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Adrenal tumours in Chinese

K.Y. Lam

Department of Pathology, University of Hong Kong, Queen Mary Hospital, Hong Kong

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Summary. Patients with adrenal tumours were identified ($n=412$). Among them, 43% (176 patients) had primary and 57% (236 patients) had secondary tumours. Of the primary tumours, 71% were adenomas, but adrenal cortical carcinoma 6.8% (12 cases), phaeochromocytoma 9.7% (17 cases), neuroblastoma 6.2% (11 cases), ganglioneuroma 1.1% (2 cases) and myelolipoma 4% (7 cases) were also seen. Rare tumours like lipoma and haemangioma were also found. Most of the metastatic tumours were carcinomas (88.2%), mainly from lung (33.2%), stomach (15.9%) and oesophagus (17.3%).

Key words: Adrenal gland – Incidence – Tumours – Primary – Metastasis

Introduction

Functional tumours of the adrenal glands are associated with a diverse and complex spectrum of clinical syndromes resulting from abnormalities in the production of hormones. Non-functional adrenal tumours are either asymptomatic or present as abdominal masses. The advent of high-resolution abdominal imaging techniques has resulted in the discovery of many non-functional lesions (Glazer et al. 1982). There has been no systematic study on various adrenal tumours in the Chinese and due to the rarity of these tumours, there was no comprehensive data in the world literature. In view of this, the autopsies and biopsies that were performed in Queen Mary Hospital, Hong Kong were reviewed to give a comprehensive view of the adrenal tumours and to see if there were any differences in Hong Kong Chinese compared with other population groups with particular reference to demographic data and clinicopathological correlations.

Materials and methods

All autopsy and biopsy records of the Queen Mary Hospital (Hong Kong) from 1978 to 1990 (inclusive) were reviewed. Queen Mary Hospital is the only regional hospital on Hong Kong Island and it serves a population of about one million. The clinical data and pathology of all tumours noted in the adrenal glands were analysed. Only Chinese patients were included in the study.

Results

Patients with adrenal tumours ($n=412$) were identified. Of these, 176 cases (43%) had primary adrenal tumours and 236 (57%) had their adrenal glands affected by metastatic tumour. Throughout this 13-year study period, 6896 autopsies and 198664 biopsies were performed.

Table 1 lists the major groups of tumours that were present in our study.

Adenomas accounted for 71% of cases (43.2% were functional adenomas, 27.8% were non-functional). Of patients with functional adenomas, 15.8% presented with Cushing's syndrome and 84.2% presented with primary hyperaldosteronism (Conn's syndrome). The age distribution of the patients with Cushing's syndrome was from 16 to 71 years with a modal peak in the third

Table 1. Primary adrenal tumours

Primary tumours	Number of cases
Functional adenoma	
– with Cushing's syndrome	12(6.8%)
– with Conn's syndrome	64(36.4%)
Non-functional adenoma	
– size > or = 1.5 cm	18(10.2%)
– size < 1.5 cm	31(17.6%)
Adrenocortical adenocarcinoma	12(6.8%)
Phaeochromocytoma	17(9.7%)
Neuroblastoma	11(6.2%)
Ganglioneuroma	2(1.1%)
Myelolipoma	7(4%)
Haemangioma	1(0.05%)
Lipoma	1(0.05%)
Total	176 cases

and fourth decades. All were females and the adenomas were 2–4.5 cm in diameter. The ratio of left to right involvement was 1.4:1. The female to male ratio for cases with Conn's syndrome was 1.6:1. Their age distribution was from 23 to 62 years and the peak incidence was in the fourth to sixth decades. The mean age of these patients was 44.7 years. The ratio of left to right involvement was 1.3:1. The diameters ranged from 1 to 10 cm.

All the non-functional adenomas of the adrenal cortex were found at autopsy. The diameters of 18 cases were equal to or greater than 1.5 cm (group 1) while the diameters of 31 cases were less than 1.5 cm (group 2) and the largest diameter of adenomas seen was 4 cm. The incidence of non-functional adenomas at autopsy was thus 0.71% (0.25% for those with diameters > or = to 1.5 cm, 0.45% for those with diameters <1.5 cm). The ratio of left to right involvement of group 1 lesions was 5:1 in males and 2.3:1 in females. The mean age for male patients with group 1 lesions was 68.9 years while for females it was 72.3 years. The ratio of left to right involvement of group 2 lesions was 0.75:1 in males and 1.2:1 in females. The mean age for the male patients was 68.4 years and that for the female patients was 69.9 years.

