ADRENAL METASTASES

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The aim of the study was an retrospective assessment of adrenal metastases based on the analysis of patients operated on in three surgical institutions between 2001 and 2005.

Material and methods. Between 2001 and 2005 169 patients (106 females and 63 males) were treated due to adrenal tumors. The age of patients ranged between 25 and 82 years (mean 55.4± 11.8 years). All patients were routinely diagnosed by means of ultrasound, computed tomography or magnetic resonance imaging and hormonal tests such as cortisol, chromogranine A, aldosterone and sodium, potassium concentrations. Patients were surgically managed after preparation dependent on general status, tumor type and concomitant diseases. Operations were carried out using classic techniques via lumbar approach in 146 cases (86.4%) or videoscopic techniques via retroperitoneal or transperitoneal approaches (13.6%).

Results. In 143 cases (84.6%) benign tumors and in 26 (15.4%)-malignant lesions were diagnosed. 16 (9.5% of all cases and 61.5% of malignant tumors) were secondary- metastases form various cancers treated previously. Adrenal metastases occurred most often in the 7th decade (43.7%), and primary site was clear cell carcinoma of the kidney (9 cases – 56.25%) and non-small cell lung cancer (4 – 25%). melanoma (2 cases – 12.5%) and rectal cancer (1 – 6.25%). During the follow-up of 1-5 years (mean 3.1 years) 12 patients died of metastatic tumors – 6 with multiple metastases and 6 with solitary adrenal metastasis. 4 patients are still alive with metastatic deposits in the adrenal glands (at the moment of adrenalectomy) – 3 with metastatic renal cancer (currently 2 without other metastases) and 1 with disseminated lung cancer.

Conclusions. 1. Adrenal metastases are the most frequent malignant tumors of these glands. 2. Metastatic tumors occur most often during the 6th and 7th decades. 3. Results of treatment are not satisfactory and dependent on the extent of spread.

Key words: adrenal malignant tumours, metastases

Malignant adrenal tumors are relatively rare. According to reports, adrenal carcinoma accounts for 0.05-0.2% of all malignancies (1, 2). An incidence rate is 0.4x10^-5 for males and 0.2x10^-5 for females (1). In the WHO classification of adrenal tumors secondary lesions are listed in the special position (2).

Adrenal tumors can originate in the adrenal cortex or medulla. From the consecutive layers of the cortex epithelial lesions can arise. They can be benign (adenoma) or malignant (carcinoma). From the medulla benign or malignant phaeochromocytoma or complex phaeochromocytoma/ paraganglioma with various grade of malignancy of the compounds can be derived.

The WHO classification of adrenal tumors also includes extraadrenal masses such as paraganglioma. Moreover, in the adrenal
glands tumors are formed by other adrenal cells than these producing steroids and catecholamines. They can be both benign (myelolipoma, hemangioma, leiomyoma, lymphangioma, schwannoma, ganglioneuroma, teratoma) and malignant (angiosarcoma, leiomyosarcoma, melanoma, PNET and others) – tab. 1 (2).

Regarding functional classification, the aforesaid masses can be hormonally active or inactive. The first group can secrete glucocorticoids, mineralocorticoids, sex hormones or catecholamines depending on the origin or transformation of the tumor cells. They can show mixed hormonal activity or produce hormones in a small amount without clinical manifestation.

Data collected in the Departments of Endocrine Surgery in Poland demonstrate that among adrenal operations cortical lesions are twice to six times more frequent as compared with the medulla (3).

Metastatic tumors are detected most often in the sixth-eighth decade of life. At this age these masses are more common in comparison with primary adrenal tumors.

The aim of the study was an retrospective assessment of adrenal metastases based on the analysis of patients operated on in three surgical institutions between 2001 and 2005.

