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CLINICAL STUDY

Importance of histological verification of mediastinal lymphadenopathy in exact staging of non-small cell bronchogenic carcinoma

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Abstract: *Background:* Diagnostics and treatment of bronchogenic non-small cell lung carcinoma is a severe clinical problem. Radical surgery is the major treatment modality with the highest chance for a long-time survival. The aim of the study was to map metastasizing of bronchogenic non-small cell lung carcinoma into homolateral mediastinal lymph nodes and to assess the importance of histological verification of mediastinal lymphadenectomy for exact staging and treatment.
Methods: Study of 29 patients with non-small cell lung carcinoma in stage IIIa, IIIb and IV (TNM classification) diagnosed from September 2006 to March 2007, with mediastinal lymph nodes invasion according to CT, and with subsequent mediastinal lymph node dissection during autopsy.
Results: 50% of the right upper lobe tumors metastasized into group 1 nodes (N1–N4) and 50% into group 3 (N7). 66% of the right lower lobe tumors metastasized into group 3 nodes (N7) and 33.3% into group 1 (N1-4). 20.0% of the left upper lobe tumors metastasized into group 1 nodes (N1-4), 33.0% into group 2 (N5-6), 25.0% into group 3 (N7) and 16.7% into group 4 (N8-9). 23.5% of the left lower lobe tumors metastasized into group 1 nodes (N1-4), 23.5% into group 2 (N5-6), 23.5 % into group 4 (N8-9) and 29.5% into group 3 (N7). 27.6% of examined patients had false positivity of lymph node metastasis according to CT.
Conclusion: Histological verification of suspect mediastinal lymph nodes via Endobronchial Ultrasound Biopsy (EBUS) or mediastinoscopy or thoracoscopy is crucial for determining the stage of the disease according to the TNM classification. False positivity of imaging methods in diagnostics of non-small cell brochogenic carcinoma can contraindicate up to quarter of potentially operable patients *(Tab. 3, Ref. 11)*. Text in PDF www.elis.sk.
Key words: mediastinal lymphadenopathy, bronchogenic carcinoma, lung cancer.

Lung cancer is one of the most frequent malignant tumors (1). 82 606 cases of malignancies were reported in the Czech Republic's National Oncological Register in 2010, that was 4 % increase compared to 2009. 27 834 patients died in the consequence of malignant diseases (0.6 % increase). The most common tumors in 2010 were colorectal carcinoma, lung cancer, breast malignancies in women and prostate carcinoma in men.

6532 cases of malignant neoplasmas of trachea, bronchus and lung were reported in the Czech Republic in 2010, that was 1.5 % increase compared to 2009. 4641 of newly diagnosed were men (incidence 89.9/100 000). Women incidence was 35.3/100 000 (1891 new cases). Men incidence has decreased and stagnated over the incidence in women for a long period in the Czech Republic. Lung cancer remains the most frequent cause of death of malignancy in men in Czech Republic. The half of cases were discovered in the clinical stage IV (2).

228 190 cases of new lung malignancies were reported in the United States in 2010, that was 13.7 % newly diagnosed malignant tumors. 159 480 patients died (27.5 % of all cause of death of malignancy). Relative incidence was 75.2/100 000 persons in men, 52.3/100 000 persons in women and in total 63.5/100 000 persons. US National Cancer Institute describes differences in Caucasians, Afroamericans, Asiatics, Indians and Latinos.

Specific mortality in the United States in 2010 was 63.5/100 000 persons in men and 39.2/100 000 persons in women and in total 51.35/100 000 persons. 56 % new cases were discovered in the clinical stage IV and their 5-year survival was 3.9 %. 15 % of the patients were diagnosed in stage I and their 5-year survival was 53.5 %. In 22 % of cases were detected metastastases in mediastinal lymph nodes and 5-year survival was 26.1 % (3).

