Pituitary surgery

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Drs. Jagannathan and Oldfield, along with their colleagues from the National Institutes of Health (NIH), have made a significant contribution to our surgical armamentarium with respect to the surgical manipulation of pituitary tumors. This manuscript is particularly refreshing to me in that it deals with the issues of tumor resection ("what to do once you're there") rather than the recent flurry of articles concerned with the preresection approach ("how to get there"). We can all understand that it is far more important to the patients harboring these tumors that cause a malignant endocrinopathy to have successful resection of the tumor than the concern about whether the surgeon pursues a sublabial endonasal microscopic or endonasal endoscopic approach, each of which is minimally invasive and designed to help the surgeon reach the tumor. Dr. Oldfield obviously has had long-standing success with the sublabial approach; his success in eradicating the hypercortisolemia constitutes the critically important consideration.

Along these lines, however, this author would take issue with the comments to the effect that the sublabial approach provides the best option for a "broad, complete exposure of the sella." Having used both the sublabial and endonasal approaches for many years, it is apparent to us that, using either approach, one can open the sella from the cavernous sinus to the cavernous sinus and from the circular sinus to the floor. The sublabial approach does provide the best access to the tuberculum and planum for an extended transsphenoidal procedure, but, for a direct approach to the sella, either approach allows excellent visualization. The authors note that, in their hands, an extrapseudocapsular dissection lends itself to a remarkably high success rate in achieving resolution of hypercortisolemia. The success appears to relate to one’s ability to identify a tumor confined by using an intact pseudocapsule as an index of a noninvasive tumor, and this report relates to their experience with this group of tumors specifically. As the authors also note, most surgeons resect the tumor from within the tumor bed without excising the tumor capsule. Support for their contention that the pseudocapsule should be resected would be enhanced if the authors had reported evidence of invasive tumor cells in the resected pseudocapsule to possibly explain why simple tumor resection does not appear to be as effective. Is there such evidence? In addition, they describe 6 patients with a pseudocapsule at surgery in which the contents were normal anterior pituitary rather than tumor. Can the authors explain this finding on the basis of the defined formation of a pseudocapsule? Furthermore, in these 6 patients it appears that resection of the nontumor-containing pseudocapsule resulted in postoperative hypocortisolemia. What is the presumed mechanism behind this?

The authors describe remission in 89% of "invasive tumors" and in 76% of patients in whom no tumor was found intraoperatively (followed by resection of 30--100% of the anterior lobe); these are truly outstanding results in these particularly complicated cases. Do the cases of invasive tumor relate primarily to invasion of the pseudocapsule or to dural and/or cavernous sinus invasion? Our experience with resection of nontumorous gland including total anterior hypophysectomy with sparing of the pars tuberalis is much more disappointing. Even with resection of the entire midline mucoid wedge, our biochemical remission rate is only about 50% in the absence of definitive tumor. For that matter, because these tumors frequently occur in young women who are interested in maintaining their fertility, we have abandoned attempts at hypophysectomy after a negative "eight segment exploration" of the gland and proceeded with adrenalectomy in this group. In a small series of 12 patients treated as such, we have not yet seen one case of Nelson syndrome during a follow-up period of up to 5 years.

The authors describe their postoperative protocol that commences on postoperative Day 3 with 3 successive days in which patients are studied for early morning cortisol and 24-hour urinary free cortisol levels to determine the efficacy of surgery. This is a commendable and highly desirable protocol, but it is probably impractical outside of the setting at the NIH, since most patients cannot be kept in hospital for at least 6 days. I suspect that Dr. Oldfield will have to change that protocol now that he has moved to the University of Virginia. In our present protocol, we do not utilize perioperative corticoids in these patients and draw a morning cortisol on the first postoperative day, give the patient 1 mg of dexamethasone that evening, and then draw another morning cor-

See the corresponding article in this issue, pp 531–539.
tisol on postoperative Day 2 prior to discharge. We have found this protocol both practical and effective in defining the early efficacy of tumor resection. Our long-term follow-up then requires performance of a 24-hour urinary free cortisol at 6 weeks and 3 months postoperatively and then every 6 months for 10 years. We have also found return of a normal diurnal variation in cortisol secretion to be an excellent index of a persistent disease-free state. This is probably a bit more accurate than completion of a survey and inquiry from the patient.

