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Adrenal tumour bigger than 5 cm — what could it be? An analysis of 139 cases

Guzy nadnerczy większe niż 5 cm — czym mogą być — analiza 139 przypadków

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Abstract

Introduction: There is an increasing number of adrenal being tumours discovered incidentally during imaging examinations performed for many different indications. Radiological findings suggesting adrenal pathology may be caused by true adrenal tumours or by other retroperitoneal masses. Generally, the larger the tumour, the higher the possibility of adrenal cancer.
Material and methods: Analysis of our data — 139 operations performed over 11 years (2004–2014) in patients with tumours in the adrenal area larger than 5 cm.
Results: The most common finding was adrenal cancer (25.2%), benign adenoma (24.5%), pheochromocytoma (12.9%), and metastatic cancer (10.1%). In total, there were 19 various histopathological diagnoses in this group.
Conclusion: Although adrenal cancer is the most likely diagnosis in large adrenal tumours, a broad spectrum of various adrenal and retroperitoneal tumours with size more than 5 cm can be found in such patients. **(Endokrynol Pol 2017; 68 (4): 411–415)**

Key words: *adrenal tumor, big adrenal mass, adrenal surgery*

Streszczenie

Wstęp: Obecnie obserwuje się zwiększoną liczbę guzów nadnerczy wykrywanych przypadkowo przy okazji badań obrazowych wykonywanych z różnych wskazań. Zmiany opisywane jako guzy nadnerczy mogą być zmianami samych nadnerczy, jak i innymi patologiami przestrzeni zaotrzewnowej. Wraz ze wzrostem wielkości guza rośnie ryzyko jego złośliwego charakteru.
Materiał i metody: Przedstawiamy analizę 139 pacjentów z guzami nadnerczy większymi niż 5 cm, operowanymi w ciągu 11 lat w latach 2004–2014.
Wyniki: Najczęstszymi rozpoznaniami były: rak kory nadnercza (25,2%), gruczolak (24,5%), guz chromochłonny (12,9%), zmiany przerzutowe (10,1%). Łącznie w tej grupie chorych postawiono 19 różnych rozpoznań histopatologicznych.
Wniosek: Rak kory nadnercza jest najbardziej prawdopodobnym rozpoznaniem u chorych z dużymi guzami nadnerczy, jakkolwiek w tej grupie chorych można się spodziewać licznych, różnych, rzadszych patologii. **(Endokrynol Pol 2017; 68 (4): 411–415)**

Słowa kluczowe: *guzy nadnerczy, duże zmiany nadnerczy, chirurgia nadnerczy*

Introduction

The presence of adrenal mass is reported in 1–4% of patients undergoing imaging studies for various reasons [1] The prevalence of such findings increases with increasing age [2, 3]. The majority of these tumours are benign non-functional lesions, but certain patient's characteristic and large size are predictors of malignancy [4].

Among all adrenal tumours the most common is non-functioning benign lesion (82.5%), followed by cortisol secreting adenoma (5.3%), pheochromocytoma (5.1%), adrenocortical carcinoma (4.7%), metastatic lesion (2.5%), and aldosteronoma (1%) [5].

However, many retroperitoneal pathologies may be confused with adrenal tumours on preoperative imaging examinations [6].

When tumour size is exceeds 6 cm, the possibility of malignancy increases [7–9]. All such patients are candidates for surgical treatment as the only one offering the chance for cure.

We would like to present our experience with 139 operations performed in our institution in patients with tumours larger than 5 cm in the adrenal area during an

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eleven-year period (2004–2014). Because our institution is part of the Institute of Oncology, the patients referred to us were preselected. All of them were presumed to have a higher risk of malignancy and/or had atypical appearance of the mass seen in cross-sectional imaging.

Material and methods

Between 2004 and 2014 a total of 287 patients with various adrenal tumours were referred to our centre from departments of endocrinology in the whole Poland. Initial diagnostic procedures (hormonal status, imaging examinations) were performed mostly in referring centres. Indications for surgery were established based on the hormonal activity of the tumour and its appearance in ultrasound, CT, MR, and sometimes PET-Ct scans. Based on NIH guidelines from 2004 [10], tumours larger 6 cm were referred to surgery independently of their other radiological and hormonal features. Tumours smaller than 6 cm were treated with surgery if they were heterogeneous, had irregular or unclear margins, high density and delayed washout, areas of necrosis, haemorrhage or calcifications, and an increase in size exceeding 1 cm on consecutive CT scans.

