MEDICAL PRACTICE

*Clinical Topics***Management of selected patients with hyperprolactinaemia by partial hypophysectomy**

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Abstract

Results are reported in 35 patients with prolactinomas who underwent pituitary surgery within the past five years. After surgery prolactin concentrations became normal in 26 patients and symptoms were alleviated, and nine normal pregnancies were achieved in seven women, including all those who had complained of infertility. Normal prolactin concentrations were restored in 16 of 17 patients with tumours 5-19 mm in diameter but in only six of 11 with tumours ≤ 4 mm and four of seven with tumours ≥ 20 mm. Normal prolactin concentrations were restored in all those with preoperative concentrations below 1000 mU/l but in none of those with concentrations above 10 000 mU/l. Although not all of the patients were followed up for five years, hyperprolactinaemia did not recur in any patient whose prolactin concentration had returned to normal six weeks after surgery. This included 16 patients with macroprolactinomas (>10 mm in diameter), who were followed up for from two to five years.

These data contrast strikingly with those reported by others at similar stages of follow up and show clearly that partial hypophysectomy offers an acceptable alternative treatment for selected patients with prolactinomas.

Introduction

Pituitary surgery has been widely practised for patients with hyperprolactinaemia due to pituitary tumours. The pioneering work of Hardy on the surgical removal of small pituitary tumours (microadenomectomy) is well known.^{1,2} Initial results were encouraging, with claims of success rates of up to 86% for the removal of small tumours and restoration of prolactin concentrations to normal.^{3,4} Despite these promising early results, however, concern about the justification for this approach has grown since Serri *et al* reported an incidence of recurrence of up to 50% for microadenomas (<10 mm diameter) and 80% for macroadenomas (≥ 10 mm diameter) five years after transsphenoidal sellotomy and selective removal of prolactinomas.¹⁰ This concern is highlighted by the availability of effective alternative treatment for such patients—namely, dopamine agonists, such as bromocriptine, or radiotherapy, or both.^{11,12}

We report the results of transethmoidal surgery in 35 patients with prolactinomas. Our results cover five years and emphasise the importance of careful endocrine assessment in the preoperative diagnosis and subsequent management of these patients. Our data are supported by detailed immunohistochemical analysis of tumour material removed at surgery.

Patients and methods

We investigated 70 patients with hyperprolactinaemia (basal prolactin concentration >420 mU/l) and a clinical diagnosis of prolactinoma over five years. Of these, 35 were treated surgically. After full investigation patients were offered surgery if they had appreciable symptoms with a history of failure to respond to, or intolerance of, dopamine agonist drugs or if they preferred surgery to the other options, including follow up without active treatment.

Of the 29 women who underwent surgery (age range 19-44), 27 complained of oligomenorrhoea, amenorrhoea, or galactorrhoea, and of these, four wanted treatment for their infertility (six were either intolerant of dopamine agonist drugs or had failed to respond to them). Of the remaining

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two women, one suffered profuse spontaneous galactorrhoea and intermittent, severe frontal headaches; the other was postmenopausal and presented with a bitemporal field defect and headaches. Five of the women suffered intermittent frontal headaches, and four complained of reduced libido. Of the six men (age range 22-68), three presented with reduced libido alone, one with reduced libido and additional evidence of hypopituitarism, one with short stature and delayed puberty, and one with severe frontal headaches associated with bitemporal heminopia. This last patient had failed to respond adequately to treatment with bromocriptine over two months, and one other man was also intolerant of bromocriptine. No other patients had received treatment with dopamine agonists during the 12 months before surgery.

Before surgery anterior pituitary function was fully assessed in each patient by measuring appropriate hormonal responses to insulin hypoglycaemia (0.1 U/kg intravenously) or metyraprone (250 mg every two hours for three days), or both, thyrotrophin releasing hormone (200 µg intravenously), luteinising hormone releasing hormone (100 µg intravenously), and domperidone (10 mg intravenously), each test being carried out separately with an appropriate interval between. Thyroid and gonadal hormone concentrations were measured using standard assay procedures. Neuroradiological investigation included lateral skull radiography and computed tomography of the hypothalamic pituitary area. Thirty patients were investigated with an EMI 1010 scanner and the five patients who had undergone surgery most recently by fourth generation computed tomography.

