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Primary Adrenal Tumors – a 16-year Experience in a Single Institution

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The incidence of primary adrenal gland tumors observed at the Pathology Department, Cracow, in the period of 16 years was examined. The frequency of adrenal lesion in males and females was studied and compared. The mean age of the patients was calculated. The results were shown in tables and diagrams and compared with data given in the WHO Classification of Tumors and the literature on the subject.

Introduction

Primary tumors of the adrenal gland are relatively rare entities, which may originate both from the adrenal cortex and adrenal medulla [4]. The majority of these lesions are benign. Malignant adrenal tumors account for only a small percentage of all cases – definitive criteria for malignancy are distant metastases and local invasion. Several morphological multiparametric systems differentiating benign from malignant tumors of the adrenal cortex and adrenal medulla have been published [2,14,16]. Adrenal tumors occur sporadically or may be associated with MEN (multiple endocrine neoplasia) [4]. Many of these adrenal masses are discovered incidentally, usually in individuals in later decades of life – the incidence of such tumors increases in frequency with age [7, 12, 15]. Less than 20% of cases represent functional tumors, which cause various clinical manifestations because of abnormal hormone secretion [13].

The purpose of this investigation was to analyze the incidence of primary adrenal tumors collected in a single pathology department during the period of 16 years.

Materials and Methods

The records of the Pathology Department in Cracow for the period spanning the years 1992-2007 were searched to find primary lesions of the adrenal glands. A case was included into the study if the clinical diagnosis had been as follows: “adrenal tumor”, “hyperplasia”, “pheochromocytoma”, “adenoma”, “retroperitoneal tumor”, “cystis”, “pseudocystis”, “angiomyolipoma” or “incidentaloma” and the morphological evidence that the tumor originated from the adrenal gland was found. The adrenals resected and referred to pathologic examination together with a kidney tumor were excluded from the study. The available clinical information and morphological data were collected and compared. The mean age of the patients and the mean tumor diameter were calculated for every tumor type. The results are shown in tables and diagrams.

Results

During the 16-year period, 212 cases of adrenal gland lesions excised independently from kidney tumors were found. After a preliminary selection, 22 cases were excluded, as they contained metastases of various neoplasms, normal pancreatic or adrenal tissue, abscesses and other non-neoplastic lesions (Table 1).

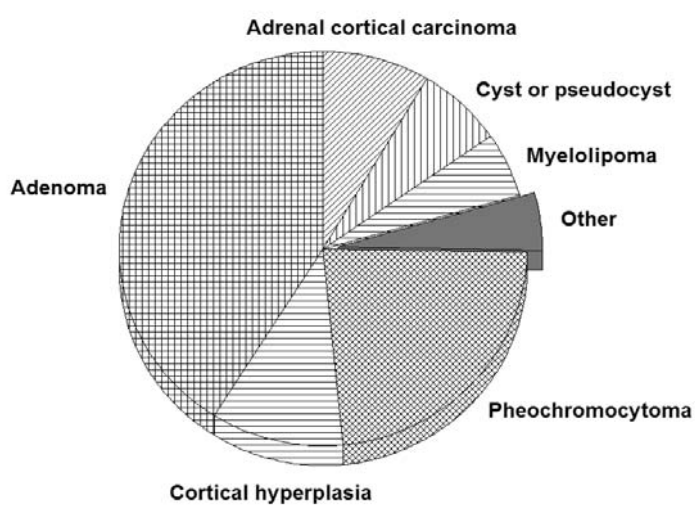
Finally, 190 primary adrenal gland lesions were included into the study: the number of particular cases is illustrated in Table 2. The number of cases in the subsequent years is shown in Table 3.

The most common single tumor of the adrenal gland was adenoma – it accounted for almost 42% of the cases. Adenomas were three times more common in women than in men. The mean age at adenoma diagnosis in men was higher then in women. The tumors were almost equally distributed between the left and right adrenal gland. The mean adenoma diameter in women and men was not significantly different (Table 4). In three cases, the patient presented with more than one adenoma (in two case – 2 tumors, in one - 3 tumors). In eight cases, cortical hyperplasia was present in

