

Multi-Year Observation of Lung Cancer Metastases to the Adrenal Glands

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Abstract: The purpose of our study was to show if there is any correlation between the location of the primary cancer site in the lungs and the appearance of metastases in the adrenal gland. 2,340 patients with confirmed lung cancer were analyzed. The study group of 2,340 patients was divided into two subgroups: 1,998 patients were diagnosed with lung cancer located only in one lung, and 342 with disseminated lung cancer. Among the group of 1,998 patients, in 218 cases, pathological lesions in the adrenal glands were detected using computer tomography (CT) or magnetic resonance (MR). In 161 out of 218 cases, suprarenal lesions were detected by ultrasound (US). All patients with suprarenal lesions detected by US (161 cases in total) underwent US-guided biopsy. Among these patients, metastases to the adrenal glands were histopathologically confirmed in 91 cases. In 70 cases, the histopathological reporting confirmed benign lesions. Altogether there were 64 adrenal metastases originated from the left lung cancer and 32 metastases from the right lung cancer. In 342 patients with disseminated cancer, four of them had confirmed metastases in both adrenal glands; seven patients had a metastatic lesion in the left and three in the right adrenal gland. Among this group, metastases to other organs such as the liver, bones, central nervous system and mediastinal lymph nodes were also detected. The authors came to the conclusion that the higher occurrence rate of adrenal metastases from the left lung carcinoma as compared to the right lung carcinoma is associated with higher blood flow in the left lung.

Key words: Ultrasound, computer tomography, magnetic resonance, fine needle biopsy, lung cancer, metastases to adrenal gland.

1. Introduction

Metastases to organs such as the liver, bones or central nervous system appear to be a frequent complication of malignant lung cancer, whereas metastases to the suprarenal glands are found less frequently [1]. Metastases of lung cancer to the spleen are a great rarity and they are described sporadically [2].

An adrenal gland tumor detected incidentally during imaging tests is described as an incidentaloma [3-7].

In the medical literature, fine needle biopsy performed under ultrasound (US) guidance is considered to be the method of choice in obtaining histopathological diagnosis [8-11].

Having vast experience in performing biopsies, the authors decided to take biopsies of metastatic deposits located in the adrenal glands [12-16]. These deposits were identified on routine computer tomography (CT) scans in patients diagnosed with lung cancer.

There are cases of regional dissemination of malignant cells described in the medical literature [18] as well as some cancers' affinity for metastasizing to certain organs [19]. Therefore, the purpose of our study was to show if there is any correlation between the location of the primary cancer site in the lungs and the location of the lesion in the suprarenal glands.

In our study, the differentiation between malignant and benign tumors (on the basis of imaging tests) was also considered, as such differentiation is of fundamental importance in patients' treatment [8].

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2. Patients and Methods

Our study was conducted from January 2003 to November 2011 with 2,340 patients who had CT and MR scans arranged due to presence of lung tumor. All analyzed patients were diagnosed with lung cancer for the first time. Histopathological diagnoses of the lung tumors were made on the basis of previously conducted investigations during which the specimens were taken either intraoperatively or during flexible bronchoscopy. All patients received treatment in the Oncology Department and Ambulatory in St. Leszczyński Hospital, Katowice. Our project has received approval from the Commission of Ethics and all patients were given detailed information about US-guided biopsy and were consented to the procedure.

CT Siemens Somatom AR.TX, Siemens Somatom Sensation Open (Fig. 1), MR GE 1,5T Signa HD XT (Fig. 2), US Hitach EUB 515 and Logiq C5 (Figs. 3-6), were used to visualize the suprarenal glands. All patients with adrenal gland tumors visualized by the US underwent US-guided biopsy of the lesions (Figs. 7 and 8).

Specimens were taken with 1.2 mm diameter biopsy needles. The criterion for performing an US-guided biopsy of the lesion in the adrenal glands (and, therefore, for including patients in our study) was to detect a lesion greater than 3 cm in diameter using CT or MR. This criterion was established based on the authors' experience that mostly adrenal gland lesions measuring at least 3 cm in diameter can be visualized by US, thereby allowing to perform US-guided biopsy.