Prolactinoma was diagnosed preoperatively if other causes of hyperprolactinaemia were absent and there were abnormal radiological findings or an exaggerated response of thyroid stimulating hormone (incremental rise >2.1 mU/l) or a reduced response of prolactin (to <200% of basal concentrations) after dopamine receptor blockade with domperidone. We also measured the prolactin response to thyrotrophin releasing hormone, a reduced response (to <200% of basal concentrations) being compatible with a prolactinoma. Evidence supports the use of these dynamic tests in the diagnosis of microprolactinomas.¹³⁻¹⁵ While abnormal radiological findings supported the diagnosis of a pituitary adenoma, normal radiological findings were not interpreted as excluding such a diagnosis, particularly when the EMI 1010 head scanner was used for computed tomography.

SURGICAL PROCEDURE

The surgical approach to the pituitary fossa was by transethmoidal sellotomy, as described by Chiari and adapted for microsurgery by James.^{16,17} We have found that this approach allows a wider exposure of the hypophysis than the more restricted trans-septal route, and visual access is further improved by the invariable use of hypotensive anaesthesia. After removal of the ethmoid air cells the sphenoid sinus was entered and the bone removed from the floor of the sella. After removal of the bone in the floor of the fossa the dura was incised and the lateral lobes of the adenohypophysis were mobilised to allow comprehensive inspection of the surface of the gland. If the prolactinoma was not readily identifiable on the surface of the gland multiple incisions were made into the gland. Biopsy specimens of the adenoma were obtained, and if the diagnosis was confirmed by frozen sections the part of the gland containing the tumour was removed.

If the adenoma was near to the neurohypophysis the adjacent part of the neurohypophysis was excised. Similarly, the dura adjacent to the tumour was removed if possible. The space left after excision of the gland was packed with a muscle graft and the dural incision sutured. Antibiotic cover was given during the operation and for seven days postoperatively.

HISTOLOGICAL PROCEDURE

Frozen sections of biopsy specimens removed during surgery were stained with haematoxylin and eosin. An adenoma was identified by frozen section in all cases in which the diagnosis of adenoma was subsequently confirmed using paraffin sections stained by the periodic acid Schiff orange G technique and a silver impregnation technique for reticulin.

We identified cell types in the tumours with a hapten sandwich immunohistochemical technique¹⁸ using antibodies to human pituitary hormones (growth hormone, prolactin, β thyroid stimulating hormone, β follicle stimulating hormone, and β luteinising hormone) kindly supplied by the National Institute of Arthritis and Metabolic Diseases and to synthetic 1-24 kindly donated by Professor L Rees, St Bartholomew's Hospital, London.

FOLLOW UP

Patients were assessed six weeks after the operation and then yearly thereafter. At the preoperative and initial postoperative assessments the full range of pituitary function was assessed by means of insulin hypoglycaemia or metyraprone, or both, and testing with thyrotrophin releasing hormone, luteinising hormone releasing hormone, and domperidone. At subsequent visits clinical state was assessed and the responses of thyroid stimulating hormone and prolactin to administration of domperidone tested. Two patients were followed up for four to five years, four for three to four years, 13 for two to three years, 12 for one to two years, and four for less than one year (mean (SD) 2.7 (1.0) years).

Results

Adenomas were clearly identified in 33 patients, but in two cases no lesion was found and further surgery was abandoned. Altogether 13 patients had microadenomas (<10 mm) and 20 had macroadenomas (≥10 mm). Table I shows the size of the adenoma at surgery and postoperative prolactin concentrations (normal circulating prolactin concentrations in our laboratory were less than 420 mU/l). According to this criterion, the overall success rate was 74%, the poorest results being found in patients with very small (≤4 mm) or very large (≥20 mm) lesions. A very high success rate was obtained in patients with adenomas of 5-19 mm diameter (92-100%). When the data were assessed in relation to the preoperative prolactin concentrations (table II) the poorest results were seen in patients with circulating prolactin concentrations greater than 10 000 mU/l and the best in patients with concentrations below 1000 mU/l.

