

ATYPICAL NON-SMALL CELL LUNG CANCER PRESENTATION: INGUINAL LYMPH NODE METASTASES AS THE FIRST SIGN OF DISEASE RELAPSE

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SUMMARY – A case is presented of a 67-year-old male patient with atypical non-small cell lung cancer, where inguinal lymph node metastases were the first sign of disease relapse. The patient had a long-term smoking history of 30 cigarettes *per* day, with no other important personal or family medical history data. Because of prolonged cough, the patient underwent diagnostic procedure, which revealed squamous cell carcinoma of the lung (stage IIIB, T3N2M0). Concomitant radio-chemotherapy and consolidation chemotherapy according to PE protocol was administered. Multi-slice computed tomography performed upon chemotherapy completion showed almost complete tumor regression and withdrawal of mediastinal lymph node enlargement, and the patient felt well. However, in the next few months, enlarged lymph nodes appeared in both inguinal regions. Histopathologic analysis revealed metastatic lung cancer. Four months after the presentation of enlarged inguinal lymph nodes, lung cancer metastases were also diagnosed in the liver and lumbosacral spine. Despite additional treatments, the patient died four months later. Although it is well known that inguinal lymph nodes can harbor lung cancer metastases, in our patient inguinal lymph node metastases were the first sign of lung cancer relapse.

Key words: *Lung neoplasms – pathology; Carcinoma, non-small-cell lung – secondary; Carcinoma, non-small-cell lung – complications; Neoplasm staging; Lymphatic metastasis; Disease progression; Case report*

Introduction

Lung cancer, the most common cause of cancer-related death in men and women, is responsible for 1.3 million deaths worldwide annually¹. The most common symptoms are shortness of breath, coughing, hemoptysis and weight loss. Only 30% of these carcinomas are diagnosed in surgically treatable stage, usually presenting with long lasting cough and hemoptysis. The vast

majority of primary lung cancers are carcinomas of the lung, derived from epithelial cells. The main types of lung cancer are small cell lung carcinoma (SCLC) and non-small cell lung carcinoma (NSCLC). This distinction is important because the treatment varies; NSCLC is sometimes treated with surgery, while SCLC usually responds better to chemotherapy and irradiation². The most common cause of lung cancer is long-term exposure to tobacco smoke. More often, NSCLC presents in advanced stage, where surgical treatment is not recommended and oncologic therapy is the treatment of choice. It is well known that NSCLC usually spreads into mediastinal lymph nodes, liver, brain and adrenals². Metastasizing of NSCLC to other parts of the body is very rare, while metastases in inguinal lymph nodes,

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Fig. 1. Multi-slice computed tomography of the chest showing tumor in the right lung.

at the same time being the first sign of disease relapse, present an exceptional situation. Lung cancer may be seen on chest radiograph and multi-slice computed tomography (MSCT). The diagnosis is confirmed by biopsy. It is usually performed by bronchoscopy or CT-guided biopsy. Our 67-year-old male patient is described as an atypical NSCLC presentation, where metastases to inguinal lymph nodes were the first sign of disease relapse.

Case Report

A 67-year-old man presented to his general practitioner because of cough lasting for four months. The patient had a long lasting smoking history of 30 cigarettes *per day*, with no other important personal

or family medical history data. On physical examination, the patient appeared fatigued. No rash or lymphadenopathy was detected. Chest x-ray performed at the time revealed no pathologic finding. Since the patient's health worsened and the symptoms progressed, two months later a new chest x-ray was performed to reveal inhomogeneous opacity in the right perihilar region. MSCT of the chest showed a tumor in the right lung lobe, measuring 5.5 cm in diameter (Fig. 1). There was also an enlarged (13 mm) mediastinal lymph node, with a very small amount of cytologically verified malignant pleural effusion. Fiberoptic bronchoscopy showed stricture in the right lower main bronchus with a tumor in its distal part. Bronchoscopic biopsy revealed the presence of abnormal histology (NSCLC, squamous cell carcinoma) (Fig. 2). The patient's performance status was 90% according to Karnofsky score (capable of normal activity, few symptoms or signs of disease). With the diagnosis of a locally advanced NSCLC (stage IIIB, T3N2M0), the patient was treated with radiotherapy (6000 cGy in 30 fractions) and 4 cycles of chemotherapy with 75mg/m² of cisplatin (Cisplatin Pliva, Pliva, Croatia). Upon completion of concomitant radio-chemotherapy, the patient was treated with additional consolidation chemotherapy following the PE protocol. The PE chemotherapy protocol consisted of 60 mg/m² of i.v. cisplatin (Cisplatin Pliva, Pliva, Croatia) on day 1 and 120 mg/m² of oral etoposide (Vepesid, Bristol-Myers Squibb, Australia) on days 1-3. This regimen was repeated every 21 days for four cycles. Chest MSCT performed after chemotherapy showed almost complete tumor re-

