Giant Pituitary Tumors: A Study Based on Surgical Treatment of 325 cases

Atul Goel, Trimurti D. Nadkarni

Department of Neurosurgery, King Edward Memorial Hospital, Seth G.S. Medical College, Parel, Mumbai

Summary

Three hundred and twenty five cases of hormonally inactive giant pituitary tumors, having their maximum dimension of more than 3 cm, treated surgically in our neurosurgical department from the year 1995 to November 2008 were analyzed. Depending on the extensions and the nature of their meningeal coverings these tumors were divided into four grades. Average duration of follow-up was thirty-six months.

There were 135 giant pituitary tumors, which remained within the confines of sellar dura and under the diaphragma sellae and did not enter into the compartment of cavernous sinus (Grade I). Transgression of the medial wall and invasion into the compartment of the cavernous sinus (Grade II) was seen in 109 cases. Elevation of the dura of the superior wall or roof of the cavernous sinus (Grade III) was observed in 59 cases. Supradiaphragmatic- subarachnoid extension (Grade IV) was seen in 22 patients.

Radical surgery by a transsphenoidal route is indicated and possible in Grade I-III pituitary tumors. Such a strategy offered a reasonable opportunity for recovery in vision and a satisfactory post-operative and long-term outcome. Biopsy of the tumor followed by radiotherapy could be suitable for Grade IV pituitary tumors.

Key Words

Giant pituitary tumors, cavernous sinus, diaphragma sella, dura.

Reprint requests: Prof. Atul Goel Head, Department of Neurosurgery King Edward Memorial Hospital & Seth G.S. Medical College, Parel, Mumbai- 400012, INDIA. Tel- 91-22-24129884, Fax- 91-22-24143435 E-mail- atulgoel62@hotmail.com

Introduction

Giant and 'invasive' pituitary tumors are amongst the more complex neurosurgical challenges (11,13,14,24). Despite the histological benign nature, some of these tumors grow into a massive size and invade into diverse anatomical structures (25,44). Due to the invasiveness and size of such tumors, surgical resection is difficult and frequently dangerous (1,5,13,18,23,44,47). The results of radiation therapy are inconsistent (13,27,34,46).

The diagnosis of the pituitary tumor can usually be made on the basis of analysis of presenting clinical features and their classical anatomical extensions seen on imaging. Biopsy of the lesion thus has little relevance. Subtotal or partial resections can be dangerous as bleeding from the residual tumor is frequent and can result in death. The clinical outcome following a successful small or partial resection is generally not satisfactory. An exact understanding of the anatomical nature of the tumor and of its extensions is mandatory for planning and execution of surgery. A successful radical resection of the tumor can lead to rapid symptomatic recovery and an excellent longterm clinical outcome. The recurrence rate of the tumor after its radical resection is reported to be low, but significantly higher than smaller sized pituitary adenomas.

We have discussed our earlier experience with 118 cases of giant pituitary tumors and presented our surgical policy on these patients (13). The present paper is an analysis of our current experience on the subject.

Material and Method

Two thousand three hundred and seventy five pituitary tumors were treated in our neurosurgical unit between the years 1995 to November 2008. We selected 325 surgically treated hormonally inactive pituitary tumors,

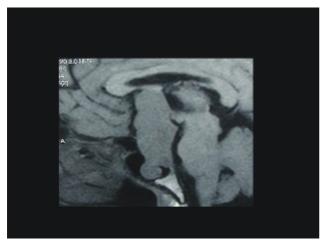
which measured more than 3 cm in their maximum dimension (Fig. 1). Patients operated upon earlier and presenting with a giant tumor were not included as it was observed that the extensions in some such tumors was bizarre and did not follow a defined pattern seen in the non-operated cases.

Results

Clinical and radiological features

The tumors were divided into four grades.

Grade I pituitary tumors were those, which were located within the confines of sella and remained underneath the superiorly elevated diaphragma sellae and did not invade into the cavernous sinus. There were 135 Grade I pituitary tumors (Figs. 1 - 4). In 31 cases in this grade, the diaphragma sellae extended superiorly up to or beyond the normal level of corpus callosum. In three cases, the tumor extended anteriorly and elevated the dura of tuberculum sellae and planum sphenoidale.



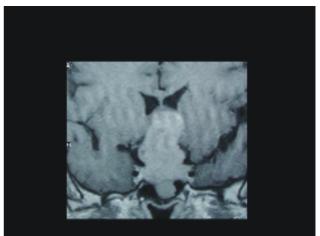
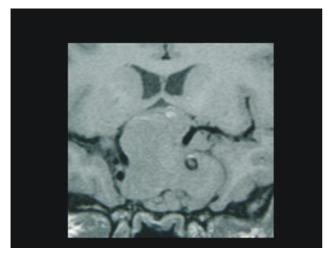


Figure 1A. Post-contrast T1-weighted sagittal MR image and **B.** coronal MR image showing the massive vertical extent of a giant pituitary adenoma (Grade I) obliterating the third ventricle and reaching upto the corpus callosum. There is no cavernous sinus invasion.

Grade II pituitary tumors were those where the tumor invaded into the cavernous sinus. There were 109 Grade II pituitary tumors (Figs. 5 and 6). Unilateral cavernous sinus invasion was more frequent (75 cases) than bilateral cavernous sinus invasion (34 cases).