Of the 21 women with normal prolactin concentrations after surgery, 19 had presented with galactorrhoea, three with decreased libido, three with headache, and one with a visual field defect; these symptoms were all alleviated by surgery. All of the 20 women in this group who had complained of amenorrhoea achieved regular menses, and ovulatory cycles were restored biochemically in at least 13 of them; most importantly, nine normal pregnancies occurred in seven women, including four who had previously complained of infertility. Of the eight women who continued to have hyperprolactinaemia after surgery, six had persistent oligoamenorrhoea with galactorrhoea and anovulation. In the remaining two prolactin concentrations were restored to near normal after surgery (486 mU/l and 500 mU/l), regular menses were restored, and galactorrhoea stopped. One of these two patients became pregnant and the other took an oral contraceptive.

TABLE I—Surgical and hormonal results in relation to size of adenoma

Size of adenoma (mm)	No of patients	No (%) with normal postoperative prolactin	No with antiprolactin immunohistochemistry	No with normal postoperative response to:				
				Domperidone			Thyrotrophin releasing hormone	
				Change in TSH*	Change in prolactin*	%Change in prolactin†	Change in prolactin*	% Change in prolactin†
0-4	11	6 (55)	4	5	6	5	4	4
5-9	4	4 (100)	4	4	3	3	2	2
10-19	13	12 (92)	12	10	6	6	5	7
≥20	7	4 (57)	7	6	3	2	2	2
Totals	35	26 (74)	27	25	18	16	13	15

TSH=Thyroid stimulating hormone.

*Difference in concentrations at 0 and 30 minutes.

†Difference in concentrations at 0 and 30 minutes expressed as percentage of basal value.

In five of the men prolactin concentrations returned to normal after surgery and this was associated with symptomatic relief. In the remaining man, who had an enlarged pituitary fossa, very high prolactin concentrations (11 000 mU/l), and a bitemporal field defect, surgery resulted in a reduction in prolactin concentrations, with improvement in his hypopituitarism and field defects.

Major surgical complications were uncommon. Four patients developed mild, transient diabetes insipidus and five developed mild, transient right frontal sinusitis some weeks after surgery. One patient showed signs of meningitis in the early postoperative period that responded readily to treatment with appropriate antibiotics. In general, surgery was well tolerated by all patients.

Two women developed panhypopituitarism after surgery. Both had large tumours, and one, who was postmenopausal, had presented with bitemporal hemianopia. Both operations had been performed early in the series, and the surgeon had chosen to clear the fossa rather than attempt partial hypophysectomy. One man with multiple endocrine adenomatosis type I who also had Cushing's disease had partial adrenocorticotrophic hormone deficiency and possible thyroid stimulating hormone deficiency, for which he received replacement treatment.

In two patients no adenoma was found at surgery and there was no histological evidence of adenoma in the small amount of pituitary tissue removed. An adenoma was identified using microscopy in 28 of the 35 patients. In these 28 immunohistochemical analysis for all six pituitary hormones was carried out. Twenty five adenomas were pure prolactinomas. Two adenomas were composed predominantly of lactotrophs but contained a minority population of somatotrophs. One adenoma contained only a few cells positive for adrenocorticotrophic hormone. The man in whom this adenoma was found had multiple endocrine adenomatosis type I, Cushing's disease, and hyperprolactinaemia, and results of tests suggested a prolactinoma. A lesion 3 mm in diameter was removed, and his prolactin concentration subsequently fell to within the normal range. As there was no lactotroph hyperplasia and multiple adenomas are common in multiple endocrine adenomatosis type I we assumed that a microprolactinoma had also been present and had been cured by the surgery.

