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Professional paper

Metastases to Rare Locations as the Initial Manifestation of Non-Small Cell Lung Cancer: Two Case Reports

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A B S T R A C T

Non-small cell lung cancer is the most common type of lung cancer (about 80% of all lung cancers). It grows and spreads more slowly than small cell lung cancer, but still, when the primary tumour treatment starts, about 60% of patients with cancer already have some kind of malignant cell spreading. Metastases to hand bones and skeletal muscles are very rare (metastatic hand lesions represent 0.1% of all osseous metastases while metastases to muscles represent from 0.8 to 16% incidence in autopsy series); in case of metastases in such sites it can be usually expected to find metastases disseminated all over the body. Fine needle aspiration cytology has an important role to give accurate diagnosis or at least diagnosis of suspicion and thus to set the guidelines to a clinician for the further specific and cost-effective treatment. We will show two cases where the metastases of non-small cell lung carcinoma were the first signs of the disease located in uncommon body parts: a man with the metastasis to distal phalanx of the right thumb and a woman with nodal metastasis to the right gluteal muscle and subcutaneous tissue near muscle which show us that we have to pay our attention to the potential development of such lesions even on rare locations and even when there are no other symptoms. In both cases, patients did not have any other symptoms related to the lung cancer.

Key words: *metastasis, non-small cell lung cancer, fine needle aspiration cytology (FNAC)*

Introduction

Non-small cell lung cancers belong to a group of malignant epithelial tumours, usually characteristic for their fast growth and quick spreading to other organs (adenocarcinoma and large cell carcinoma) but sometimes for their perfidious and slow growth and later spreading (squamous cell carcinoma). This is the most common cancer in the men population and the most common cause of lung cancer is long-term exposure to tobacco smoke[1]. But the majority of tobacco users do not develop such tumors and at least 10–15% of lung carcinomas occur in non smokers[2]. In these people, reason could be environmental risk factors such as radon gas, second hand smoking and exposure to carcinogens such as asbestos, radiation, arsenic, chromates, nickel etc[1]. Some studies suggested that viruses like HPV may play an etiologic role in bronchial carcinogenesis[2]. Often, the first signs of the disease are persistent cough, breathlessness, pain in chest, blood in phlegm, and harshness but, in a smaller number of patients (about 10%[3]), these symptoms may not appear and, sometimes but very rarely, the first sign of the disease can be revealed by the appearance of near or distant metastasis. Approximately 60% of the patients with this type of cancer have microscopic or clinically evident metastasis at the time of primary tumour treatment[4]. In case of the local spreading, intrathoracic sites include mediastinal lymph nodes, pleura, diaphragm, chest wall and pericardium, whereas the most common extrathoracic sites include adrenal gland, big bones, brain and liver[5]. In the advanced disease stages, lung cancer metastases can be found practically in every part of the body. Metastases of lung carcinoma can be discovered by the image techniques such as ultrasound, radiography, CT, MRI or PET and they are confirmed by the fine needle aspiration or core and open biopsy and then analysed cytologically or pathohistologically. Very uncommon sites of lung cancer metastases refer to muscles and small

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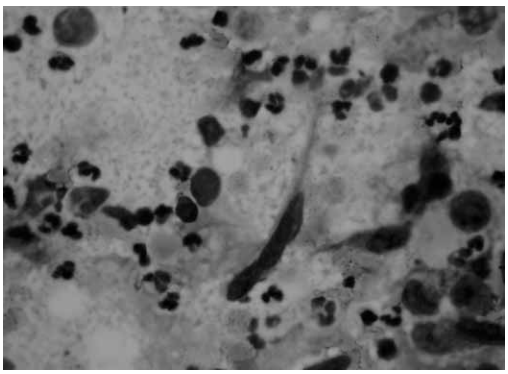
hand and feet bones as in our two reported patients; these sites almost always indicate an extended metastatic disease with poor prognosis.

Case Report No. 1

This was a 63-year-old woman who felt a palpable mass in her right gluteal region. The ultrasound scan showed hypoechoic irregular mass 3x2.5 cm in size with semi-liquid and hyperechoic parts, partly involving muscular and subcutaneous tissue. All the tumour markers were normal except elevated Ca 125 (98.6 U/ml). Fine needle aspiration biopsy was done and cytological diagnosis was as follows: metastasis of squamous cell carcinoma (Figure 1 and 2). It was thought that the carcinoma originated from the gynaecological system, probably uterus, because of the increased Ca 125 level. However, the gynaecologist found normal findings, and PAP smear was also normal. Just one and a half week later, patient started to complain on the pain in the left arm and the left hip. The scintigraphy of bones showed an increased accumulation of activity in the lower lumbar segment of spine and the wing of the left iliac bone. The radiological finding of X-rayed left shoulder referred to an osteolytic lesion (2 cm) with malignant characteristics at the proximal diaphysis of humerus. The patient went to another clinical centre for further examinations. During bronchoscopy, the biopsy of tumour tissue was made. Pathohistological diagnosis was non-small cell lung carcinoma. A month later, she had a pathological fracture of humerus and the pathohistological diagnosis on surgical bone biopsy was the following: probably metastasis of lung adenocarcinoma. Finally, we may presume that it was a mixed type of carcinoma (non-small cell lung cancer). The patient died three months and a few days after the initial diagnosis had been made.