In the first group, suspicious lesions in the adrenal glands were detected using CT or MR in 218 of 1,998 patients (Table 1).

In 161 (which meet 3 cm criterion) of the 218 cases included, we were able to visualize the lesions by the US; in 57 cases the lesions were undetectable by US. All 161 patients with lung cancer limited only to one lung (T1, T2, T3, T4) underwent US-guided biopsy of

the adrenal gland lesions (Table 2).

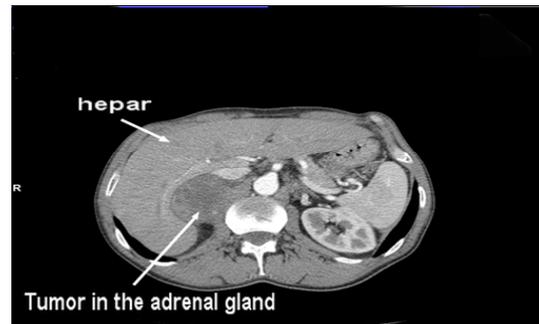


Fig. 1 KT image, tumor in right adrenal gland, metastasis from right lung carcinoma.



Fig. 2 MR image, tumor in left adrenal gland, metastasis from left lung carcinoma.



Fig. 3 US image, tumor in right adrenal gland, metastasis from right lung carcinoma.



Fig. 4 Ultrasound image, right adrenal gland tumor, metastasis from left lung carcinoma.



Fig. 5 US image, enormous right adrenal gland tumor, metastasis from left lung carcinoma.



Fig. 6 Ultrasound image, tumor in left adrenal gland, metastasis from left lung carcinoma.



Fig. 7 US image, biopsy needle in a left adrenal gland tumor, metastasis from left lung carcinoma.

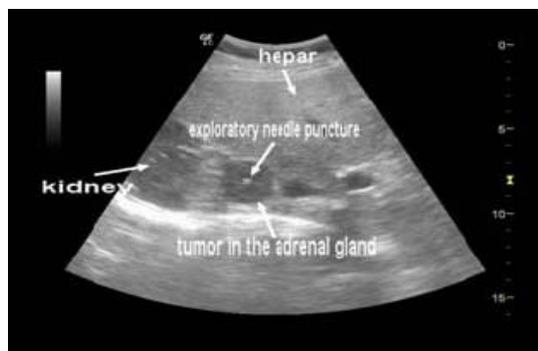


Fig. 8 US image, biopsy needle in a right adrenal gland tumor, metastasis from right lung carcinoma.

All pictures submitted in our manuscript were taken during the study.

In our study group of 2,340 patients, 1,998 were diagnosed with lung cancer (initially classified as located only in one lung: T1, T2, T3, T4), and 342 with disseminated lung cancer (M1a, M1b) metastasizing to the liver, bones, central nervous system and mediastinal lymph nodes in addition to the adrenal glands.

Among the second group of 342 patients with disseminated lung cancer, in 18 cases CT examination confirmed the presence of lesions in the adrenal glands. fourteen of them (which meet 3 cm criterion) were detectable by US and US-guided biopsies were performed (Table 3).

Among this group in four cases metastases were detected in both adrenal glands; in seven cases in the left and in 3 cases in the right adrenal gland (Table 3). In this group, apart from adrenal metastases, in ten cases metastatic deposits were detected in the liver, in two cases in the liver and in the central nervous system, and in two cases in the liver, bones and the mediastinum.

Table 4 shows the location of adrenal gland metastases in patients with lung cancer limited only to one lung (T1, T2, T3, T4) and statistically significant differences (Table 4).

Statistical analysis was performed using Chi-square goodness-of-fit test (χ^2) by Person. Unfortunately, it was only possible to perform PET scans on less than half of the patients and the results we obtained were ambiguous, even in biopsied patients with histopathological confirmation of metastasis in the adrenal gland or in the spleen. Under these circumstances we decided to omit the analysis of the PET scan reports in our study.

3. Results

In 1,998 of the 2,340 analyzed patients with single lung cancer (T1, T2, T3, T4), single and isolated adrenal tumors were detected by US in 161.

