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ORIGINAL ARTICLE

PHAEOCHROMOCYTOMA: EXPERIENCE FROM A REFERRAL HOSPITAL IN SOUTHERN INDIA

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Background: Phaeochromocytoma has been traditionally called the 'Tumour of Tens'. Many investigators have reported the prevalence of extra-adrenal phaeochromocytoma to be more than 10%.
Methods: All consecutive adult patients diagnosed to have phaeochromocytoma by the departments of endocrinology and surgical endocrinology of the Christian Medical Hospital, India, over a period of 10 years from 1988 to 1998, were included in the study.
Results: A total of 30 patients were diagnosed to have phaeochromocytoma. Extra-adrenal phaeochromocytoma accounted for 26.6% of cases. Ten per cent of cases were bilateral, 6.6% were malignant and one patient had a familial tumour (multiple endocrine neoplasia IIB). The tumours were localized pre-operatively in all patients. Multicentric extra-adrenal tumours were not found in this series. All patients except one were explored by the anterior transperitoneal approach. Persistent hypertension was noted in 30% of patients.
Conclusions: Our series shows a higher prevalence (26.6%) of extra-adrenal tumours than the traditionally described 10%. With accurate pre-operative localization, a transperitoneal approach may not be necessary. The laparoscopic approach needs to be evaluated in light of these findings.

Key words: adrenal gland neoplasms, paraganglioma, phaeochromocytoma.

INTRODUCTION

Phaeochromocytoma is a rare tumour which arises from chromaffin tissue located in the adrenal medulla or in the sympathetic nervous system. Extra-adrenal phaeochromocytoma are most commonly found in the para-aortic region in the abdomen. They are also known to occur below the aortic bifurcation, in the thorax, neck, heart, brain and urinary bladder. Phaeochromocytomas account for 0.1% of hypertensives.[1]

Phaeochromocytoma has been characterized by the 'rule of tens' (i.e. 10% extra-adrenal, malignant, bilateral, familial, multicentric and in children).[2] Many investigators have reported prevalence of extra-adrenal tumours to be in the range of 14 to 30%.[3–7] Some studies feel that the higher prevalence is due to referral or reporting bias. In a review of the cancer registry of Sweden, where there has been mandatory reporting of all tumours since 1958, 22% of phaeochromocytomas were extra-adrenal.[8]

Extra-adrenal phaeochromocytomas occur with greatest frequency in the second and third decades. No sex predominance has been noted. These tumours are often multicentric. They are more likely to be malignant than their adrenal counterparts.[9–11]

We analysed our series to determine the behaviour of phaeochromocytomas in the Indian setting.

METHODS

All consecutive adult patients diagnosed to have phaeochromocytomas and managed by the departments of Endocrinology and Surgical endocrinology of the Christian Medical Hospital, during a 10-year period from 1 July 1988 to 30 June 1998, were included in the study.

Phaeochromocytoma was suspected when 24 h urinary vanillyl mandelic acid (VMA) was found to be elevated in hypertensives. Tumour localization was done by computed tomographic scanning. ^{131}Meta-iodo-benzyl-guanidine scanning (MIBG) was introduced in this hospital in 1994. This isotope scanning technique was found to be of value in patients with normal or borderline VMA, in whom there was a high index of suspicion. In such patients it was found to be a useful confirmatory as well as a localizing test. This scanning was also used in young patients with extra-adrenal tumours to detect multicentricity and in patients with malignant tumours to detect metastases.

Data were collected regarding patient profiles, diagnostic methods, pathology, operative treatment and results of operation.

RESULTS

Thirty patients had biopsy proven phaeochromocytoma in the study period. There were 13 males and 17 females. Eight tumours (26.6%) were located at extra-adrenal sites. Table 1 shows patient profiles.