MATERIAL AND METHODS

Adrenal tumors were analyzed in patients operated on in the Department of Endocrine and General Surgery, Department of Thoracic and General Surgery and Surgical Oncology of Medical University in Łódź and Department of Surgery, Ministry of Internal Affairs’ Hospital in Łódź. In the evaluated period 169 patients with adrenal lesions were treated. Among them there were 106 women (62.7%) and 63 men (37.3%), respectively. Their age ranged between 24 and 82 years, mean 55.4±11.8. The age of females ranged between 25 and 82, mean 56.5±11.3 years of age, and in males between 24 and 79, mean 53.7±12.6 years of age, respectively.

All patients were routinely diagnosed, namely ultrasound and computed tomography scans or magnetic imaging resonance and hormonal tests depending on the clinical status and symptoms were performed. In case of clinically silent lesions (incidentaloma) cortisol, chromogranine A, natrium, potassium and aldosterone concentrations were determined.

Patients were operated on after preparation regarding the general status, tumor type and functional status and concomitant diseases. Procedures were carried out using a classic lumbar approach – 146 cases (86.4%) or video-endoscopic technique via transperitoneal or retroperitoneal approaches – 23 cases (13.6%). In laparoscopic techniques the retroperitoneal approach was preferred.

The excised specimens were examined in the Department of Pathology, Chair of Oncology (Head: Prof. Radzisław Kordek, MD, PhD), Department of Clinical Pathomorphology and Cytopathology, Medical University in Łódź (Head: Prof. Krzysztof Ziełinski, MD, PhD) and Department of Pathomorphology, Ministry of Internal Affairs’ Hospital (Head: Dr Jacek Kuroszczyk, MD).

RESULTS

The number of operations in relation to age groups is presented in tab. 2. As shown in

Table 1. WHO histological classification of tumours of the adrenal gland

<table>
<thead>
<tr>
<th>Adrenal cortical tumours</th>
<th>Adrenal cortical carcinoma</th>
<th>Adrenal cortical adenoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal medullary tumours</td>
<td>Malignant pheochromocytoma</td>
<td>Benign pheochromocytoma</td>
</tr>
<tr>
<td>Extra – adrenal paraganglioma</td>
<td>Carotid body</td>
<td>Jugulotympanic</td>
</tr>
<tr>
<td>Other adrenal tumours</td>
<td>Adenomatoid tumour</td>
<td>Sex-cord stromal tumour</td>
</tr>
<tr>
<td>Secondary tumours</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Tab. 1 (2).
Adrenal metastases

Table 2. Number of adrenal gland operations according to age

<table>
<thead>
<tr>
<th>Age</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>3 (2.8%)</td>
<td>5 (7.9%)</td>
<td>8 (4.7%)</td>
</tr>
<tr>
<td>31-40</td>
<td>5 (4.7%)</td>
<td>4 (6.4%)</td>
<td>9 (5.4%)</td>
</tr>
<tr>
<td>41-50</td>
<td>22 (20.8%)</td>
<td>13 (20.6%)</td>
<td>35 (20.7%)</td>
</tr>
<tr>
<td>51-60</td>
<td>37 (34.9%)</td>
<td>22 (34.9%)</td>
<td>59 (34.9%)</td>
</tr>
<tr>
<td>61-70</td>
<td>28 (26.4%)</td>
<td>15 (23.8%)</td>
<td>43 (25.4%)</td>
</tr>
<tr>
<td>&gt; 70</td>
<td>11 (10.4%)</td>
<td>4 (6.4%)</td>
<td>15 (8.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>106 (100%)</td>
<td>69 (100.0%)</td>
<td>169 (100.0%)</td>
</tr>
</tbody>
</table>

Table 3. Number of adrenal gland operations because of metastatic tumor according to age and gender