TABLE 1
Cases excluded from the study

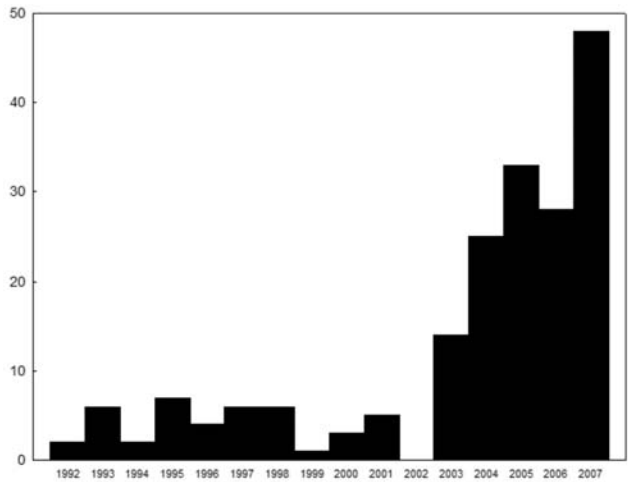
METASTASES	adenocarcinoma	3
	planoepithelial ca.	2
	microcellular ca.	3
	hepatocellular ca.	1
	DLBCL	3
	T-cell lymphoma	1
	Wilms' tumor	1
	leiomyosarcoma	1
MPNST	(without adrenal tissue)	1
ABSCESS		1
PANCREATIC TISSUE		1
VESSEL INVAGINATION		2
NORMAL ADRENAL TISSUE		2
		22

TABLE 2
Incidence of adrenal gland tumors diagnosed between 1992 and 2007 in Pathology Department, Cracow



Diagnosis	Number of cases	Percentage
Adenoma	78	41%
Pheochromocytoma	44	23,1%
Cortical hyperplasia	20	10,5%
Adrenal cortical carcinoma	16	8,4%
Cyst or pseudocyst	13	6,8%
Myelolipoma	10	5,2%
Angiomyolipoma	2	1%
Ganglioneuroma	2	1%
Schwannoma	2	1%
Angiosarcoma	1	0,5%
Oncocytoma	1	0,5%
Medullary hyperplasia	1	0,5%
	190	100%

TABLE 3
Number of cases included into the study every year



the adrenal cortex near the adenoma. In three cases, there were small areas of myelolipoma within the adenoma.

Pheochromocytomas constituted more than 23% of primary adrenal tumors. They occurred with an almost equal frequency in men and in women, but compared to adenomas, were seen in significantly younger patients. The tumors were more frequent in the right adrenal gland. The mean diameter of pheochromocytomas in men was larger than in woman – Table 5. The tumors were usually solitary, but four patients (three of them with MEN syndrome) had bilateral or unilateral but multiple pheochromocytomas. One of these tumors was a composite pheochromocytoma with a small area of ganglioneuroma; three were malignant according to the PASS criteria [16].

In the analyzed period, five extraadrenal pheochromocytomas (paragangliomas) were diagnosed in our Department. Three of them were located in the retroperitoneum near the aorta (so-called Zuckerkandle organs paraganglioma). Two were found in the posterior thorax. Four of the five extraadrenal pheochromocytomas were observed in women with the mean age at diagnosis being much higher then in adrenal pheochromocytomas.

In 10% of cases, the diagnosis of cortical hyperplasia was made. Adrenal cortical hyperplasia was twice as common in women as in men. It had the smallest mean diameter of all adrenal tumors. The lesions were usually diagnosed in the sixth decade of life, similarly as in the case of adenomas. Multiple adrenal tumors were most commonly represented by cortical hyperplasia – Table 6.

Adrenal cortical carcinomas accounted for less than 10% of adrenal tumors. The diagnosis was based on the Weiss Revisited System [2] and Van Slooten Index [14]. Cortical carcinomas were more common in women and were usually diagnosed in the sixth decade of life. These lesions were usually larger than 4cm in diameter. – Table 7.

Adrenal cysts were diagnosed in relatively younger patients than other adrenal lesions; they were two times more common in women then in men and had the largest mean diameter – Table 8.

Of ten cases of myelolipoma, nine developed in women in the early sixth decade of life.

Angiomyolipoma, ganglioneuroma, schwannoma, angiosarcoma, oncocytoma and adrenal medullary hyperplasia each constituted less than 1% of all tumors.

Discussion

Adrenal masses represent a heterogeneous group of lesions and include benign and malignant adrenocortical tumors, pheochromocytomas, cysts, metastases and other rare entities.

In the analyzed records, adenoma was the most common primary adrenal tumor, what was consistent with data presented in the literature [9, 12, 15, 17]. Adenomas were three times more common in women than in men and were usually diagnosed in the fifth and sixth decade of life. According to the literature, adenomas could also be found in children [13], however, we did not find any such instances in young patients because our Department does not service any children's hospital. In three patients adenomas were multiple, the majority of the lesions were solitary. Also in the literature only few cases with multiple adenomas were described [6].

