Efficacy of cryohypophysectomy in the treatment of acromegaly

Evaluation of 54 cases

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Between 1963 and 1974, 54 patients with acromegaly (28 men and 26 women) ranging in age from 23 to 61 years were evaluated. Each patient underwent thorough preoperative neurological, roentgenographic, and endocrinological surveys; most demonstrated mild-to-severe abnormalities in growth hormone immunoassay and oral glucose tolerance. Of those who underwent stereotaxic cryohypophysectomy, approximately 80% were considered to have a beneficial result. The efficacy of this form of therapy was judged on the basis of: 1) significant overall clinical improvement and regression of acromegalic features; 2) improvement in the glucose tolerance curve; and 3) a fall of serum growth hormone below 10 ng/ml. Complications including rhinorrhea, meningitis, and hemorrhage occurred in only a small number of cases. A comparison is made between this technique and others, including craniotomy, radiotherapy, and transnasal transsphenoidal hypophysectomy. The efficacy, low morbidity, and the ease with which the procedure may be performed make this our treatment of choice when dealing with growth-hormone-producing pituitary adenomas with no suprasellar extension.

KEY WORDS: acromegaly • cryohypophysectomy • cryosurgery • growth hormone • glucose tolerance • transsphenoidal hypophysectomy

ACROMEGALY is a progressive, disfiguring, and potentially fatal disease. The latter aspect is particularly emphasized by Evans, et al., whose survey demonstrated a 50% death rate before middle age and 90% mortality before the sixth decade. The cause of death varies and may range from intracerebral tumor extension to diabetic coma, although Wright, et al., described cardiovascular disease as the most frequent cause. In view of the morbidity associated with the clinical and metabolic manifestations of this disease, few surgeons disagree with the recommendation for prompt and aggressive intervention. Controversy exists concerning the choice of modality rather than the need for therapy. At present, the preferred alternatives include craniotomy, microsurgical transsphenoidal hypophysectomy, conventional radiotherapy, heavy particle irradiation, and cryohypophysectomy.
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Despite the clinical aspects, the definitive endocrinological diagnosis was made on a metabolic basis by radioimmunoassay of human serum growth hormone (HGH). An elevated fasting specimen, which subsequently failed to suppress during glucose tolerance testing (GTT), was considered a major criterion of this disease. At the UCLA hospital, normal HGH levels include those values below 10 ng/ml in the fasting, basal state, or below 5 ng/ml in response to the glucose tolerance suppression test. Simultaneous blood sugar levels were also obtained to determine the degree of associated diabetic involvement.

Our method of patient selection was simple; because of the appreciable disfigurement and considerable mortality, we believed that all acromegalic patients should receive some form of treatment. Transfrontal craniotomy was reserved for those patients with evidence of pituitary apoplexy, sudden or marked loss of either visual acuity or peripheral fields, and significant suprasellar tumor extension associated with cranial nerve palsies or obstructive hydrocephalus. Transphenoidal cryohypophysectomy was performed on all of our other cases of acromegaly. In each individual, HGH levels were obtained pre- and postoperatively to evaluate the efficacy of this particular therapy. To determine the adequacy of other pituitary functions, the pituitary adrenal axis was studied by urinary hydroxy- and ketosteroids, and thyroid output by protein-bound iodine testing (PBI), T₃, and ¹³¹I thyroid uptake.

Operative Procedure

The details of the operative procedure have been discussed elsewhere. The liquid nitrogen-cooled cryoprobe is guided under stereotaxic manipulation and with fluoroscopic control into the sella turcica. Several overlapping cryogenic lesions are produced on either side of the midline at cryoprobe tip temperatures ranging from −170° to −180° C for 10 to 15 minutes. Except in rare cases of exceedingly large tumors, an average of only five lesions are made. The temperature gradient 8 to 10 mm from the freezing site rises sharply to a range of −5° to +10° C. The patient is awake under local anesthesia and sedation. During the creation of the lesion, extraocular movements, visual acuity,
Cryohypophysectomy for acromegaly and visual fields are carefully monitored. About 15% of the patients developed incipient palsies as adjacent cranial nerves became cooled below +15°C, but these palsies invariably disappeared with probe warming. In none of our 54 patients was there any postoperative evidence of residual deficit.