The aim of this prospective study was to map metastasizing of bronchogenic non-small cell lung carcinoma into homolateral mediastinal lymph nodes and to assess the importance of histo-

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logical verification of mediastinal lymphadenectomy for exact staging and treatment.

Methods

We included into the study patients with non-small cell lung carcinoma diagnosed in the Department of Respiratory Medicine of the Thomayer´s Hospital, Prague, from September 2006 to March 2007. Inclusion criteria were the following: patients with stage IIIa, IIIb and IV (TNM classification) with mediastinal lymph nodes invasion according to CT, and died of generalization or due to terminal complication during generalization, and with mediastinal lymph node dissection during autopsy (all zones 1–4, lymph nodes No. 1–9 according TNM classification vol. 7).

Results

There were in total 29 patients, 21 men (72.4 %) with average age 71.8 years (50–85 years) and 8 women (27.6 %) with average age 63.5 years (47–83 years).

Malignancy in family history was reported in 9 cases (24.1 %) and bronchogenic carcinoma was reported in 3 cases.

In personal history was malignancy reported in 4 cases (13.8 %), and one patient underwent surgery and adjuvant chemotherapy for bronchogenic carcinoma.

The most frequent comorbidity was arterial hypertension (45.2 %) followed by ischemic heart disease and chronic obstructive pulmonary disease (62.1 %) and diabetes mellitus (31.0 %).

There were 25 smokers (86.2 %), who had smoked in average 38.8 years (20 to 63 years) and had smoked in average 250 591 cigarettes (56 575–536 550). 12 patients quit smoking (25.8 %) and the mean non-smoking time was 3.0 years (2–25 years).

The most frequent tumor localization was the upper right lobe (URL) – 9 cases, 15 patients had tumor in the left lung, 8 cases in the lower lobe (LLL) and 7 cases in the upper lobe (LUL). The mean tumor size was 63.8 mm.

In the time of diagnosis were mediastinal lymph node metastases detected in 21 patients (69,0%) according to CT, 82.2 % hilar lymph nodes N1 were affected, 72.4 % N2 and 31.0 % N3.

Bronchoscopy showed pathological findings in 25 patients (86.2 %): 16 stenosis of subsegmental bronchial tube, 4 granulations, in 5 cases inflammatory changes. Only in 2 patients (7 %) cytological examination didn't raised suspicion of non-small cell lung carcinoma.

Histopathological examination confirmed 5 types of the lung carcinoma (Tab.1).

In total 755 mediastinal lymph nodes were dissected, in average 26 nodes per patient. Metastases were detected in 264 lymph nodes, representing 35.0 % of all collected nodes. The mean value of the affected lymph nodes was 9.1 lymph nodes with metastases per patient.

In case of the lymph node positivity, all lymph nodes in the appropriate stage were affected. In case of the lymph node negativity, all the lymph nodes in the appropriate stage were without metastasis.

Tab. 1. Histopathological finding.

Type	No.	%
Squamous cell carcinoma	15	51.7
Adenocarcinoma	7	24.1
Bronchioalveolar carcinoma	1	3.5
Anaplastic carcinoma	4	13.8
Large cell carcinoma	2	7.0

Tab. 2. Comparison of CT and autopsy findings of mediastinal lymph nodes.

CT/ autopsy	%
conformity	62.1
CT false negative finding	10.3
CT false positive finding	27.6

Tab. 3. Cause of death.

The cause	No.	%
Generalization	11	37.9
Pneumonia	14	48.3
Pulmonary embolism	1	3.4
Acute pancreatitis	1	3.4
stroke	2	7.0

Tumors of the right upper lobe metastasized in 50.0 % into group 1 nodes (stages N1–N4) and in 50.0 % into group 3 nodes (stage N7).

There were no metastasis of the tumors of the right middle lobe.

Tumors of the right lower lobe metastasized in 66.7 % into group 3 (stage N7) and in 33.3% group 1 nodes (stages N1–N4).