Diagnostic methods

Screening was done by measuring 24-h urinary VMA excretion. The normal value for our laboratory is 7 mg in 24 h. However, a number of patients with essential hypertension were found to have VMA values between 7 and 14 mg in 24 h (M. S. Seshadri, unpubl. obs., 1991). Vanillyl mandelic acid values greater than 14 mg/24 h were taken as diagnostic of phaeochromocytoma. Urinary VMA was found to be more than 14 mg/24 h in all except four patients. However, MIBG scans were diagnostic in these

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patients (Table 2). Computed tomographic scans were done in all patients, and accurately localized the tumour in all.

Operative approach

One patient was operated on by the flank approach in 1988. All other patients were operated on by the anterior transperitoneal approach. This approach was chosen because both adrenals as well as the common extra-adrenal sites could be inspected intra-operatively for multicentric tumours missed by pre-operative imaging. However, no patient had a tumour that was not detected pre-operatively. Most adrenal tumours were unilateral. The extra-adrenal tumours were predominantly para-aortic. Table 3 shows the tumour characteristics. There was no operative mortality.

Associated syndromes

One patient had multiple endocrine neoplasia (MEN IIB) which consisted of phaeochromocytoma, medullary carcinoma thyroid and hypertrophic corneal nerves. One patient had Von Hippel Lindau syndrome (i.e. phaeochromocytoma, medullary haemangioblastoma and retinal haemangiomata).

Table 1. Patient profiles

	Adrenal	Extra-adrenal
No. tumours	22 (73.4%)	8 (26.6%)
Age		
Mean (SD)	32.6 (13.7)	23.5 (14.5)
Range	13–58	14–58
Sex		
Male	11 (50%)	2 (25%)
Female	11 (50%)	6 (75%)

Table 2. Diagnostic tests

	Adrenal (n = 22)	Extra-adrenal (n = 8)
24-h urinary VMA (mg/24 h)		
Minimum	9.4	6.9
Maximum	103	83
Mean (SD)	31.8 (23.5)	35.85 (24.7)
MIBG scanning	Eight (36.4%); positive in all	Three (37.5%); positive in all

Results of operation and follow up

Persistent hypertension was found in 30% of patients at discharge. In this group (n = 9), six patients had normal postoperative urinary VMA. Two patients are expected to come for follow up and VMA estimation shortly. One patient was completely lost to follow up. Follow up was available in 21 patients (70%) (Table 4).

DISCUSSION

Extra-adrenal phaeochromocytomas were encountered in 26.6% of our patients, in contrast with the often quoted figure of 10%. This finding has also been reported by others.[3–8]

Our study confirmed previous reports of extra-adrenal tumours occurring in the second and third decades of life. Unlike other series, our findings show a female preponderance in the extra-adrenal group. No malignant tumour was encountered in the extra-adrenal group, in contrast with previous reports.[9–11]

An anterior transperitoneal approach has been recommended by many investigators.[12–14] Advocates of this approach argue that the high incidence of multicentricity in extra-adrenal phaeochromocytomas would necessitate thorough abdominal examination. We used this approach in all patients except one. However, multicentric tumours were not found. The routine use of a transperitoneal approach is probably not required when accurate pre-operative localization is available. The laparoscopic approach has been recommended by some studies[15,16] and this needs further evaluation.

Persistent hypertension is known to occur in 25% of cases after excision of the tumour. This has been attributed to permanent vascular changes.[1] In this series, 30% had persistent hypertension. The majority of patients who were found to have persistent hypertension had normal urinary VMA levels suggesting that the persistence of hypertension is probably due to vascular changes rather than to recurrent tumours or missed multicentric tumours. However, because follow up was incomplete, this observation should be interpreted with caution.