**Results**

The efficacy of cryohypophysectomy was judged on the basis of three criteria: 1) substantial overall clinical improvement and regression of acromegalic features; 2) improvement in the glucose tolerance curve; and 3) a reduction of HGH to below 10 ng/ml.

After undergoing this therapy, many patients demonstrated significant subjective and objective improvement in many of the previously described clinical signs and symptoms (Table 1). Acral enlargement diminished in 63% and facial enlargement in 61%. Improvement occurred during the first 24 hours and progressed for several months. Despite lowered HGH levels, radiographic studies demonstrated little if any change in previously described osseous deformities. Consequently, the therapeutic regression of acromegalic features was attributed to the loss of excess fluid from hypertrophic collagenous structures. Also following cryohypophysectomy, heel-pad thickness ranged from 20 to 30 mm (mean 24.4 mm). Hand volume, when measured by water displacement, was lessened by almost 15%. Initially, 63% of these patients demonstrated hypertension with an average blood pressure of 164/101, but after therapy they exhibited a more normal range, averaging 128/86. Skin characteristics such as oiliness, coarseness, and increased pigmentation disappeared altogether or markedly improved in 56% of those affected. Body weight returned to premorbid status in half of the cases, while headache vanished in more than one third. Furthermore, distressing arthralgias and acroparesthesias were relieved or lessened without need for further medication in at least 40% of cases. However, certain complaints were resistant to operative intervention; these included hyperhidrosis and diminished libido.

Fasting blood sugar (FBS) and GTT levels were evaluated in all patients. After oral administration of 100 gm of glucose, serum sugars were sampled at 30, 60, 120, and 180 minutes. The average of these four values was subsequently designated the mean GTT. In random nondiabetic individuals, FBS ranges between 100 and 120 mg%, whereas mean GTT approaches 128 mg%. By using these criteria it soon became evident that within this series at least 34% of our acromegalic patients demonstrated severe chemical diabetes; these patients averaged an FBS of 198 mg% and a mean GTT of 250 mg%. After surgery, these figures rapidly improved to 137 mg% and 158 mg%, respectively. Conversely, patients with an initially normal glucose tolerance curve remained unchanged after cryohypophysectomy.

Comparing the intensity and duration of the initial clinical symptomatology, there appeared to be little difference between the diabetic and nondiabetic populations, but the former group displayed greater morbidity in relation to certain other clinical aspects. Hypertension was common, with an average blood pressure of 153/99, and the incidence of cardiomegaly was almost doubled. Subsequent to surgery, the blood pressure approached a more normal range of 128/82. Finally, significant visual field deficits were recorded in 36% of the diabetic and only 11% of the nondiabetic acromegalic patients. Within each of these groups, visual impairment was associated with definite, although not extensive, suprasellar tumor extension.

The metabolic criterion of successful endocrinological therapy is a lowering of the fasting basal HGH level below 10 ng/ml. At the time of the latest follow-up, an average of 5 years postoperatively, this requirement was fulfilled in 77% of our patients: 56% were below 5 ng/ml, and 21% between 5 and 10 ng/ml. In the successfully treated group, preoperative values ranged from 13 to 185, with a mean of 50 ng/ml (Table 2).
TABLE 3
Number of patients requiring exogenous hormonal therapy before and after cryohypophysectomy

<table>
<thead>
<tr>
<th>Radiation Therapy</th>
<th>No Radiation Therapy</th>
<th>Total Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>before cryosurgery</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>after cryosurgery</td>
<td>20</td>
<td>7</td>
</tr>
<tr>
<td>total</td>
<td>28</td>
<td>26</td>
</tr>
</tbody>
</table>

Postoperatively, HGH averaged 4.05 ng/ml. By comparison, those patients who were categorized as unsuccessful displayed preoperative HGH levels between 30 and 140, with a mean value of 66 ng/ml. Although these preoperative values are similar to those in the successful group, the postoperative mean of 39 ng/ml was far above the acceptable therapeutic range.