There were 12 patients (6 males and 6 females) who presented with adrenal cortical carcinomas, making up 6.8% of the primary adrenal tumours under investigation. All except 1 female patient had endocrine manifestations and as a group, 7 out of 12 cases (58%) had endocrine manifestations. All male patients had their tumours on the left side while the ratio of right to left side involvement was 2:1 for female patients. The age distribution was from 4.5 to 63 years with a mean of 38 year. The diameters were from 4 cm to 25 cm, ranging from 65 g to 2800 g.

Seventeen a phaeochromocytomas (8 males and 10 females) were noted, comprising 9.7% of all the primary adrenal tumours found in this survey, with an autopsy incidence of 0.05%. The mean age for male patients with phaeochromocytomas was 56 years with a modal peak incidence in the sixth decade; that for females was 39 years and the peak incidence was in the fourth decade. Twelve patients had right-sided tumours, 3 had left-sided tumours and one had bilateral tumours. The side of involvement in 1 patient was not known. The diameters of the tumours were in the range of 1–13 cm and their weights were from 34 to 278 g.

Autopsies were performed in 11 patients with neuroblastoma (6.2% of primary adrenal tumours analysed), with an incidence of 1 in 625 autopsies (0.16%). Most male children were 2 years old (range 1.5–5 years). The right adrenal glands were involved in 2 patients and the left adrenal in 3 patients. For female patients, the age distribution was from 2–22 months with a mean of 7 months. Two patients had both adrenal glands, 3 patients had their right adrenal glands and 3 had their left adrenal glands affected by neuroblastoma.

Two patients with ganglioneuroma (1.1% of all cases) were noted (1 male and 1 female).

Seven patients with myelolipomas (5 from autopsy records and 2 from biopsy records) were found; the weights of their tumours ranged from 4 to 210 g. The incidence was 4% of primary adrenal tumours in this survey and the incidence of myeliolipoma found at autopsy was 0.07%. The male to female ratio was 1.3:1. The mean age of male patients was 49.8 yeras and that of female patients was 76.7 years.

One patient with cavernous haemangioma and 1 with lipoma were noted.

Table 2 shows the number of various groups of neoplasms with metastasis to adrenal glands. Out of 236 cases, 208 (88.2%) were metastatic carcinomas. Malig-

Table 2. Metastatic tumours in adrenal gland

Types of tumour	Number of patients
1. Carcinoma	208(88.2%)
Oesophagus	28
Lung	69
– Adenocarcinoma	(44)
– Large cell carcinoma	(9)
– Squamous carcinoma	(8)
– Small cell carcinoma	(8)
Stomach	33
Breast	9
Bile duct	11
Pancreas	14
Liver	10
Colorectal	13
Cervix	2
Prostate	1
Ovary	1
Bladder	5
Kidney	8
Gall bladder	4
2. Malignant lymphoma	14(5.9%)
3. Malignant melanoma	2(0.9%)
4. Sarcoma	6(2.5%)
5. Carcinoid	1(0.4%)
6. Malignant mesothelioma	1(0.4%)
7. Others	4(1.7%)
Total	236 cases

Table 3. Metastatic carcinoma in both sexes

Carcinoma	Male	Female	Both sexes
Oesophagus	24(17.3%)	4(5.8%)	28(13.5%)
Lung	44(31.7%)	25(36.2%)	69(33.2%)
Stomach	23(16.5%)	10(14.5%)	33(15.9%)
Pancreas	10(7.2%)	4(5.8%)	14(6.7%)
Colorectal	9(6.5%)	4(5.9%)	13(6.3%)
Breast	0(0%)	9(13.0%)	9(4.3%)
Bladder	2(1.4%)	3(4.4%)	5(2.4%)
Liver	10(7.2%)	0(0%)	10(4.8%)
Gallbladder	2(1.4%)	2(2.9%)	4(1.9%)
Bile duct	8(5.8%)	3(4.4%)	11(5.3%)
Prostate	1(0.7%)	0(0%)	1(0.5%)
Ovary	0(0%)	1(1.4%)	1(0.5%)
Kidney	6(4.3%)	2(2.9%)	8(3.8%)
Cervix	0(0%)	2(2.9%)	2(1%)
Total	140(100%)	69(100%)	208(100%)