In conclusion, extra-adrenal phaeochromocytomas are more common than what is usually described. Routine transperitoneal

Table 4. Blood pressure at discharge

Blood pressure	Adrenal (%)	Extra-adrenal (%)	All patients (%)
Normal	14 (63.6)	7 (87.5)	21 (70)
Elevated	8 (36.4)	1 (12.5)	9 (30)

Table 3. Tumour characteristics

Tumour	Adrenal (n = 22)	Extra-adrenal (n = 8)	
Side		Sites	
Right	13 (59.1%)	Upper para-aortic	5 (62.5%)
Left	6 (27.3%)	Organ of Zuckerkandl	2 (25%)
Bilateral	3 (13.6%)	Just below bifurcation	1 (12.5%)
Size (in cm)			
Mean (SD)	7.86 (4.3)		5.87 (1.45)
Minimum	3		4
Maximum	20		8
Histopathology			
Benign	20 (90.9%)		8 (100%)
Malignant	2 (9.1%)		

approach is unnecessary with accurate pre-operative localization of the tumour. Nevertheless, when localization is uncertain, when there is an extra-adrenal tumour, bilateral adrenal tumours or malignant tumours, an anterior approach would be appropriate.

REFERENCES

1. Landsberg L, Young JB. Pheochromocytoma. In: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, Hauser SL, Longo DL. (eds) *Harrison's Principles of Internal Medicine*, 14th edn. New York: McGraw Hill Co., 1998; Chapter 333.
2. Tierney LM, McPhee SJ. *Current Medical Diagnosis and Treatment*, 36th edn. Appleton and Lange, Stamford, 1997.
3. Hume DM. Pheochromocytoma in the adult and in the child. *Am. J. Surg.* 1960; **99**: 458–96.
4. Scott HW Jr, Oates JA, Nies AS, Burko H, Page DL, Rhamy RK. Pheochromocytoma: Present diagnosis and management. *Ann. Surg.* 1976; **183**: 587–92.
5. Modlin IM, Farndon JR, Shepherd A *et al.* Phaeochromocytomas in 72 patients: Clinical and diagnostic features, treatment and long term results. *Br. J. Surg.* 1979; **66**: 456–65.
6. Scott HW Jr, Halter A. Oncological aspects of pheochromocytoma: The importance of follow up. *Surgery* 1984; **96**: 1061–5.
7. Cullen ML, Staren ED, Straus AK *et al*. Pheochromocytoma: Operative strategy. *Surgery* 1985; **98**: 927–9.
8. Stenstrom G, Svardsudd K. Pheochromocytoma in Sweden 1958–1981. An analysis of the National Cancer Registry data. *Acta Med. Scand.* 1986; **220**: 225–32.
9. Goldfarb DA, Novick AC, Bravo EL, Straffon RA, Montie JE, Kay R. Experience with extra adrenal pheochromocytoma. *J. Urol.* 1989; **142**: 931–6.
10. Hartley L, Perry-Keene D. Phaeochromocytoma in Queensland: 1970–1983. *Aust. N.Z. J. Surg.* 1985; **55**: 471–5.
11. Whalen RK, Althausen AF, Daniels GH. Extra adrenal pheochromocytoma. *J. Urol.* 1992; **147**: 1–10.
12. Remine WH, Chong GC, Van Heerden JA, Sheps SG, Harrison EG Jr. Current management of pheochromocytoma. *Ann. Surg.* 1974; **179**: 740–7.
13. Stewart BH. Adrenal surgery: Current state of the art. *J. Urol.* 1983; **129**: 1–6.
14. Vaughan ED Jr, Blumfield JD. The adrenals. In: Walsh PC, Retik AB, Vaughan ED, Wein AJ (eds) *Campbell's Urology*, 7th edn. Philadelphia: WB Saunders Co., 1997; Chapter 96.
15. Staren ED, Prinz RA. Adrenalectomy in the era of laparoscopy. *Surgery* 1996; **120**: 706–11.
16. Duh DY, Siperstein AE, Clark OM *et al*. Laparoscopic adrenalectomy. Comparison of the lateral and posterior approaches. *Arch. Surg.* 1996; **131**: 870–5.