In this series it was difficult to evaluate postoperatively the function of the remaining pituitary trophic hormones since a majority (28 of 54) of our patients had undergone previously unsuccessful courses of radiation at other institutions. Even before coming to UCLA, 24% of these patients had been placed on maintenance thyroid therapy, and 28% required some form of exogenous steroid. After surgery, 50% (27 of 54) of our cases ultimately employed supplemental therapy (Table 3). However, 24 of the 27 who demonstrated postoperative pituitary dysfunction had required some type of endocrine replacement even before cryohypophysectomy. Obviously, a major consideration (as well as a confusing aspect) is the large number of patients with a history of previous therapy. Conversely, it also is evident that of 26 patients treated solely with cryosurgery, only seven (27%) required postoperative exogenous hormones. We feel, therefore, that the latter group provides a valid indication of the degree of residual pituitary function one might expect when cryohypophysectomy is the initial procedure of choice in those acromegalics with otherwise normal endocrine status.

Complications were transient and infrequent. Of all 54 patients, 13% developed diabetes insipidus and 7% demonstrated rhinorrhea, but neither of these conditions lasted beyond 4 days. In the latter group, three patients progressed to inflammatory, noninfectious meningitis, which usually cleared within 1 week.

Discussion

For many years authors have debated the efficacy of various surgical and radiotherapeutic techniques in the treatment of acromegaly. The degree of success for any given procedure depends upon specific clinical and biochemical criteria of 1) an improvement and regression of symptomatic acromegalic complaints, and 2) simultaneous association with a fall in HGH level to below 10 ng/ml. Unfortunately, the formulation of a single therapeutic approach has been hindered by certain limitations within each of the proposed methods.

Intracranial Approach

The transfrontal intracranial approach was initially attempted by Horsley in 1889, and its relative safety has subsequently been documented by several others. Cush ing, in his last 200 cases, demonstrated a 2.4% operative death rate. More recently, Krayenbühl and MacCarty, et al., have reported respective mortality rates of 5.9% and 3.4%. In those studies where distinction was made between large and small tumors, the latter incurred an average mortality of 4.3%. Microneurosurgical technique has undoubtedly caused a further reduction in this statistic. In each of the above series, the major causes of death were related to intraoperative hemorrhage, postoperative swelling of residual tumor, cerebral edema, and pituitary insufficiency.

Obviously, when dealing with suprasellar extension and visual impairment, the intracranial approach provides the best opportunity for direct surgical exposure of the chiasmatic region. German and Flanigan in referring to Cushing's series, described successful rehabilitation and improvement in more than two thirds of 247 patients with preoperative visual complaints. Of 165 cases with bitemporal hemianopsia, 80% experienced a successful result. Bakay, in reporting Olivecrona's series, noted significant return of function in 64% of acromegalics with bitemporal hemianopsia. More recently, reports by Ray and his colleagues, Elkington and McKissock,

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and Fager, et al., have demonstrated postoperative improvement in visual acuity and peripheral fields ranging from 60% to 75%.

Unfortunately, among the various studies concerning the intracranial approach to pituitary adenomas, only two mention specifically the postoperative course observed in acromegalic patients. In Bakay's series of 30 women with amenorrhea, only 16% regained regular menses following hypophysectomy. Other characteristics apparently refractory to this mode of therapy included diminished libido, diabetes mellitus, and hypertension. Postoperatively, 40% of these patients died within 6 years as a result of progression of the primary disease. Despite the lack of endocrine replacement, Bakay attributed only one death to pituitary insufficiency. He concluded that only 10% of his cases demonstrated any clinical improvement from surgical intervention. A more recent study by Ray and Horwith describes the alleviation of headache, hypertension, and acromegalic features in a majority of affected patients. Unfortunately, the clinical criteria that led to these conclusions were not discussed. Although the result is beneficial, there still is no adequate study documenting the effect of the transfrontal approach upon HGH levels in acromegalic patients.

