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Synchronous two distinct neuroendocrine lung cancer lesions

Dwa synchroniczne neuroendokrynne nowotwory płuca

The authors declare no financial disclosure

Abstract

The synchronous primary lung tumors is a rare condition and presented patient is the first reported case of simultaneous two distinct neuroendocrine lung cancer lesions in the same lobe. We present the case of a 55-year-old woman with synchronous two distinct neuroendocrine lung cancer lesions in the right upper lobe. Initially she showed no signs or symptoms related to lung lesions and was admitted to Thoracic Surgery Ward for the investigation of two oval, solitary pulmonary nodules (11 and 19 mm in diameter) detected on a chest X-ray performed three months earlier. The radiological imaging showed a variability of growth of both lesions (smaller tumor has enlarged while the larger one remained unchanged). After the CT-guided lung biopsy, patient underwent right upper lobectomy. Histological examination revealed a small cell carcinoma in one of the tumors and a large cell neuroendocrine carcinoma in the other one. The patient was discharged in good condition and lung inflation in chest X-ray and qualified for adjuvant chemotherapy with a combination of cisplatin and etoposide and the prophylactic cranial irradiation. Very important issues, having impact on outcome of patients with multiple lung tumours is differentiation whether the lesions are metastases or synchronous primary lung tumors and the optimal management of these patients.

Key words: synchronous primary lung cancer, large cell neuroendocrine carcinoma, small cell carcinoma

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Streszczenie

Synchroniczne nowotwory płuc są rzadką chorobą, a prezentowany przypadek to pierwszy opublikowany opis jednoczesnego wystąpienia dwóch pierwotnych neuroendokrynnych raków płuca zlokalizowanych w jednym płacie. Przedstawiono przypadek 55-letniej pacjentki z dwoma pierwotnymi, odrębnymi neuroendokrynnymi rakami płata górnego płuca prawego. Pacjentka została przyjęta na oddział chirurgii klatki piersiowej w celu diagnostyki dwóch cieni okrągłych płuca prawego (o średnicy 11 i 19 mm) uwidocznionych na zdjęciu RTG klatki piersiowej wykonanym trzy miesiące wcześniej. Przy przyjęciu pacjentka nie prezentowała żadnych objawów związanych ze zmianami w płucu. Dalsze badania obrazowe wykazały zmienność wzrostu obu zmian (mniejszy guz uległ powiększeniu, natomiast średnica większego pozostała bez zmian). Po dalszej diagnostyce obejmującej biopsję płuca pod kontrolą tomografii komputerowej, pacjentkę poddano operacji usunięcia płata górnego płuca prawego. Wynik badania histopatologicznego usuniętej tkanki płucnej wykazał, że jeden z guzów jest rakiem drobnokomórkowym, drugi natomiast wielkokomórkowym rakiem neuroendokrynnym. Po kontrolnym zdjęciu RTG klatki piersiowej, które wykazało pełne upowietrznienie obu płuc, pacjentka została wypisana do domu w stanie ogólnym dobrym. Pacjentkę zakwalifikowano do adjuwantowej chemioterapii z zastosowaniem cisplatyny oraz etopozydu, a także do profilaktycznego naświetlania czaszki. Bardzo ważnym zagadnieniem mającym wpływ na wyniki leczenia pacjentów z mnogimi guzami w płucach jest różnicowanie zmian przerzutowych od nowotworów synchronicznych, a także szybkie wdrożenie właściwego leczenia.

Słowa kluczowe: synchroniczny rak płuca, wielkokomórkowy neuroendokrynny rak płuca, drobnokomórkowy rak płuca

