TECHNICAL NOTES

THE CASE FOR TRANSSPHENOIDAL APPROACH TO HYPOPHYSIAL TUMORS*

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Hypophysial tumors are endowed with variable biological properties and hazardous anatomical relationships. At the Harvey Cushing Society's Symposium on Pituitary Tumors† it was concluded that there is no rigid regime for handling these difficult cases when the growing neoplasm indicates need for reducing its encroachment on contiguous neurovascular structures. The panelists agreed that effectively proven measures like transfrontal surgery or irradiation should receive fair consideration with respect to the individual problem—but not transsphenoidal surgery. The latter was condemned on the basis of 30- to 40-year-old evidence derived from the work of Cushing when he was developing gradually the parasellar exposure during the late twenties as one of his basic intracranial techniques.

Cushing did not depreciate his experience with the transsphenoidal operation in 1932 when he expressed preference for the transfrontal approach. In that era the infrasellar procedure, performed sublabially with primitive instruments and less exposure than the septal route, scarcely could provide adequate removal nor reaccess to deal with recurrence. Nevertheless, his 5-year results by intra-or subcranial attack (with or without secondary irradiation) still present an extraordinary target. His statement—"It is certain that no one method is applicable for all conditions of pituitary tumor and that for some no satisfactory procedure has been devised."—still holds true.

The transsphenoidal approach deserves fair consideration—which is not granted by a court whose judges have had so little actual and no recent experience with it. The method should be utilized as well as transfrontal surgery and roentgen-ray therapy to reduce further the morbidity and mortality in a most important group of benign, albeit wicked neoplasms.

Dr. Ray inveighed against recognition of two camps who use roentgen-ray treatment exclusively or who rely wholly on surgery; rather we should consider what may be best for the individual patient. The same admonition applies to the surgical method. There are patients who have received maximum benefit at the right time from one or the other procedure and from certain types of irradiation as well, with appropriate credit to each.

Dr. Davidoff cited 20–25 per cent less protection against recurrence in small samples selected out of context from Henderson's4 follow-up monograph (1939) on Cushing's 338 patients as "one of the major reasons" for rejecting the transsphenoidal approach. Another important reason: failure of many senior neurosurgeons to give credence to earlier good results and recent progress in transsphenoidal treatment, disparaging by hearsay and diverting their apprentices from seeking knowledge of its usefulness. Satisfaction with the method, however, has been sustained in reports from Scandinavia, Britain, and France; and it was encouraging to hear favorable comment by neurosurgical mentors like Professors Edgar Kahn and Hugo Krayenbühl at the Second International Congress of Neurological Surgery in October 1961.

In Cushing's cases of chromophobe adenoma there were 167 transsphenoidal and 91 transfrontal operations analyzed by Henderson.† In those of acidophil adenoma transsphenoidal operation in 60 cases was designated as preferable to transfrontal operation in 7 cases, the latter having incurred 15 per cent higher mortality. Among the patients with chromophobe adenoma who had received supplementary irradiation and who could be traced for 5 years, improvement was recorded in 32 out of 49 after transsphenoidal operation and 27 out of 31 after transfrontal operation (major premise of Davidoff). Considering that most of the transsphenoidal operations
had been done during the earlier decade when roentgen-ray treatment was not utilized, and comprised the vast majority of operations in the cases of 260 chromophobe, 67 chromophil, and 11 malignant adenomas, the statistical incongruity of the comparative data becomes apparent. Complications were distributed about equally. Henderson remarked on the variation in rate of growth and surgical anatomy of the tumors. He commented on the good outcome of transsphenoidal operations in patients with homonymous hemianopia or central scotomata, usually associated with prefixed chiasm. Instances were cited of stable improvement (without supplementary irradiation) for 7 1/2, 9 1/2 and 10 1/2 years; and 5 of 11 patients so treated in 1920 remained symptom-free for 16 years. Remissions for 20-30 years in 33 transsphenoidal cases have been documented by Hirsch, and his 5-10 year remissions among 392 others are equally impressive.

