Endobronchial Metastasis Of Ovarian Cancer: A Case Report And Literature Review

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Case report

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Abstract

Background: Metastasis to the endobronchial from primary ovarian carcinoma (OC) is very rare. To enhance our understanding of this disease, we report a case of endobronchial metastasis from primary OC and review the literature.

Case presentation: This is a case report and retrospective analysis of bronchial tumor patient secondary form primary OC. The patient was a 51-year-old woman who presented intermittent cough and expectoration for 3 month, and suffocating pneumonia for 3 weeks. Multiple nodular masses at the right upper lobe and thickening soft tissue with surrounding invasion of bronchi at the left upper lobe were found. The chest X ray scan demonstrated that enlarged right and left upper hilar, spreading mediastinum, elevated right septum were observed. Bronchoscopy showed that stenosis of the opening of right main bronchus and apical, middle and posterior segmental bronchi at right lobe was identified and the opening of left main bronchus was almost completely blocked by some visible neoplasm. The pathological result indicated that the disease was bronchial tumor derived from primary OC. Until now, only 12 cases were reported. The latent period ranged from 2 months to 21 years and the overall survival time ranged from 1.5 months to 5.5 years.

Conclusions: The endobronchial is one of metastasis site of OC. The latent period of the disease is long and after active treatment, good prognosis can be acquired. This is the first study on endobronchial metastasis from primary OC, in China.

1. Introduction

Ovarian cancer (OC) is considered as the most lethal gynecologic malignancy for the highest mortality and the absence of specific symptoms at the early stage [1]. The endobronchial metastasis from primary OC is extremely rare in clinical. From the first case of endobronchial metastasis from primary OC reported by Westerman in 1980, there are only 12 reported cases until now [2]. Since the latent period is long and the clinical characteristics are atypical, it is difficult to distinguish it from the primary bronchial tumor. Here, we report a case of endobronchial metastasis from primary OC.

2. Case Report

A 51-year-old female patient showed intermittent cough and expectoration for 3 month and suffocating pneumonia for 3 weeks. The patient presented chest tightness, back pain on the right side, weakness, night sweats during the examination in the 3 months prior to admission. Besides, multiple nodular masses at the right upper lobe, thickening soft tissue with surrounding invasion of bronchi at the left upper lobe, enlargement of the bilateral hilar and mediastinal lymph nodes were found by the chest computed tomography (CT) scan. The patient showed intensive suffocating pneumonia, blood-stained sputum, legs edema at 3 days before admission. The treatment of moxifloxacin combined with doxofylline and hydrocortisone didn't relieve her cough. Therefore, the patient was admitted to our hospital in Nov.2018.

Due to the OC, the patient was treated by taxol and oxaliplatin for 1 cycle of chemotherapy. Then, the patient was conducted resection of ovarian, uterus, greater omentum and lymph nodes on the left clavicle in Aug. 2016. After the resection, the patient was treated by taxol and oxaliplatin for 5 cycles of chemotherapy and next, by irinotecan and oxaliplatin for 5 cycles of chemotherapy, until Sep. 2017. After that, she has been taking traditional Chinese medicine for improvement.

On physical examination, she was conscious. Her abdomen was flat and soft, and there was no tenderness. She had clubbing fingers and legs edema. The carcinoembryonic antigen levels in serum were increased and her other indexes in routine testing were listed in Table 1. The chest X ray scan showed that enlarged right and left upper hilar, spreading mediastinum, elevated right septum and multiple nodular masses at the right upper lobe were observed (Fig. 1). To differentiate primary tumor and metastasis, the flexible bronchoscopy was performed for her. The mucosa was congestive, edema and the tracheal carina was broadening (Fig. 2a). Granuloma was projected from the opening wall of right main bronchus (Fig .2b). Stenosis of the opening of right main bronchus and apical, middle and posterior segmental bronchi at right lobe was observed (Fig. 2c) and the opening of left main bronchus was almost completely blocked by some visible neoplasm (Fig. 2d). For the further observation, neoplasm was removed using clip and electric needle knife, and we saw the thickening and uneven mucosa. The hematoxylin-eosin (HE) staining of the neoplasm revealed that tumor cells arranged tightly and was irregular in shape (Fig. 3a). After

magnification, tumor cells and nucleus were not uniform in size and cells exhibited obvious atypia (Fig. 3b). The immunohistochemistry staining of the neoplasm showed anti-pan cytokeratin (CK) positivity in cytoplasm and anti-wilms tumor protein (WT-1) positivity in nucleus (Fig. 4a and b). Besides, the immunophenotypes of neoplasm were evaluated by antibodies to various makers and the results indicated that p53 were positively expressed and the rate of Ki-67 expression was more than 70% (Table 2). Integrating all above research, the pathological result was endobronchial tumor from primary OC. The patient didn't receive any chemotherapy for intolerance. Due to the terminal OC and multiple metastasis, the disease progresses fast. The patient abandoned treatment and died on 17 Dec. 2018.

