TRANSSPHENOIDAL MICROSURGERY FOR PITUITARY ADENOMAS

K H Ho

Department of Neurosurgery I
Tan Tock Seng Hospital
Moulmein Road
Singapore 1130

K H Ho, MBBS, FRACS
Sr Registrar

SYNOPSIS

The transsphenoidal approach to the pituitary fossa has become the most commonly used approach in the surgical femoval of pituitary tumours in many neurosurgical centres. The author reviews the results of transsphenoidal pituitary microsurgery in 19 patients over a 36-month period. There was no operative mortality and very low morbidity. Excellent visualization of the contents of the pituitary fossa resulted in preservation of pitultary function in all patients who did not have panhypopituitarism prior to surgery. Total macroscopic resection was achieved in all but 2 patients. Normalization of growth hormone levels was achieved in 6 out of 8 acromegalics. Both patients with Cushing's disease had normal ACTH following surgery. Vision improved in 4 of the 5 who had preoperative visual dysfunction.

INTRODUCTION

The rhinoseptal transsphenoidal approach to the pituitary fossa used in modern neurosurgical practice is a modification of the method first employed by Harvey Cushing in 1910. However in the late 1920's, he abandoned the approach in favour of the transcranial route, probably because of the greater risks of infection and subsequent meningitis, and the poorer visibility and therefore difficult haemostasis associated with the former (1). With the introduction of the operating microscope and the image intensifier in the early 1970's, the transsphenoidal route became popular again.

The first transsphenoidal removal of a pituitary tumour in the Department of Neurosurgery, Tan Tock Seng Hospital was performed by Dr C F Tham and the author in August 1983. Since then, 18 more cases have been performed in this Unit: 15 by the author and 3 by Dr P L Ong. This paper presents the clinical characteristics and results of surgery on these 19 patients.

MATERIALS AND METHODS

19 patients of Unit I, Department of Neurosurgery, Tan Tock Seng Hospital underwent transsphenoidal microsurgery for pituitary adenomas between August, 1983 and July, 1986.

With the exception of a patient who had emergency surgery for pituitary apoplexy, all other patients underwent preoperative assessment of pituitary function, including at least assay of serum cortisol, T4, and prolactin levels. All patients with acromegaly also had growth hormone levels measured during glucose tolerance test. Gonadotropin levels were measured in some patients.

The size of the tumours were estimated from the CT scans. They were classified according to their size and biologic characteristics into microadenomas, diffuse adenomas and invasive adenomas, using the classification proposed by Laws (2). Microadenomas are those intrasellar lesions 100 mm or less in diameter. Diffuse adenomas are those that essentially fill the sella but remain enclosed by the dura mater — they may have suprasellar extension. Invasive adenomas are those that invade the dura mater, bone, or both. This is determined either at surgery or by demonstration of microscopic invasion of the dura.

All patients were treated wtih preoperative dexamethasone and prophylactic antibiotics. Thyroxine was not given if the patient had normal preoperative thyroid function.

The transseptal transsphenoidal approach described by Laws and Kern is used in the majority of cases (3). The operation is carried out under general anaesthesia with the patient supine and the left ear cocked towards the left shoulder. A right-sided intranasal hemitransfixion incision is made along the caudal septal skin. The nasal mucosa is then dissected off te left side of the septal cartilage. When the bony cartilage is reached, the mucosa is stripped on both sides until the rostrum of the sphenoid body is reached. The bony septum is removed but the cartilagenous septum is left attached to the right septal mucosa. Dissection is next extended to the premaxilla and from there, the nasal mucosa is dissected off the nasal floor. A sublabial incision is now made and a Hardy nasal speculum is inserted into the septal space to straddle the anterior nasal spine and the crest of the premaxilla. The position of the speculum is checked using the image-intensifier and the operating microscope is moved into position. The sphenoid sinus is then opened and entered. The bony floor of the pituitary fossa is resected and the dura excised. The tumour is removed as completely as possible with preservation of the compressed pituitary gland. The pituitary fossa is packed with subcutaneous fat taken from the patient's abdomen and the speculum removed. The mucosal incisions and any lacerations are closed with absorbable suture material. The nasal septum is sutured back to the anterior nasal spine, supported with nasal stents and the nasal cavities packed.