nant lymphomas (5.9%), malignant melanomas (0.9%), and sarcomas (2.5%) made up much of the remainder. Forty-five patients (19%) had their right adrenal glands affected by metastatic tumours while 66 (28%) had the left involved. Bilateral involvement was noted in 125 patients (53%). Table 3 shows the primary sites of various metastatic carcinomas. The lung was the most common primary site (69 cases, 33.2%) and 44 of 69 patients (63.8%) had adenocarcinomas. The other common sites were stomach (15.9%) and oesophagus (13.5%). For male patients (139 cases), lung (31.7%), oesophagus (17.3%) and stomach (16.5%) were the most common primary sites. Sixty-nine female patients were affected by metastatic carcinomas. The three most common primary sites were lung (36.2%), stomach (14.5%) and breast (13%).

Discussion

Of the 412 patients with adrenal tumours, 43% had primary tumours and 57% metastases.

The majority of primary adrenal tumours noted in this study were adrenal cortical adenomas (70.7% of all primary tumours). For patients with functional adenomas, more were associated with Conn's syndrome than with Cushing's syndrome (84.2% vs 16.8%). The age distribution for patients with adenomas associated with Conn's syndrome was from 23 to 62 years with peak incidence in the fourth to sixth decades and left to right ratio of 1.3:1, similar to series reported from Manchester (Lins and Adamson 1987). Female predominance was also noted in this survey (F:M = 1.6:1) and by Ferris et al. (1978). In contrast to other studies (Harrison et al. 1973; Neville and Symington 1966), which showed that the size of adenomas in Conn's syndrome was usually small (0.2–3.5 cm or less than 1.5 cm in diameter), the diameters of adenomas found in this study were from 1 to 10 cm. In this study, patients with Cushing's syndrome who had their adrenal cortical adenomas removed were all female. In agreement with other studies (Lack et al. 1990), there was left side predominance (L:R = 1.4:1). The diameter of adenomas was 2–4.5 cm, which was similar to those found by Harrison et al. (1973). In addition, the age distribution was from 16 to 71 years with a modal peak in the third and fourth decades.

According to Lack et al. (1990), non-functional adrenal cortical adenomas are rarely diagnosed during life. In this survey, all the non-functional adenomas were also discovered as incidental findings in autopsies and their distinction from incidental cortical nodules was difficult; in the case of solitary dominant macronodules such a distinction may be impossible as suggested in the literature (Lack et al. 1990). According to Shamma et al. (1958), most cortical nodules had diameters of 0.5–0.8 cm and patients with non-functional adenomas were in the range of 1.5–10.5 cm. Therefore, in this study, patients with non-functional adenomas were divided into two groups; those with diameters of adenomas larger than or equal to 1.5 cm (group 1) and those solitary tumours with diameters less than 1.5 cm but with diameters larger than cortical nodules defined by Shamma et al. (1958) (group 2). Both groups had a mean age similar for both sexes (68.9 years for males and 72.3 years for females in group 1 lesions, 68.4 years for males and 69.9 years for females in group 2 lesions); a predilection for the left side was noted in group 1 lesions (the left to right ratio was equal to 5:1 in males and 2.3:1 in females). This was not true for patients with group 2 lesions (the left to right ratio was 0.75:1 in males and 1.2:1 in females. As a whole, the incidence of non-functional adenomas was 0.71% in Chinese patients (0.25% for group 1 lesions and 0.45% for group 2 lesions).

Adrenal cortical carcinoma accounted for 6.8% of primary adrenal tumours under investigation. The age distribution of patients with adrenal cortical carcinoma was from 4.5 to 63 years. There was no sex predilection, as stated by Lack et al. (1990). One very remarkable feature of this study was that all the male patients had their tumours on the left side while in females, the right side was more likely to be involved (R:L = 2:1). The diameters of the tumours were from 4 to 25 cm and the weights were in the range of 65–2600 g. These findings were consistent with most recent studies in that adrenal cortical carcinomas were likely to be heavier than adenomas (Lack et al. 1990). Most studies have shown a wide variation (24–96%) in the percentage of adrenal cortical carcinoma that were functional (Didolkar et al. 1981; Hutter and Kayhoe 1966) and in the present series, all except one female had endocrine manifestations (83.3%) of their tumours. As a whole, 58% had endocrine manifestations.