Case Report No. 2

This was a 68-year-old man who was under pulmologists' control because of lung fibrosis and emphysema. He had a trauma of right hand thumb. X-rays showed a multi-fragmental fracture of thumb distal phalanx with osteolysis. Fine needle aspiration (FNA) was performed and the cytologist found mostly poorly differentiated malignant cells in the smear (Figure 3). The X-ray of the lung showed circular nodal mass, 5 cm in diameter, in the right infraclavicular and paratracheal region. The thumb was surgically removed. The pathohistological finding was: probably metastatic adenocarcinoma; immunohistochemistry in other hospital was well-matched with the diagnosis. The ultrasound scan found enlarged cervical lymph nodes and fine needle aspiration



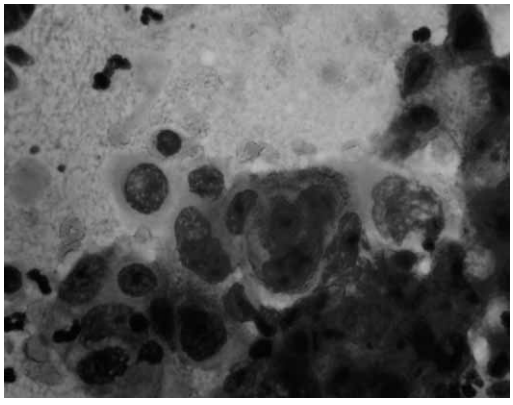


Fig. 1 and 2. FNAB shows malignant cells of squamous cell carcinoma from the gluteal metastasis (MGG stain x1000).

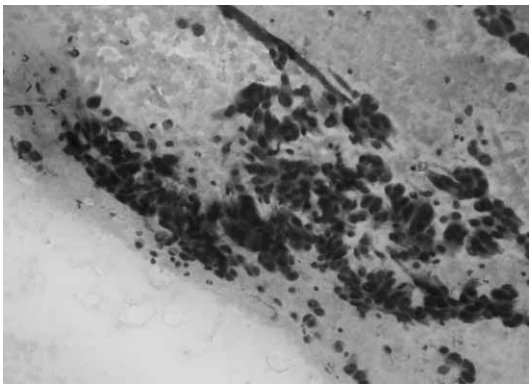


Fig. 3. FNAB of the thumb distal phalanx shows mostly poorly differentiated malignant cells (MGG stain x400).

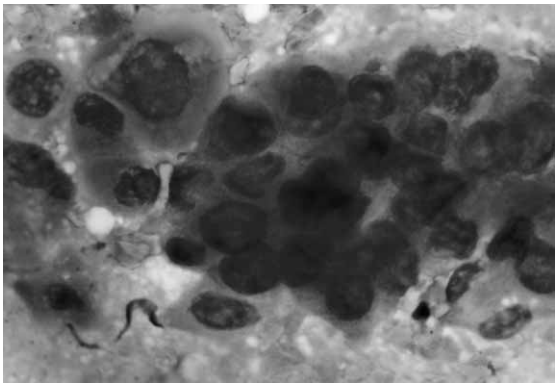


Fig. 4. Smears from bronchoscopy shows moderately differentiated malignant squamous cells (MGG stain x1000).

cytology showed non-small cell carcinoma metastasized to lymph node. It was intriguing; the patient began feeling pain in his left big toe. X-rays showed again an osteolytic focus in the head of proximal phalanx of the left big toe but it was no longer examined and it was presumed that it referred to cancer metastases, too. Bronchoscopy found enlarged carina and the right main bronchus. The cytological brushing was done and the diagnosis was moderately differentiated squamous cell carcinoma of the lung (Figure 4). The patient was exposed to chemotherapy but there was no success, though. Metastases started developing in inguinal lymph nodes, in the abdominal wall and liver. Finally, all the right lung was infiltrated with carcinoma (lymphangitis carcinomatosa), which was proved by X-rays. Because of the differences between cytological and pathohistological diagnoses in this case, we can assume that this cancer was made of mixed subtypes, as well. The patient died three and a half months after the diagnosis had been made.