There was no difference in the incidence of pheochromocytomas in men and women; the tumors were usually unilateral and solitary in the adrenal gland, with the mean diameter of 3-6 cm, what is consistent with data given in pathology textbooks [4, 13]. The only difference was the younger mean age of pheochromocytoma patients, a phenomenon that was especially pronounced in women. In two patients (both diagnosed as MEN2A syndrome), pheochromocytomas were bilateral. Three of these tumors showed morphological signs of malignancy according to the PASS criteria [16]. The fourth lesion was a composite pheochromocytoma with a small area of ganglioneuroma. A composite pheochromocytoma-ganglioneuroma was also reported in association with MEN 2A by other investigators [3].

Adrenal cortical hyperplasia is probably associated with localized ischemia – the idea of an ischemic origin of cortical hyperplasia was first suggested by Dobbie [5].

TABLE 4
Adenoma – details of incidence

	female	male	total
left adrenal	27	11	38
right adrenal	29	8	37
no information	1	2	3
together	57	21	78 = 41,5%
mean diameter	3,7 cm	4,0 cm	
mean age	54,4	58,2	

TABLE 5
Pheochromocytoma – details of incidence

	female	male	total
left adrenal	7	9	16
right adrenal	13	9	22
no information	3	3	6
together	23	21	44 = 23%
mean diameter	3,8 cm	5,6 cm	
mean age	44,8	50,3	

TABLE 6
Adrenal cortical hyperplasia – details of incidence

	female	male	total
left adrenal	8	4	12
right adrenal	5	2	7
no information	-	1	1
together	13	7	20 = 10,5%
mean diameter	2 cm	2,6 cm	
mean age	55,4	57,5	

TABLE 7
Adrenal cortical carcinoma– details of incidence

	female	male	total
left adrenal	4	3	7
right adrenal	4	1	5
no information	2	2	4
together	10	6	16 = 8,5%
mean diameter	4,5	10	
mean age	55,5	45	

TABLE 8
Cysts – details of incidence

	female	male	total
left adrenal	2	2	4
right adrenal	5	2	7
no information	2	-	2
together	9	4	13 = 7%
mean diameter	5,8 cm	4,5 cm	
mean age	40,5	51,5	

Adrenal cortical hyperplasia is classified as diffuse, nodular or combined [8]. The nodules, if present, are usually small, often less than 1 cm in diameter, having the form of the so-called micronodules. Computed tomography allows for detecting lesions as small as having the diameter below 0.5cm. In our series, in adrenal hyperplasia the tumors found in a particular patient were often multiple, but each single lesion was small. Our observations are consistent with data given by other investigators – the nodules in adrenal cortical hyperplasia were the smallest primary adrenal lesions.

Adrenal cortical carcinoma is a rare tumor, which is usually diagnosed in patients in the fifth and sixth decade of life [7, 10, 13] – 15 of 16 cases in our series represented patients from this age group. We also had one tumor originating from a 6-year old boy. We observed a predilection for carcinoma in women (10:6), what is consistent with data given in the literature [18]. The diameter of adrenal cortical carcinomas is usually larger than 5 cm [15], and cortical tumors smaller than 4 cm are most commonly benign [1, 9]. In our material, the mean diameter of carcinomas in women was smaller as compared to data provided by pathology textbooks [13]. However, malignant cortical tumors with the diameter smaller than 4 cm were also described in the literature [11].

The number of adrenal tumors treated surgically in the years 2003-2007 was significantly higher than in the period 1992-1997 and 1998-2002. Furthermore, the number of cases continued increasing every year. This phenomenon might be explained by a more common use of modern techniques, like CT or MRI, during imaging procedures involving the abdomen, usually performed for non-adrenal conditions [12, 15]. These modern techniques significantly increased the detection rate of non-functional, small adrenal masses, which did not cause clinical symptoms – the so-called incidentalomas. The majority of the resected adrenal incidentalomas were found to be non-functioning cortical adenomas after pathological examination [15].

Conclusions

1. The incidence of particular adrenal tumors in our records was very similar to the incidence rates presented in the literature.
2. Unilateral, multiple adrenal gland tumors usually represented adrenal cortical hyperplasia.
3. Pheochromocytomas in MEN patients were often bilateral and showed morphological features of malignancy.
4. The number of adrenal tumors, especially the so-called incidentalomas, increased every year due to a more widespread use of modern imaging techniques.

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