Freedom from recurrence is an important factor in considering any particular mode of therapy. Bakay noted a recurrence rate of 20% for acidophilic tumors. Other authors have combined their results for eosinophilic lesions with those for other types of pituitary adenomas. MacCarty, et al., described an 11% reappearance of symptomatology while Elkington and McKissock and Ray and Horwith each noted an 8% recurrence.

The intracranial approach seems best suited for those individuals who have large suprasellar lesions; however, its role in smaller intrasellar lesions is questionable. When functioning or secretory, such tumors require complete obliteration of adenomatous tissue to insure the most beneficial results. Because it limits direct visualization of the abnormal intrasellar tissue, the transfrontal approach commits the surgeon to a course of total hypophysectomy with subsequent apituitarism. This is described in Ray and Horwith's study, in which all patients required postoperative maintenance therapy with cortisone and thyroid.

External Beam Irradiation

In 1951, Kelly reported a differential radiosensitivity between normal and adenomatous pituitary tissue. Based upon this supposition, conventional radiotherapy has been used to reduce the excessive production of HGH in acromegalic patients. Sheline, et al., in an investigation of 37 patients, emphasized the necessity of an adequate initial dosage. In their series, 78% of the patients receiving at least 3500 rads showed some degree of clinical improvement. A subsequent study demonstrated normal HGH levels in 76% of these individuals 10 years after therapy.

Despite early enthusiastic reports, various medical centers have subsequently noted conflicting results. In Emmanuel's series, the average patient survived only 6.5 years after therapy, usually dying by the age of 49 years; he therefore concluded that radiotherapy did little to alleviate the systemic manifestations related to cardiovascular collapse and abnormal carbohydrate metabolism. Similarly, after evaluating his irradiated patients, Kozak, et al., remained unconvinced of the efficacy of this treatment.

The availability of growth hormone radioimmunoassay since 1969 has assisted substantially in evaluating various modes of therapy. Roth, et al., presented the results of conventional pituitary irradiation in 30 acromegals seen from 1964 to 1968. They reported that 4000 rads produced a 51% mean fall in plasma growth hormone during a period of 1 to 2 years, although 58% still remained above 10 ng/ml. It is interesting to note that half of the 42% with a therapeutic response had already shown normal HGH levels even before irradiation. Unfortunately, acral enlargement and carbohydrate metabolism improved in only 15% of these patients. In 1973, Gordon and Roth reported similar results, also demonstrating that after treatment 11 of 16 patients (69%) finally attained normal levels of HGH. Inexplicably yet importantly, 14 of the original patients were excluded from these figures. Nine of these had demonstrated a nontherapeutic response to the initial irradiation. Kramer employed conventional super-voltage therapy on 29 patients between 1957 and 1971. Growth hormone assays were subsequently performed on 16 patients within 9
months to 2 years after treatment; values ranged between 1.2 and 17.8 ng/ml (average 6.12 ng/ml). When these figures are compared to normal values observed in Kramer's laboratory (men, 0 to 2.5 ng/ml; women, 0.15 to 20.5 ng/ml), it becomes evident that the designation of a beneficial response following irradiation must take into consideration the patient's sex. It is unfortunate that throughout this study the therapeutic implications of various HGH levels are overshadowed by a failure to distinguish between male and female populations. Although no reference was made to symptomatic improvement, it was noted that 23% of the patients required endocrinological replacement following irradiation.

In 1972 Jenkins, et al. discussed results obtained in acromegalic patients who were exposed to a 5-week course of 4300 rads. Before treatment, HGH levels had ranged between 15 and 340 ng/ml. Following irradiation, these values remained unchanged in 60%, rose in 30%, and fell in only 10% of the cases. Subsequently, none of the patients demonstrated either a change in acromegalic features or compromise of residual endocrinological function.

