for gigantism), with 479 by the trans-sphenoidal and 19 by the transcranial route. A consecutive series of 224 patients had an overall cure rate of 56%, with normalization in 71% when the criterion was only basal GH. Endocrine remission occurred in 72% of microadenomas, 50% of macroadenomas, and only 17% of giant adenomas. Seventy-three percent of the patients with preoperative GH levels less than 10 ng/mL were cured, but only 33% with GH greater than 100 ng/mL. Our cure rate for invasive adenomas was 38%. Surgical reexploration can lead to a 50% cure rate. Overall morbidity was low. Pretreatment of large adenomas with octreotide may soften them and facilitate their removal, and one third shrink. It also relieves the symptoms of acromegaly and improves the patient's general condition for surgery. Octreotide as first-line therapy is indicated in patients with risk factors for surgery, and it is becoming an alternative to radiotherapy after surgery. It is more potent than dopamine agonists in lowering GH levels. We recommend postoperative radiotherapy (± octreotide) if GH levels are fairly high after surgery or if the adenoma shows major invasiveness. Surgery is still the initial therapy of choice in acromegaly due to its high cure rate and low morbidity.

ACROMEGALY is a serious disease that markedly reduces life expectancy. Aggressive management is mandatory once the diagnosis has been confirmed. Surgery offers the advantages of (1) an immediate decline of growth hormone (GH) levels, (2) a high cure rate, (3) low morbidity, and (4) lower costs in comparison with other treatment modalities. We report on our surgical experience with acromegaly in the context of other treatment options, such as medical therapy and radiotherapy.

In the past 12 years, 498 operations have been performed in our department for pituitary adenomas in acromegaly and gigantism. The vast majority of operations (n = 479) have been performed by the trans-sphenoidal route. Transcranial surgery was required for adenomas with asymmetrical suprasellar, retrosellar, and/or supraclinoidal parasellar extension or for adenomas with general invasiveness. Nineteen patients underwent transcranial surgery. Nine of our patients who underwent trans-sphenoidal surgery presented with gigantism.

GH LEVELS AND CURE RATE

Normalization of basal GH levels (<5 ng/mL) and suppression of GH to less than 2 ng/mL during an oral glucose tolerance test proved reliable criteria for a surgical cure. Once these criteria were fulfilled, no clinical signs of acromegaly were found and recurrence was exceptionally rare. Even diabetes mellitus or arterial hypertension improved or regressed in a considerable number of patients. The endocrine outcome of surgery could be predicted as soon as 1 week after surgery by reassessment of GH secretion, and by the time of discharge patients had already been informed about their endocrine results and further management.

INITIAL SURGERY AND REEXPLORATION

We have reviewed a consecutive series of 224 of our patients[1] and found an overall cure rate of 56%. If only basal GH was considered, normalization was obtained in 71% of patients. The likelihood of remission largely depended on tumor size, preoperative GH levels and invasiveness of the tumors. An endocrine remission was obtained in 72% of microadenomas, 50% of macroadenomas, and only 17% of giant adenomas. While 73% of patients with preoperative GH levels less than 10 ng/mL were cured, the cure rate decreased to 33% for patients presenting with GH levels greater than 100 ng/mL. With improved microsurgical techniques and increasing personal experience, we are now able to deal with invasive adenomas and to remove adenomas from within the cavernous sinus and the clivus. We have achieved a cure rate of 38% with invasive adenomas. Surgical reexploration is helpful with noninvasive adenomas that are not cured by surgery. It improves the overall remission rates. Reexploration is particularly indicated if magnetic resonance imaging (MRI) demonstrates a residual tumor, and yielded a cure in up to 50% of such cases.

MORBIDITY RATE

The overall morbidity rate of trans-sphenoidal surgery was low. Meningitis and CSF leak each occurred in fewer than 1% of patients, and there was no mortality. Deterioration of pituitary function was rare following surgery and was exceptional with microadenomas.

OCTREOTIDE PRETREATMENT

Recent achievements in the field of medical therapy for acromegaly have supplemented the classical treatment, which consisted of surgery and radiotherapy. Pretreatment of large adenomas with octreotide is increasingly used before surgery and finds wide acceptance by pituitary surgeons. Evidence suggests that pretreatment softens the pituitary adenomas and facilitates their removal. A softer consistency is especially helpful with invasive adenomas extending beyond the confines of the sella. We now pretreat all invasive adenomas over a 2- to 3-month period using octreotide 100 μg three times daily. An additional benefit is

From the Neurochirurgische Klinik, Universität Erlangen-Nürnberg, Erlangen, Germany.

Address reprint requests to Professor R. Fahlbusch, MD, Neurochirurgische Klinik, Universität Erlangen-Nürnberg, Schwabachanlage 6, 91054 Erlangen, Germany.

0026-0495/96/4508-1023$03.00/0

shrinkage of the adenomas before surgery in one third of cases. Furthermore, pretreatment relieves the symptoms of acromegaly and improves the patient's general condition for subsequent surgery.

OCTREOTIDE AS FIRST-LINE THERAPY AND IN POSTOPERATIVE MANAGEMENT

Severe cardiopulmonary disease (grade III-IV according to the American Society of Anesthesiology [ASA] classification) is the most frequent contraindication to surgery in acromegaly. Octreotide as first-line therapy is indicated in patients with considerable risk factors to surgery. The issue of the ideal management of persistent acromegaly after surgery has not been resolved. Octreotide is becoming an alternative to radiotherapy. Octreotide therapy is more potent in lowering GH levels than treatment with dopamine agonists. Octreotide therapy is indicated if some degree of GH hypersecretion persists after surgery. However, we still recommend postoperative radiotherapy (with addition of octreotide in some cases) if GH levels are fairly high after surgery or if the adenoma showed major invasiveness.

CONCLUSION

Exclusive medical treatment with octreotide is relatively much more expensive and requires a more intensive follow-up regimen than surgical therapy. In conclusion, surgery is still the therapy of choice in acromegaly due to its high cure rate and low morbidity. However, octreotide pretreatment before surgery is becoming an increasingly recognized supplement in the management of acromegaly. If surgery cannot totally eradicate GH oversecretion, octreotide therapy and/or radiotherapy provide long-term control of residual GH activity.

REFERENCE

1. Fahlbusch R, Honegger J, Buchfelder M: Surgical management of acromegaly. Endocrinol Metab Clin North Am 21:669-692, 1992