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Bilateral endobronchial metastases from prostate cancer: A case report with literature review

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| ARTICLEINFO | A B S T R A C T |
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| <i>Keywords:</i> Prostate cancer Endobronchial metastases Hormonal therapy | Endobronchial metastases from prostate cancers are a rare phenomenon with only limited cases reported to date. Bronchoscopic biopsy and immunohistochemical test are essential for determining the diagnosis. And serum PSA level is a significant biomarker to assist the diagnosis. Our case describes a 68-year-old man presenting with bilateral endobronchial metastases after 5 years disease-free survival of prostate cancer. |

1. Introduction

The vast majority of endobronchial malignancies consist of primary bronchogenic carcinomas. Endobronchial metastases from extrathoracic tumors are exceedingly rare. The most common metastatic site of prostate cancers is bone [1]. Only limited cases of prostate cancers presenting as endobronchial metastases have been reported. Here, we share a case of prostate cancer presenting with bilateral endobronchial metastases. And we also review the literature to summarize the clinical features of prostate cancer with endobronchial metastases through searching for "prostate cancer" or "prostate carcinoma" and "endobronchial metastases" or "endobronchial malignancies" from 2005 to now in Pubmed.

1.1. Case report

A 68-year-old man was referred to the oncology department with a 3month history of coughing and chest distress in October 2019. He had undergone a surgery of prostate cancer 5 years ago. After surgery he also received adjuvant hormonal therapy for 2 years. There was no detailed data about the tumor staging and treatment.

Physical examination was unremarkable. Tumor markers, including carbohydrate (CA) 125, cytokeratin 19 fragment, squamous cell carcinoma antigen (SCC), carcinoembryonic antigen (CEA) and neuron-specific enolase (NSE) were normal. The serum total prostate-specific antigen (PSA) was 535.8 μ g/L. Computed tomography of chest showed bilateral pulmonary nodules and enlarged left hilum.

Bronchoscopy indicated multiple tumors in the bilateral mainstem bronchi (Fig. 1). The biopsy specimen showed adenocarcinoma. Immunostaining for PSA and NKX3.1 was positive (Fig. 2C and D). The specimens demonstrated negative immunoreactivity to thyroidtranscription factor-1 (TTF-1) (Fig. 2E). The immunostaining results confirmed the prostate origin. PET-CT showed multiple lymph nodes in bilateral hilar and mediastinum, parts of bilateral pulmonary patchy infiltrating shadows, left iliac bone and right ischium which were all considered as distant metastases with increased FDG uptake (Fig. 3).

The patient received total androgen blockade treatment with goserelin monthly and flutamide 250 mg PO tid. One month later, the serum total PSA was only 15.26 μ g/L. And the level of serum PSA declined to normal range two months after treatment.

2. Discussion

Endobronchial metastases from extrapulmonary solid tumors are an unusual event often reported as limited cases. Alessandro and colleagues documented a large case series of 174 patients with endobronchial metastases from extrathoracic solid tumors accounting for about 4% of all bronchoscopic biopsies performed for suspected malignancy [2]. Among them, breast cancer, colorectal cancer, renal cell cancer and gastric were the most common primary tumors presented as endobronchial mass. Prostate cancers having endobronchial metastases were relatively rare. There are only eighteen cases reported to date from 2005 searched in PubMed (Table 1).

The definition of endobronchial metastases is normally classified

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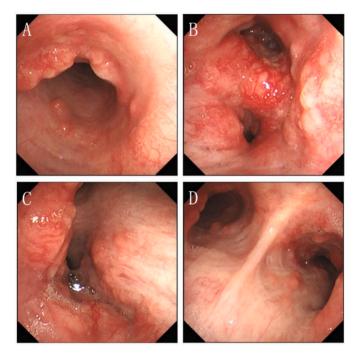


Fig. 1. Bronchoscopy showing neoplasms in the left main bronchus(A), left lobe bronchus(B), right main bronchus(C), and right lobe bronchus(D).

into four types proposed by Kiryu, Akoglu and colleagues [3,4]. Type I lesions occur as the direct metastasis to the bronchus through blood or lymphatic vessel. Type II to IV lesions result from the invasion by adjacent lesions such as parenchymal focus, mediastinal or lymph node metastasis and lymphangitis carcinomatosa. Our case accords with the type I lesions likely.