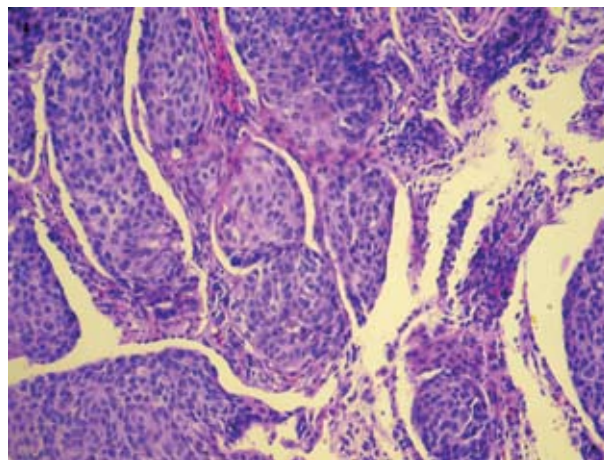
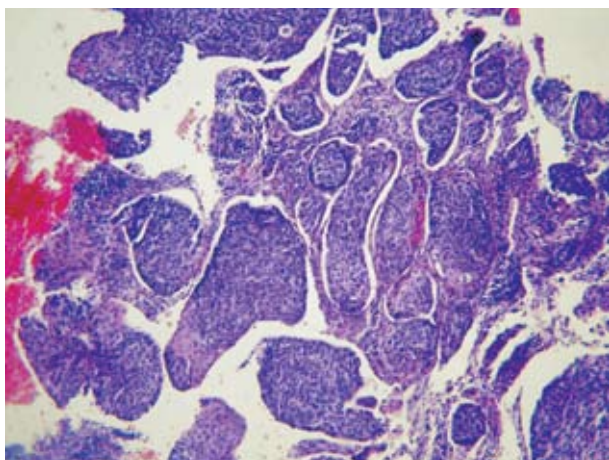


Fig. 2. Lung biopsy: squamous cell carcinoma; (A) H&E, X100; (B) H&E, X200.

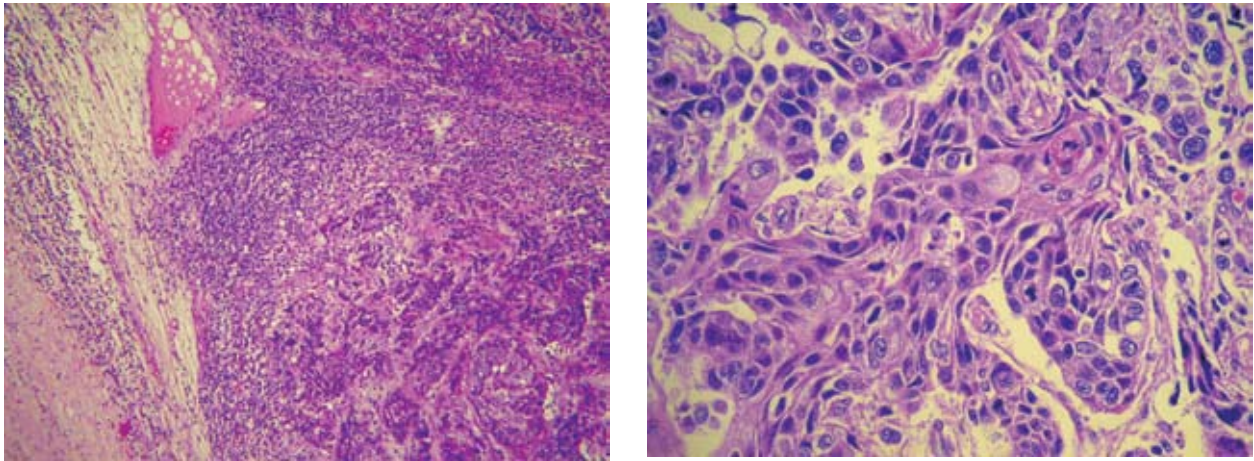


Fig. 3. Lymph node biopsy: metastatic lung cancer; (A) H&E, X100; (B) H&E, X400.

gression (measuring 0.6 cm in diameter) and complete withdrawal of enlarged mediastinal lymph nodes. The patient felt very well, with no other symptoms or signs of the disease. In the next few months, enlarged semi-mobile lymph nodes measuring 2x1 cm and 3x2 cm appeared in both inguinal regions. Because the inguinal region is an unusual location for metastasis from lung carcinoma, the patient was not suspected to have developed metastatic disease. Tumor markers were all within the normal range. Surgical extirpation of the lesion was performed for differential diagnosis. Histopathologic examination of the lymph node revealed a metastatic low-grade squamous lung carcinoma (Fig. 3). On immunohistochemistry, tumor cells were positive for high weight keratin, cytokeratin 5 (CK5) and cytokeratin 7 (CK7). Cytokeratin 20 (CK20), CEA, LCA, HMB45, PSA, chromogranin and synaptophysin were all negative. Therefore, thorough work-up was performed including x-ray of the lumbosacral spine and pelvis, brain, chest and abdominal MSCT, analysis of different tumor markers (CEA, CA 19.9, CA 72.4 and PSA), cystoscopy and colonoscopy. This work-up revealed no other primary tumor, and lung cancer metastases were also found in the liver and lumbosacral spine. Despite additional treatments, the patient died four months later.