<table>
<thead>
<tr>
<th>Age</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>41-50</td>
<td>3 (42.9%)</td>
<td>1 (11.2%)</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>51-60</td>
<td>0 (0%)</td>
<td>4 (44.4%)</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>61-70</td>
<td>3 (42.9%)</td>
<td>4 (44.4%)</td>
<td>7 (43.7%)</td>
</tr>
<tr>
<td>&gt;70</td>
<td>1 (14.2%)</td>
<td>0 (0%)</td>
<td>1 (6.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>7 (100%)</td>
<td>9 (100%)</td>
<td>16 (100%)</td>
</tr>
</tbody>
</table>

Table 4. Secondary adrenal gland tumours according to primary focus, gender, time and number of metastasis

<table>
<thead>
<tr>
<th>Primary focus</th>
<th>Number</th>
<th>Female</th>
<th>Male</th>
<th>Wiek</th>
<th>Time (years)</th>
<th>Multiple metastases at the time of diagnosis (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>9 (56.25%)</td>
<td>4</td>
<td>5</td>
<td>58±9.2</td>
<td>2±3.1</td>
<td>3 (33.3%)</td>
</tr>
<tr>
<td>Lung</td>
<td>4 (25%)</td>
<td>1</td>
<td>3</td>
<td>63±7.4</td>
<td>1.5±1.7</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>Skin</td>
<td>2 (12.5%)</td>
<td>1</td>
<td>1</td>
<td>57±11.3</td>
<td>1.2</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>Large bowel</td>
<td>1 (6.25%)</td>
<td>1</td>
<td>0</td>
<td>65</td>
<td>0.15</td>
<td>0</td>
</tr>
</tbody>
</table>

DISCUSSION

The rate of adrenal tumors found during autopsies ranges between 1.5-7% (4). The number of adrenal tumors diagnosed in the lifetime is dependent on the used diagnostic techniques. The introduction of imaging diagnostics especially magnetic resonance imaging and high resolution computed tomography increased the rate of intravital and incidental detection of adrenal pathologies to a few percent among patients examined due to other causes than diseases of the adrenal glands (5, 6).

Malignant adrenal tumors account for 0.05-0.2% of all malignancies (1, 2). Carcinoma of the cortex occurs with the frequency of about 1x10^-6 per year. Women suffer 2.5-fold more often as compared with men and the average age of the onset of disease is 40-50 years. Approximately 80% of cancers is hormonally active. The vast majority of them secrete glucocorticoids (45%), glucocorticoids and androgens (45%), androgens (10%) and aldosterone (up to 1%) (2).
Pheochromocytoma is the most common hormonal tumor. It occurs with the frequency of $8 \times 10^{-6}$ per annum and 3-13% of tumors are malignant (2). Cortical adenomas secreting glucocorticoids and mineralocorticoids occur with a lower incidence. Other primary lesions are rare or described as case reports (7, 8). Among histological reports adrenal metastases amount to 22.2-50% of malignant tumors (9, 10, 11). Therefore, they are the most common adrenal pathologies. Their incidence increases with age and is the most frequent in the 6th, 8th decades of life (12). On the basis of autopsies it was detected that metastatic tumors were more often than primary lesions and the adrenal glands are the fourth site of metastatic spread after lung, liver and bones (2).

Adrenal metastases were detected in 27% patients who died of cancer (13). In the light of these data the incidence rate of secondary adrenal tumors presented in our study is high (9.5% of all adrenal tumors and 61.5% of malignant lesions) and confirms observations made by other authors.

Lung, kidney, gastric, esophageal, biliary tract, breast, rectal cancers and melanoma metastasize most frequently (2, 14). Also metastatic spread from (others) epithelial cancers such as prostate carcinoma, mesothelioma and non-epithelial lesions such as rhabdomyosarcoma and Kaposi’s sarcoma were described (2, 14, 15).

Computed tomography is an essential prerequisite for the diagnosis of adrenal metastases, sometimes supplementary to other techniques and also fine-needle aspiration is used for cytologic verification (10).