Phaeochromocytoma represented 9.7% of all the primary adrenal tumours under study. It is a relatively rare neoplasm that has been reported to occur in 0.005%–0.1% of unselected autopsies (Page et al. 1986); the autopsy incidence was 0.05% in this study. There was a slight predominance of female patients affected (10 females and 8 males) as reported in earlier studies (Melicow 1977; Scott et al. 1976), but there was no significant sex predilection here. In most large studies, the right adrenal gland was affected more often than the left; this could be due to the slightly greater amount of medullary tissue which has been noted in the right adrenal gland when compared with the left (Quinan and Berger 1933). The same findings were also noted in this study (R:L = 4:1). Of the phaeochromocytomas 5% were bilateral. This finding was similar to that of Remine et al. (1974), who found that the incidence of bilaterality in sporadic cases was approximately 5%. In addition, Medeiros et al. (1985) found that the tumour was most common in the fourth and fifth decades of life. In the present series, the peak incidence for female patients was in the fourth decade, a similar finding to that of Medeiros et al. (1985). However, in males, the peak incidence was in the sixth decade. Lastly, according to Medeiros et al. (1985), 81% of tumours measured between 2 and 10 cm in size and the largest tumour measured 20 cm in diameter. In this survey, the diameters of phaeochromocytomas were in the range of 1.5–12 cm and their weights were from 34 to 278 g.

Of the primary adrenal tumours found in this series 6.2% were neuroblastomas. All of them were autopsy cases, giving an autopsy incidence of 1 in 625 autopsies (0.16%). According to the literature, the peak age at presentation is 2 years with over half of the new cases diagnosed in the 1st year of life (Jaffe 1976; Rosen et al. 1984). In this study, female patients with neuroblastomas were younger than males with a peak age at presentation of 7 months (range 2–22 months). For male patients, the peak age was 2 years (range 1.5–5 years). In addition, only 2 patients were affected by ganglioneuromas. They accounted for 1.1% of all primary adrenal tumours found in the study period.

Myelolipomas comprised 4% of primary adrenal tumours in the survey. The incidence in autopsy cases was 0.07%, slightly lower than the frequency of myelolipomas reported by Vyberg et al. (1984) (0.08–0.2%). The sex distribution has been reported to be about equal (Del Gaudio and Solidoro 1986) and the male to female ratio in this study was 1.3:1. Moreover, it has been noted that adrenal myelolipomas are most common in the fifth decade of life and are unusual below the age of 30 years (Del Gaudio and Solidoro 1986; Plaut 1958). However, in this study, the mean age for male patients was in the fifth decade (49.8 years) and for females in the eighth (76.7 years). Although myelolipomas weighing up to 5900 g have been reported (Boudreaux et al. 1979), the weights of myelolipomas found in this study were from 4 to 210 g.

Per unit weight, the adrenal glands are the organs most frequently affected by tumour metastases (Glomset 1938). In this series, over half (57.1%) of the tumours found in the adrenal glands were metastatic tumours, of which 53% were bilateral. Most metastatic tumours were carcinoma (88.2%), and malignant lymphoma (5.9%), malignant melanoma (0.9%) and sarcoma (2.5%) made up much of the remainder. In Glomset's series, the most common primary sites of tumours were lung and breast. In our series, lung was the most common primary site (33.2%) for adrenal metastasis. Adenocarcinomas were the most common subtype (found in 63.8% of patients with primary tumours in the lung). The second and third most common sites were stomach (15.9%) and oesophagus (13.5%). For male patients, lung (31.7%), oesophagus (17.3%) and stomach (16.5%) were the most common primary sites; in females, lung (36.2%), stomach (14.5%) and breast (13%) predominated.

A wide range of adrenal tumours may be seen in Chinese and these show certain distinct features when compared with the established data from other studies.

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