External beam irradiation, despite its simplicity and low morbidity rate, is not without complications. Delayed radionecrosis of cerebral tissue has been reported by several authors. Peck and McGovern, in a review of three cases, described intense gliosis stemming from the destruction of vasculature and supporting elements of the nervous system. Arnold defines the vulnerability of the hypothalamus as the primary limiting factor in pituitary radiotherapeutic doses greater than 600 rads. Consequently, Richmond suggested the current regimen of 3750 rads delivered over a period of 4 weeks.

Roth described alopecia as a common complication in their patients; it usually occurred within 2 weeks of therapy and in some cases became permanent. Kramer, in reporting a morbidity of 14%, described optic nerve vasculitis, memory loss, central scotomata, and empty sella syndrome. In the series of Sheline, et al. and Sheline, several patients developed transient nausea, vomiting, and headache following irradiation, but 9% experienced more serious complications such as scalp necrosis, carcinoomatous involvement of paranasal sinuses, and sarcomatous degeneration of pituitary tissue. The latter problem has been described by several authors as a possible long-term complication of radiotherapy. The prolonged latent period between irradiation and appearance of the sarcoma (average 10.4 years) may explain the relatively infrequent observation and documentation of this particular hazard. Possibly, a greater frequency may be defined after studying many of these patients over a longer period of time.

A common drawback associated with external beam irradiation is the lengthy delay preceding therapeutic improvement. Even its enthusiastic proponents agree that often a beneficial response may not be attained before 1 to 4 years following treatment.

**Interstitial Irradiation**

Some physicians who have been dissatisfied with the technique of external beam irradiation have turned to implantation of interstitial radioactive substances. Molinatti, et al. reported the results of radioactive yttrium (90Y) in 16 patients. Within 1 month of therapy, half of their patients showed clinical improvement with respect to acromegalic features, headaches, and fatigue, while maintaining normal residual pituitary function. Unfortunately, the follow-up period was too brief to eliminate the possibility of recurrence. Utilizing both radioactive gold (198Au) and 90Y, Hartog, et al. noted a beneficial HGH response in only five of nine patients. In another study Hartog, et al. reported additional results in 22 cases. Within 19 months of implantation, only 32% of the patients experienced a satisfactory response as defined by 1) a loss of symptoms, 2) a recognizable regression of acromegalic facies, and 3) a return to the normal glucose tolerance curve. Nine patients underwent a second implantation, subsequently raising to 60% the number who achieved a successful result. Ultimately, 41% required some form of endocrine replacement therapy.

Similarly, Wright evaluated results in 80 patients implanted between 1958 and 1967; they observed that 53% showed clinical improvement of headaches, paresthesias, and acromegalic appearance. Glucose tolerance tests returned to normal in 45% of those cases with previous evidence of diabetes. Although HGH levels fell an average of 54%, a majority of patients (59%) continued to demonstrate
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values in excess of 10 ng/ml. Bloom also noted that HGH levels even when greatly reduced did not regularly return to normal values.

The hazards of this particular technique have been well documented. Molinatti, et al., reported cranial nerve palsies in 13% and diabetes insipidus in 38% of their cases. Hartog, et al., described complications in 39% of their patients; the most frequent among them were pituitary abscess, rhinorrhea, meningitis, diabetes insipidus, and visual impairment. In the series of Wright, et al., similar problems occurred in only 13% of the cases but, unfortunately, these were accompanied by three operation-related deaths.

Heavy Particle Irradiation

After disappointing experiences with the conventional and interstitial techniques of irradiation, some medical centers have instead employed high-energy heavy particles such as neutrons, deuterons, or protons. With this noninvasive method, the Bragg peak effect is used to produce a local, destructive pituitary lesion. Lawrence, et al., and Linfoot, et al., reported results in 120 patients treated over a period of 11 years. Within 2 years of therapy, growth hormone was somewhat lower in 73% but normal in only 27% of patients. The authors noted, however, that most of the 21 patients evaluated 5 to 9 years later did fall within the normal range. Acral enlargement and facial features remained unaffected in 66%, and 35% of these patients required some form of endocrine replacement.