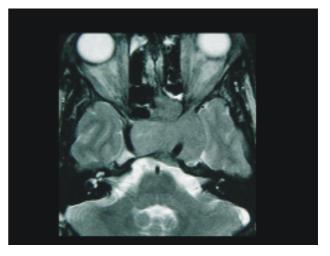
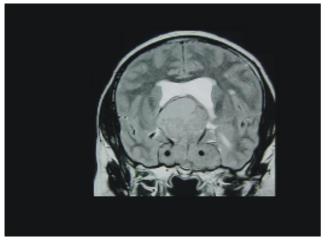


Figure 5A. T1-weighted coronal image and **B.** Axial T2-weighted MR image demonstrating a Grade II giant pituitary tumor with unilateral cavernous sinus involvement. The internal carotid artery during its course in the cavernous sinus is encased by the tumor. The diameter of the artery is not compromised.



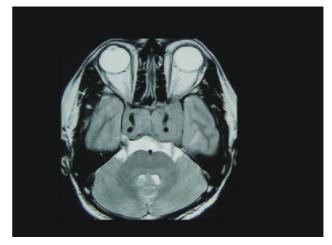
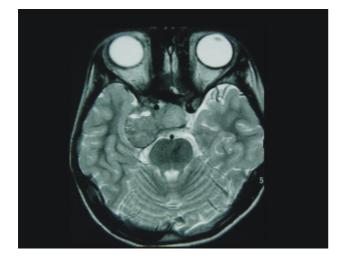


Figure 6A. T2-weighted MR image showing Grade II pituitary tumor with bilateral cavernous sinus invasion. Both cavernous carotid arteries are encased without luminal compromise. **B.** T2-weighted axial image shows the bilateral involvement of the cavernous sinus.

Grade III pituitary tumors were those giant pituitary tumors where the roof of the cavernous sinus was elevated superiorly as shown in the figures 6 and 7. There were 59 Grade III pituitary tumors. In 45 cases there was elevation of one superior wall of cavernous sinus (Figs. 7-8) and in 14 patients both the superior walls of

the cavernous sinus were bloated up (Figs. 9 - 10). In 31 cases both the diaphragma sellae and one of the superior walls of the cavernous sinus were elevated. In 4 patients superior walls of both the cavernous sinuses and the diaphragma sellae were elevated, each elevation having its own distinct neck.



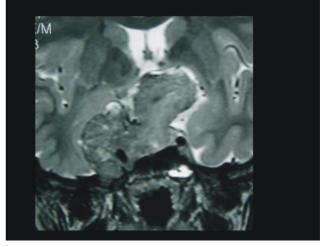


Figure 7A. T2-weighted axial and **B.** coronal MR image shows a Grade III tumor. The tumor has elevated the superior wall of the cavernous sinus unilaterally.

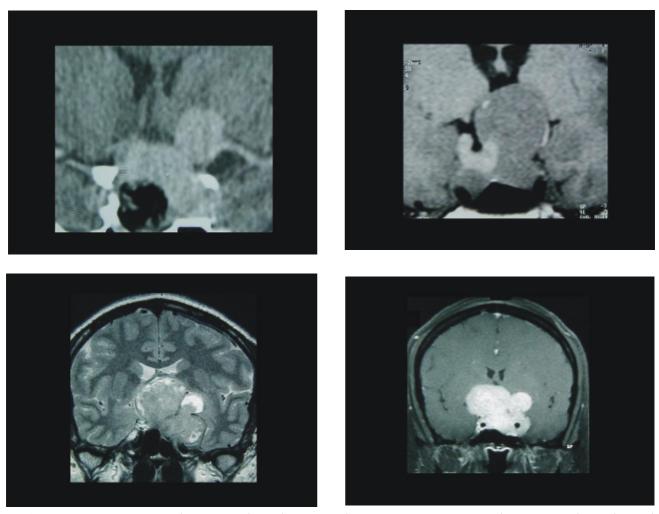


Figure 8A - D. Coronal images that show Grade III giant pituitary adenoma with unilateral cavernous sinus superior wall elevation and encasement of carotid artery.

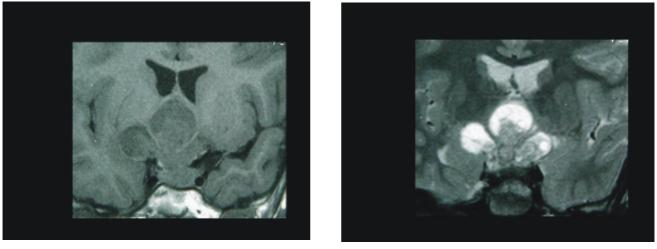
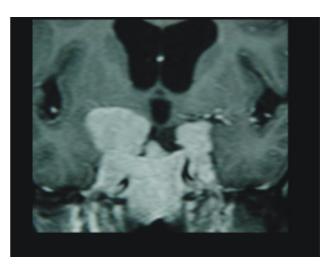


Figure 9A. Coronal MR image demonstrates a Grade III giant pituitary adenoma with bilateral cavernous sinus invasion. The tumor elevates roofs of both cavernous sinuses and diaphragma sella. **B.** T2-weighted coronal image shows the trifoliate tumor.