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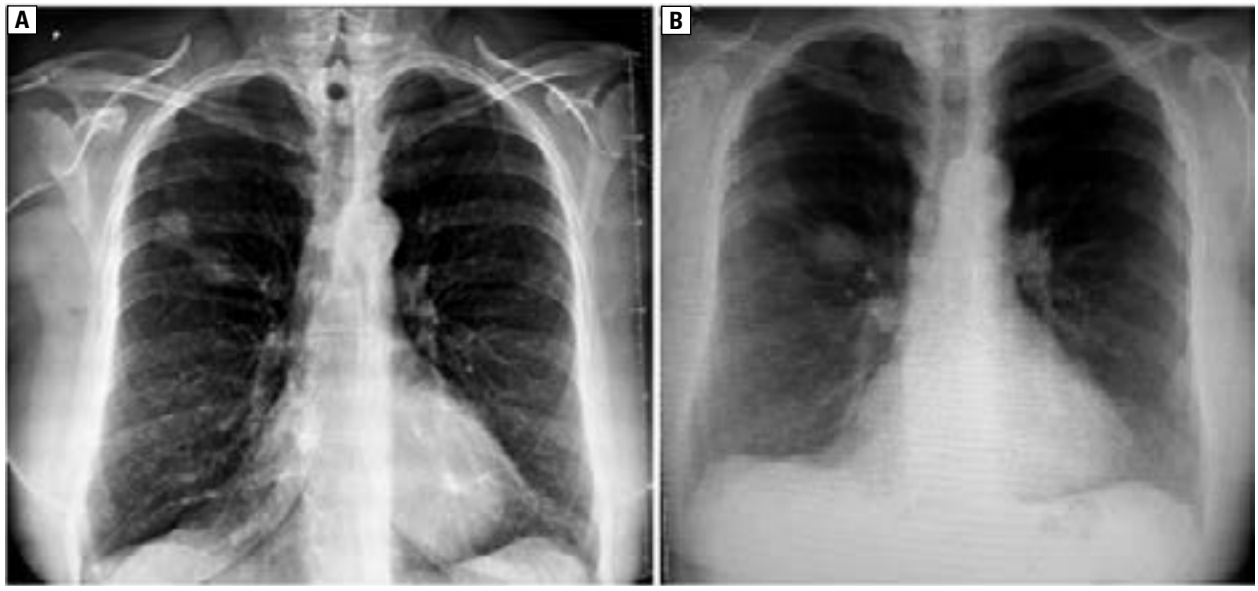

Figure 1. Chest roentgenograms showing progression of the lesions, taken at (**A**) three months and (**B**) one week prior to the surgery

Rycina 1. Zdjęcia retgenowskie obrazujące przyrost zmian, zrobione trzy miesiące (**A**) i tydzień (**B**) przed zabiegiem operacyjnym

Introduction

Multiple synchronous primary lung cancers are unusual and the incidence is reported around 0.2–20% [1]. Recently its rise has been noted due to widespread use and improvements in computed tomography (CT), positron emission tomography (PET) and other diagnostic methods. Once the detection of multiple solitary pulmonary nodules has been made, a very important issue, having a tremendous impact on treatment, is differentiation whether these lesions are metastases or synchronous primary lung tumors. There are several factors included in the criteria given by Martini and Melamed for the diagnosis of synchronous multiple primary lung tumors, such as histological characteristic of the tumors, their location, metastasis or vascular invasion occurrence [2]. In this article, we present the patient with two synchronous neuroendocrine lung cancer lesions in the right upper lobe.

Case report

A 55-year-old woman was admitted to Thoracic Surgery Ward for the investigation of two oval, solitary pulmonary nodules, 11 and 19 mm in diameter detected on a chest X-ray (Fig. 1). This was performed three months earlier prior to resection of retrosternal goiter, complicated by vocal cord paralysis, which necessitated tracheotomy. On admission, the patient showed no signs or symptoms related to lung lesions. Total tobacco consumption exceeded 32 pack-years. Control chest roentgenogram and CT showed progression of the lesions — medial tumor has enlarged from 11 mm to 23 mm, while the lateral one remained unchanged (Fig. 1). Due to the radiological imaging, the patient was qualified for CT-guided lung biopsy, which revealed poorly differentiated non-small cell carcinomas cells. Patient underwent right upper lobectomy. The lateral thoracotomy procedure was performed under general anaesthesia with single lung ventilation. Lymph node station 7 and 10 were sampled. Histological examination of the resected lung tissue revealed medially localized tumor to be a small cell carcinoma and the lateral tumor to be a large cell neuroendocrine carcinoma (Fig. 2). Immunochemical staining of the large cell neuroendocrine carcinoma showed positive reactions to cytokeratin, chromogranin A and synaptophysin, as well as negative reaction to TTF1; Ki67 (proliferation index marker) was 70%. Small cell carcinoma was focal positive ("dot like") to cytokeratin, positive to chromogranin A and synaptophysin and focal positive to TTF1; Ki67 was 70%. Histological analysis of taken lymph nodes revealed no evidence of cancer cells. The post-operative recovery was complicated by persistent parenchymal air leakage, which required talc pleurodesis. Chest drains were removed in 3rd and 6th postoperative day. The patient was discharged in good condition and lung inflation in chest X-ray. Afterwards the patient was qualified for adjuvant chemotherapy. A combination