In this group a total of 139 patients with tumours larger than 5 cm were identified. There were 85 women and 54 men. The female/male ratio was 1.57, and the age range was 23–85 years. Mean age at the time of operation was 54.9 years (SD 13.6), and it was slightly higher for men 56.6 years (SD 14.5) than for women 53.8 years (SD 13.2).

Based on preoperative investigations, presumptive diagnoses were: adrenal carcinoma — 41 patients (F-33, M-8), pheochromocytoma — 18 patients (F-9, M-9), myelolipoma seven patients (F-2, M-5), and metastatic cancer — 15 patients (F-5, M-10). Most of these patients were the ones with "non-adenoma" lesions 58 (F-40, M-18). In these cases, presumptive diagnosis was not established, but their phenotype was estimated as not typical for adenoma.

Various hormonal disturbances were present in 79 patients (56.8%). Subclinical hypercortisolaemia was a more frequent disorder, found in 41 subjects (29.5%). In 23 patients (16.5%) pheochromocytoma was suspected due to increased urinary catecholamine secretion; however, histological examination confirmed this diagnosis only in 18 tumours. In six cases primary hyperaldosteronism, and in nine cases hyperandrogenism were diagnosed.

Twenty-four out of 139 patients had previously diagnosed and treated cancer in another localisation: colon and rectum — six patients, lung — seven, breast — three, kidney — three, uterus — one, bladder — one, prostate — one, anal cancer — one, and shwannoma (mediastinum) — one.

All patients were operated under general anaesthesia with appropriate antibiotic prophylaxis using the second generation of cephalosporin (cefuroxime) according to hospital standards. All patients received perioperatively low-molecular-weight heparins as venous thromboembolism prophylaxis. Cross-matched blood was reserved for patients with large tumours or essential comorbidities. The typical surgical approach was transabdominal lateral flank. Laparoscopic technique is applied in our institution, but had not been used in patients with tumours measuring more than 5 cm and with suspected cancer.

Seventy left adrenalectomies, 59 right, and 10 bilateral adrenalectomies (at least one of the tumours was larger than 50 mm), as well as two resections of other retroperitoneal tumours, were performed. The decision to perform of bilateral adrenalectomy was always made together with the referring endocrinological centre.

Results

The size of the tumour measured on histopathological examination ranged from 50 to 250 mm. Results of this findings are displayed in Table I. The five most common adrenal lesions, including cancer, adenoma, pheochromocytoma, metastatic cancer, and myelolipoma, were responsible for 78.4% of adrenal tumours in this series.

Thirty-eight of 139 patients (27.3%) had very large tumours (not smaller than 10 cm) removed. Among this group of patients, the most common diagnosis was adrenocortical cancer — 24 (63.2 %) and metastases — 5 (13.2 %). The mean age of patients with metastases was higher than of those with the cancer. Characteristics of this group are presented in Table II.

In the whole series of 139 operations, we performed 10 bilateral adrenalectomies. In such patients at least one of the tumours measured more than 5 cm. Characteristic of patients with bilateral tumours are presented in Table III.

Discussion

Adrenal tumours represent a wide spectrum of pathologies, ranging from benign non-functioning cortical adenoma to adrenocortical carcinoma. In an increasing number of patients, the adrenal tumours are discovered incidentally during abdominal imaging performed for other clinical indications. The indications for adrenalectomy are hormone excess or increased risk of malignancy. The risk of malignancy in adrenal tumour is determined by several factors including tumour size and radiographic features, such as irregular margins, high density, slow washout of contrast medium presence of necrosis, area of haemorrhage, and calcifications.

