

CASE STUDY

LUNG NODULE 25 YEARS AFTER LOBECTOMY – RECURRENCE OF BRONCHIAL CARCINOID

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ABSTRACT

Introduction: Bronchopulmonary (BP) carcinoids are low and intermediate grade tumors, seen in adults between fourth to sixth decade, where no clear association with tobacco smoking is established. Most often they are sporadic lesions (95%). Half of patients have no symptoms and the tumor is incidentally found on a chest x-ray. BP carcinoids have a good prognostic, however there is a risk of distant metastasis and the recurrences are frequent. Therefore a crucial role of vigilant follow-up, extending far beyond 5 years.

Case presentation: We report a case of 73 years old woman, with history of recurrent pulmonary infections, and positive family history for lung cancer. Patient underwent left inferior lobectomy for BP carcinoid 25 years before and completed a 5 years long follow-up. On a thoracic computed tomography scan a nodule in the right lung was detected. Patient benefited from surgery and the pathological result was typical carcinoid with Ki67 < 1%. Follow-up CT scans showed stable images, with no signs of spread or recurrence.

Conclusions: Although there is a low risk of distant spread in such tumors, the recurrences are frequent. Moreover, patients may exhibit a higher risk of development of second tumors and there is a risk of metachronous tumors. The post-operative follow-up should be prolonged.

KEY WORDS: Bronchopulmonary carcinoid, neuroendocrine tumors, typical carcinoid

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INTRODUCTION

The steady rise in incidence and prevalence of neuroendocrine tumors (NETs) is possibly related to increased use of imaging procedures and an earlier detection [1, 2]. Approximately 70% of neuroendocrine tumors are located in gastro- entero- pancreatic system [3]. Lung is the second most common site of NETs, although these tumors account for only 1-2% of lung neoplasm. The incidence of bronchial carcinoids ranges from 0.2 to 2/100,000 population per year in the USA and European countries [1]. These tumors have a good prognostic, however a risk of distant spread exists and the recurrences are frequent.

CASE PRESENTATION

PATIENT INFORMATION

We present a case of a 73 years old woman, treated for arterial hypertension, who has been admitted to Internal Medicine Department (23.05.2016) after fainting without loss of consciousness. Patient reported excessive tiredness, recurrent respiratory infections, and also complained about intermittent chest pain in territory of prior left inferior lobectomy. The surgery was performed 25 years before for a lung nodule and the histopathological diagnosis was bronchial carcinoid (not specified whether typical or atypical). Patient never smoked and had no professional exposure. The following cases of lung

cancer within her family members were found: father (smoker, age of disease onset 70 years) and son (lung adenocarcinoma-non-smoker, age of disease onset 37 years).

CLINICAL FINDINGS

Various medical examinations have been performed, including chest X-ray, which showed diffused shadowing in the territory of former surgery. Thoracic computed tomography (CT) scan with contrast (25.05.2016) displayed a polycyclic nodule in X segment of the right lung, measuring 17x20x34mm (Fig. 1).

DIAGNOSTIC ASSESSMENT

Bronchoscopy performed in Respiratory Medicine Department revealed patent bronchi with unchanged mucosa. No carcinoma cells appeared in bronchoalveolar lavage. No obstruction was confirmed on spirometry. Blood tests did not differ from normal ranges. A fine needle biopsy was performed that demonstrated neoplastic cell with no cytological signs of malignancy and finely granular nuclear chromatin of neuroendocrine type (08.06.2016).

THERAPEUTIC INTERVENTION

It was followed by segmentectomy (VI) with lymph nodes excision (01.07.2016). The histopathologic diagnosis was typ-

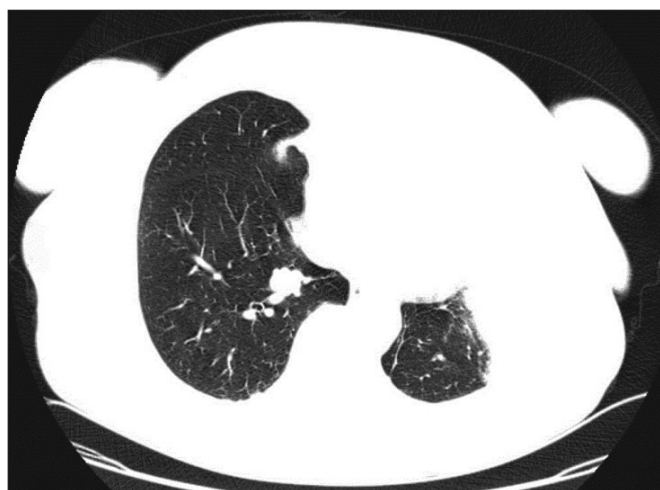


Fig. 1. Thoracic computed tomography (CT) scan with contrast (25.05.2016): a polycyclic nodule in X segment of the right lung, measuring 17x20x34 mm.