Out of concern for cellular infiltration in the tumor bed, we have, for years, bathed the tumor bed in absolute alcohol for a minute after tumor removal (in the absence of any CSF leakage) in addition to using bipolar coagulation of the tumor bed and any adjacent dural attachment. Using these augmentations, we have reported a short-term biochemical remission rate of 92% in patients harboring defined adrenocorticotropic hormone microadenomas with a 3% recurrence rate in that group followed for 5–15 years.1 It is our thesis that the alcohol and cauterization combination affects any cellular infiltration into the tumor pseudocapsule, constituting a parallel to the proposal put forth by Dr. Oldfield and his colleagues.

It is apparent from this careful study that simple curettage of the tumor from the tumor bed in cases involving these tumors may not yield optimal results. We are indebted to Dr. Oldfield and his group for advising us of the need for a more vigorous resection protocol.

Response

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We share Dr. Weiss’ conclusion that in the past several years enough attention has been given to the “pre-resection” procedure, how to get to the sella, and that it is time to emphasize the act of removing the tumor.

In patients with nostrils large enough to accommodate a normal-sized Hardy-type speculum, it is the pyriform aperture that limits the width of exposure with either operative approach. However, in many women and most children the size of the nostril requires use of a smaller retractor and thus limits the width of the exposure with the endonasal approach. Although a wide variety of approaches have been used successfully to access the sella in patients with Cushing disease, the sublabial approach offers a wider exposure for direct view of the sella and the medial portion of both cavernous sinuses while maintaining the normal nasal anatomy (that is, retention of the fully intact nasal mucosa and middle turbinates). Furthermore, anatomical studies performed by Dr. Weiss and his colleagues demonstrate that a sublabial approach provides a volume of sellar exposure of 213 mm³ rather than the 80 mm³ associated with an endonasal approach, a 2.7-fold enhancement of exposure.3 Although their study demonstrated that most of the increased exposure was the product of an enhanced superior view, in practice the experience of one of us (E.H.O.) is that the sublabial approach provides a substantially wider and more complete view of the sella than any other approach to directly view the sella for microsurgery. The increased exposure is especially important in Cushing disease as it allows the surgeon to thoroughly and systematically inspect the entire sella, which is particularly important in finding adenomas in patients with negative MR imaging,1,3,4 in whom the tumor may lie completely outside the pituitary gland, either superiorly in the pituitary stalk5 or laterally in the wall of the cavernous sinus.6,12 Additional disadvantages of the endonasal approach are that it has a more oblique view of the sella, and the speculum is less stable because its inferior rim does not engage the osseous margin of the pyriform aperture.4 Finally, it is notable that the high success rate reported by Dr. Weiss and his colleagues described below was achieved using a sublabial approach in all patients.

We use the so-called pseudocapsule to describe the area of compressed gland and its concentric reticulin layers that surround an adenoma.10 The focus in our current report is on the outcome of the intraoperative use of this capsule (via the extracapsular approach) to treat tumors thought to be contained within the pituitary gland at surgery. Although there are no studies that focus on differences in the thickness of the tissue envelope that contains the adenoma after extracapsular dissection compared with removal of the adenoma from within, histological assessment of some tumors suggests the presence of an irregular margin at the interface of the innermost levels of the pseudocapsule and the contained adenoma, as demonstrated in Fig. 1. Inspection of this adenoma clearly suggests that dissection with a ring curette from the inside of the tumor may leave residual tumor cells behind with the potential for lack of endocrine remission, or recurrence. An added advantage, as outlined in our report, is the increased likelihood of using the pseudocapsule to identify an adenoma in patients with negative MR imaging, removal of which produces a high remission rate in patients with Cushing disease, as demonstrated in our study.

That 6 patients (2.3%) underwent removal of a lesion intraoperatively considered to be an adenoma but which proved not to be adenoma on pathological examination is easily understood. In very small tumors the development of the histological pseudocapsule is not as thick or as well defined as it is in larger tumors.10 Thus, during a search for tumors as small as 2–4 mm in diameter, what appears to be tumor at surgery may not prove to be tumor in all cases. This was the case in 6 of the 261 patients in our

References