Discussion

Primary solid malignant tumors of inguinal region are very rare^{3,4}. Just opposite to primary tumors, meta-

static tumors frequently involve either inguinal lymph nodes or spermatic duct, and they are most commonly of gastrointestinal or urologic origin³.

Metastases of lung cancer usually occur in the liver, brain, bones, kidneys and adrenals, however, metastases of lung cancer to the spleen, skin, lungs and spermatic duct are also described. Extrathoracic nodal metastasis is a rare clinical finding in patients with NSCLC⁵. Therefore, the first signs of malignant lung disease relapse usually are related to these organs. It is well known that inguinal lymph nodes can harbor lung cancer metastases, and we describe a case where inguinal lymph node metastases were also the first sign of lung cancer relapse. Rare cases of inguinal metastases from tumors above the diaphragm have been reported, only three of them with inguinal metastasis recognized antemortem. In these cases, primary tumors were malignant mesothelioma, salivary duct carcinoma and breast carcinoma⁵. Kocak *et al.* report a case of lung carcinoma metastatic to inguinal lymph node as the only evidence of progressive lung cancer⁵.

Blood-borne, lymph-borne and *per continuitatem* metastases are the types of lung cancer metastasizing, especially in cases of T2 tumors². Inguinal lymph nodes and spermatic duct metastases are the examples of blood-borne and lymph-borne lung cancer metastases^{6,7}. However, lymph-borne or blood-borne metastases in inguinal region are parameters of advanced disease (stage IV) and poor prognosis. The five-year survival rate for stage IV lung cancer is only 5% regardless of radiotherapy or chemotherapy received^{8,9}.

Surgical treatment is not appropriate for advanced NSCLC, but it remains a cornerstone of radical treatment for IIIA and lower stage NSCLC¹⁰.

In conclusion, although extremely rare, metastatic disease to the inguinal region in patients with a history of lung cancer should be considered on differential diagnosis of any lesion in the groin. Thorough pulmonologic work-up is mandatory in such cases, although metastatically enlarged inguinal lymph nodes are more commonly due to gastrointestinal or urologic malignancies.

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Sažetak

ATIPIČNA MANIFESTACIJA NEMIKROCELULARNOG KARCINOMA PLUĆA: METASTAZE U INGVINALNE LIMFNE ČVOROVE KAO PRVI ZNAK RECIDIVA BOLESTI

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Prikazuje se slučaj 67-godišnjeg bolesnika s neuobičajenim razvojem kliničke slike planocelularnog karcinoma pluća, kod kojeg su metastaze u preponskim limfnim čvorovima bile prvi znak recidiva bolesti. Dugogodišnji je pušač koji puši oko 30 cigareta na dan, a osobna i obiteljska anamneza su bez osobitosti. Zbog dugotrajnog kašlja učinjena mu je dijagnostička obrada koja je pokazala da se radi o planocelularnom karcinom pluća (stadij IIIB, T3N2MO). S obzirom na stadij proširenosti tumora ordinirano je provođenje konkomitantne radio-kemoterapije i konsolidacijske kemoterapije, prema protokolu PE. Iako je kontrolna kompjutorizirana tomografija pokazala gotovo potpunu regresiju tumora i iako se bolesnik osjećao značajno bolje, nekoliko mjeseci nakon provedene konsolidacijske kemoterapije pojavili su se povećani limfni čvorovi u obje preponske regije, patohistološka analiza kojih je pokazala metastatski planocelularni karcinom pluća. Četiri mjeseca nakon pojave metastaza u preponskim limfnim čvorovima dijagnosticirane su metastaze u jetri i lumbosakralnoj kralježnici. Unatoč provedenoj terapiji bolesnik je preminuo. Iako je poznato da preponski limfni čvorovi mogu biti sjelo metastatskog karcinoma pluća, ovdje se opisuje slučaj gdje su povećani preponski limfni čvorovi bili prvi znak recidiva bolesti.

Ključne riječi: *Plućne novotvorine – patologija; Karcinom, ne-malih plućnih stanica – sekundarni; Karcinom, ne-malih plućnih stanica – komplikacije; Stadiji novotvorine; Limfatična metastaza; Napredovanje bolesti; Prikaz slučaja*