Lung Adenocarcinoma Complicated with a Carcinoid Microtumor: A Case Report and Literature Review

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Abstract

Background: Adenocarcinoma is the most common primary lung malignant tumor. However, pulmonary carcinoid tumorlets are rare neuroendocrine tumors, and the coexistence of adenocarcinoma and pulmonary carcinoid tumorlets is extremely rare. Herein, we describe a case of lung adenocarcinoma complicated with carcinoid tumorlets.

Case presentation: A 71-year-old female patient was admitted to the hospital after physical examination, multiple micronodules were in the inferior lobe of the left lung and right lung for 2 years, and a tumor was in the superior lobe of the left lung for 1 month. The patient underwent resection of the superior lobe of the left lung and wedge resection of the inferior lobe of the left lung by Video-assisted Thoracoscopic Surgery(VATS). The pathology of the superior lobe of the left lung was adenocarcinoma (pathological stage pT1cN0M0, IA3 stage), and the pathology of the inferior lobe of the left lung was carcinoid tumorlets. The patient was discharged from the hospital one week after the operation and recovered well after follow-up without recurrence.

Conclusions: The lack of understanding of carcinoid tumorlets in the clinic causes their misdiagnosis or missed diagnosis. At the same time, the lack of understand also suggests that we should pay attention not only to mass-type lung tumors but also to pulmonary micronodules.

Background

Double primary lung cancer is rare in the clinic and was first reported by Beyreuther in 1924 [1]. According to the literature, its incidence is approximately 3% [2]. Recently, we treated a patient with double primary lung cancer. The pathology of the superior lobe of the left lung was adenocarcinoma, and the pathology of the inferior lobe of the left lung was carcinoid tumorlets. Adenocarcinoma is the most common primary lung malignant tumor. Moreover, pulmonary carcinoid tumorlets are rare neuroendocrine tumors, and the coexistence of adenocarcinoma and pulmonary carcinoid tumorlets is extremely rare. Therefore, we report this patient.

Case Presentation

A 71-year-old female patient was admitted to our hospital on October 21, 2020. The major cause of admission was multiple micronodules in both lungs for 2 years and tumors in the superior lobe of the left lung for 1 month. One month prior, the patient underwent chest enhanced CT (September 16, 2020); a lesion in the apicoposterior segment was found in the superior lobe of the left lung. Multiple micronodules were present in both lungs. After that, bronchoscopy was performed on September 18, 2020. No obvious neoplasm was found under bronchoscopy, and blind brush examination was carried out in the apicoposterior segment. The cytopathology report revealed that the cancer cells were not detected. Chest-enhanced CT examination in our hospital on October 16, 2020, showed that there was a high possibility of lung cancer in the apicoposterior segment in the superior lobe of the left lung, and

there were multiple micronodules in both lungs (Fig. 1). The patient had no chest tightness, shortness of breath, cough, hemoptysis, fever, etc. but had occasional diarrhea. There was a previous history of hypertension, coronary heart disease and diabetes that could be controlled well. The patient had no history of drinking and smoking. The patient had no family history of lung disease or cancer. There were no abnormalities found in the physical examination. The tumor markers found in the hospital were squamous cell carcinoma antigen (0.29ng/mL), carcinoembryonic antigen (3.0ng/mL), soluble cytokeratin (2.13ng/mL) and neuron-specific enolase (10ng/mL). Brain magnetic resonance imaging, bone imaging and abdominal CT excluded distant metastasis. The patient refused PET-CT examination.