TABLE II—Surgical results in relation to preoperative prolactin concentrations

Preoperative prolactin (mU/l)	No of patients	No (%) of patients with normal postoperative prolactin
≤1000	6	6 (100)
>1000	29	20 (69)
≤2000	18	15 (83)
>2000	17	11 (65)
≤3000	24	20 (83)
>3000	11	6 (55)
≤4000	26	21 (81)
>4000	9	5 (56)
≤5000	28	23 (82)
>5000	7	3 (43)
≤6000	30	25 (83)
>6000	5	1 (20)
≤10000	31	26 (84)
>10000	4	0 (0)

In a further five cases the tissue identified by the surgeon as adenoma was either insufficient for pathological examination or damaged during surgery so that immunohistochemical analysis could not be performed. In four of these cases, however, other fragments of normal adenohypophysis were examined immunohistochemically, and no evidence of lactotroph hyperplasia was found. In the fifth case there was insufficient material for any immunohistochemical analysis. All these five patients, however, had microadenomas (<10 mm in diameter) and hormonal responses to dynamic tests suggestive of prolactinomas. These findings together with the restoration of prolactin concentrations to normal after surgery indicated that the microadenomas were probably prolactinomas. Table I gives the details of the restoration of normal responses of thyroid stimulating hormone or prolactin, or both, to domperidone and thyrotrophin releasing hormone after surgery. Patients who continued to have hyperprolactinaemia after surgery showed persistent abnormalities in one of these hormonal responses. Of the patients whose prolactin concentrations returned to normal after surgery, only four continued to have a marginally exaggerated response of thyroid stimulating hormone to domperidone; of these, one had developed primary hypothyroidism, which could account for this finding. Persistent reduction in prolactin responses to thyrotrophin releasing hormone and domperidone was much commoner after surgery. Further follow up of these patients is required, however, to assess how this pattern alters with time.

Discussion

Our findings show clearly that pituitary surgery is an acceptable alternative treatment for selected patients with prolactinomas. In accordance with the findings of other groups,^{2,5} our results in restoring normal prolactin concentrations were poor in patients with large tumours (>20 mm) or high circulating prolactin concentrations preoperatively (>10 000 mU/l), or both. In addition, our data indicate that results of surgery are equally poor in patients with small lesions. For instance, no adenoma could be identified in two patients whose history, circulating basal prolactin concentrations, and persistently abnormal responses of thyroid stimulating hormone and prolactin to dopamine antagonists strongly suggested a prolactinoma. We believe that these two patients probably harbour small intrapituitary groups of cells secreting prolactin and functioning autonomously but that the lesions were so small as to render visual identification impossible. It is important, therefore, that patients should have lesions that can be readily identified before surgery is considered, and we suggest that assessment of hormonal responses to domperidone or thyrotrophin releasing hormone, or both, and the finding of a definite lesion on fourth generation computed tomography are essential prerequisites to surgery.

Hyperprolactinaemia did not recur in any patient who had normal prolactin concentrations six weeks after surgery. This finding contrasts with those reported by some workers,^{10,19} who showed incidences of recurrence of hyperprolactinaemia of about 5% at two years, 15% at three years,¹⁰ and 18-50% at four to five years^{6,20} after microadenomectomy. In addition, Rodman *et al* reported an incidence of recurrence of 17% at 16 months after resection of microadenoma.²¹ With regard to macroadenomas (>10 mm), Serri *et al* reported an incidence of recurrence of 40% at two years and 80% at three years after surgery,¹⁰ whereas we did not find any recurrences in our group with macroadenomas (delineated by size according to Serri *et al*¹⁰) whose prolactin concentrations returned to normal after surgery (n=16). Although we did not follow up all patients for five years, 19 were followed up for two to five years, and we would have expected some recurrence by this stage were we to obtain results comparable with those previously reported.

There are two possible reasons for this discrepancy. The first relates to surgical technique. Hardy described the procedure of selective microadenomectomy, whereas we used that of partial hypophysectomy, in which a generous rim of normal tissue is excised with the adenoma. The second relates to the adequacy of endocrine documentation, a point highlighted in our series by two women whose prolactin concentrations were restored to near normal by surgery yet who, according to strictly applied criteria, continued to have slight hyperprolactinaemia and showed persistently abnormal responses of thyroid stimulating hormone and prolactin to dynamic testing. Despite this slight hyperprolactinaemia regular menses were resumed and galactorrhoea stopped and one of the patients had a normal pregnancy. Without adequate endocrine investigation such patients might have been classified as cured after surgery and might therefore have contributed to recurrence figures at follow up.