The patient's vital signs, water balance and vision are monitored closely following the operation. If the pre-operative plasma cortisol is normal, dexamethasone is tapered off rapidly over the next 3 or 4 days. Plasma cortisol is measured on the 7th postoperative day and the patient is restarted on oral replacement therapy till the result of the test is known. Thyroid and gonadal functions are assessed during outpatient follow-up. Basal growth hormone levels are measured in acromegalics.

1 patient, a foreigner who left the country, was lost to follow-up. The remaining 18 patients were followed up for 3 to 36 months, with a mean of 16 months.

RESULTS

Age and Sex

Table 1 shows the patient distribution by sex and age. There were 11 males and 8 females with a mean age of 40 years (range, 20 to 68), at the time of surgery.

Clinical Features

12 of the patients had hypersecreting adenomas: 8 patients had acromegaly, 2 had prolactinomas, and 2 with Cushing's disease. The remaining 7 patients had non-secretory adenomas (Table 5). The multiple endocrine neoplasia syndrome, type I was not seen in any patient.

TABLE 1: DISTRIBUTION BY AGE AND SEX

Age (years)	20—29		30—39		40—49		50—59		60—69		All age groups	
Sex	M	F	M	F	M	F	M	F	M	F	M	F
Number of patients	2	3	4	2	1	2	2	0	2	1	13	6
Total	5		6		3		2		3		19	

The patients' symptoms at the time of presentation are shown in Table 2. Although headache was the chief complaint in only 4 patients, a total of 8 patients had headache when they sought medical attention. 4 of these had acromegaly.

Results of surgery

Total macroscopic removal of tumour was not achieved in 2 patients. Both of them had large invasive tumours that had grown into the cavernous sinuses.

TABLE 2: SYMPTOMS AT TIME OF CONSULTATION

	Patients with symptom as first complaint		All patients with symptom	
Symptom	Number	(%)	Number	(%)
Headache	4	21	8	42
Diminished vision	4	21	5	26
Infertility/amenorrhoea/ oligomenorrhoea	3	16	4	21
Cushingoid features	2	10	2	10
Acromegalic appearance	4	21	8	42
Epilepsy	1	5.5	1	5
Sleepiness	1	5.5	1	5

Of the 5 patients with impaired vision, 1 was not aware of her bitemporal hemianopia. The visual defect consisted of diminished visual acuity with bitemporal hemianopia in 4 patients and bitemporal superior quadrant defects in the remaining patient. The results of visual assessment before and after surgery are shown in Table 6.

1 patient with a non-secretory adenoma presented with the syndrome of pituitary apoplexy.

Clinical pan-hypopituitarism was not detected in any patient but the serum cortisol was low in 2 patients. 1 patient with a large non-secretory adenoma was amenorrhoeic for 8 years despite normal gonadotropin and prolactin levels. Pre-operative diabetes insipidus was present in 1 patient.

Tumour size and extent

The size of the tumour estimated from the CT scan ranged from 0.5 cm to 3.5 cm (Table 3). Although only 5 patients had visual field defects, 13 of the 19 patients had tumours with suprasellar extension.

Employing the classification proposed by Laws (2), microadenomas appeared in 4 patients, 2 of whom had Cushing's disease and the other 2 had acromegaly. 6 patients had diffuse adenomas and 9 had invasive adenomas. (Table 4)

TABLE 3: SIZE OF TUMOUR

Tumour size	Number of patients
$\leq$ 1.0 cm	4
1.1 — 2.0 cm	5
2.1 — 3.0 cm	9
$>$ 3.0 cm	1

TABLE 4: TUMOUR CLASSIFICATION

Tumour	Number of patients
Microadenoma	4
Diffuse adenoma	6
Invasive adenoma	9

Post-operative CT scans were performed on all patients with non-secretory tumours. 6 out of 7 patients showed no remnant tumour.