Two years ago, the micronodules were found to be located in the inferior lobe of the left lung and right lung, and their maximum diameters were less than 5 cm. After regular reexamination, the size and number of micronodules did not change during the two years. No special treatments were given during this period. On September 16, 2020, the patient underwent another physical examination, and a tumor was found in the superior lobe of the left lung, but micronodules were not found in the superior lobe of the left lung. At that time, according to the patient's medical history, the micronodules in the inferior lobe of the left lung and the right lung were considered benign nodules. On October 28th, 2020, after preoperative preparation, wedge resection of the left superior lobe was performed by VATS. An examination of an intraoperative frozen section showed adenocarcinoma. The patient underwent surgery for left superior lobectomy and systematic lymph node dissection by VATS. Only wedge resection was performed in the inferior lobe of the left lung, and two nodules were identified by intraoperative frozen sectioning; atypical cells were visible, and paraffin pathology was needed for diagnosis. The paraffin pathology report after operation showed that the size of pulmonary nodules in the superior lobe of left lung was 3 cm×3 cm×2.5 cm, with invasive adenocarcinoma (approximately 80% acinar, approximately 20%volt wall-like), no definite vascular tumor thrombi, and no invasion of visceral pleura. Diagnosis of the nodules in the inferior lobe of the left lung was carcinoid tumorlets(Fig. 2). Lymph nodes were as follows: 0/1 in group 4L, 0/2 in group 5, 0/7 in group 7, 0/2 in group 9, 0/1 in group 10, 0/1 in group 11, 0/2 in group 12 and 0/1 in group 13. Tumor immunohistochemistry in the superior lobe of the left lung showed: ALK negative (-), ALK (VENTANA D3F3) (-), C-Met (60% moderate intensity), HER2 (0), ROS1 (0), and BRAF (-). Immunohistochemistry of nodules in the inferior lobe of the left lung showed: AE1/AE3 (+), Syn (+), CgA (+), CD56 (+), TTF-1 (+), LCA (-), Ki-67 (2% positive cells), and P40 (-).Pathological staging of the superior lobe of the left lung after the operation was pT1cN0M0 (IA3 stage). We detected the whole adenocarcinoma gene in the superior lobe of the left lung and carcinoid tumorlets in the inferior lobe of the left lung. Epidermal growth factor receptor (EGFR) has a exon 21 L858R point mutation in adenocarcinoma, and TPS was negative in the PD-L1 test. The carcinoid tumorlets did not have this EGFR mutation. The patient was discharged from the hospital one week after the operation and recovered well after follow-up without recurrence.

Discussion And Conclusion

The incidence of lung adenocarcinoma is increasing year by year, and it has become the most common subtype of lung cancer, accounting for almost 50% of all lung cancers [3]. The 2015 edition of the WHO classification of tumor of the lung reclassifies lung adenocarcinoma based on the growth patterns of cancer: preinvasive lesions, including adenocarcinoma in situ and atypical adenomatoid hyperplasia; early invasive lesions were named tiny invasive adenocarcinoma; and infiltrating adenocarcinoma, including volt wall-like type, acinar type, nipple type, micropapillary type and solid type, and invasive mucinous adenocarcinoma, colloid adenocarcinoma, fetal adenocarcinoma and intestinal adenocarcinoma were introduced [4]. EGFR is a typical driving oncogene in lung adenocarcinoma. The global prevalence of mutations in this gene is still difficult to estimate, and there are great racial differences. According to the literature reports, the incidence of EGFR mutations is 10–15% in Caucasian individuals, 20%-40% in Asian individuals, and even more than 60% in nonsmoking Asian individuals [5]. Therefore, the detection of EGFR gene mutations is not only helpful for the early diagnosis of lung adenocarcinoma patients but also provides a basis for gene-targeted therapy and prognostic evaluation of lung adenocarcinoma.

Pulmonary carcinoid tumorlets are fibrotic nodules formed by hyperplastic pulmonary neuroendocrine cells (PNECs) continuously breaking through the airway mucosal epithelial basement membrane, and the diameter of these nodules is less than 5 mm. If the size of the nodule was greater than or equal to 5 mm, it is diagnosed as a carcinoid tumor. Pulmonary carcinoid tumorlets are a rare disease in primary lung tumors. This disease is often found accidentally in operation or autopsy specimens and is most common in lung inflammation and fibrosis [6].

Pulmonary carcinoid tumorlets have a hidden onset, slow development and lack of specific clinical manifestations. The main symptoms are closely related to the accompanying lung diseases. When hyperplastic PNECs cause tracheal obstruction, stenosis and inflammatory reactions, they can manifest as cough, expectoration, hemoptysis, chest tightness, shortness of breath or progressive dyspnea, and some patients have carcinoid syndromes, such as facial flushing, skin pigmentation, muscle weakness, and diarrhea [7]. Pulmonary carcinoid tumorlets are usually multiple pulmonary nodules that can occur in a single lobe, in multiple lobes, or even in both lungs, and the number ranges from several to dozens [8]. Because of the small volume of these lesions, the common X-ray or CT examination easily leads to missed diagnosis; the different thicknesses of CT may also affect the imaging number of pulmonary nodules, and the disease is often accompanied by some pulmonary disease, which is easy to cause misdiagnosis.