The literature were searched from http://med.wanfangdata.com.cn and http://www.ncbi.nlm.nih.gov/pubmed. 11 papers published in English and no papers in Chinese reported 12 cases who suffered endobronchial metastasis from primary OC, until now (Table 3) [2-12]. The current patient was the 13th one.

3. Discussion And Conclusions

OC is considered as the most lethal gynecologic malignancy and ovarian cancer cells can directly attack the surrounding pelvis organs such as bladder (17%) and colon. Besides, ovarian cancer cells can also arrive at peritoneum and omentum (86%), intestinal (50%) and spleen (20%), through peritoneal fluid transportation [13]. The common metastatic routes are lymphatic metastasis and direct invasion, while the hematogenous metastasis only accounts for 16% and the hematogenous metastatic sites are always liver, lung and pleura [13]. Although the end-stage OC can metastasize to lung, the endobronchial metastasis is extremely rare and there is no study on this disease in China, before our research. The intervals between primary OC and endobronchial metastasis are always long with the mean interval as 65.3 months, and the maximum time was up to 21 years [10]. The development of endobronchial metastasis from primary OC is a slow progress and the media survival time of 10 cases before 2018 ranged from 6 to 24 months [14]. Compared with metastatic chest tumors, the endobronchial metastasis from primary OC often showed good prognosis [15].

The potential mechanisms of endobronchial metastasis from primary OC were complicated and that may include mediastinal lymph nodes metastasis, hematogenous metastasis, lymphatic metastasis and parenchymal metastasis [7, 9, 16]. In addition, the routine imaging examination can't clearly distinguish endobronchial metastasis from primary bronchial tumors. Clinical manifestations of endobronchial metastasis are dyspnea, dry cough, hemoptysis, anhelation and hoarsness. However, 52% ~ 62.5% patients showed no respiratory symptoms [16]. Stenosis of airway and thickening vessel walls observed by chest CT, may be due to diseases from intratracheal site, tracheal mucosa and airway surroundings. Furthermore, only 50% endobronchial diseases can be found by chest CT. Therefore, physician scientists always misdiagnose the endobronchial metastasis from primary OC as primary bronchial tumors [3].

Flexible bronchoscopy is a direct detection method for endobronchial metastasis and its characteristics vary widely, including benllones combined with necrosis and nodular masses. However, flexible bronchoscopy can't differentiate between benign tumor, primary lung cancer and tumor metastasis. Therefore, pathological and immunohistochemistry assay are necessary to identify the tumor origins. According to the metastatic modes, the tumors metastasis to airways can be divided into four types, □ type, direct metastatic tumor; □ type, airway tumors invaded from pulmonary solid lesions; □ type, airway tumors invaded from lymph nodes of mediastinum and hilum; □ type, airway tumors invaded from peripheral lesions [17]. □ and □ types are in the majority. Dhillon et al reported a unique endobronchial metastasis combined with airway calcification [11]. Unfortunately, the clinical manifestations of airway calcification and broncholithiasis are very similar, which may result in misdiagnose. Ayub et al described an unusual endobronchial metastasis combined with aspergillosis and the patient showed hemoptysis [12].

The treatments for endobronchial metastasis, such as resection, chemotherapy and radiotherapy, depends on multiple aspects, like patients' status, age, and tumor size, location and others. Choi et al firstly reported that needle electrical knife was applied to remove the bronchial metastasis focuses and this method effectively relieved patients' dyspnea and hemoptysis [8]. The endobronchial intervention such as stent, local radiotherapy and photodynamic therapy, may be efficient methods for alleviating patients' dyspnea, hemoptysis and stenosis induced by endobronchial metastasis. However, endobronchial intervention showed little effect on patients with submucosa metastasis. Some research indicated that atomizing

chemotherapy might be an ideal method for patients with submucosa metastasis, for the long detention and high drug concentration in lesions, and it was estimated that the drug concentration in tumor tissues was almost 5 ~ 15 times higher than that in normal lung tissues [16]. By now, some novel therapeutic regimens are still necessary for the treatment of endobronchial metastasis.