Adrenal metastases can occur in one gland or bilaterally. Sebag and al. demonstrated 16 cases of isolated metastases to the adrenals including 10 synchronous and 6 metachronous lesions. The primary sites were most frequently lung cancers (9 cases) and melanoma – 3 (14). Other authors described apart from solitary, also bilateral metastases. Kocijanic et al. presented the group of 50 patients with non-small cell lung cancer in whom adrenal metastases were detected. In 20 patients they were ipsilateral, in 15 – contralateral and in 15 bilateral (16). In cases of bilateral metastases to the adrenal glands symptomatic hormonal insufficiency can be diagnosed which ought to be treated with substitution doses of glucocorticoids before and also after adrenalectomy (17, 18, 19). In our material we found 2 cases of synchronous bilateral adrenal metastases from lung cancer in which at the time of diagnosis in one patient hormonal insufficiency of the adrenal glands regarding glucocorticoid secretion was diagnosed. Adrenal insufficiency is caused mainly by lung and breast cancer metastases. The first option is confirmed in our article. Others such as kidney, gastric and intestinal cancers lead to adrenal insufficiency less frequently (18). In the article published by Italian authors adrenalectomy due to metastatic spread, led to long survival - 37-80 months, without relapse in 3 out of 10 patients and in one case the patient has been living with recurrence in the site of adrenal removal for 44 months (19).

Renal cancer spreads quite often to either ipsilateral and contralateral adrenals. Hence, conception of routine simultaneous resection of the ipsilateral adrenal gland even if it is not infiltrated. In the studies published by the authors who removed the adrenals routinely with the kidney, metastases to the adrenal glands were detected in 4 (1.4%) out of 285 patients and 26 (2.7%), out of 914 patients respectively (20, 21). Based on these results the authors of both papers do not recommend routine ipsilateral adrenalectomy as a necessary component of radical nephrectomy when macroscopically normal adrenal glands can be seen intraoperatively and on CT scan, and the tumor is not located in the superior pole of the kidney. We have not analyzed this feature because our patients after nephrectomies were previously treated in different institutions.

Adrenal tumors can be managed via classic open technique- anterior transabdominal, lumbar or posterior approach and using laparoscopic techniques- transabdominal or retroperitoneal (3, 22, 23, 24). In our paper the majority of patients – 146 out of 169 (86.4%) were managed through open procedures. Minimal access was used in 23 patients (13.6%). The low rate of minimally invasive techniques performed in our study has increased in recent years and currently video-surgical operations are of vital importance. When malignancy is suspected classic operations were made assuming that malignancy or tumor size over 6cm are contraindications for laparoscopic procedures. The authors from some institutions very experienced in the field
of videoscopic operations of the adrenals point out the successful outcome of such procedures in many patients with tumors when malignancy was suspected and/or over 6cm in diameter. The percentage of conversion to open procedures was 1% – 2 out of 216 and 3 out of 325 patients, respectively (22, 23). The percentage of major complications was 1.8% (23). In minimally invasive techniques 2 essential approaches are used such as transperitoneal and retroperitoneal. Budzyński et al. comparing 2 groups of patients operated on using laparoscopy (110 retroperitoneal and 75 transperitoneal approaches) did not find any differences concerning morbidity and conversion rate between these groups (24).

Adrenalectomy due to metastases has a beneficial impact on survival, especially in patients with lung, renal cancer and melanoma. A survival rate after adrenalectomy can amount to 80 months, but approximately to 8 months (12, 19). Five year survival rates occur only in 5% of patients with symptomatic metastases (12). When adrenal metastases are suspected total adrenalectomy is suggested and gland preserving procedures are not recommended (23).

The results of follow-up reveal that adrenal spread is a symptom of dissemination in the majority of cases. Other sites harbor metastases later.

CONCLUSIONS

1. Adrenal metastases are the most frequent malignant tumors of these glands.
2. Metastatic tumors occur most often during the 6th and 7th decades.
3. Results of treatment are not satisfactory and dependent on the extent of spread.

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