ical carcinoid (TC) and included immunohistochemistry for synaptophysin SYN (+), chromogranin CHR (+), thyroid transcription factor-1 TTF1(-), CD56 (+), Ki- 67<1% (Fig. 2-4). Blood tests revealed normal levels of tumor markers such as: Ca 19-9- 2,03 U/ml (N<27U/ml), CEA- 1,82 ng/ml (N<5 ng/ml), chromogranin A 34,59 ug/l (N<100 ug/l), serotonin 102 ng/ml (reference range 80-450 ng/ml), 5-hydroxyindoleacetic acid 1,22 mg/24h (reference range 2-9 mg/24h) (2-9). There was no pathological uptake of radioisotopes on somatostatin receptors scintigraphy (SRS) using ⁶⁸Ga-DOTATATE positron emission tomography PET/CT (Fig. 5 and 6). According to TNM staging system it has been evaluated as pT2aN0M0.

FOLLOW- UP AND OUTCOMES

Follow-up thoracic CT scans (24.05.2017 and 20.08.2018) have been compared and consulted by experienced radiologist- they displayed a solitary subpleural nodule in VIII segment, measuring 6 mm. The radiological images were stable, with no signs of spread or recurrence. These results lead to “watch and wait” follow- up strategy- further examinations are scheduled.

DISCUSSION

Bronchopulmonary carcinoids grow slowly and occur in fourth to sixth decade. About half of patients is asymptomatic [4], and the tumor’s finding is incidental on a standard chest x-ray. For others, their clinical presentation can be uncharacteristic, with cough, hemoptysis, dyspnea, thoracic pain or, as was in case of this patient, recurrent pulmonary infections.

There is a low risk of distant spread in typical carcinoids, but the recurrences are frequently observed. In case of our patient, second tumor has appeared 25 years after first curative surgery. However, it was not a local recurrence of the same carcinoid after years. The second carcinoid was a metachronous tumor, as can be attributed by a different location – opposite lung.

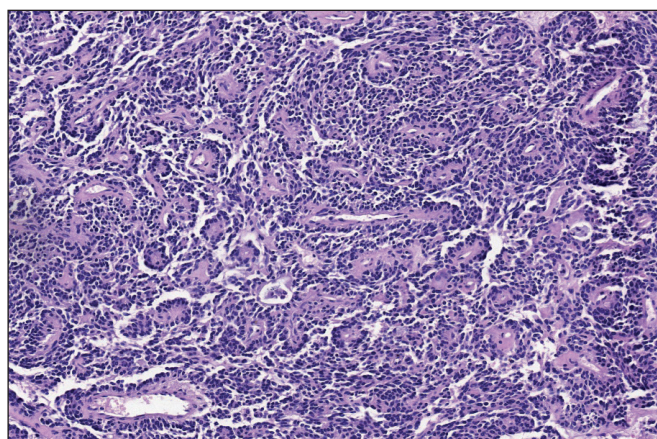


Fig. 2. Histopathology of typical carcinoid without mitotic activity and necrosis (HE stain, 400X).

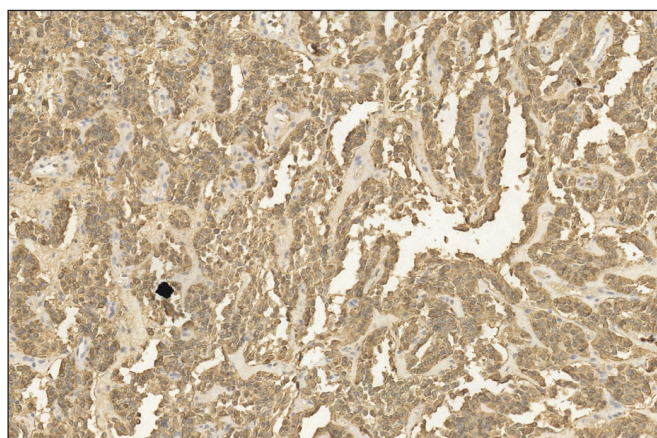


Fig. 3. Immunohistochemistry: The neoplastic cells are positive for Synaptophysin (IHC stain, 400X).