In conclusion, endobronchial metastasis from primary OC is extremely rare. The latent period of this disease was long and clinical manifestation are always hiding. Flexible bronchoscopy combined with imaging and immunohistochemistry tests are efficient diagnostic approach. Endobronchial intervention, radiotherapy and chemotherapy could be taken for the patients' treatment. The individual endobronchial metastasis can be acquired good prognosis after active treatment, while the prognosis of patients with multiple metastasis is usually poor.

List Of Abbreviations

OC: ovarian carcinoma;

CT: computed tomography scan

HE: hematoxylin-eosin staining

CK: cytokeratin (CK)

WT-1: wilms tumor protein 1

Declarations

Ethics approval and consent to participate

This research was approved by the Ethics Committee of the Tianjin Chest Hospital and the informed consent and medical record were obtained from the patients' family.

Consent for publication

The patient's medical record and individual data were consented to publish by the patients' family.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Author contribution

RZ and LY performed the chest X-ray, flexible bronchoscopy images, HE and Immunohistochemistry staining. RZ, LY and WJ analyzed and interpreted the patient's data. WJ wrote the manuscript and all authors read and approved the final manuscript.

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Tables

Table 1. Routine texting results of the patient in this study.

index	value	index	value
Blood routine texting		neu (%)	72.1 %
Hb	126 g/L	PLT	337.00 × 10^9 L
Fg	5.35 g/L	D-dimer	1.00 μg/mL
ESR	49.0 mm/h	WBC	5.29 × 10^9 L
Arterial blood gas		pH	7.472
pCO_2	37.0 mmHg	pO_2	69.0 mmHg
$cHCO_3^-$	27.4 mmol/L	sO_2	94.7 %
FiO_2	29.0 %		
Tumor makers		NSE	58.07 ng/mL
CYFRA21-1	18.57 ng/mL	CA125	86.82 U/mL
Echocardiography		EF	56 %
PAP	30 mmHg	RVOT	28 mm
RVAW	3 mm		

Table 2 Immunohistochemistry results of the neoplasm from current patient.

antibody	Carcinomatous component	antibody	Carcinomatous component
ER	-	PR	-
WT-1	+	TTF-1	-
NapsinA	-	CD56	-
CK	+	P53	+
P40	-	PAS	-
Ki-67	> 70%		

- = negative, + = positive

Table 3 Summary of endobronchial tumor from primary ovarian carcinoma.

First Author	Age	type	Time (years)	Imaging examination	Clinical manifestations	Therapy	prognosis	
							Metastasis to other sites	Survival (months)
Westerman[2]	51	PC	7	Compact shadow in trachea	dyspnea	Radiotherapy	NR	NR
Merrill[3]	45	SCC	12	Compact shadow in right middle lobe	cough	Right lower lobe resection	NR	NR
Merimsky[4]	83	PA	0.2	Airway obstruction	dyspnea	Laser therapy	abdomen	4
Mateo[5]	62	SA	5	Bronchial obstruction	dyspnea, cough	Chemotherapy + radiotherapy	brain	22
Wholey[6]	49	NR	2	Bronchial obstruction	dyspnea	NR	NR	NR
Petru[7]	40	SPA	2.7	lymphadenovarix	dyspnea	Laser therapy + Chemotherapy	NR	6
Choi[8]	33	SPA	7	Airway obstruction	dyspnea, hemoptysis	Chemotherapy + radiotherapy	No	> 66
Harrington[9]	42	SPA	0.92	Right middle lobe atelectasis	hemoptysis	Chemotherapy + radiotherapy Chemotherapy + radiotherapy	NR	NR
Upadhyay[10]	62	SA	21	NR	dyspnea, cough	Chemotherapy	No	> 18
Upadhyay[10]	53	SA	6.3	NR	dyspnea, cough	Intervention	NR	18
Dhillon[11]	61	SPA	12	Lymphadenovarix and calcification	hemoptysis	Radiotherapy + laser therapy	No	> 36
Ayub[12]	22	PA	2	Bronchial obstruction	hemoptysis	No	NR	6

PC = papillary cystadenocarcinoma, Time = time metastasis to EC, SCC = serous cystadenocarcinoma, PA = papillary adenocarcinoma, NR = none reported, SPA = serous papillary adenocarcinoma, SA = serous adenocarcinoma,

