

PITUITARY ADENOMAS, EAST AND WEST

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SYNOPSIS

The clinical and radiological features, and results of treatment of two series of patients with pituitary adenomas seen over 10 years in Western Australia and Singapore are analysed. There appears to be fewer acromeglics in Singapore and the patients with non-secreting chromophobe adenomas present late with larger tumours often causing severe hydrocephalus that require preliminary shunting. In Western Australia, surgical decompression alone was usually used, initially. The overall recurrence rate was 32 per cent. Where radical surgery with magnification was used, no recurrence have yet been noted. In Singapore, decompression followed by DXT is the Norm, with a recurrence rate of 9 per cent.

INTRODUCTION

This study proposes to analyse the clinical and radiological characteristics of 2 series of verified non-secreting pituitary adenomas, one comprising of an oriental or Asian population and the other, Caucasian. Since the regimes of treatment were also different, opportunity was taken to compare the results, bearing in mind that these do not reflect differences between Asian and European neurosurgical centres in general.

CLINICAL MATERIAL AND METHOD

The total number of clinically diagnosed pituitary tumours seen and treated by the interhospital Neurosurgical Services of Western Australia from January 1963 to December 1972, and those similarly treated at the only Neurosurgical Unit in Singapore were collected and analysed according to a standardised proforma. All radiological investigations were reviewed. Visual field examination were done routinely by neurosurgeons in Singapore and by ophthalmic surgeons in Western Australia using standard Bjerrum screens and Keeler Aimark perimeters. Differentiation of the pathological cell types of the Mallory Heidenhains and Periodic Acid Schiff stains were used in both centres. Follow-up periods vary between two to nine years. Percentages are taken to the nearest whole figure.

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CASE RECORDS

There were 62 clinically diagnosed cases in Western Australia, 35 males and 27 females, all Caucasians. Twenty-two cases (or 36 per cent) showed acromegaly with operations performed in 8. Six of those were acidophilic adenomas and 2 chromophobe. Two patients presented with Cushing's syndrome, with radiological evidence of pituitary neoplasia but received no surgical intervention. One patient with Nelson's syndrome was found operatively to have a basophilic adenoma. The other 37 cases presented with non-secreting features, of which 34 were verified histologically. Thus, of 43 verified tumours, 36 or 84 per cent were chromophobes, 6 or 14 per cent were acidophils and 1 or 2 per cent was basophilic.

In the Singapore series, 26 cases, 14 males and 12 females were clinically and radiologically diagnosed. Twenty three (88 per cent) had non-secretory features and three showed acromegaly (12 per cent). Histology was obtained in 23 cases, with 22 chromophobes, and one acidophilic tumour. All the verified chromophobe adenomas were non-secretory. No basophilic tumours were seen.

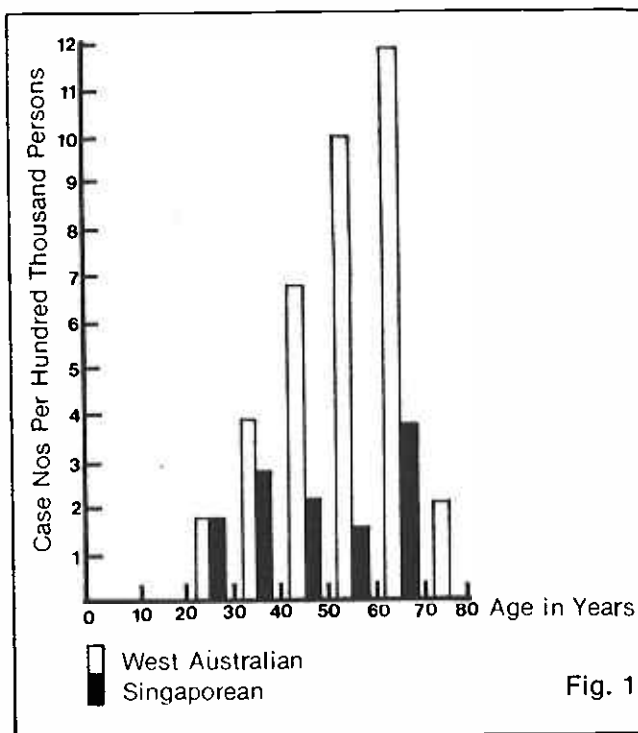
As hypersecretory tumours present their own management problems and as there was an inadequate number of such tumours seen in Singapore, the following analysis will compare only the characteristics of verified non-secreting chromophobe adenomas of each population.

RESULTS

The age incidence of the 2 series of tumours are shown on the histograms in Fig. 1, after correction for the relative population structure in each country. Before correction the Singapore patients appeared younger but this was due to the younger population structure present.

The visual characteristics (Table I) shown that all the Singapore patients suffered from severe loss of visual acuity whereas only 59 per cent of the Australian patients had visual acuity worse than 6/12 bilaterally. More Singapore patients (91 per cent) complained of visual field loss than the Australian patients (71 per cent) and more remarkably 77 per cent of the Singapore patients had more than half the temporal field loss bilaterally as against only 17 per cent of the Australian patients.