Similarly, Kjellberg, et al., and Kjellberg and Kliman employed stereotaxic Bragg peak proton ablation in 233 cases of acromegaly. Following hypophysectomy, 53% reported clinical remission of their acromegalic features, 32% showed partial improvement, but 15% remained unchanged or worse. Of 149 patients followed for varying intervals, only 51% demonstrated HGH levels within the therapeutic range.

The mortality rate associated with this form of therapy is low. In the entire series of Kjellberg and Kliman there was only one death, a consequence of pulmonary embolus following general anesthesia. Complications, although bothersome, are usually transient. Lawrence, et al., described visual field changes, cranial nerve palsies, and temporal lobe epilepsy in 4% of their cases. Kjellberg and Kliman also discussed additional undesirable sequela ranging from diabetes insipidus (2%) to temporary extraocular dysfunction (21%).

Because of the potential hazard to surrounding structures, strict attention must be paid to defining the borders of the pituitary for spatial distribution of the radiation. Consequently, this technique should not be used on patients who show evidence of suprasellar extension. An additional contraindication to heavy particle therapy is a history of previous irradiation, since the cumulative dose exceeds safe neural tissue tolerance levels.

Transnasal Transsphenoidal Microsurgery

The transsphenoidal approach, employed by Schloffer in 1907, provided the first successful means for partial resection of a pituitary lesion. Subsequently, Cushing used this method in 90% (69 of 76) of his acromegalic patients with an operative-related mortality of only 6.6%. His switch to the transfrontal operation in the latter part of his series stemmed not from disenchantment with the extracranial technique but rather from a desire to evaluate other types of suprasellar pathology, such as meningioma and aneurysm. Of the various symptomatic complaints, visual deficit seemed to benefit most from surgical intervention. Henderson, in evaluating Cushing's results, noted that of 36 patients with severe loss of vision, 86% showed marked postoperative improvement. Headache also diminished in 55% of these patients. The systemic deleterious effects of the functionally secreting lesion persisted in a significant number of patients. Five years after transsphenoidal hypophysectomy, 49% of the patients were alive and functioning, but 38% had died from symptomatic recurrence. In order of frequency, the chief causes of death in those 25 patients were: diabetes mellitus, acute myocardial failure, hypertension and intracranial tumor extension.

The most recent applications of the operating microscope and microneurosurgical technique have reduced the incidence of morbidity and greatly enhanced the accuracy of the transsphenoidal approach. With this technique, Hardy was able to distinguish between normal pituitary and acidophilic adenomatous tissue. Under such circum-
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TABLE 4
Comparison of various characteristics between two groups of treated acromegalic patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Successful Therapy</th>
<th>Failure</th>
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<tr>
<td>age</td>
<td>33 ± 6 yrs</td>
<td>41 ± 8 yrs</td>
</tr>
<tr>
<td>duration of symptoms</td>
<td>9 ± 3 yrs</td>
<td>13 ± 3 yrs</td>
</tr>
<tr>
<td>blood pressure</td>
<td>146/89</td>
<td>146/94</td>
</tr>
<tr>
<td>glucose</td>
<td>preoperative</td>
<td>165 ± 26 mg%</td>
</tr>
<tr>
<td>tolerance</td>
<td>postoperative</td>
<td>107 ± 22 mg%</td>
</tr>
<tr>
<td>fasting</td>
<td>preoperative</td>
<td>135 ± 41 mg%</td>
</tr>
<tr>
<td>glucose</td>
<td>postoperative</td>
<td>101 ± 22 mg%</td>
</tr>
<tr>
<td>growth</td>
<td>preoperative</td>
<td>50 ± 14 ng/ml</td>
</tr>
<tr>
<td>hormone</td>
<td>postoperative</td>
<td>4 ± 2 ng/ml</td>
</tr>
<tr>
<td>CSF glucose</td>
<td>82 ± 15 mg%</td>
<td>91 ± 23 mg%</td>
</tr>
<tr>
<td>protein</td>
<td>38 ± 8 mg%</td>
<td>57 ± 10 mg%</td>
</tr>
</tbody>
</table>