Table 1 The number of US-guided biopsies of suprarenal gland tumors (greater than 3 cm in diameter) shown by CT and MR ($n = 236$).

The total number of adrenal glands lesions as shown in CT and MR ($n = 236$)	The total number of adrenal glands lesions detected by US and US-guided biopsy ($n = 175$) (74.15%)
The number of adrenal glands lesions in lung cancers limited to one lung (T1, T2, T3, T4) ($n = 218$)	The number of adrenal gland lesions detected by US and US-guided biopsy ($n = 161$) (73.85%)
The number of adrenal glands lesions in disseminated lung cancer (M1a, M1b) ($n = 18$)	The number of adrenal gland lesions detected by US and US-guided biopsy ($n = 14$) (77.7%)

Table 2 Characteristics of adrenal gland lesions in patients with lung cancer limited only to one lung (T1, T2, T3, T4) ($n = 161$).

Metastases in the adrenal glands (T1, T2, T3, T4)	$N = 91$	Small cell carcinoma $n = 20$ Squamous cell carcinoma or adenocarcinoma $n = 71$
Benign lesions, incidentalomas	$N = 70$	

Table 3 The location of biopsied metastases ($n = 14$) in the adrenal glands in disseminated lung cancer (M1a, M1b). Total number of patients with disseminated lung cancer $n = 342$.

US-guided biopsy of the adrenal gland lesions $n = 14$	Right adrenal gland $n = 3$	$p > 0.05$ (not statistically significant)
	Left adrenal gland $n = 7$	
	Both adrenal glands $n = 4$	

Chi-square goodness-of-fit test (X^2), not statistically significant differences $p > 0.05$

All 161 patients underwent US-guided biopsy of the lesions in the suprarenal glands and the histopathological reporting confirmed the cancerous pattern of the lesions in 91 cases. Benign lesions were found in 70 cases.

The biopsy had to be done twice in 15 cases and 3 times in nine cases in order to obtain clear histopathological results.

The presence of metastases in the adrenal glands (as well as in the liver, bones, mediastinum and central nervous system) was confirmed in 18 out of 342 patients with disseminated lung cancer (M1a, M2a), 14 of them we were detectable by US. In this group, four patients had metastases in both adrenal glands, three in the right and seven in the left adrenal gland.

In our opinion, the relatively small number of cases (14 of 342) with metastatic dissemination to the adrenal glands is most likely the result of limited time for tumor growth in the adrenal glands (due to tumors' rapid progression and dissemination to other parts of the body). There was, therefore, limited time to achieve the minimal size required for us to perform diagnostic biopsies of the lesions.

In addition, the early occurrence of systemic

symptoms and prompt institution of treatment may have affected (decreased) the size and progression rate of the adrenal lesions.

4. Discussion

On the basis of the references, we found in the medical literature and in our own experience, it ought to be noted that cancer metastases, including lung cancer metastasizing to the suprarenal gland, have been well analyzed [1, 9, 10]. Diagnostic methods used to differentiate benign from malignant suprarenal gland tumors can be divided into invasive methods, such as biopsies and surgical procedures [10, 11] and non-invasive, based on imaging techniques [3, 8]. Both methods were described and presented by many authors.

In 218 out of 1,998 patients with single lung cancer, a pathological suprarenal gland structure was found by CT or MR scans. In 161 of them, the adrenal gland lesion was visualized by US (Table 1), and in all 91 patients the cancer pattern was confirmed after a sample was taken from the patient's lesion using US-guided biopsy. Benign lesions were found in 70 cases (Table 2).

It seems interesting to analyze the location of the lesions in the lung in order to compare to the confirmed location of the metastasis in the adrenal gland.

The group of 91 patients with histopathologically confirmed adrenal gland metastases was then analyzed after being divided into two subgroups: in 30 patients metastases originated from right, and in 61 patients from left lung cancer.

In all 30 cases of metastatic right lung cancer, in 11 of them metastases were found in the right adrenal gland, in 17 cases in the left adrenal gland and in two cases metastatic deposits were found in both adrenal glands. It gives the total number of adrenal gland metastases from right lung cancer of 32:13 (11 + 2) which were located in the right and 19 (17 + 2) in the left adrenal gland.