Lung adenocarcinoma and carcinoid tumorlets are two kinds of tumors with different tissue sources. Their coexistence is rarely reported. Only Flynn et al [9] reported a case of right superior lobe carcinoma in the literature in 2004, and low differentiated squamous cell carcinoma, moderately differentiated adenocarcinoma and typical small carcinoid were simultaneously detected in the surgically resected specimen of the right superior lobe.

At the same time, several medical records of lung adenocarcinoma complicated with carcinoids were found. Jung-Legg et al [10] reported a case of three concurrent lung malignant tumors in 1986; two of them were central bronchial carcinoid and peripheral small cell carcinoma in the superior lobe of the right lung, and the third was peripheral adenocarcinoma in the middle lobe of the right lung. Sen et al [11] reported a case of resection of the lower lobe of the left lung in 1998, and adenocarcinoma and typical carcinoid coexisted in postoperative specimens. Metastasis occurred in the ipsilateral hilar lymph nodes, but the metastatic components were composed of well-differentiated adenocarcinoma. Yano et al [12] reported a case of resection of the middle and lower lobes of the right lung in 2002. Pathology confirmed that the tumor in the lower lobe of the right lung was bronchial carcinoid, but the tumor in the middle lobe of the right lung was adenocarcinoma. Nagamatsu et al [13] reported in 2012 a case of adenocarcinoma found in the resection of the superior lobe of the right lung, and carcinoid was detected in the central fibrous scar of the adenocarcinoma. Abbi et al [14] reported a case of a tumor found during resection of the superior lobe of the right lung in 2014. Postoperative pathological examination showed that the tumor was a collision tumor composed of micropapillary adenocarcinoma and typical carcinoid. Saladi et al [15] reported an elderly male cachexia patient with massive pleural effusion in the right lung in 2018. No cancer cells were found in the right pleural effusion puncture. Neoformation was found in the left lower lobe bronchus by bronchoscopy, which was confirmed as carcinoid by pathological biopsy. The cause of pleural effusion was unknown, so thoracoscopic exploration was performed. Multiple pleural nodules were found in the right pleura during the operation, and these nodules were confirmed to be adenocarcinoma by biopsy and gene detection; however, EGFR mutation, KRAS mutation, ALK rearrangement and PD-L1 expression were all negative. The patient was given palliative chemotherapy after the operation. Drpa et al [16] reported a case of adenocarcinoma in stage IIIB found in the right superior lobe that coexisted with bronchial carcinoid of the left lower lobe. Then, the patient underwent gene detection. The adenocarcinoma had an EGFR mutation, while the carcinoids did not have any EGFR mutations. After the patient was treated with erlotinib for 50 months, the adenocarcinoma progressed, but the carcinoid completely disappeared. The patient eventually died of intestinal obstruction due to abdominal metastasis.

This patient was diagnosed with adenocarcinoma in the left superior lobe combined with carcinoid tumorlets in left lower lobe. The two types of lung tumors were located in different lobes, which is very rare. This patient had symptoms of intermittent diarrhea, which may be a manifestation of carcinoid syndrome. However, diarrhea is not serious, and there is no special treatment. The pathological stage of adenocarcinoma of the left superior lobe is IA3 stage(T1cN0M0).

Although the EGFR mutation was positive, but according to the eighth edition of the UICC lung cancer stage, adenocarcinoma of the left superior lobe needs no further treatment and periodic follow-up. We consider that the micronodules of the right lung may also be carcinoid tumorlets. In view of the good prognosis of carcinoid tumorlets, it is recommended that patients do not need radiotherapy and chemotherapy and that close follow-up should be performed. This patient recovered well since the operation follow-up, with no recurrence.