Longer term follow up is also required for the large number of patients who showed persistently abnormal responses of prolactin to domperidone and thyrotrophin releasing hormone after successful surgery. One report suggests that such dynamic responses tend to return to normal over many months,⁶ although this is not a common finding.^{22,23} In our patients restoration to normal of the response of thyroid stimulating hormone to domperidone was much commoner than restoration to normal of the response of prolactin to thyrotrophin releasing hormone or domperidone.

Surgery was well tolerated by all patients, and symptomatic improvement was extremely satisfactory in all those whose prolactin concentrations returned to normal. In particular, all those who had previously been troubled by their infertility achieved normal pregnancies postoperatively.

In conclusion, we believe that the combination of complete endocrine evaluation (supported by the identification of a lesion on fourth generation computed tomography) and partial hypophysectomy represents a satisfactory alternative treatment for some

patients with pituitary adenomas secreting prolactin. Data obtained after longer follow up are obviously required, but our early results over five years using this approach are more encouraging than those of other groups.^{6 10 19}

References

- Hardy J. Transsphenoidal microsurgery of the normal and pathological pituitary. *Clin Neurosurg* 1969;16:185-217.
- Hardy J. Le prolactinome. *Neurochirurgie* 1981;27:1-110.
- Ludecke D, Kantzy R, Saeger W. Selective removal of hypersecreting pituitary adenomas; an analysis of endocrine function, operative and microsurgical findings in 101 cases. *Acta Neurochir* 1976;35:27-42.
- McLanahan CS, Christy JH, Tindall GT. Anterior pituitary function before and after transsphenoidal microsurgical resection of pituitary tumours. *Neurosurgery* 1979;3:142-5.
- Fahlbusch R. Surgical failures in prolactinomas. In: Deroma PJ, Jedynak CP, Peillon F, eds. *Pituitary adenomas: biology, physiopathology and treatment. 2nd European workshop*. Paris: Axlepios, 1980:273-82.
- Tucker HStG, Lanaford HV, Gardner DF, Blackard WG. Persistent defect in regulation of prolactin secretion following successful pituitary tumour removal in women with galactorrhoea-amenorrhoea syndrome. *J Clin Endocrinol Metab* 1980;51:968-71.
- Llandolt AM. Surgical treatment of pituitary prolactinomas: post-operative prolactin and fertility in 70 patients. *Fertil Steril* 1981;35:620-5.
- Randall RV, Laws ER, Abbond CF, et al. Transsphenoidal microsurgical treatment of prolactin-producing pituitary adenomas. Results in 100 patients. *Mayo Clin Proc* 1983;58:108-21.
- Teasdale G. Surgical management of pituitary adenoma. In: Scanlon MF, ed. *Neuroendocrinology*. London: Saunders, 1983:789-823. (Clinics in Endocrinology and Metabolism No 12.)
- Serri O, Rasio E, Beauregard H, et al. Recurrence of hyperprolactinaemia after selective transsphenoidal adenomectomy in women with prolactinoma. *N Engl J Med* 1983;309:280-7.