Figures

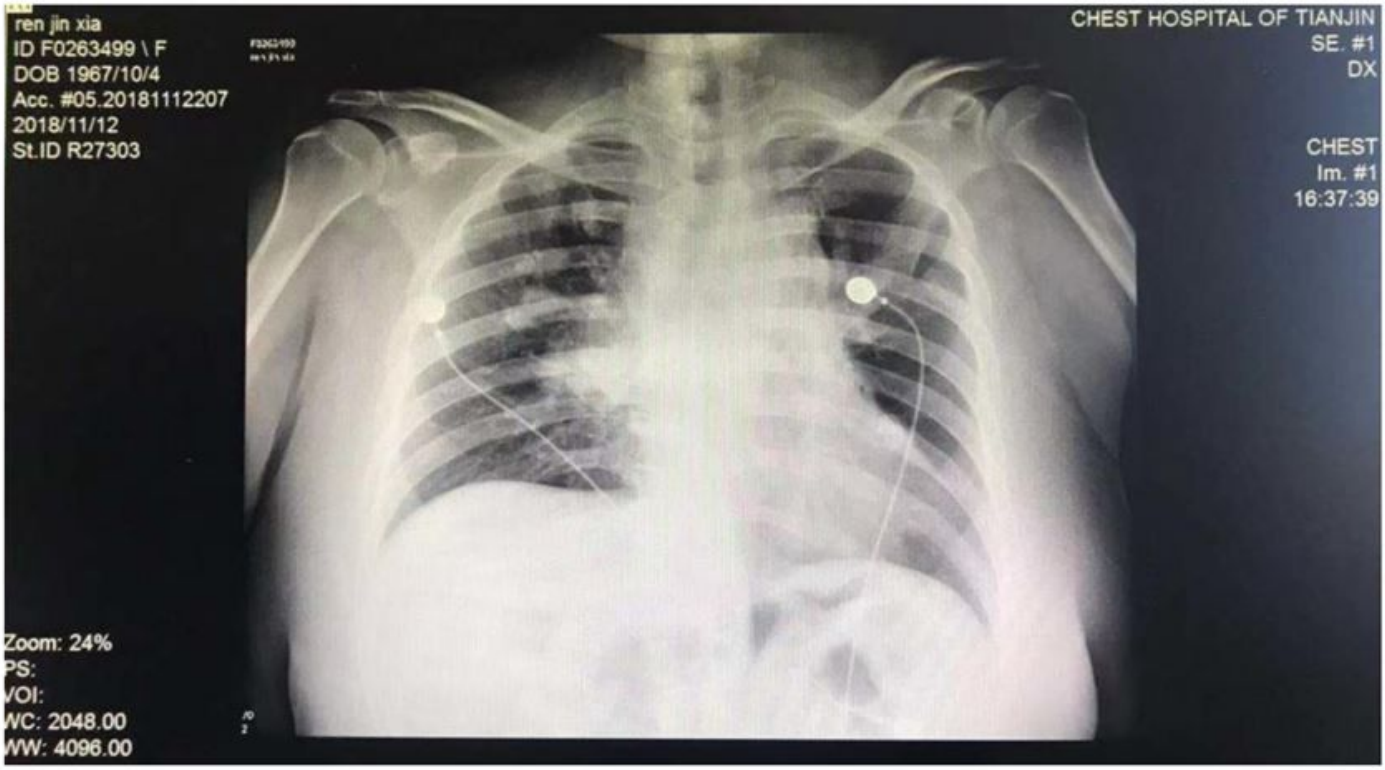

Figure 1

The chest X-ray of the current patient.