Basal fasting growth hormone level was lowered to 5ng/ml or less in 6 acromegalics. The remaining 2 patients had growth hormone levels lowered from 85.8ng/ml and 65.8ng/ml to 21.2ng/ml and 12.1ng/ml respectively.

Both patients with Cushing's disease had normal ACTH level following surgery, although in 1 patient ACTH could not be detected during the first 3 months following surgery.

Serum prolactin level was brought down from 119.3ng/ml to 2.7ng/ml in 1 patient with a diffuse prolactinoma. She also had resumption of menstruation after being amenorrhoeic for 3 years prior to surgery. No improvement was achieved in the other patient who had a large invasive prolactinoma.

A 46 year old patient who had not menstruated for 8 years started menstruating about 2 months after a non-secretory macroadenoma was removed. Her blood levels of prolactin and gonadotropins were normal both before and after surgery.

Table 6 shows the result of surgery in the 5 patients with impaired vision. Vision became normal in 2 patients, almost normal in 1, and improved slightly in another. The remaining patient did not show any improvement. Deterioration was not seen in any patient.

Complications

One patient developed transient disbetes insipidus, but this had resolved spontaneously by the time he was discharged from hospital on the 7th day after surgery. Another patient who had mild diabetes insipidus prior to surgery had aggravation of the condition for several weeks following surgery but eventually returned to normal.

The first patient in this series developed mild saddling of the nose as a result of excessive resection of the cartilagenous septum. However, her overall appearance was much improved because of resolution of Cushingoid features following surgery.

Vision was not made worse in any patient. Anterior pituitary function was also preserved in all patients. There was no case of cerebrospinal fluid rhinorrhoea, meningitis or hypothalamic damage.

TABLE 5: SECRETORY ACTIVITY

Secretory activity	Present series	Wilson's series (5)	Laws' series (2)
Growth hormone	8 (42%)	195 (19.5%)	173 (18%)
ACTH	2 (10.5%)	167 (16.7%)	139 (14%)
Prolactin	2 (10.5%)	410 (41%)	394 (41%)
TSH	—	2 (0.2%)	—
Non-secretory	7 (37%)	226 (22.6%)	262 (27%)
Total	19	1000	968

TABLE 6: VISION BEFORE AND AFTER SURGERY

Patient number	Eye	Visual acuity		Visual field	
		Before	After	Before	After
1	Rt	6/6	6/6	Normal	Normal
	Lt	6/24	6/6	Superior temporal quadrant defect	Near normal
2	Rt	6/36	6/9	Central scotoma	Normal
	Lt	HM (*)	6/9	Temporal hemianopia	Normal
3	Rt	CF (**)	6/9	Temporal hemianopia	Normal
	Lt	6/36	6/6		Normal
4	Rt	6/36	6/18	Temporal hemianopia	Temporal hemianopia
	Lt	6/36	6/6	Temporal hemianopia	Temporal hemianopia
5 (***)	Rt	6/9	6/9	Not done	Not done
	Lt	CF (**)	CF (**)	Not done	Not done

* HM = detects hand movements only
** CF = able to count fingers at 1 meter only
*** Pituitary apoplexy — Lost to followup 1 week after surgery because he left the country

DISCUSSION

Forty-eight operations for the removal of pituitary tumours were performed in the Department of Neurosurgery I, Tan Tock Seng Hospital between August, 1983 and July, 1986 (4). The nineteen cases In this report thus represent 40% of the patients th pituitary tumours who were treated surgically in this Unit over a 3-year period.