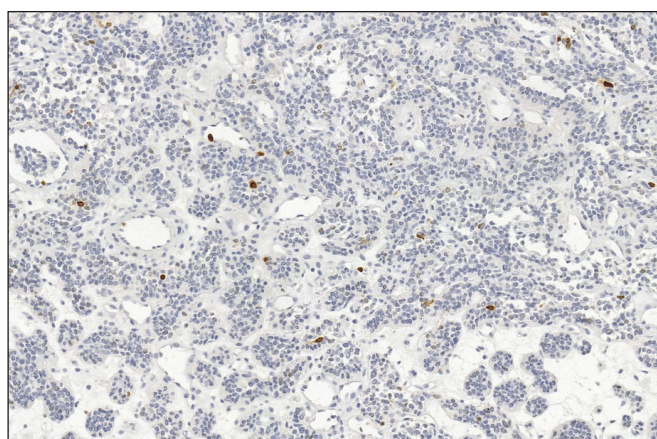


Fig. 4. Immunohistochemistry: Ki-67 index is less than 1%. (IHC stain, 400X).

Multicentric bronchopulmonary carcinoids are not very often reported in literature [5-7]. A case of metachronous central TC was described by surgeons from the University of Padova- the second tumor was detected 3 years after resection of the first TC and concerned the opposite lung [5]. It was a case of a 33-year old man. Manoutcheri et al. reported a case of 51-year women, with metachronous TC 12 years after the first diagnosis [6].

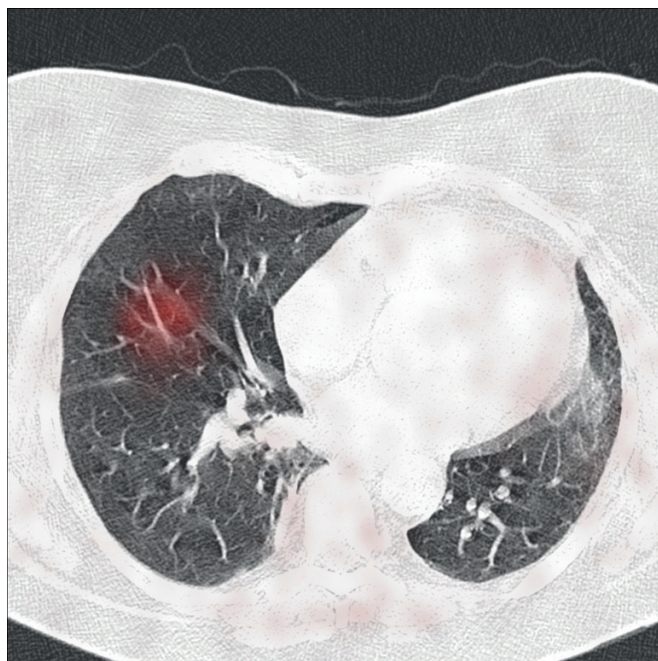


Fig. 5. Hybrid imaging positron emission tomography with computed tomography using ^{68}Ga -DOTATATE (^{68}Ga -DOTA-TATE PET/CT): no pathological uptake of radioisotopes.

This case is interesting because it comprehensively deals with three points of bronchopulmonary carcinoids' management:

1. the role of biopsy
2. the necessity of parenchyma-sparing surgery
3. the necessity of prolonged follow-up

Bronchopulmonary neuroendocrine tumors (BP NETs) are divided into histological groups, according to number of mitoses per 2mm^2 and the presence of necrosis [1]. The pathological distinction between typical or atypical carcinoids might be difficult on cytologic samples from fine needle biopsies. Moreover, histopathological diagnosis should always be confirmed by immunohistochemical examination, including determination of chromogranin A expression, synaptophysin and Ki-67 [8]. The Ki-67 antigen may be helpful to differentiate the high-grade NETs from the bronchopulmonary carcinoids [9,10]. It predicts the patients outcome better than mitotic count, histology and tumor stage [11]. The lung biopsy of discussed patient was performed and did not provide sufficient information. It was therefore followed by segmentectomy, allowing final and accurate diagnosis. A surgical specimen enables to obtain sufficient tissue and proper diagnosis. It is always preferred over lung biopsies [4].