Table I. *Histopathological diagnosis — tumours larger than 50 mm*
Tabela I. *Rozpoznania histopatologiczne — guzy powyżej 50 mm*

Diagnosis	Number [%]	Sex	Age [years]	Age [years] mean / SD	Tumour size [mm]	Tumour size [mm] mean/SD
Cancer	35 (25.2)	28K, 7M	23–73	49.5/13.6	50–250	122.5 /45.5
Adenoma	34 (24.5)	25K, 9M	27–78	55.1/12.0	50–85	62.9/10.2
Pheochromocytoma	18 (12.9)	8K, 10M	30–77	55.8/12.6	55–135	75.4/19.3
Metastases	14 (10.1)	3K, 11M	58–79	66.3/6.6	51–130	88.6/25.1
Myelolipoma	8 (5.75)	3K, 5M	30–78	59.8/17.3	60–110	83.75/17.7
Ganglioneuroma	4 (2.8)	2K, 2M	39–74	53.3/14.7	50–85	67.5/15.6
Cysts	4 (2.8)	3K, 1M	43–68	51.5/11.3	50–95	66.3/19.7
Cortical hyperplasia	4 (2.8)	3K, 1M	31–62	49.8/13.2	50–110	81/26.8
Pseudocysts	3 (2.15)	2K, 1M	33–56	47/12.3	60–100	80/20
Haemorrhage with post-haemorrhage changes	3 (2.15)	1K, 2M	49–76	65.3/14.4	55–90	71.7/17.6
Shwannoma	2 (1.4)	1K, 1M	25–46	35.5 /14.8	60–110	85/35.4
Paraganglioma	2 (1.4)	1K, 1M	64–60	57/4.2	60–65	62.5/3.5
Hemangioma	2 (1.4)	2K	64–67	65.5/2.1	50–85	67.5/34.7
Haemangiolipoma	1 (0.7)	M	63		65	
Both adrenocortical carcinoma and malignant pheochromocytoma	1 (0.7)	K	25		170	
Leiomyosarcoma	1 (0.7)	M	85		120	
primary myelofibrosis	1 (0.7)	K	40		70	
Neurogenic sarcoma	1 (0.7)	M	65		125	
Lipoma	1 (0.7)	K	70		90	

Table II. *Histopathological diagnosis — tumours larger than 100 mm*
Tabela II. *Rozpoznania histopatologiczne — guzy powyżej 100 mm*

Diagnosis	Number [%]	Sex	Age [years]	Age [years] mean/SD	Tumour size [mm]	Tumour size [mm] mean/SD
Cancer	24 (63.15)	18K, 6M	23–73	50.5/14.6	100–250	144.8/38.0
Metastases	5 (13.15)	1K, 4M	59–79	65.8/7.7	100–130	116/13.4
Myelolipoma	2 (5.3)	2M	56–74	65/12.7	100–110	105/7.1
Pheochromocytoma	1 (2.6)	K	55		135	
Leiomyosarcoma	1 (2.6)	M	85		120	
Pseudocysts	1 (2.6)	M	56		100	
Neurogenic sarcoma	1 (2.6)	M	65		125	
Shwannoma	1 (2.6)	M	25		110	
Cortical hyperplasia	1 (2.6)	M	53		110	
Both adrenocortical carcinoma and malignant pheochromocytoma	1 (2.6)	K	25		170	

Regardless of all these features, presumptive diagnosis is often delusive because of numerous different pathologies which may exist in the adrenal area.

The 2002 National Institutes of Health consensus statement on incidentaloma recommended adrenalectomy for all non-functioning tumours greater than 6 cm in size. For tumours 4 to 6 cm, is recommended to take into account such factors as the tumour's features on imaging studies, age, and general condition of the patient [10]. Some authors, however, suggest lowering absolute cut-off to 4 cm because most adrenocortical carcinomas (ACC) are > 4 cm in size [11]. In recently

Table III. *Characteristic of patients and histopathological findings with bilateral adrenalectomies*

Tabela III. *Charakterystyka pacjentów i rozpoznania histopatologiczne w przypadkach obustronnych adrenalektomii*