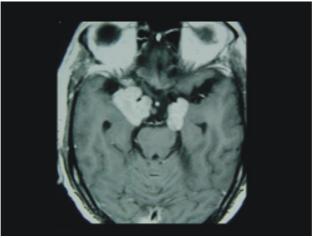
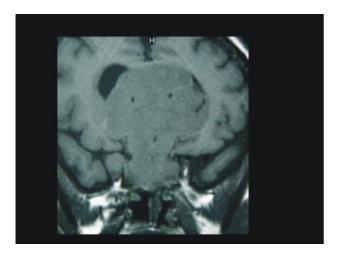
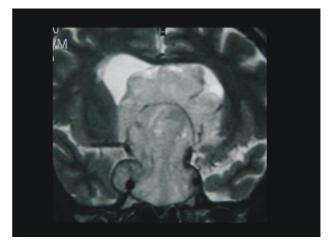
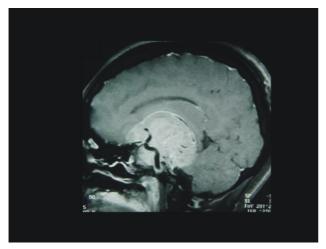


Figure 10A. Coronal CT image shows a Grade III pituitary adenoma with bilateral cavernous sinus invasion. **B.** Post-contrast coronal and **C.** Axial MR images show the tumor more vividly.

Grade IV pituitary tumors were those, which transgressed the diaphragma sella or the superior wall of the cavernous sinus boundary and entered into the subarachnoid spaces of the brain. These tumors encased the arteries of the circle of Willis. There were 22 Grade IV pituitary tumors (Fig. 12).







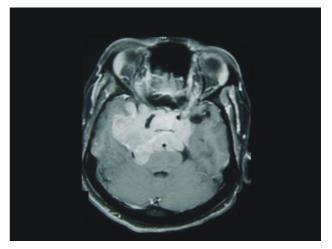


Figure 12 A-D. Grade IV pituitary adenoma. **A.** Coronal T1-weighted MR image, **B.** Coronal T2-weighted MR image and **C.** Post-contrast sagittal MR image show the encasement of anterior communicating artery complex within the tumor mass. **D.** Post-contrast axial MR image demonstrates the encasement of the basilar artery.

Transgression of the sellar dural layer and extension into the paranasal air sinuses was observed on radiology and confirmed during surgery in 18 cases, 8 of them being Grade I pituitary tumors, 7 Grade II pituitary tumors and 3 Grade III pituitary tumors.

The maximum tumor size ranged from 3 to 9 cm and the mean of the maximum tumor size was 4.5 cm. Each tumor was divided into proximal (part nearest to the sella) one third, middle one third and distal one third. One hundred and thirty-seven tumors had cysts of varying sizes. The cysts were predominantly located in the proximal third of the tumor in 18 cases, middle third of the tumor in 48 cases and in the distal third of the tumor in 71 cases. Intratumoral hemorrhage in the form of a well-defined liquefied or organized clot was seen in 64 cases.

Clinical features

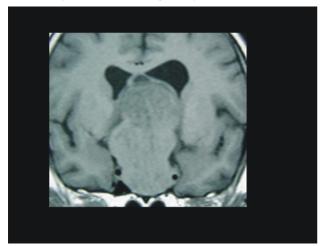
The clinical presenting features are shown in the Table 1. The mean age of the patient was 43.6 years. The youngest patient was 10 years old and the oldest was 70 years old. One hundred and twenty-eight patients were males and 197 were females. Visual worsening was the primary presenting symptom in 319 cases. Vision was affected in both eyes in 272 patients. Eighty-five patients were blind in one eye and 34 patients were blind in both eyes. Field defect was predominantly bitemporal in majority of cases. Menstrual irregularities were present in

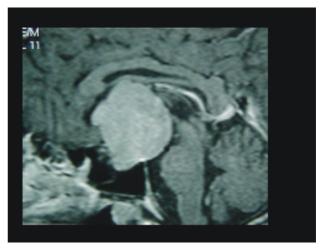
77 patients. Records of preoperative hormonal assessment were available in 210 cases. Hormonal deficiency was detected in 92 cases, of which 61 patients were hypothyroid and 37 patients had hypocortisolemia. There was mild to moderate hyperprolactinemia in 56 patients.

Surgery and outcome

Grade I pituitary tumors: Trans-sphenoidal surgery was effective and relatively safe in Grade I pituitary tumors (Figs. 2 - 4). The surgical strategy was to expose the sellar part of the tumor and debulk the tumor mass. As the tumor mass was debulked the suprasellar component progressively fell into the operative field. Valsalva maneuver was used during surgery to facilitate the descent of the tumor mass. Wherever there was difficulty in exposure of the dome of the tumor mass, additional bone in the region of the tuberculum and planum sphenoidale were removed and the dural incision was extended. The extent of tumor resection, after the initial trans-sphenoidal operation, was confirmed on postoperative imaging. Radical gross tumor excision was achieved in 97 cases and a relatively small residual tumor was left behind in 38 cases. Following surgery 96 patients improved in their vision. Two patients worsened in vision after surgery. Six patients died in the post-operative phase. Eight patients developed CSF leak, which stopped after drainage lumbar punctures. Three patients developed post-operative transient or

permanent diabetes insipidus. Radiotherapy was avoided in this group. Patients with nonsymptomatic residual lesion were observed clinically and radiologically. In the period of observation, the residual tumor grew in size in 8 cases. The lesion in two of these patients was subjected to radiation treatment and the other six patients were re-operated.





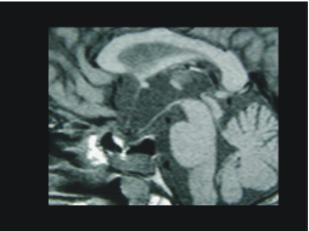
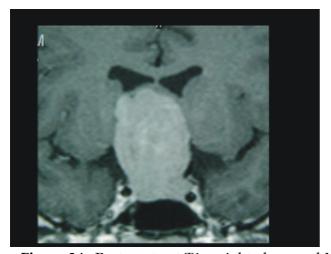


Figure 2A. T1-weighted coronal MR image and **B**. sagittal image showing a Grade I giant pituitary tumor. The tumor does not invade into the cavernous sinus. **C**. Post-operative sagittal image shows a total excision of the tumor.