Dr. Horrax was cited on the basis of the same source material as estimating the transsphenoidal operation to afford “two to three times less protection against recurrence” for chromophobe adenomas than the transfrontal operation. Such a conclusion cannot be extrapolated from Henderson’s material. In a later article Horrax et al., attempted to demonstrate “the tremendous gain” during 1950-53 accomplished through rotational bombardment of enlarged sellec, presumably containing adenomas, with 2-million-volt photons. The report served rather to add evidence that combined surgery and irradiation is more effective than either alone. The ambiguous statistics that were concocted to support their contention received effective criticism by McCort in a later issue of the same journal. During 1932-49 among 173 patients who were irradiated (115 histologically unverified; 74 with no visual loss) nearly 60 per cent required subsequent surgery; during 1940-53, 53 patients were irradiated (45 unverified; 15 with no visual loss), follow-up not being mentioned.

The actuarial validity of unmatched or unrandomized sets of data concerning disease states depends largely on their relative degree of biological variability. Unitary control of therapy was the conformable factor for the Cushing cases. Subsequent published series have reflected more complexity with respect to homogeneity of cases, treatment, and follow-up observation so that accurate statistical comparison can be only approximate.

Credit must be given to the efficacy of various sorts of irradiation that have sustained or initiated improvement in patients who first had either type of surgery or no surgery. There are many factors that render positive pronouncement on therapy with radiation versus surgery specious. One should complement the other. The interven-

tion of either can be demonstrated to have been valuable at a particular time for the individual patient. Scrutiny of the records wherein each case is so unique indicates the importance of weighing the factors of divergence that affect the analysis and conformity of such material. Priority by “two or three times” for any proven form of treatment over another, as implied by Horrax for all pituitary tumors, is not warranted. Further unpublished observation after 1940 on Cushing’s cases was expressed by Eisenhardt who commented upon how well some of Dr. Cushing’s patients had fared after the transsphenoidal procedure.*

Dr. Chamlin presented an admirable ophthalmological analysis of methods of testing and interpretation of visual defects caused by pituitary tumors. His logical opinion, however, that “reversibility of visual loss depends on the duration and severity of pressure on the optic nerve” is not in accord with the alleged proof that measurable response need not appear for 6 months up to 2-3 years after irradiation has been completed. The author’s 20-case chart in support of this contention records the initial increment of improvement to have occurred within a matter of weeks in 14 patients, at 4-6 months in 4, and at 12-16 months in 2.

Reference was made to the remarkable progress in modern intracranial surgical technique and its adjuvants that have mitigated the risk of operating in the parasellar area. The transsphenoidal procedure also has accrued considerable technical advance since 1940; it has reduced its mortality rate for a recent series of 104 patients, including 10 with craniopharyngiomas, from 5.4 to less than 2 per cent.† The risk of meningitis is minimal, having occurred in 3 among 104 cases since 1945; in 2 cure was effected by antibiotic therapy. There were 6 instances of cerebrospinal rhinorhea, 4 earlier in misdiagnosed nontumor cases; in all 6 cases successful closure was performed by endonasal mucosal flap.‡

Among the 100 odd recent patients followed for at least 5 years, 62 have maintained visual and somatic improvement, the majority having been treated with secondary radiation. All received additive benefit during their treatment from gains in diagnostic maneuvers and endocrine-metabolic aids. It is usually a symptom of pituitary deficiency that brings the patient with hypophysial tumor to a physician; many such individuals are maintained successfully by endo-

* Personal communication.
† One patient, a hypopituitary dwarf, died 6 weeks after operation of postmenigitic hypoadrenalism; autopsy revealed craniopharyngioma located above an empty sella. The other succumbed to a pulmonary embolus on the 5th postoperative day following subtotal removal of a large chromophobe adenoma.
crine support without resort to surgery or radiation. Any measurable visual loss is a warning of encroachment on optic nerve or chiasm which should be investigated promptly. Fractional pneumoencephalography and carotid arteriography, either or both, should be performed to determine the precise anatomical relationship of the suspected neoplasm. If the sella is ballooned so that the major portion of the tumor is judged radiographically to be below the level of the diaphragma sellae, transsphenoidal exploration should be performed forthwith in order to decompress the chiasm and adjacent structures, and to determine the nature of the tumor which should furnish guidance for future therapy.