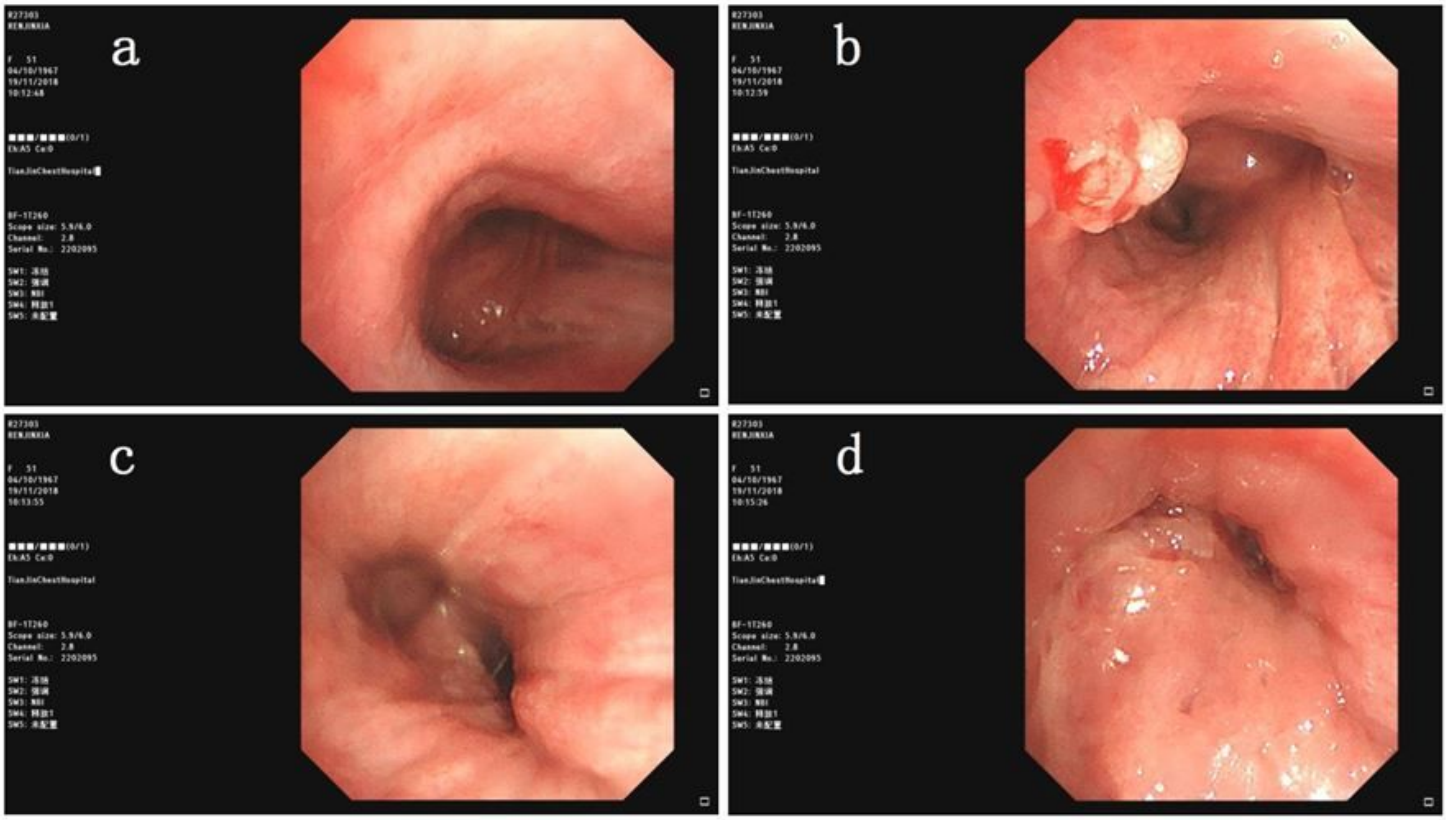

Figure 2

Flexible bronchoscopy images of trachea (a), right main bronchus (b), right middle bronchus (c), left main bronchus (d).