On the other hand, in all 61 cases of metastatic left lung cancer, in 35 of them metastases were detected in the left adrenal gland, in 23 cases in the right adrenal gland and in three cases metastatic deposits were found in both adrenal glands giving the total number of adrenal gland metastases from left lung cancer of 64:38 (35 + 3) in the left and 26 (23 + 3) in the right adrenal gland.

Our study shows that metastases from left lung cancer to the adrenal glands occurred almost two times more often than adrenal gland metastases from right lung cancer (statistically significant differences $p < 0.05$) (Table 4).

No significant statistical difference in the frequency

of metastases occurring in the suprarenal glands was found in relation to the cancer pattern. Analysis of the relationship between the type of cancer and the location of the lesions in the suprarenal glands showed that both squamous cell carcinoma and small cell carcinoma metastasize to the adrenal glands, more or less, with the same frequency (Table 2).

Some authors attribute such possible dissemination to the higher blood flow in the left lung as compared to the right lung [19], which could also explain the higher number of isolated metastases observed from the left lung to the adrenal gland as compared to the number of metastases from the right lung to adrenal gland.

The authors observed no significant statistical difference in the frequency of metastatic occurrence in the right and left adrenal gland in disseminated lung cancer (Table 4). This finding confirms that distribution of metastases in the adrenal glands in cases with single lung tumors is related to the unbalanced blood flow in the lungs.

The two cases of detecting metastases in the liver, bones, adrenal glands and mediastinal lymph nodes suggest the possibility of concurrent dissemination of the lung cancer via both the blood and the lymphatic vasculature.

We noticed that 175 of 232 (75.43%) adrenal gland lesions (greater than 3 cm in diameter) detected by CT or MR scans could be visualized by ultrasonography (Table 1).

Table 4 The location of adrenal gland metastases in patients with lung cancer ($n = 91$) limited only to one lung (T1,T2,T3,T4) Total number of metastases in adrenal gland ($n = 96$).

(a) Number of metastases from right lung $n = 32$	$p < 0.05$ (statistically significant)	(a) Number of metastases in both adrenal glands ($n = 4$) (2 left + 2 right)	$p > 0.05$ (not statistically significant)
		Left adrenal gland ($n = 19$) (17 left + 2 in left from point a. = 19)	
(b) Number of metastases from left lung $n = 64$	$p < 0.05$ (statistically significant)	Right adrenal gland ($n = 13$) (11 right + 2 in right from point a. = 13)	$p > 0.05$ (not statistically significant)
		(b) Number of metastases in both adrenal glands ($n = 6$) (3 left + 3 right)	
		Left adrenal gland ($n = 38$) (35 left + 3 in left from point b. = 38)	
		Right adrenal gland ($n = 26$) (23 right + 3 in right from point b. = 26)	

Chi-square goodness-of-fit test (X^2) a to b (statistically significant difference $p < 0.05$)

Despite the ambiguous explanation of the observed findings, considering the significant practical value of these observations, in our opinion, the obtained results could be incredibly helpful in making decisions regarding patients' treatment.

5. Conclusions

Lung cancer may return in 4.55% of cases as metastasis to the adrenal glands.

In patients with lung cancer and suprarenal gland tumors (greater than 3 cm in diameter) shown by computer tomography, 75.43% can be detected by ultrasound imaging. The specimens can be obtained using US-guided biopsy of the adrenal gland lesions in 100% of affected patients.

Metastases from left lung cancer to the adrenal gland occurred twice more often statistically significant, test of goodness of fit Pearson's (χ^2) than metastases to the adrenal gland from right lung cancer.

In departments which lack invasive diagnostic methods such as fine needle biopsy, this observation could be helpful in both, estimating the character of pathological lesions in the adrenal glands and trying to qualify patients for surgical treatment.

The number of adrenal metastases originating in the right lung (13 were found in the right and 19 in the left adrenal gland) as well as in the left lung (26 were detected in the right and 38 in the left adrenal gland) were analyzed, meaning that not the number of metastasizing lungs but the number of adrenal glands affected by metastases underwent analysis.

It has been proven that metastases found in the adrenal glands originated comparatively more frequently in the left lung than in the right lung.

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