- Thorner MO, McNeilly AS, Hagen C, Besser GM. Long term treatment of galactorrhoea and hypogonadism with bromocriptine. *Br Med J* 1974;iii:419-22.
- Grossman A, Besser GM. Prolactinomas. *Br Med J* 1985;290:182-4.
- Cowden EA, Thomson JA, Doyle D, Ratcliffe JG, MacPherson P, Teasdale GM. Tests of prolactin secretion in diagnosis of prolactinomas. *Lancet* 1979;ii:1155-8.
- Scanlon MF, Rodriguez-Arnan MD, Weightman D, et al. Altered dopaminergic regulation of thyrotrophin release in patients with prolactinomas: comparison with other tests of hypothalamic function. *Clin Endocrinol* 1981;14:133-43.
- Massara F, Camanni F, Martra M, Dolfin GC, Muller EE, Molinatti GM. Reciprocal pattern of the TSH and PRL responses to dopamine receptor blockade in women with physiological or pathological hyperprolactinaemia. *Clin Endocrinol* 1983;18:103-10.
- Chiari O. Über ein Modifikation der schlofferschen Operation von Tumoren der Hypophyse. *Wien Klin Wochenschr* 1912;25:5-6.
- James A. The hypophysis. *J Laryngol Otol* 1967;81:1283-307.
- Jasani B, Wynford-Thomas D, Williams ED. Use of monoclonal antihapten antibodies for immunolocalisation of tissue antigens. *J Clin Pathol* 1984;34:1000-2.
- Charpentier G, de Plunkett T, Jedymak CP, et al. Short and long term results of surgical treatment of pituitary adenomas. In: Lamberts SWJ, Tilders SJ, Van der Veen DEE, Assies J, eds. *Trends in the diagnosis and treatment of pituitary adenomas*. Amsterdam: Free University Press, 1983.
- Gordon D, Richards A, Bulloch R, et al. Prolactin dynamics and tumour size in the prediction of surgical outcome for prolactinoma. *Q J Med* 1985;54:141-51.
- Rodman EF, Molitch ME, Post KD, et al. Long-term follow-up of transsphenoidal selective adenomectomy for prolactinoma. *JAMA* 1984;252:921-4.
- Camanni F, Ghigo E, Ciccarelli E, et al. Defective regulation of prolactin secretion after successful removal of prolactinomas. *J Clin Endocrinol Metab* 1983;57:1270-6.
- Samaan NA, Elhaj GE, Leavens ME, Franklin RR. The clinical and biochemical features in 26 patients with prolactinoma before and after transsphenoidal microresection. *Acta Endocrinol* 1980;94:450-8.

(Accepted 23 July 1985)

Treatment of presumed prolactinoma by transsphenoidal operation: early and late results

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Abstract

Seventy seven patients who were presumed to have a prolactinoma on the basis of biochemical findings underwent transsphenoidal operation between October 1977 and September 1983. Sixty one patients were found to have a microadenoma, and hyperprolactinaemia was cured in 46 of these, amenorrhoea in 39 (80% of those with the symptom), galactorrhoea in 32 (80%), and infertility in 31 (82%). Four of eight patients found to have a macroadenoma were also satisfactorily treated with surgery. Two patients had a lesion other than a prolactinoma, and in six a tumour could not be found at operation; four of these last eight patients had a normal serum prolactin concentration after operation. Recurrent hyperprolactinaemia was rare, occurring in only three patients in the series overall; among the 32 patients followed up for more than five years only two of the 22 whose operation had initially been successful developed recurrent hyperprolactinaemia.

Introduction

An operation on the pituitary is now widely accepted as the best method of treating acromegaly and Cushing's disease, but the management of tumours producing prolactin remains controversial. Series reported from Britain have concentrated on radiotherapy and treatment with dopamine agonists such as bromocriptine; surgery has to some extent been neglected and sometimes misrepresented.^{1,2}

We have treated a consecutive series of 77 patients with hyperprolactinaemia by transsphenoidal operation. We have previously reported the laboratory diagnosis of prolactinoma,³ the radiological findings,⁴ the initial results of operation in the first 14 patients,⁵ the restoration of fertility and the outcome of pregnancy,⁶ and the factors affecting prognosis.⁷ This report provides an overview of the clinical and biochemical results and pays special attention to the long term outcome.

Methods

The patients included in this review each presented with amenorrhoea, galactorrhoea, or infertility. Each had a serum prolactin concentration that was persistently above normal and impaired responses to dynamic testing with thyrotrophin releasing hormone or metoclopramide.³ The serum prolactin concentration was estimated using a radioimmunoassay; the coefficient of variance of the assay was 5% within batches and 10% between batches, and our normal reference range for serum prolactin concentration was 60-360 mU/l.³

Radiological investigation evolved during the years of the study. In each patient a plain x ray film of the skull was obtained, initially coupled with tomograms of the pituitary fossa. Each patient also underwent computed tomography. Orbital phlebography was used routinely to display the venous and arterial relations of the pituitary gland.⁸ Carotid angiography and metrizamide cisternography and ventriculography⁹ were used selectively to clarify detailed anatomical abnormalities and were needed in only seven and

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