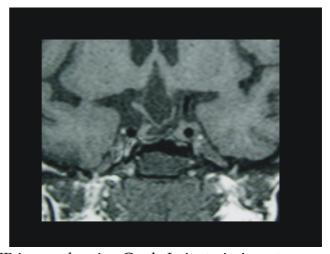
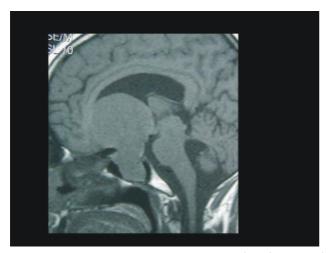


Figure 3A. Post-contrast T1-weighted coronal MR image showing Grade I giant pituitary tumor. **B.** Post-contrast post-operative T1-weighted coronal MR image showing complete excision of the tumor.



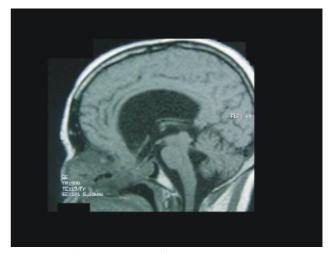
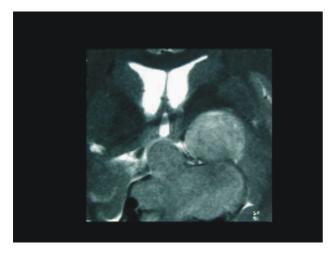


Figure 4A. Post-contrast T1-weighted sagittal MR image showing Grade I giant pituitary tumor with a sub-frontal extension. **B.** Post-contrast post-operative T1-weighted coronal MR image showing complete excision of the tumor including the sub-frontal extension.

Grade II pituitary tumors: The component of the tumor under the superiorly elevated diaphragma sellae was relatively easily and safely resected by the trans-sphenoidal route. An attempt was made in the later cases of the series to resect the part of the tumor invading into the cavernous sinus by changing the direction of the vision through the microscope. However, post-operative imaging showed that residual tumor in the cavernous sinus was left behind in majority of cases. Complete resection of the part of the tumor in the cavernous sinus was done in 8 cases. Sixty-one patients improved in vision after surgery. One patient died in the post-operative phase. One patient developed hemiplegia after surgery and had progressive but incomplete recovery at 19 months followup. One patient reportedly died at home after 2 months of surgery. Exact details of the events leading to death were not available. Radiation therapy was given in cases where the residual tumor in the cavernous sinus was relatively large and/or there were visual symptoms and symptoms related to the cranial nerves coursing through the cavernous sinus. In this group, 34 patients received radiation therapy following surgery. In 16 cases the tumor size reduced on radiation therapy while there was no change in the tumor size in 18 cases. In two of these patients there was improvement in the vision and in diplopia after radiotherapy.

Grade III pituitary tumors: Transsphenoidal

route was effective for Grade III tumors. It was observed that cases with expansion of the superior wall of the cavernous sinus had a relatively narrow neck at the level of the roof of the cavernous sinus. This feature and the angle necessary to access the extensions made resection of the supra-cavernous sinus extensions of the tumor mass relatively difficult. Complete or radical resection of the extension of the tumor in relationship to the superior wall of the cavernous sinus was possible in three cases (Fig. 11). A transcranial route was employed for re-exploration whenever the intracranial cavernous sinus extensions were large or the lesion was symptomatic. A transcranial route following the initial transsphenoidal surgery was employed in six cases. In two patients the relationship of the tumor to the third cranial nerve could be identified during surgery; it was seen that the third cranial nerve was displaced medial to the elevation of the superior wall. Cases with significant residual but clinically asymptomatic tumor were subjected to radiation treatment. Post-surgery tumor irradiation was carried out in 42 cases. There was radiologically demonstrated reduction in the tumor size in 14 cases, whilst in the rest of the cases there was no appreciable change in tumor size. During the period of follow-up four tumors grew in size. All the four patients had received radiation treatment. One of these cases was re-operated.



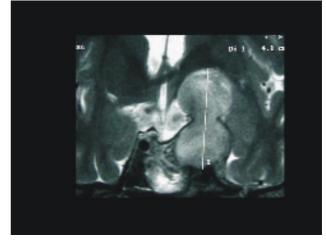


Figure 11A. T2-weighted coronal image shows a Grade III pituitary tumor with unilateral cavernous sinus invasion. **B.** Post-operative T2-weighted coronal image shows complete excision of the midline tumor. Residual tumor is noted in the cavernous sinus.

Grade IV pituitary tumors: In two cases a radical surgical resection was attempted. Both these patients died in the immediate postoperative phase. Subsequent to this experience, a biopsy followed by radiation therapy was used in rest of these cases. During the period of follow-up four patients died. Three patients were lost to follow-up. Growth of the tumor size was observed in two patients. One of these patients was readmitted on multiple occasions with complaints of generalized and uncontrolled convulsions.

The follow-up in the entire series ranged from 3 months to 11 years (average being thirty-six months). The visual outcome at an interval of 3 months after surgery are presented in Table 2.