Sex and age	Histopathology	Size of the tumours
F-44	Bilateral pheochromocytoma	40 and 75 mm
M-67	Bilateral metastases of prostate cancer	65 and 95 mm
K-44	Bilateral adenomas	55 and 55 mm
K-31	Bilateral cortical hyperplasia	90 and 95 mm
M-63	Bilateral haemangiolipoma	43 and 65 mm
M-61	Bilateral adenomas	60 and 70 mm
M-62	Bilateral metastases of lung cancer	35 and 130 mm
M-59	Bilateral adenomas	45 and 60 mm
M-53	Bilateral cortical hyperplasia	100 and 95 mm
K-62	Bilateral adenomas	60 and 10 mm

published guidelines, authors voted against a certain cut-off in diameter of the tumour, and suggested that an individualised approach was most appropriate [12]. It is worth remembering that although attenuation value of < 10 Hounsfield units is the most widely used attenuation value for the diagnosis of lipid-rich benign adenomas, lipid poor adenomas with higher value represent 10–40% of all adenomas [13]. Even such tumours as myelolipomas, although they are benign, are recommended to be surgically removed when they are bigger than 4 cm [14, 15]. According to current Polish recommendations, tumour size larger than 5 cm is one of the additional criteria for the surgical treatment of an incidentaloma [16], so we decided to analyse tumours of this size. Although adrenal cancer was the most common pathological finding in our series of patients, its incidence accounted for just above a quarter of all tumours (25.2%). This percentage is still much higher than previously published by our co-workers — 14% for primary and metastatic adrenal cancers [17]. This discrepancy is caused by preselection of the referred to oncological centre patients with "unclear" or "suspicious" imaging phenotype of the tumours.

The presented material shows also a large variety of pathologies preoperatively estimated as oncologically suspicious adrenal mass. Among 19 pathologic diagnoses, the five most common (cancer, adenoma, pheochromocytoma, metastatic cancer, and myelolipoma) accounted for 78.4% of cases. A wide spectrum of histological profiles of removed adrenal tumours was previously described [6]. Also, in our series we found some unexpected and rarely occurring lesions, for example Schwannoma (two cases), haemangiolipoma (one case), or leiomyosarcoma (one case). These rare cases constitute up to 21.6% of all operated tumours. Tumours like primary adrenal leiomyosarcoma are extremely rare, and only approximately 30 cases have been reported so far in the English language literature [18]. We present as many different pathological diagnoses as previously reported on a similar number of patients, but we report many more malignant lesions [19].

Concerning the tumour size, the highest mean size on histopathological examination was seen for adrenal cancers, followed by metastases and myelolipomas. For all these tumours the mean size was greater than 80 mm. The size of adenomas in this series reached 180 mm, but the median size of carcinomas was still almost twice as big. The percentage of adrenal carcinomas in the subgroup with tumours larger than 10 cm was over 60%. Since the probability of adrenal carcinoma is extremely high in large adrenal tumours, the diagnosis in such cases should be completed very quickly to shorten the time to surgery.

A distinct diagnostic challenge is posed by bilateral masses, which constitute about 15% of incidentally discovered adrenal tumours [20, 21]. In the literature, metastatic or infiltrative tumours, changes with underlying congenital adrenal cortical hyperplasia, bilateral adrenal cortical adenomas, or ACTH-independent macronodular adrenal hyperplasia (AIMAH) have been described as the most likely diagnoses in such cases. Attention is also paid to the necessity for "oncological vigilance" after detection of bilateral lesions [22]. However, a higher frequency of malignant lesions in bilateral adrenal tumours was not found in a larger series of patients with adrenal incidentalomas, compared to unilateral ones [21]. Also in our material, despite exceptionally large dimensions of the tumours, the most frequent diagnoses were bilateral adrenal adenomas or AIMAH (6/10 cases). Some authors found a higher incidence of subclinical hypercortisolaemia among patients with benign bilateral adrenal tumours than in patients with unilateral lesions [23]. In the cases of large bilateral lesions operated in our clinic there were no subclinical hypercortisolaemia; we only found hyperaldosteronism in one case. Even in two cases of large bilateral metastases, there was no adrenal insufficiency in these patients. Adrenal insufficiency, a state which is often suspected in cases of metastases to both adrenal glands, is in fact a rare symptom in such patients [24].

Conclusion

In conclusion, we have stated that the incidence of malignant lesions among tumours larger than 5 cm is high. In our opinion, all patients with large adrenal tumours should be considered for surgical treatment, often as the only one offering a chance of cure.

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