stances, one might ideally expect complete eradication of small pathological lesions with subsequent preservation of residual pituitary function, but Hardy noted that in his series of 40 acromegals, only 63% were candidates for "selective total surgical excision." Unfortunately, "microadenomas" represented only 25% of all acidophilic lesions, while the separation of larger tumors from pituitary tissue could not always be reliably performed. He described favorable results in 88% of cases; 62% of these patients experienced both clinical and metabolic relief from pituitary hyperactivity. Of the remaining cases, 25% demonstrated symptomatic improvement but continued to show elevated HGH levels, and 13% were classified as unaltered by surgery. As a result of the transsphenoidal procedure, seven of 12 patients experienced functional recovery from preoperative pituitary insufficiency. Although not specifically documented, the statistics implied that acromegals with normal pituitary function suffered no further endocrinological deficit as a result of transsphenoidal microsurgery.

Hardy and Guiot described similar mortalities of 1.5% to 2% in transsphenoidal operations involving over 800 patients. Guiot noted the postoperative complications of rhinorrhea in 2%, recurrent hematoma and/or diplopia in 1%, and meningitis in 1%. In Hardy's series, no reference was made to the presence or absence of recurrent disease.

It is apparent from the foregoing review of the literature that each alternative for the treatment of acromegaly presents certain inadequacies. Since our initial experience with cryosurgery, we have had ample opportunity to refine our techniques and evaluate our results in relation to other modalities of therapy. Our success in the amelioration of acromegalic features (62%), the enhancement of carbohydrate metabolism, and the alleviation of hypertension (63%) compares favorably with any of the studies that have evaluated the clinical results of surgical intervention. In a similar manner, none of the alternative modes of therapy, except possibly transfrontal craniotomy, has provided both the magnitude (postoperative mean of 4.05 ng/ml in 77% of the patients) and the rapidity of improvement in previously elevated HGH levels. Despite our enthusiasm for cryohypophysectomy, we must still agree that no single approach or therapeutic regimen seems applicable to all cases of acromegaly. At present, the major disadvantage of this procedure lies in the restriction of its use to intrasellar lesions. Although we are displeased with a morbidity rate of 13%, we can report that during the past 5 years of additional experience, we have significantly reduced this figure. Another hindrance has been our inability to predict accurately which acromegalic patient might be refractive to cryohypophysectomy; in this particular series, 23% of the cases were described as unsuccessful results.

Categorization and preoperative elimination of these potentially unresponsive individuals would greatly enhance the use and applicability of this surgical technique. Table 4 compares various characteristics between

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successfully and unsuccessfully treated acromegalics, and indicates that there is little significant difference with regard to age, duration of symptoms, blood pressure, or serum fasting glucose. It is apparent that carbohydrate metabolism, as measured by mean GTT, returns to normal levels following cryohypophysectomy in successfully treated individuals. Conversely, in those patients categorized as therapeutic failures, there was little significant difference between pre- and postoperative mean GTT values.

Although it constitutes an important retrospective observation, this information provides no assistance in the preselection of individuals with a predilection for endocrinological recovery. Of all the preoperative factors evaluated, only the CSF protein showed any significant variation between the two groups of patients categorized as successful and unsuccessful responses to cryotherapy. As yet we are unable to explain or extrapolate the importance of this observation with regard to identifying potential candidates for this surgical procedure.

We consider cryohypophysectomy the procedure of choice in those acromegalics with intrasellar tumor demonstrating only minimal extension. In the near future, as acromegaly becomes recognized in progressively earlier stages, we believe that this technique will become the most frequently used surgical procedure.

References


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