All tumors were confirmed on histological examination to be pituitary adenomas. There was no evidence of malignancy in any case.

Discussion

Various classifications of pituitary tumors have been proposed on the basis of size, radiographic appearance, cytogenesis, staining properties, and endocrine function. There is no consensus regarding the terminology to be used in describing large pituitary tumors (9). They have been described as invasive adenoma (30), malignant adenoma (3) and carcinoma (7). Hardy classified pituitary tumors on the basis of their biological behavior (16). Some authors refer to pituitary tumors with size in excess of

40 mm, or those extending less than 6 mm from the foramen of Monro as 'giant' irrespective of their invasiveness (8). Jefferson observed an incidence of giant pituitary tumors in about 6% of all cases (19). The histological characters of giant pituitary tumors do not usually correlate well with the gross features and generally comprise of benign cells (22,26,28,39,44,49).

In the present report those pituitary tumors, which measured more than 30 mm in maximum diameter have been labeled as being 'giant' (8,13,14,24,42,43,44). These tumors constituted 13.7 % of the total number of pituitary tumors seen during the period. The relatively larger percentage of giant pituitary tumors in our series could be related to ignorance of early symptoms due to high rate of illiteracy and poverty and difficulty in availability of specialized medical help in our country. The extent of the radicality of tumor resection increased and the clinical outcome improved with more experience in all varieties of giant pituitary tumors.

Giant non-functioning pituitary tumors are frequently soft in consistency, are slow growing and therefore considering the massive size they have relatively innocuous presenting symptoms. The general growth pattern of pituitary tumor is that after the origin from the pituitary gland the tumor grows in size and expands within the confines of the sella, which is enlarged and ballooned (24,29,33). The diaphragma sellae is elevated superiorly as the tumor grows in size.

There were 135 Grade I pituitary tumors in

this series. This group of tumors was confined inferiorly to the sellar dura, was underneath the elevated diaphragma sellae and

laterally was bordered by an intact medial wall of the cavernous sinus. Diaphragma sellae was markedly thinned out at places and frequently formed big or small daughter balloons. The rounded superior wall of the tumor was suggestive of the fact that the diaphragma sellae was intact. The presence of an intact diaphragma sella was confirmed during surgery and this feature had surgical relevance as it formed an important protective barrier and such tumors could be resected radically through a relatively small exposure by a transsphenoidal route (13,15,17,33,36,38,48). Gross tumor resection was achieved 72 % in our series. 71% patients improved in their symptoms following surgery.

Grade II variety of the giant pituitary tumors was where the tumors crossed the boundary formed by the sellar dura and by the medial wall of the cavernous sinus (1,5,13,35). Cavernous sinus invasion could be confirmed on MR imaging if the tumor extended on both sides of the carotid artery. Carotid artery encasement as a true indicator of cavernous sinus invasion has also been referred to in other papers on this subject (10,20,41,43). When the artery is displaced, the entire cavernous sinus (including the medial wall) is usually displaced laterally as Although bulged out laterally, transgression of the lateral dural wall of the cavernous sinus was not observed, suggesting the relative firmness and the resistance offered by the lateral dural wall of the cavernous sinus (10). In cavernous sinus, the tumor encases the internal carotid artery but the diameter of the artery is seldom compromised and was not encountered in our series. Despite the invasion of the cavernous sinus, symptoms related to involvement of cranial nerves coursing through the cavernous sinus are a relatively rare feature. Majority of the patients where there were symptoms of involvement of cranial nerves in the cavernous sinus, the clinical course was acute in nature. Cavernous sinus invasion was observed even in some small or moderately large pituitary tumors. The ease of invasion of the pituitary tumor into the cavernous sinus and

transgression of its medial dural wall suggests that this wall of the cavernous sinus may not actually be dural in nature (38). Various authors have considered cavernous sinus as an extradural structure and this observation could lend support to this concept. However, it was observed in the present series and those reported by us earlier (11,13) that the tumor never actually elevated the entire cavernous sinus (1,5) or elevated the middle fossa or temporal dural layer superiorly or extended into the extradural compartment. This suggests that the medial wall of cavernous sinus actually allows the tumor to enter into the 'compartment' of cavernous sinus and not in the 'extradural' space.

Complete resection of the part of the tumor in the cavernous sinus was possible in 11% cases. Resection of the tumor in the cavernous sinus will necessarily require a wide exposure of the entire cavernous sinus and subject the cranial nerves to a risk of functional compromise. For resection of the part in the cavernous sinus, medial route through an extension of transsphenoidal route was seen to be most appropriate. However, extensions lateral to the carotid artery was difficult to resect as it necessitated displacement of the internal carotid artery. From our anatomical and operative experience, manipulation of the anterior and medial loop of the artery was difficult as this portion of the artery was relatively firmly positioned and mobilization of the artery, particularly without local control was a formidable surgical task. Mobilization of the artery also subjected the sixth cranial nerve to risk of injury. For patients having hormonally 'active' pituitary tumors where resection of the intracavernous sinus portion of the tumor was necessary to cure the hormonal dysfunction, a radical resection was attempted by the transsphenoidal route. In selected patients a lateral extradural approach as described by Dolenc was used (4). However, these cases are not discussed in the present report.

Extension of the tumor into the sphenoid or other paranasal air sinus by transgressing the sellar dura was a relatively infrequent feature despite the massive tumor sizes seen in the series. In a large proportion of cases the sellar dura remained intact despite the massive ballooning of the sella. We observed that a thinned out sellar bone was also preserved in most of these cases.