With the advent of radioimmunoassay for pituitary hormones, the classification of pituitary adenomas into chromophobe, basophilic and eosinophilic on the basis of light microscopy has become obsolete. The current system classifies adenomas according to the hormone(s) they secrete (2,5). The distribution of tumour type in this study is rather different from that in other large series. Table 5 compares the distribution in this series to the series of 968 cases and 1000 cases of pituitary adenoma treated by transsphenoidal microsurgery reported by Laws (2) and Wilson (5) respectively. Acromegalics constituted 42% of the cases in this study while the 2 studies had an incidence of 18% and 19.5% respectively. The author's interest in transsphenoidal microsurgery could be the reason for the difference because this condition is not known to be more common in Singapore. Gwee, et al (6) managed to study only 2 giants and 17 acromegalics over a 23-year period in the National University Department of Medicine. On the other hand, several patients with non-secretory macroadenomas underwent transcranial surgery by other surgeons. Some of these patients might have been suitable candidates for transsphenoidal microsurgery.

The percentage of patients with prolactinomas in this study is low, at 10.5%, compared to 41% in both the other two. The relatively small number of patients with prolactinomas undergoing microsurgery in this report could be due to the use of bromocryptine by endocrinologists and gynaecologists in Singapore for treatment of prolactin-secreting microadenomas. It is uncertain at this point in time whether surgical or medical treatment should be advised as the primary treatment modality. However, several neurosurgeons have found that preoperative treatment with bromocryptine for a long period of time results in interstitial fibrosis and reduces the surgical cure rate

(7,8). When recommending medical treatment for prolactin-secreting microadenomas, one also has to bear in mind the fact that the lower the initial prolactin value, the more probable is the surgical cure (5,6). Wilson discussed four indications for operative removal of prolactin-secreting microadenomas (5). In patients for whom nonoperative management is elected at the time of diagnosis, he listed 2 subsequent developments when surgery should be recommended. They are: "1) progressive elevation of PRL levels approaching 200ng/ml in an untreated patient or a progressive elevation of PRL values in a patient whose symptoms and hyperprolactinaemia were initially controlled by bromocryptine and who is still receiving the drug; and 2) enlargement of the tumour, as determined by serial CT scans."

The primary treatment of prolactin-secreting macroadenomas should be by surgery (5,7,8). Some authors recommend medical treatment for all prolactinomas based on the fact that most prolactinomas regress when treated with bromocryptine (10,11). However, this cannot be accepted because histological studies have revealed that the tumour shrinkage is due to decrease in cytoplasm and reduction in size of the tumours cells without any cytotoxic effect or evidence of increased cell necrosis (7,8,9,12). Life-long administration of a dopamine agoinst without knowing what the long-term side effects might be cannot be recommended (7).

Headache was experienced by 8 of the patients at the time of presentation, although it was the chief complaint in only 4 patients. The patient with pituitary apoplexy complained of severe headache. Of the remaining 7 patients, 4 were acromegalics. Although several authors have noted that this symptom is more common among acromegalic patients (13,14), the reason for this is not known.

Pituitary tumours may affect the patient's mentrual cycle and fertility by production of prolactin or by compression of the remaining portions of the gland or pituitary stalk, thereby interfering with the gonadtropin-releasing factor-gonadotropin-gonadal axis. The only female patient with a prolactinoma in this series first presented to a gynaecologist complaining of amenorrhoea for 3 years. With reduction of serum prolactin to normal levels, regular menstrual cycles resumed within 2 months of transsphenoidal microsurgery. The resumption of menstrual cycles in the 46-year-old patient mentioned earlier is interesting because her prolactin and gonadotropin levels were all normal prior to surgery. Compression of the pituitary stalk had probably disrupted the normal pulsatile release of gonadotropin hormone-releasing hormone by the hypothalamus (15).

Of the 5 patients with impaired vision, 4 showed improvement. 2 of these had complete restoration of visual fields and improvement of visual acuity from only being able to count fingers to 6/9. These results are similar to those of Cohen, et al (16), who found that postoperatively, visual acuity was normal or improved in 79% of the eyes, and visual fields were normal or improved in 74% of 100 patients with visual dysfunction who underwent transsphenoidal microsurgery for treatment of macroadenomas.