Typical carcinoids are potentially curable even in case of distant recurrence or appearance of metachronous tumor. Their management should be discussed with multidisciplinary team [1]. Surgery is treatment of choice in patients with localized tumor. The aim is to resect the tumor and to preserve as much lung tissue as possible and [12]. It is especially important in young, active patient, in which reduced postoperative respiratory function can influence the quality of live [5]. The extension of surgery depends on histological type and location of primary lesion. Peripheral TC should be managed by an anatomic resection – lobectomy or segmentectomy [4].

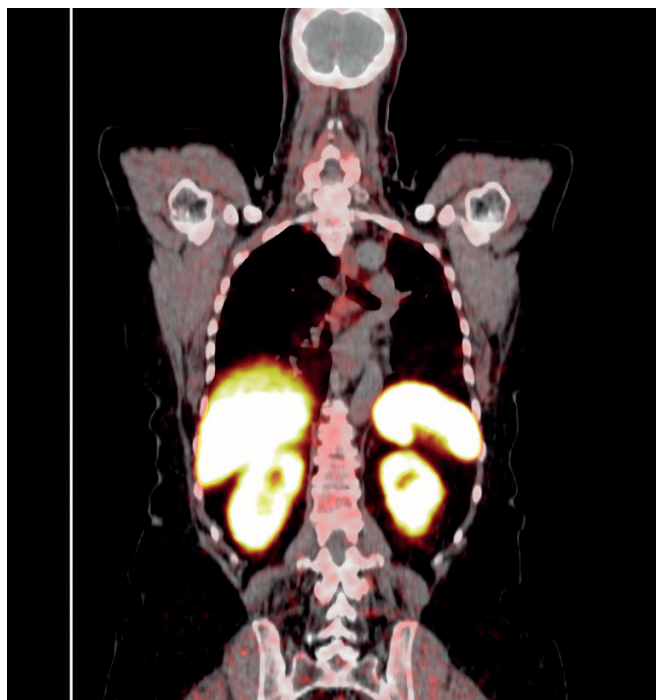


Fig. 6. Hybrid imaging positron emission tomography with computed tomography using ^{68}Ga -DOTATATE (^{68}Ga -DOTA-TATE PET/CT coronal): no pathological uptake of radioisotopes.

In this patient, segmentectomy of right lung was a treatment of choice, permitting to preserve the pulmonary function more significantly than another lobectomy. In patients with centrally located typical carcinoids, bronchial sleeve resection, sleeve lobectomy or endobronchial treatment is possible [13-15]. Recurrences in these cases are rare and the survival is excellent.

There is no consensus about how long to follow up should be proposed to patients after lobectomy for a typical carcinoid. According to European Neuroendocrine Tumor Society expert consensus, it is recommended to perform a CT chest scan in localized TC at first and third year, and every 3 years, if a tumor is more than pT1, during 15 years [1]. However, some authors reject close surveillance in completely resected, node-negative, typical carcinoid as ineffective and cost-consuming [16]. In addition, scheduled surveillance imaging often fails to detect most recurrences [17]. On the other hand, it was demonstrated that pulmonary carcinoids may exhibit a higher risk of development of second tumor and therefore a prolonged follow-up might be beneficial [18-19]. As showed in this case and reported by colleagues from different scientific centers in Europe, metachronous tumors may appear many years after the first diagnosis of TC and might require special management, regarding previous surgical burden of disease.

CONCLUSIONS

In conclusion, the lung- preserving surgery is a treatment of choice in all eligible cases of typical carcinoids. Recurrences are frequent, but other tumors or metachronous carcinoid tumors of the lung can appear as well and therefore an oncological vigilance is highly recommended. A “watch and wait” follow-up strategy

should be employed and further examinations, especially in case of any new clinical symptoms, should be scheduled.

List of Abbreviations

NETs – neuroendocrine tumors

CT – computed tomography

SYN- synaptophysin

CHR – chromogranin

TTF1 – thyroid transcription factor-1

SRS- somatostatin receptors scintigraphy

PET – positron emission tomography

TC – typical carcinoid

AC – atypical carcinoid

BP NETs – bronchopulmonary neuroendocrine tumors

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Conflict of interest

Authors declare no conflict of interest.

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