The incidence of headaches were about the same (Table II) present in less than a quarter and being localised to the frontal or temporal regions in the majority. Papilloedema was present in 14 per cent



of the Singapore cases and only 3 per cent in the Western Australian series. All these features are explained by the late presentation and larger tumours seen in the Singapore series.

Table III show similar characteristics in both series. Loss of libido was noted early and some loss of secondary sexual characteristics were seen in about half the cases. Intolerance to cold was seen less in Singapore (23 per cent) than in Western Australia (44 per cent) probably due to the tropical climate of the former. Skin changes consisting of pallor and increased softness was seen in 23 per cent and 32 per cent respectively. Signs of hypothalamic compression was marked mainly by somnolence and noted in 9 per cent and 12 per cent respectively. No incidence of preoperative diabetes insipidous was seen. Pituitary apoplexy was present in 5 cases or 15 per cent in the Western Australian series but not seen in Singapore.

The laboratory endocrine investigation were unsatisfactory in both series, being fully worked up only in the recent cases and no attempts were made to analyse these.

Comparison of plain radiographic features show that "double flooring" due to asymmetrical erosion of the floor and usually an early change was seen in 25 per cent of the Western Australian cases and 14 per cent of the Singapore series. Ballooning of the fossa was however more common in the latter series (84 per cent) compared to 56 per cent in the Western Australian series. Similarly non-specific enlargement of the fossa with destruction of the

TABLE I: Comparison of Visual Characteristics

	W. A. Series (34 cases)		Singapore Series (22 cases)	
	Nos.	%	Nos.	%
Complaint of visual blurring with visual acuity less than 6/12 both eyes	20	59%	22	100%
Visual field loss as main complaint	24	71%	20	91%
Visual field loss bilaterally more than 1/2 temporal field	4(4/24)	17%	17	77%
Visual field loss 1/2 temporal field or less	20(20/24)	83%	6	23%

*These are percentages of 24 cases as visual field data was lacking in 10.

TABLE II: Incidence of Headaches and Papilloedema

	W. S. Series (34 cases)		Singapore Series (22 cases)	
	Nos.	%	Nos.	%
Headaches as a severe symptom	8	24%	5	23%
Headaches localised	18	62%	12	55%
Headaches generalised	11	32%	10	45%
Papilloedema present	1	3%	3	14%

TABLE III: Analysis of Endocrine Features

	W. A. Series (34 cases)		Singapore Series (22 cases)	
	Nos.	%	Nos.	%
Early loss of libido with partial loss of secondary sex characteristics	14	41%	12	55%
Lethargy and intolerance to cold	15	44%	5	23%
Skin Changes	11	32%	5	23%
Signs of Hypothalamic Insufficiency	4	12%	2	9%
Pituitary Apoplexy	5	15%	0	0%

TABLE IV: Plain Radiographic Changes

	W.A. Series (34 cases)		Singapore Series (22 cases)	
	Nos.	%	Nos.	%
"Double flooring"	9	26%	3	14%
"Ballooning of fossa"	19	56%	19	84%
Non-Specific enlargement with erosion of Dorsum sella — post. clinoids	13	38%	14	62%

dorsum sellae and posterior clinoids was also more common with the larger lesions of the Singapore series. Combinations of 2 of the 3 features listed were also common.

Angiography was used in 17 or half of the Western Australian cases and 14 of the 22 Singapore

cases only.

The angiographic changes confirm that displacement of the internal carotid arteries were the most reliable sign of a suprasellar space effect. The displacement of the A1 segment of the anterior cerebral arteries was seen in half the Singapore cases and two-thirds of the Australian cases.

Air studies were the most popular definitive investigation, being used in all the Singapore series and 25 of the Western Australian series. Displacement and distortion of the anterior part of the 3rd ventricle was noted in over 80 per cent of both series but obstructive hydrocephalus was seen only in the Singapore series. These cases require ventricular shunting before definitive surgery was feasible.

The usefulness of the air study showing the relationship of the tumour to optic chiasm although the latter is seldom prefixed, was tested. In only 2 cases (8 per cent) of the Western Australian series and 1 (5 per cent) of the Singapore cases could the relationship be discussed.

RESULTS OF TREATMENT

In the Western Australian series, 17 cases had simple decompression alone without radiotherapy. Of these, there were 9 recurrences, mainly occurring between the second and sixth year. These recurrences were treated by reoperation and radiotherapy. 3 cases remain well after decompression alone. There were 5 deaths in this group. 3 were due to hypothalamic infarction in cases that had presented with acute pituitary apoplexy. One died from post-operative pulmonary embolism and one died from an associated frontal astrocytoma. One case had decompression and radiotherapy but was followed by a recurrence after 3 years and another recurrence occurred in a case who had Yttrium implantation done elsewhere. One case had cryogenic ablation performed in another country and remains well. 13 cases had a radical subtotal or "total" excision done using the operating microscope. No recurrences have been noted in this group yet although the follow-up in this group is only from 2 to 5 years.