Among a series of approximately 400 tumors operated upon by the transsphenoidal procedure, nearly 25 per cent were cystic.4 Subsellar decompression in such cases had often been delayed to await the negative effects of roentgen-ray therapy. Following exenteration of as much of the tumor as possible, immediate implantation of radioactive chronic phosphate (P32), a beta-emitting short-range isotope, has proven to be a safe and effective form of direct radiation to the neoplastic remnant. It also is believed to be locally bacteriostatic. Focal destruction of neoplastic cells occurs slowly in relation to decay of nuclear energy, tending to spare normal pituitary cells which are less susceptible. Occasionally a cystic tumor after it has been emptied from below will become decompressed permanently by the pressure of pulsation of the intracranial contents. The capsule of the tumor, however, often becomes sealed off at the subsellar site of evacuation with insidious recurrence of symptoms caused by reaccumulation of cystic content. The transsphenoidal approach leaves a permanent infra sellar corridor to the operative site for subsequent re-exploration. The superior capsular covering of the tumor remains intact, separating the sellar compartment from the supradiaphragmatic region. Infrasellar formation of scar across the obliterated sphenoid sinus forms a barrier against contamination if suprasellar operation becomes necessary.

Transsphenoidal biopsy is an answer to Dr. Love's plea for a definite diagnosis on patients with disorders suggesting hypophysial tumor before committing them to a trial of radiation. In addition to 25 craniopharyngiomas (hypophysial duct or Rathke-pouch tumors) the transsphenoidal explorations cited above have disclosed examples of chordoma, meningioma, teratoma, dermoid, carcinoma, sarcoma, mucocele, aneu-

Dr. Ray's final statement—"When the operation is indicated, there is no substitute for it."—implies the right procedure for the right situation. The corollary is that suitable operation should be performed without delay when there is measurable loss of vision caused by presumed tumefaction expanding from the sella. The transsphenoidal aim is to preserve optic pathways and pituitary-hypothalamic function by discrete removal and subsequent long-term control which would include irradiation and additional surgery as required. A prospective patient rarely is turned down because of age or associated physical ailment. When the main mass of the lesion appears to extend above the level of the diaphragma the operative exposure should be transfrontal, although decompression and biopsy through a ballooned sella usually can be performed from below.

Pathologic identification, therefore, is urged before traversing the parahypophyseal domain with superpowered atomic particles that are suspect for delayed deleterious effects on normal tissues. Primary trial of irradiation, however, may be the correct choice in certain cases of grave surgical risk or active intrasellar tumor (i.e., acromegaly) without loss of sight.

The transsphenoidal operation was developed on the sound anatomical principles of midline dissection, adequate exposure and visualization.† You have to see it to believe it. It is a simple, not an easy procedure, but neither is the transfrontal operation. Surgeons of consummate skill and experience like Drs. Ray and Poppen make it look easy. The transsphenoidal operation has a lower morbidity and mortality throughout its history than the transfrontal, notably so with 25 craniopharyngiomas among 425 cases, 11 in the recent series of 104. At the present time, in proper hands, there is no more risk of difficulty in exposure, meningitis or cerebrospinal rhinorrhea in attacking an intrasellar tumor from below than from above. The amount of safe removal and supplementary radiation depend on the individual pathological anatomy.

Analysis of results of the transsphenoidal operation in 104 patients (Fig. 1) treated since 1945 shows that nearly 65 per cent of the 102

* Cystic dilatation of the 3rd ventricle or carotid aneurysm should be identified by preliminary contrast studies. During operation, as the floor of the sella is being removed, exploratory puncture through dural periosteal capsule is performed routinely.

† The lateral ethmoidal entry to the sella is rejected mainly because it does not provide safe midline orientation with minimal hemorrhage, and does not leave reaccess to the operative site.

* Better designated as semimystic or cystic-degenerated, whether related to prior radiation or spontaneous ischemic autolysis of tumor.
survivors have maintained visual gain or stability and betterment in other ways for at least 5 years. About 15 per cent of the remainder stay improved over shorter periods. Approximately one-third of the total had undergone prior ineffective transfrontal surgery or roentgen-ray therapy; 78 per cent received secondary infrasellar application of radium or direct isotope implant at operation, or multiportal roentgen-ray treatment and/or additional operative maneuvers, mostly through endonasal reaccess, 5 by craniotomy.

The case for the transsphenoidal approach to hypophysial tumors now rests—with hopeful reliance on a fair-minded jury.

REFERENCES