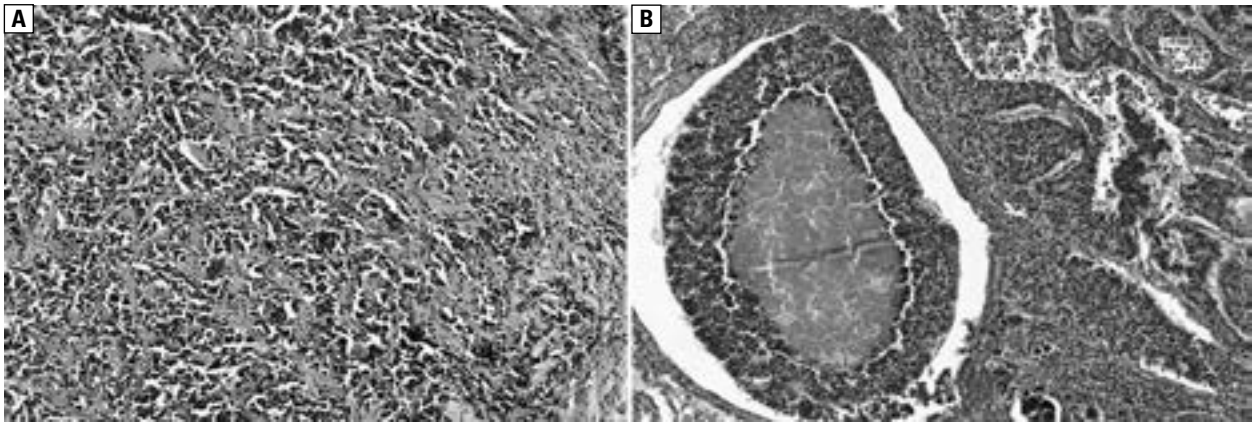

Figure 2. Histological appearance of lung carcinomas. (**A**) Small cell carcinoma. (**B**) Large cell neuroendocrine carcinoma

Rycina 2. Obraz histopatologiczny raków płuca. (**A**) rak drobnokomókowy; (**B**) neuroendokrynny rak wielkokomórkowy

of cisplatin and etoposide was given in a three series of treatments over a period of three months, with a two weeks breaks in between. CT scans of chest, brain and abdomen, performed after treatment showed no signs of distant metastasis. The last stage of treatment was prophylactic cranial irradiation, which patient underwent without any complications.

Now, 22 months after surgical treatment, being under thorough surveillance, the lady is fit and well showing no signs of relapse.

Discussion

The synchronous primary lung tumors are a rare condition and despite several reported series of patients [1–3], or case reports describing even three synchronous histologically different primary tumors in one lobe [4]. We present the first reported case of simultaneous two distinct neuroendocrine lung cancer lesions in the same lobe.

Large-cell neuroendocrine carcinomas of the lung are aggressive tumors. Patients with that kind of carcinoma have an extremely poor prognosis since the biological behavior is similar to that of small cell lung carcinomas [5, 6]. The classification of high-grade neuroendocrine lung tumours currently recognises large-cell neuroendocrine carcinoma and small-cell lung carcinoma as distinct groups [7, 8]. However Jones et al. [9] suggest that a single high-grade neuroendocrine lung tumours classification would be more appropriate due to a similarity in histology for these two carcinomas and uncertain clinical course. The WHO lung cancer classification distinguishes combined type of small cell carcinoma with elements of large cell neuroendocrine carcinoma. However in our patient lesions were physically distinct and separate and therefore meets the criteria given by Martini and Melamed for the diagnosis of synchronous multiple primary lung tumors [2]. Evident difference in the rate of growth of these two types of carcinomas also confirms primary nature of each tumors.

Still controversial remains the optimal management of patients with synchronous lung tumors. The operative management of these patients requires careful analysis at each stage of evaluation and the extension of resected lung tissue depends on localization of each tumors [1, 10]. The treatment for patients with large cell neuroendocrine carcinoma has been based on non-small cell carcinomas. To improve the result of treatment these kind of carcinoma, very important issue is to understand its clinicopathological characteristics, including preoperative diagnoses, the effectiveness of adjuvant chemotherapy, tumor recurrence rates and the prognosis of different stages [5, 11, 12]. Kocaturk et al. evaluated the benefits resulting from the use of adjuvant chemo- or radiotherapy to improve the three year survival in comparison with patients not undergoing adjuvant therapy (66.7 vs. 56.3%) [13].

As this is a case report, it is obvious that our patient will be treated on the individual basis, depending on the pathological characteristics of potential recurrence. It is to some extent likely that the relapse, if any, will appear as a small cell cancer lesion due to higher metastasizing capability and proliferation rate, compared to large cell cancer. In such circumstances the patient should be treated with second-line chemotherapy supplemented with radiotherapy. However, if the

large cell cancer clone will be predominant, then, paradoxically, the prognosis may be poorer due to chemo- and radiotherapy insesitiveness.

Conflict of interest

The authors declare no conflict of interest.

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