In the Singapore series, all the cases were treated by simple decompression and radiotherapy. There were 2 recurrences (9 per cent) occurring in the 3rd and 4th post-operative years respectively. There were 2 deaths. One was due to post-operative hypothalamic infarction and one from post-operative hepatic failure. One case was permanently incapacitated from radionecrosis, complicating radio-

therapy.

DISCUSSION

The tumour incidence appear relatively small in the Singapore series. This is due largely to a poorer pick-up rate from a large sector of the population that is uniformed and superstitious, thus unwilling to subject to investigations and treatment. The same factors explain the late presentation and larger tumours which account for the gross visual deficits, and marked radiological changes when first seen. The number of acromegalics clinically seen in the Western Australian series was 36 per cent, a higher incidence than the 12 per cent seen in Singapore. The latter figure is similar to that reported by Grant (1948) and others.

Elkington and McKissock (1967) in reviewing 260 cases treated mainly by surgical decompression and radiotherapy reported a mortality of 10 per cent and recurrence rate of 7.5 per cent. Improvement of vision occurred in 55 per cent and as unchanged in 26 per cent. This was worse in 17 per cent. Ray and Patterson (1962) also using the transfrontal method for decompression with radiotherapy reported no operative mortality. They had a recurrence rate of 8 per cent and 75 per cent had visual improvement. The results of the Singapore series with 9 per cent recurrences, a mortality rate of 9 per cent and improvement of vision in over 80 per cent are comparable to these. The West Australian regime of using surgery only initially, reserving radiotherapy

TABLE V: Angiographic Changes

	W. A. Series (17 cases had angiography)		Singapore Series (14 cases had angiography)	
	Nos.	%	Nos.	%
Displacement of terminal portion of INTERNAL CAROTID.	12	71%	13	93%
Displacement of A1 segment of anterior cerebral artery	11	65%	7	50%

TABLE VI: Air Study Changes

	W. A. Series (25 cases with AEG performed)		Singapore Series with AEG performed (22 cases)	
	Nos.	%	Nos.	%
Displacement of anterior part of 3rd ventricle-	22	88%	18	82%
Obstructive hydrocephalus	0	—	5	23%
Showing relationship of chiasm to tumour	2	8%	1	

TABLE VII: Results of Treatment (W. A. Series — 34 Cases)

Programme of Treatment	Nos	Well with improved vision	Incapacitated	Died	Recurrence
Simple Decompression	17	3	—	5	9
Decompression & DXT	1	1	—	—	1
Radical Excision with Magnification	13	13	—	—	—
DXT alone	1	1	—	—	—
Yttrium Implantation	1	—	1	—	1
Cryogenic ablation	1	1	—	—	—
Total No of cases	34	19(56%)	1(2%)	5(15%)	11(32%)

TABLE VIII: Results of Treatment Singapore Series (22 Cases)

Programme of Treatment	Nos	Well with improved vision	Incapacitated	Died	Recurrence
Simple decompression	—	—	—	—	—
Decompression & DXT	22	19	1	2	2
Radical Excision with magnification	—	—	—	—	—
DXT alone	—	—	—	—	—
Total No of cases	22	19(86%)	1(5%)	2(9%)	2(9%)

for recurrences only, provide a controlled study. Those 17 cases with decompression alone suffered 9 recurrences, a rate of 53 per cent. This is similar to Cushing's series as reviewed by Henderson (1939), of the transfrontal operation alone, where the recurrence rate was 57.5 per cent. Those treated by similar decompression and radiotherapy suffered a recurrence rate of 13 per cent only. The reason, according to Lekias (1972) for omitting radiotherapy in the West Australian programme of treatment was due to an unsatisfactory experience of radionecrosis. This, however, was rare in the Singapore and other series so treated. Interestingly, the 13 cases with radical excision performed using operating microscope have so far been without recurrences. The follow-up period of 2 to 5 years may be inadequate for critical comment but the general impression is that only if Microsurgery is used to perform a radical excision safely, should radiotherapy be perhaps reserved. Otherwise, adequate decompression followed by radiotherapy remains the treatment of choice.

REFERENCES

1. ELKINGTON, S. G. and MCKISSOCK, W. (1967). Pituitary Adenomas: "Results of Combined Surgery and Radio-

- therapeutic treatment in 260 patients" Br. Med. J. 1, 263
2. GRANT, F.C. (1948). Surgical experience with tumours of the pituitary gland. J. AM. Med. Ass. 136, 668
 3. HENDERSON, W.R. (1939). The Pituitary Adenomata. A follow-up study of the Surgical Results in 338 cases (Dr Harvey Cushing's series)" Br. J. Surg. 26, 811.
 4. LEKIAS, J.S. (1972) Personal Communication.
 5. RAY, B.S. and PATTERSON, R.H. (1962). Surgical Treatment of Pituitary Adenomas. J. Neurosurgery, 19, 1.