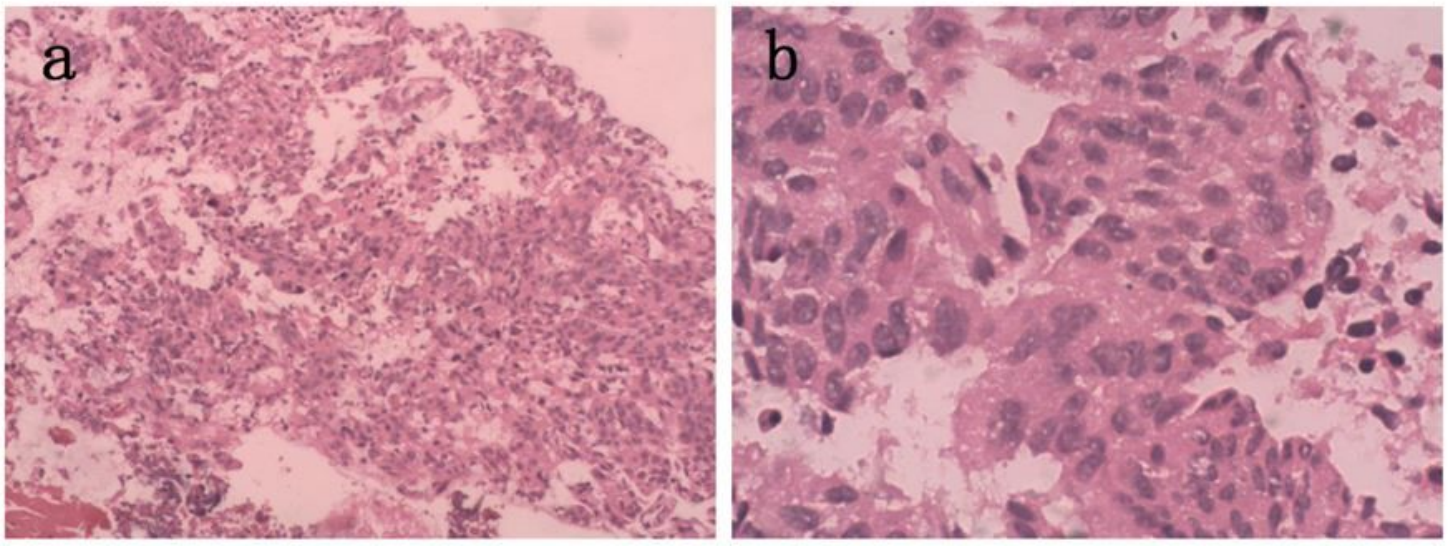

Figure 3

Hematoxylin-eosin (HE) staining of the neoplasm from the patient's bronchus. (a) Tumor cells arranged tightly and was irregular in shape. (magnification, 100 ×). (b) Tumor cells and nucleus were not uniform in size and cells exhibited obvious atypia. (magnification, 400 ×).

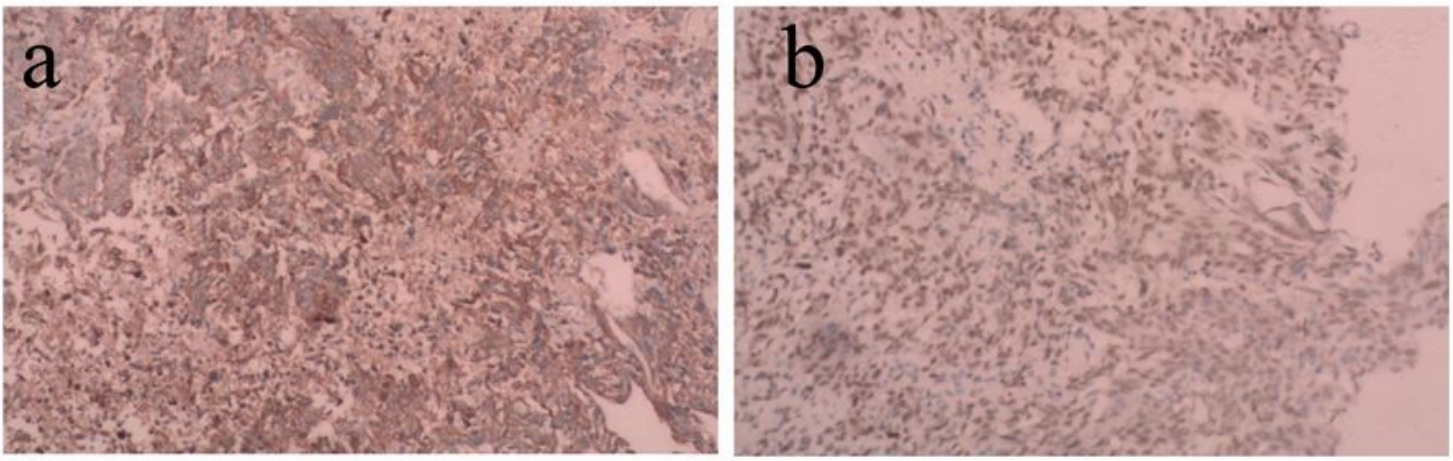

Figure 4

Immunohistochemistry (IHC) of the neoplasm from the patient's bronchus. (a) Staining with anti-CK antibody was positive, suggesting epithelial tumor. (magnification, 100 ×). (b) Staining with anti-WT-1 antibody was positive, suggesting ovariogenic tumor. (magnification, 100 ×).