Due to the lack of clinical understanding of microneoplastic carcinoids, misdiagnosis or missed diagnosis can easily occur. Therefore, we should pay attention not only to lump-based lung tumors but also to pulmonary micronodules in the clinic.

Abbreviations

EGFR: Epidermal growth factor receptor; PNECs: pulmonary neuroendocrine cells; VATS: Video-assisted Thoracoscopic Surgery

Declarations

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Not applicable.

Authors' contributions

XYZ reviewed the literature and contributed to manuscript drafting; SBK and SP collected data, reviewed the literature; ZF and GCY reviewed the literature; HM and TZQ were responsible for the revision of the manuscript for important intellectual content and reviewed the literature. All authors issued final approval for the version to be submitted.

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Availability of data and materials

We do not wish to share the data because that it might identify the patient.

Ethics approval and consent to participate

Written informed consent was obtained from the patient.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Competing interests

we declare that we have no competing interests.

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Figures

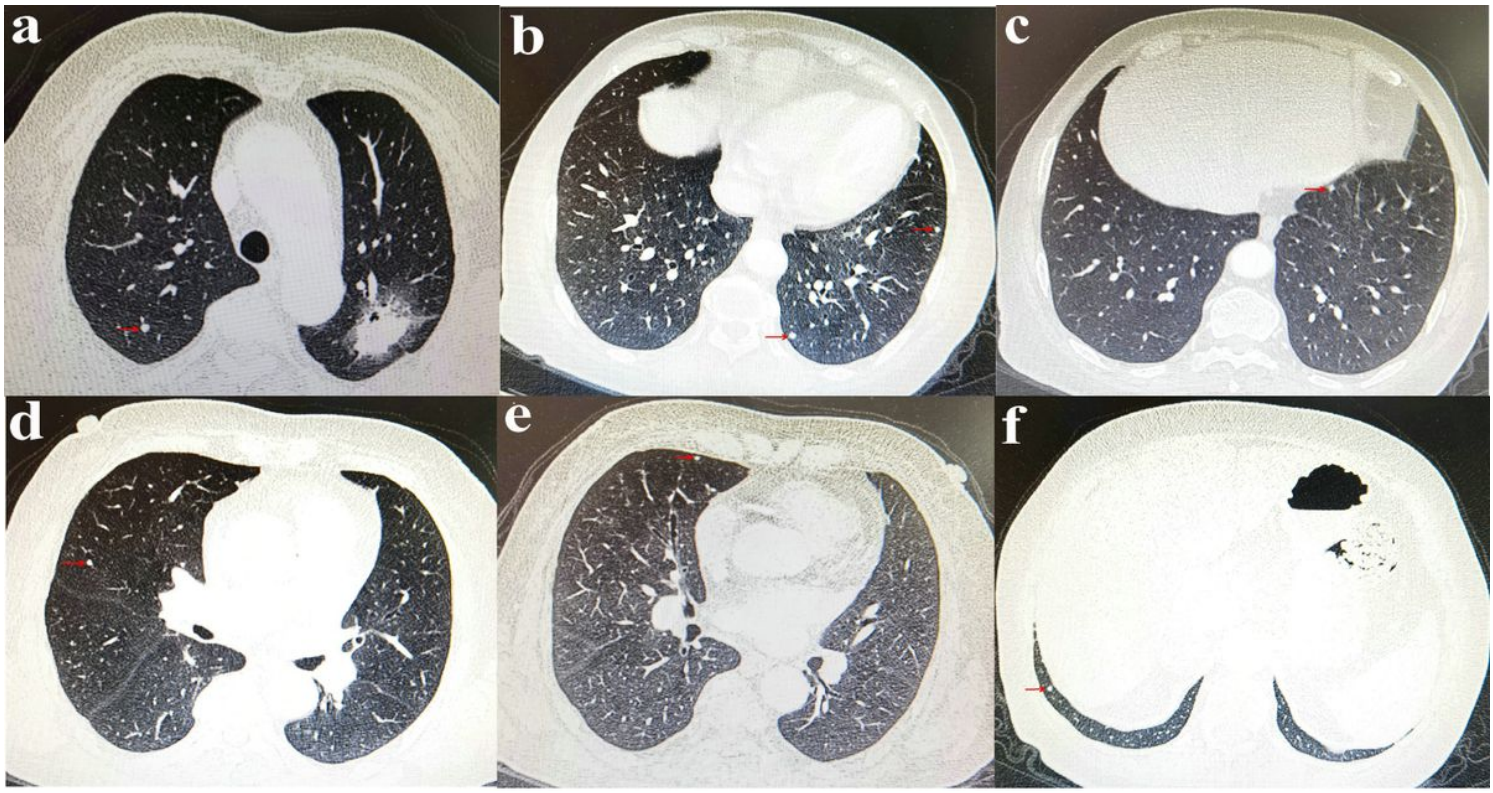

Figure 1

a: Tumor in the superior lobe of the left lung and micronodules in the superior lobe of the right lung. b and c: Micronodules in the lower lobe of the left lung; dand e: Micronodules in the middle lobe of the right lung. f: Micronodules in the lower lobe of the right lung.

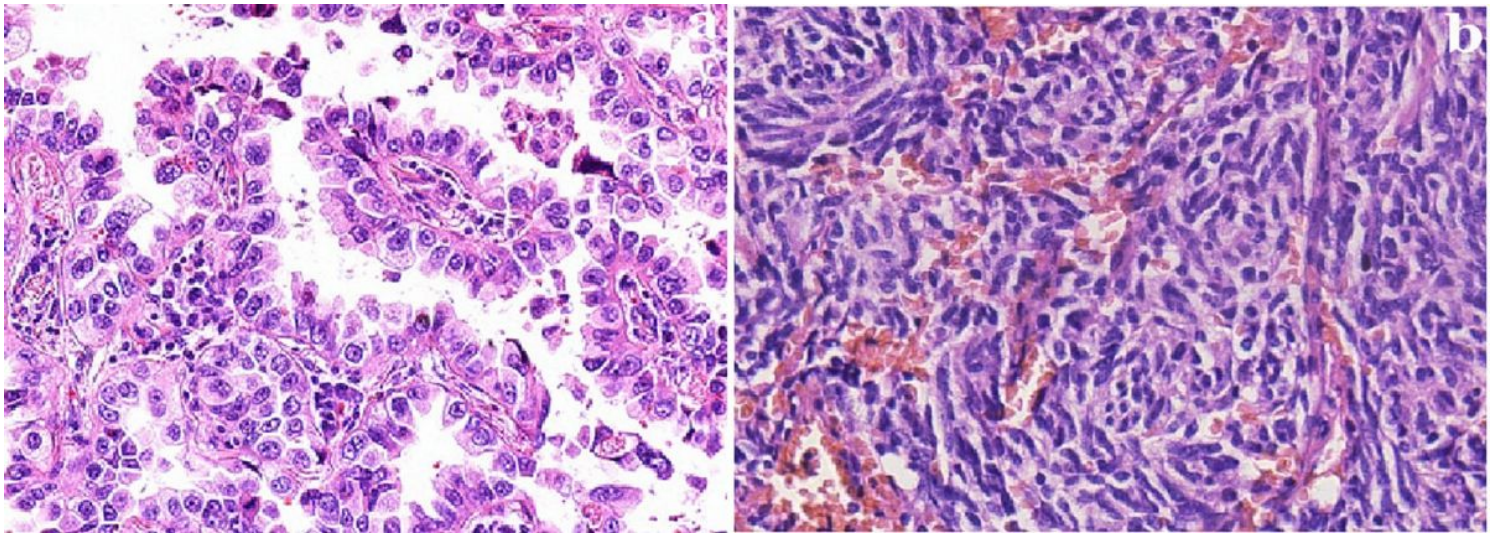

Figure 2

a:adenocarcinoma of the superior lobe of the left lung: under the microscope, the adenocarcinoma cells were single-layer cubic or columnar, with the same size and shape, such as hanging on the surface of the alveoli in the shape of spikes (×200).b: Carcinoid tumorlets of the lower lobe of the left lung: microscopic microtubular carcinoid of the left lung is relatively uniform in size, with round, oval or short fusiform nuclei; there is less cytoplasm, with deeply stained or fine-grained nuclei and no obvious nucleoli. The tumor cells form multifocal cellular nests or small round nodules (×200).