'Weakness' of the superior wall of the cavernous sinus and its elevation as a result of the presence of intracavernous sinus tumor has been described earlier (21). We observed that a significant number of giant pituitary tumors, which invaded into the cavernous sinus, elevated the superior dural wall of the cavernous sinus. Such tumors, which selectively elevated the roof of the cavernous sinus, were labeled as Grade III pituitary tumors. On review of the cases in the previous series reported by us (11,13), and analysis of radiology of cases reported in literature, we observed that a significant number of cases labeled to have an 'intracranial sub-arachnoid extension' could actually be Grade III pituitary tumors. In all cases the superior dural wall of the cavernous sinus covered the dome of the tumor mass. It was observed that majority of cases where the superior wall of the cavernous sinus was bloated up, the area of the superior wall involved was relatively small, and it gave an appearance of a balloon with the base towards the roof of the cavernous sinus. This suggested that a part of the superior wall of the cavernous sinus was thinner than the rest of the wall and could not resist the pressure (21). The superior wall of the cavernous sinus matched in the elasticity but was significantly thinner than the diaphragma sellae. Trans-sphenoidal surgery was used to resect majority of these tumors. An attempt was made to remove the portion of the tumor extending into the cavernous sinus and along its superior wall. However, radical resection of the part of the tumor along the superior wall of cavernous sinus was possible in only 3 cases due to difficulty in adequate exposure of the tumor mass and the narrowness of the dural neck at the level of the roof of the cavernous sinus Transcranial surgery was employed where the intracranial extension was large or was symptomatic.

It was observed that either of the diaphragma sellae or the dura of the roof of the cavernous sinus continued to cover the intracranial extension of the giant pituitary tumors in majority of cases. This was also supported by

the fact that the evidence of cerebral parenchymal edema was a rare feature despite the massive size of the tumor. The giant pituitary tumors, which transgressed the diaphragma sellae boundary and encased the arteries of the circle of Willis, were included in Grade IV. In these cases it appeared that the tumor extended into the subarachnoid space of the brain and encased arteries and perforators. The exact site of dural dehiscence could not be confirmed. Invasiveness of such tumors matches an epidermoid tumor, wherein it spreads into the available spaces, engulfs or encircles the blood vessels and cranial nerves without actually invading these structures, rarely compromising the lumen of the artery and resulting in only moderate displacements. In two cases a radical surgical resection was attempted. However, resection was incomplete in both these cases, and both suffered post-operative hemorrhage in the region and subsequently died. Considering this experience, in all subsequent cases in this group, surgery was aimed at only a biopsy, as it was observed that radical tumor resection in this group was difficult and dissection between the perforators could lead to their compromise.

On histological examination of the material, there was no evidence of malignancy in any case. There was no significant histological difference between the different grades of the giant pituitary adenomas. Immunohistochemical analysis of the tumors was not carried out in our series. Yokoyama et al report no statistical difference between tumors encasing cavernous carotid artery and those, which did not, in terms of Ki-6, cathepsin metalloproteinase-9 and matrix immunostaining (51). On the other hand, some authors have found that pituitary adenomas invading into the cavernous sinus expressed a high Ki-67 labeling index, a high DNA index, and a high percentage of cells in S-phase (23,31,32,45).

There was a suggestion of recent or old hemorrhage within the confines of the 20% giant tumors. In 42% tumors presence of a single or multiple cysts was observed. The presence of cyst was more frequently encountered in the distal third, part remote from the sella. The

presence of cyst in the distal aspect of the tumor suggests that this part could be more remote from vascular supply and necrosis and cystic degeneration was more likely to occur in this location. In giant tumors, majority of the frontal, temporal or retrosellar extensions contained a cyst. This could suggest necrosis of part of the tumor probably due to the constriction of the tumor at the level of the roof of the cavernous sinus.

The clinical course and surgical outcome in cases with giant pituitary adenomas have generally been reported to be (11,12,17,24,33,37). A transsphenoidal route was used for surgery in majority of giant pituitary tumors (13). This approach was in variance with our previously published series where a transcranial route was used for such cases (11). We feel that the understanding of the dural coverings of these tumors and more experience with transsphenoidal surgical route were factors responsible for the change in the surgical strategy. In most of the reported cases of giant pituitary adenomas, either a transcranial route or a combined transsphenoidal and transcranial routes have been employed (2,6,11,13,17,33,40,48). Reports of high surgical mortality have been attributed to a breach of sub-arachnoid spaces and ischemia within the hypothalamus, brainstem or cerebral hemisphere caused by small and large vessel traction (12,17,24). A subtotal resection can lead to infarction and edema of the residual tumor, a phenomenon reported by us earlier as 'postoperative pituitary apoplexy' (12). Such a tumor swelling can cause compression of adjacent vital neural structures or acute obstructive hydrocephalus.

In our present series, the indication of radiation therapy was different for the four grades of giant pituitary tumors (8,13,50). Due to the relative ease of surgical resection of the tumor in Grade I cases, the radiotherapy was generally avoided and re-exploration of the tumor was preferred in cases with large or symptomatic residual or recurrent tumors. Cases with relatively small and asymptomatic residual tumor were clinically and radiologically observed. Radiotherapy has been proven to be effective in long-term control of non-functioning pituitary adenomas. Modern high precision techniques like stereotactic conformal methods have the potential to minimize radiotherapy induced morbidity (8,13,50). In Grade II and III cases, radiotherapy was given to the patient whenever the residue in the cavernous sinus was significant in size or was symptomatic. Reexploration for resection of the part of the tumor within the cavernous sinus was avoided. Grade IV patients were subjected to radiation treatment. In all, 29% patients received radiation treatment. It was observed that although radiation treatment was effective in stalling the progress of tumor growth in a large majority of patients.