The author operated on 12 of the 13 patients with suprasellar extension of tumour. No difficulty was encountered in removing the suprasellar component in all but 1 patient in whom neither injection of air into the subarachnoid space nor repeated Valvsava manoeuvres succeeded in displacing the suprasellar component of the tumour into the sella. This is one of the 2 patients in whom total macroscopic excision could not be achieved. Hashimoto (17) recently described the transsphenoidal extracapsular approach for total removal of such tumours. Suprasellar extension of tumour is not a contraindication to the transsphenoidal approach (18). This approach is, however, contraindicated if there is extension of the tumour into the anterior, middle, or posterior fossae. High resolution axial and coronal CT scan with sagittal reconstruction is most useful in demonstrating the extent of tumour growth. The role of high resolution CT scanning has been reviewed by Taylor (19).

Both patients with ACTH-secreting tumours were cured. This is probably because of the small size of the tumours at the time of surgery. Among microadenomas, a high cure rate of 90% to 96% was also reported by other authors (2,5,20). It should be emphasized that a period of ACTH and cortisol deficiency is often found in patients following successful removal of the adenoma. Withdrawal from maintenance glucocorticoid therapy should be carried out carefully over a period ranging from 1 to 6 months (20,21).

The results of surgical removal of growth hormone secreting tumours is encouraging. Of the 8 patients in this series, 6 have had their basal growth hormone levels brought down to normal values (5g/ml). Recurrence has occured in some patients with normal postoperative basal growth hormone levels. Some authors have suggested that the response to provocative and suppressive stimuli should also be normal if the adenoma has been completely removed (22,23,24,25). A paper is being prepared to address this aspect in detail. In the remaining 2 patients, the levels of growth hormone were reduced to approximately 25% of that prior to surgery.

No difficulty was encountered in identifying and preserving the compressed pituitary gland during surgery. In this study, no patient who did not have panhypopituitarism before surgery was made worse after surgery. Nelson et al (26) studied the residual pituitary function following transsphenoidal resection of pituitary adenomas greater than 1 cm in diameter. Of the patients who had normal anterior pituitary function before surgery, 78% retained normal function after surgery. The risk of sacrificing remaining anterior pituitary function was found to be greater for patients with impaired preoperative function and for patients with larger tumours.

The very low morbidity and mortality associated with transsphenoidal microsurgery for pituitary adenomas has been emphasized by several authors (2,5). For example, the mortality rate of transcranial pituitary operations ranged from 1.2% to 16%, while that by transsphenoidal route ranged from 0.4% to 2% (14). As discussed earlier, no patient in this series suffered deterioration of vision or pituitary function. There was also no CSF leakage, meningitis or epilepsy. Only one patient developed transient diabetes insipidus requiring a few injections of pitressin. Permanent diabetes insipidus did not develop in any patient. The first patient in the series suffered mild nasal deformity. No patient developed nasal septal perforation or denervation of the teeth.

CONCLUSION

The characteristics of 19 patients with pituitary adenomas who underwent transsphenoidal microsurgery are presented. Normalization of elevated hormone levels in patients with hypersecreting adenomas was achieved in a percentage of patients comparable to other larger series. Visual recovery was demonstrated in 80% of patients who had preoperative visual impairment. The morbidity was very low and there was no operative mortality.