In tumors of the left upper lobe were metastases detected in 20.0 % in group 1 nodes (stages N1–N4), in 33.0 % into group 2 nodes (stages N5–N6), in 25.0 % into group 3 nodes (stage N7) and in 16.7 % into group 4 nodes (stages N8–N9).

Tumors of the left lower lobe metastasized in 23.5 % into group 1 nodes (stages N1–N4), 23.5 % into group 2 nodes (stage N5–N6), 23.5 % into group 4 nodes (stage N8–N9) and 29.5 % into group 3 nodes (stage N7).

More than 1/4 of examined patients had false positivity of lymph node metastasis according to CT (Tab. 2). 10 patients underwent chemotherapy. These patients were treated by combination of cisplatin and navelbine. All the patients suffered from minor side effects of chemotherapy. 5 patients died of generalization or due to terminal complication during chemotherapy.

8 patients were treated by actinotherapy. All the patients suffered from minor side effects of actinotherapy. 3 patients died of generalization or due to terminal complication during actinotherapy. 5 patients had adjuvant chemoradiotherapy.

All the patients died during 12–1644 days. The average survival was 221.7 days. The most frequent cause of death was generalization of the disease or bronchopneumonia (Tab.3).

Discussion

There were in total diagnosed 29 patients with non-small cell lung carcinoma in stage IIIb and IV (TNM classification) with

mediastinal lymph nodes invasion, who died of generalization or due to terminal complication during generalization.

In total 755 mediastinal lymph nodes were dissected, in average 26 nodes per patient. In 264 lymph nodes were detected metastases, representing 35.0 % of all collected nodes. The mean value of the affected lymph nodes was 9.1 lymph nodes with metastases per patient.

Relatively a high number of mediastinal lymph nodes affection was caused by late stage of the disease (stage IIIb and IV). In case of one lymph node positivity in an appropriate stage were affected all the lymph nodes in the appropriate stage. In case of the lymph node negativity were all the lymph nodes in the appropriate stage without metastasis.

Determining the extent of the lung cancer is essential for setting of the adequate therapy. Similar to other malignancies, we used the TNM classification vol.7.

The aim of the diagnostics is to determine the histological classification of tumor (typing), malignity degree (grading), the extent of the malignant process (staging) and the performance status with comorbidities (6).

Diagnostics is based on the imaging methods, bronchoscopic examination, cytological and histological examination (7).

In 21 patients (69.0 %) were mediastinal lymph node metastasis detected at the time of diagnosis. According to CT were affected 82.2 % hilar lymph nodes N1, 72.4 % homolateral N2 and 31.0 % contralateral N3 lymph nodes.

4 patients (13.8 %) were classified in the stage IIIa, 4 patients (17,2%) in the stage IIIb and 20 patients (69.0 %) in the stage IV.

Comparison of CT findings and the results of dissected mediastinal lymph nodes in the autopsy showed confirmation in 62.1 %, CT false negative finding was in 10.3 % and CT false positive finding was 27.6 %. Only 2/3 correctness of CT examination was caused of advanced stages of the disease with many mainly respiratory complications. Described enlarged false positive lymph nodes were caused mainly of pneumonitis behind tumor obstruction with inflammatory lymph nodes reaction.

27.6 % of examined patients had false positivity of lymph node metastasis according to CT. CT false positivity in diagnostics of lung malignancies can contraindicate up to 1/4 of potentially resectable patients, therefore histological verification of suspect mediastinal lymph nodes via EBUS (Endobronchial Ultrasound Biopsy) or mediastinoscopy or thoracoscopy is requisite (8).

Conclusion

Imaging methods false positivity in diagnostics of non-small cell brochogenic carcinoma, can contraindicate up to quarter of potentially operable patients.

Histological verification of suspect mediastinal lymph nodes via Endobronchial Ultrasound Biopsy (EBUS) or mediastinoscopy or thoracoscopy is crucial for determining the stage of the disease according to the TNM classification.

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