Our current opinion is that radiation treatment is mandatory for tumors larger than 5 cm, tumors having hemorrhage and/or multiple cysts and where there is a residual tumor following surgery.

The growth rate, growth potential, pattern of clinical course and management issues of giant pituitary adenomas have not yet been clearly elucidated in the literature and will have to be analyzed on the basis of larger series with longer follow-up period. Understanding of the anatomical subtleties and an aggressive surgical resection can lead to a satisfactory clinical outcome. Giant pituitary tumors usually have a meningeal cover and extend into well-defined anatomical pathways

Table 2. Visual outcome-3 months after surgery

Visual status	Grade I	Grade II	Grade III	Grade IV
Improvement	96	61	21	-
Same	29	20	15	9
Deteriorated	2	15	11	11

Table 1. Clinical presentation

Clinical features	Grade I (135)	Grade II (109)	Grade III (59)	Grade IV (22)
Headaches	113	85	49	22
Diminution of vision	135	104	58	22
Hypothalamic affection	21	23	5	22
Hormonal deficiences	41	23	28	-
Hemiparesis	-	1	3	-
Epistaxis	-	-	3	-
Seizures	-	-	-	1
Cranial nerves affection				
Third nerve	4	10	5	-
Sixth nerve	4	10	5	-
Fifth nerve	-	11	5	-

References

- Ahmadi J, North CM, Segall HD, Zee CS, Weiss MH (1985) Cavernous sinus invasion by pituitary adenomas. AJNR 6:893-898
- 2. Alleyne CH Jr, Barrow DL, Oyesiku NM (2002) Combined transsphenoidal and pterional craniotomy approach to giant pituitary tumors. Surg Neurol 50:380-390
- 3. Bailey OT, Cutler EC (1940) Malignant adenomas of the chromophobe cells of the pituitary body. Arch Pathol 29:368-399
- 4. Dolenc VV (1997) Transcranial epidural approach to pituitary tumors extending beyond the sella. Neurosurgery 41:542-550
- 5. Fahlbusch R, Buchfeler M (1988) Transphenoidal surgery of parasellar pituitary adenomas. Acta Neurochir (Wien) 92:93-99
- Fahlbusch R, Ganslandt O, Buchfelder M, Schott W, Nimsky C (2001) Intraoperative magnetic resonance imaging during transsphenoidal surgery. J Neurosurg 95:381-390
- 7. Feiring EH, Davidoff LM, Zimmerman HM (1953) Pituitary carcinoma of the pituitary. Neuropathol Exp Neurol 12:205-223
- 8. Fisher BJ, Gasper LE, Noone B (1993) Giant pituitary adenomas: role of radiotherapy. Int J Radiat Oncol Biol Phys 15:677-681
- Garibi J, Pomposo I, Villar G, Gaztambide S (2002) Giant pituitary adenomas: clinical characteristics and surgical results. Br J Neurosurg 16:133-139

- Goel A (1998) Meningeal architecture of the cavernous sinus: Clinical and Surgical implications. Neurosurgery 42:430-431
- 11. Goel A, Nadkarni T (1996) Surgical management of Giant Pituitary Tumors - A Review of 30 cases. Acta Neurochir (Wien) 138:1042-1049
- 12. Goel A, Deogaonkar M, Desai K (1995) Fatal postoperative pituitary apoplexy: its case and management. Br J Neurosurg 9:37-40
- 13. Goel A, Nadkarni T, Desai K, Muzumdar D, Phalke U, Sharma P (2004) Giant Pituitary tumors: A study based on surgical treatment of 118 cases. Surgical Neurology 61:436-46
- 14. Grote E (1982) Characteristics of giant pituitary adenomas. Acta neurochir (Wien) 60:141-153
- 15. Hardy J (1978) Transsphenoidal hypophysectomy. Neurosurgical techniques. J Neurosurg 48:13-22
- 16. Hardy J (1979) Transphenoidal microsurgical treatment of pituitary tumors. In: Linfoot JA, (ed) Recent advances in the diagnosis and treatment of pituitary tumors. Raven, New York, pp 375-388
- 17. Hashimoto N, Handa H, Yamashita J, Yamagami T (1986) Long term follow up of large or invasive pituitary adenomas. Surg Neurol 25:49-54,1986
- 18. Hashimoto N, Kikuchi H (1990) Transsphenoidal approach to infrasellar tumors involving the cavernous sinus. J Neurosurg 73:513-517
- Jefferson G (1940) Extrasellar extensions of pituitary adenomas. Proc R Soc Med 33:433-458