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REFERENCES

1. McDonald T J, Laws E R. Historical aspects of the management of pituitary disorders with emphasis on transsphenoidal surgery. In: Laws E R, Randall R V, Kern E B, Abboud C F. eds. Management of pituitary adenomas and related lesions with emphasis on transsphenoidal microsurgery. New York, Appleton-Century-Crofts, 1982: 1-13.
2. Laws E R. Pituitary adenomas. In: Current Therapy in Neurologic Disease. C B Decker Inc, 1985-1986: 220-5.
3. Kern E B, Laws E R. The rationale and technique of selective transsphenoidal microsurgery for the removal of pituitary tumours. In: Laws E R, Randall R V, Kern E B, Abboud C F. eds. Management of pituitary adenomas and related lesions with emphasis on transsphenoidal microsurgery. New York, Appleton-Century-Crofts, 1982: 219-44.
4. Ho K H. Unpublished data.
5. Wilson C B: A decade of pituitary microsurgery. J Neurosurg 1984; 61: 814-33.
6. Gwee H M, Chua D, Cheah J S, Lim P: Gigantism and acromegaly in Singapore. Sing Med J 1981; 22: 266-70.
7. Derome P J, Kouadri M, Kujas M, et al. Surgery of PRL and GH secretlng adenomas after long term treatment with bromocryptine. In: Lamberts S W J, Tilders F J H, et al. eds. Trends in diagnosis and treatment of pituitary adenomas. Amsterdam: Free University Press, 1984: 133-7.
8. Barrow D L, Tindall G T, Kovacs K, et al: Clinical and pathological effects of bromocryptine on prolactin-secreting and other pituitary tumours. J Neurosurg 1984; 60: 1-7.
9. Randall R V, Laws E R, Abboud C F, et al: Transsphenoidal microsurgical treatment of prolactin-producing pituitary adenomas. Mayo Clin Pro 1983; 58: 108-21.
10. Fossati P, Dewailly D, Thomas-Desrousseaux P, et al: Medical treatment of hyperprolactinaemia. Hormone Res 1985; 22: 228-38.
11. Tan S L, Morris D, Jacobs H S: The management of hyperprolactinaemia. Sing Med J 1986; 27: 190-5.
12. Landolt A M, Keller P J, Froesch E R, et al: Bromocryptine: does it jeopardise the results of later surgery for prolactinomas? Lancet 1982; ii: 657.
13. Northfield D W C. The surgery of the central nervous system. Blackwell Scientific Publications, 1973: 289.
14. Landolt A M, Wilson C B. Tumours of the sella and parasellar area in adults. In: Youmans J R. ed. Neurological surgery. W B Saunders, 1982; Vol 5: 3129.
15. Antunes J L: Neural control of reproduction. Neurosurgery 1979; 5: 63-70.
16. Cohen A L, Cooper P R, Kupersmith M J, et al: Visual recovery after transsphenoidal removal of pituitary adenomas. Neurosurgery 1985; 17: 446-52.
17. Hashimoto N, Handa H, Yamagami T: Transsphenoidal extracapsular approach to pituitary tumours. J Neurosurg 1986; 64: 16-20.
18. Hardy J: Transsphenoidal Hypophysectomy. J Neurosurg 1971; 34: 582-94.
19. Taylor S. High resolution computed tomography of the sella. In: Leeds N E. ed. The radiologic clinics of North America. W B Saunders, 1982; Vol 15 No 1: 207-36.
20. Ludecke D K, Niedworok G: Results of microsurgery in Cushing's disease and effect on hypertension. Cardiology 1985; 72 (suppl 1): 91-4.
21. Bigos S T, Soma M, Rasio E, et al: Cushing's disease: Management by transsphenoidal pituitary microsurgery. J Clin Endocrinol Metab 1980; 50: 348-54.
22. Pearson O H, Arafah A M, Brodkey J: Management of acromegaly. Ann Intern Med 1981; 95: 225-7.
23. Arafah B M, Brodkay J S, Kaufman B, et al: Transsphenoidal microsurgery in the treatment of acromegaly and gigantism. J Clin Endocrinol Metab 1980; 50: 578-85.
24. Schuster L D, Bantle J P, Oppenheimer J H, Seljeskog E L: Acromegaly: Reassessment of the long-term therapeutic effectiveness of transsphenoidal pituitary surgery. Ann Intern Med 1981; 95: 172-4.
25. Tucker H St G, Grubb S R, Wigan J W, et al: The treatment of acromegaly by transsphenoidal surgery. Arch Intern Med 1980; 140: 795-802.
26. Nelson A T, Tucker H St G, Becker D B: Residual anterior pituitary function following transsphenoidal resection of pituitary macroadenomas. J Neurosurg 1984; 61: 577-80.