Discussion

It is uncommon to see the metastases of bronchogenic carcinoma to the bones distal to the elbow and knee[6]. Metastatic lesions to the hand are very rare and comprise 0.1% of all osseous metastases[7]. The most common site of metastatic deposits to the hand is the distal phalanx[8]. The incidence of metastasis to the hand is to the metacarpals 17%, phalanges 66% and carpal bones 17%[9]. The lung is the most common source (42%), followed by the breast and the kidney each of which account for 11%[8–10]. Other sources are colon, prostate, stomach, liver and rectum[8]. Men are more involved than women, even double[8,11]. Metastases in the hand are the first clinical sign of an undiagnosed tumour in only 16% of all metastases[11]. Tumour deposits occur mainly in hematopoetically active bones and multiply to produce a typical lytic lesion or, occasionally, formation of reactive bone[12]. The infrequent development of metastases to the hand may be related to the smaller amount of red marrow in these bones[6]. The recent trauma with increased blood flow onto this site can become a nidus for tumor cells[7,10]. The clinical sign refers to a swollen, painful, reddish part of the hand[11,12]. X-rays show the bone lytic zone lesion[6]. The prognosis for these patients is poor with the median survival of six months[8,11]. The treatment is a combination of radiotherapy and chemotherapy but amputation must be considered for metastasis at the distal phalanx[6]. Skeletal muscle metastases are also rare (0.8 to 16% incidence in autopsy series)[13]. The reason is not well clarified but can be influenced by the turbulent blood flow, β--adrenergic stimulation, tissue oxygen levels and host immune responses as protective mechanisms to skeletal muscle against tumour metastases[5] maybe including even the effect of lactic acid on tumour cell production[14]. Most case reports of muscle metastases report death within 1 year. Generally, metastatic lung cancer has only 7.5% five-year survival[15].

Conclusion

Lung cancer is still a big public health problem because of its late detection in the majority of cases. Even if the metastases of non-small cell carcinoma of the lung are rare in muscles and hand bones, it is important to have them in mind as much as possible. Metastases in these sites usually indicate an extended metastatic disease and usually have a poor prognosis. After the lesion is found by radiological image techniques, cytology plays a great role defining an accurate diagnosis quickly or at least suggesting the diagnosis and thus enables a specific and cost-effective treatment. Better cytological results are achieved when metastatic tumour cells are not poor differentiated. It is important to have a good cooperation between pulmologists, radiologists, cytologists, pathologists, oncologists and surgeons to avoid an over-treatment for the disease with already poor prognosis. Fine needle aspiration cytology in combination with cytochemistry and immunocytochemistry, which increase specific quality is one of the best approaches to establish a correct primary diagnosis and set the guidelines to a clinician for further treatment. Identifying and effectively treating these metastases in a timely manner sometimes can lead to the improvement in quality regarding the next period of patient's life.

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METASTAZE NA RIJETKIM LOKALIZACIJAMA KAO PRVE MANIFESTACIJE PLUĆNOG KARCINOMA NE-MALIH STANICA: PRIKAZ DVA SLUČAJA

S A Ž E T A K

Karcinom pluća ne-malih stanica je najčešći tip karcinoma pluća (oko 80% svih karcinoma pluća). Raste i širi se sporije nego karcinom pluća malih stanica, ali ipak u trenutku početka terapije oko 60% pacijenata već ima metastaze. Metastaziranje u kosti šake ili skeletne mišiće vrlo je rijetko (metastatske lezije u šake predstavljaju 0,1% svih metastaza u kosti, a metastaze u mišiće predstavljaju se incidencijom od 0,8% do 16% na obdukcijskim serijama), i u slučaju metastaza na takvim sijelima može se obično očekivati naći metastaze diseminirane po cijelom tijelu. Citološka punkcija tankom iglom ima važan zadatak dati točnu dijagnozu ili barem sumnju na određenu dijagnozu i na taj način usmjeriti kliničara na daljnju specifičnu i novčano isplativu terapiju. Prikazat ćemo 2 slučaja u kojem su metastaze karcinoma pluća ne-malih stanica bile prva manifestacija bolesti na rijetkoj lokalizaciji u tijelu: muškarac s metastazom u distalnoj falangi palca desne šake te žena s nodalnom metastazom u desnom glutealnom mišiću i potkožju uz mišić što nas upućuje da moramo obratiti pozornost na mogućnost razvitka ovakvih lezija na rijetkim lokalizacijama čak i kad nema drugih simptoma. U oba slučaja pacijenti nisu imali bilo kakve druge simptome pridružene karcinomu pluća.