- Kaufman B, Kaufman BA, Arafah BUM, Rossemann U, Selman WR (1987) Large pituitary gland adenomas evaluated with magnetic resonance imaging. Neurosurgery 21:540-546
- Kawase T, van Loveren H, Keller JT, Tew JM (1996) Meningeal architecture of the cavernous sinus: Clinical and Surgical Implications. Neurosurgery 39:527-536
- Kernohan JW, Sayre GP (1956) Tumors of the pituitary gland and infundibulum. In: Atlas of tumor pathology. Sect X., Fasc 36. Armed Forces Institute of Pathology, Washington, DC, 81
- 23. Knosp E, Kitz K, Steiner E, Matula C (1991) Pituitary adenomas with parasellar invasion. Acta Neurochir (Wien) 53:65-71
- Krisht AF (1999) Giant invasive pituitary adenomas.
 In: Krisht AF, Tingdall GT (eds) Pituitary Disorders
 Comprehensive Management. Lippincott, Baltimore, pp 287-294
- 25. Krisht AF (1999) Giant invasive pituitary adenomas: management plan. Contemp Neurosurg 21:1-6
- Landolt AM, Wilson CB (1982) Tumors of the sella and parasellar area in adults. In: Youmans JR (ed) Neurological surgery. Saunders, Philadelphia, pp 3107-3162
- Lawson LJ (1958) Intranasal chromophobe adenocarcinoma. Report of a case. Arch Otolaryngol (Chicago) 68:704-709
- 28. Lundberg PO, Drettner B, Hemmingsson A, Stenkvist B, Wide L (1977) The invasive pituitary adenoma. A prolactin producing tumour. Arch Neurol 34:742-749
- 29. Majos C, Coll S, Aguilera C, Acebes JJ, Pons LC (1998) Imaging of giant pituitary adenomas. Neuroradiology 40:651-655
- 30. Martins AN, Hayes GJ, Kempe LG (1965) Invasive pituitary adenomas. J Neurosurg 22:268-276
- 31. Mastronardi L, Guiducci A, Buttari FM, Cristallini EG, Puzilli F, Maira G (2001) Relationships among DNA Index, S-Phase, and invasive behavior in anterior pituitary adenomas: A cytometric study of 61 cases with Feulgen-positive DNA analysis. Surg Neurol 56:27-32
- 32. Mastronardi L, Guiducci A, Spera C, Puzilli F, Liberati F, Maira G (1999) Ki-67 labelling index and invasiveness among anterior pituitary adenomas: Analysis of 103 cases using the MIB-1 monoclonal anyibody. J Clin Pathol 52:107-111
- 33. Mohr G, Hardy J, Comtois R, Beauregard H (1990) Surgical management of giant pituitary adenomas. Can J Neurol Sci 17:62-66
- Newton TH, Burhenne HJ, Palubinskas AJ (1962) Primary carcinoma of the pituitary. Am J Roentgenol 87:110-120
- 35. Nichols DA, Laws ER, Houser OW, Abboud CF (1988) Comparison of MRI and computed tomography in the preoperative evaluation of

- pituitary adenomas. Neurosurgry 22:380-385
- Oruckaptan HH, Senmevsim O, Ozcan OE, Ozgen T (2000) Pituitary adenomas: results of 684 surgically treated patients and review of the literature. Surg Neurol 53:211-219
- 37. Pia HW, Grote E, Hilderbrandt G (1985) Giant pituitary adenomas. Neurosurg Rev 8:207-220
- 38. Post KD, Biller BJ, Adelman LS, Molitch ME, Wolpert SM, Reichlin S (1979) Selective transsphenoidal adenomectomy in women with galactorrhea-amenorrhea. JAMA 242:158-162
- 39. Russel DS, Rubenstein LJ (1977) Tumors of adenohypophysis. In: Pathology of tumors of the nervous system, 4th ed. Williams and Wilkins, Baltimore, pp 312-323
- 40. Sandeman D, Moufid A (1998) Interactive imageguide pituitary surgery. Neurochirurgie 44:331-338
- 41. Scotti G, Yu CY, Dillon WP, Norman D, Newton TH, DeGroot J, Wilson CB (1988) MR imaging of cavernous sinus involvement by pituitary adenomas. AJNR 9:657-664
- 42. Shrivastava RK, Arginteanu MS, King WA, Post KD (2002) Giant prolactinomas: clinical management and long-term follow up. J Neurosurg 97:299-306
- 43. Steiner E, Imhof H, Knosp E (1989) Gd- DTPA enhanced high resolution MR imaging of pituitary adenomas. Radiographics 4:587-598
- 44. Symon L, Jakubowski J, Kendall B (1979) Surgical treatment of giant pituitary adenomas. J Neurol Neurosurg Psychiatry 42:973-982
- 45. Thapar K, Kovacs K, Scheithauer BW, Stefaneanu L, Horvarth E, Pernicone PJ, Murray D, Laws ER Jr (1996) Proliferative activity and invasiveness among pituitary adenomas and carcinomas: An analysis using MIB-1 antibody. Neurosurgery 38:99-107
- 46. Terry RD, Hayams VJ, Davidoff LM (1959) Combine non-metastasizing fibrosarcoma and chromophobe tumor of the pituitary. Cancer 12:791-798
- 47. Wilson CB (1979). Neurosurgical management of large and invasive pituitary tumors. In: Tindall GT, Collins WF (eds) Clinical management of pituitary disorders, Raven, New York, pp 335-342
- 48. Wilson CB (1984) A decade of pituitary microsurgery.
 The Herbert Olivecrona lecture. J Neurosurg 61:814-833
- 49. Wise BL, Brown HA, Naffziger HC, Boldrey EB (1955) Pituitary adenomas, carcinomas, and craniopharyngiomas. Surg Gynec Obstet 101:185-193
- 50. Yildiz F, Zorlu F, Erbas T, Atahan L (1999) Radiotherapy in the management of giant pituitary adenomas. Radiother Oncol 52:233-237
- 51. Yokoyama S, Hirano H, Moroki K, Goto M, Imamura S, Kuratsu JI (2001) Are nonfunctioning pituitary adenomas extending into the cavernous sinus aggressive and/or invasive? Neurosurgery 49:857-863