In the reported cases, the most common symptoms of endobronchial metastases were dyspnea, coughing and hemoptysis which were nonspecific in respiratory diseases. Nevertheless, some patients had no symptom. The patient of our case just sought medical advice on account of coughing. Meanwhile, radiologic characteristics of endobronchial metastases are also nonspecific and similar to those of primary

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bronchogenic carcinomas. Therefore, bronchoscopic biopsy and pathologic findings are especially important in making a definite diagnosis. In addition, the history of prostate cancer and detection of serum PSA level are critical. In our case, because of the high serum PSA level and the patient's medical history of prostate cancer, we performed immunohistochemistry for PSA to obtain the final diagnosis. In all cases, the serum PSA levels were elevated in varying degrees. As a result, serum PSA level is a significant biomarker to assist the diagnosis of endobronchial metastases from prostate cancer.

The interval between endobronchial metastases and primary diagnosis of prostate cancers varied individually. In some cases, they were synchronous. In other cases, they were heterochronous ranging from years to decades. Until now, the known longest interval was 20 years reported by Yukihisa and colleagues [5]. In our case, the interval was five years.

Alessandro et al. reported that endobronchial metastases from all kinds of solid tumors occurred in the right more frequently than the left bronchus [2]. Whereas, in the cases of endobronchial metastases from prostate cancer, there was no predilection site. It could happen in the right bronchus, left bronchus or bilateral bronchus. And in the previous reported cases, bilateral endobronchial metastases only occurred in partial bronchial branches. Our case showed prostate cancer could spread to all main and lobar bronchus extensively and concurrently. Bones are the most common metastatic sites in prostate cancer. Moreover, the bronchus could be the only metastatic site. In our case, prostate cancer also metastasized to the bones simultaneously.

The therapeutic strategy differs on the basis of primary solid tumors having endobronchial metastases. Hormone deprivation therapy has been the standard treatment for endobronchial metastases from prostate cancers. However, the androgen refractory prostate cancers require chemotherapy. In our case, the patient obtained the treatment of total androgen blockade with a rapid decline of serum total PSA level.

In conclusion, endobronchial metastases from prostate cancers are rare. In order to get the correct diagnosis, we need to realize the previous history of prostate cancer and detect the serum PSA level. Furthermore, histopathology is the gold standard for diagnosis.

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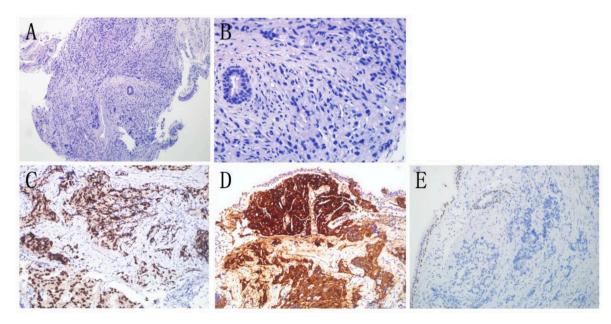


Fig. 2. Immunohistochemistry of the biopsied bronchial issue. Hematoxylin and eosin stained section(A,B), positive labeling with prostate-specific antigen(D) and NKX3.1(C), negative labeling with thyroid transcription factor-1(E), Original magnification \times 100(A), \times 400(B), \times 200(C,D,E).

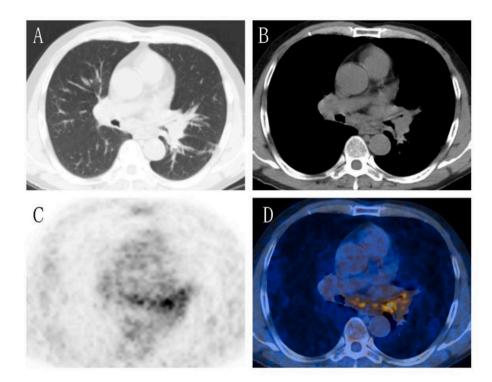


Fig. 3. ¹⁸F-FDG PET/CT was performed. Transverse CT(A,B),corresponding PET(C), and fusion(D) image showed intense FDG uptake of multiple nodules.

| Table 1 |
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| Case reports of endobronchial metastases from prostate cancer. |

| Author | Year | Age (years) | Symptoms | Time from primary diagnois | Bronchus location | Treatment | Total PSA (ng/ml) level | Follow- up | Extrathoracio metastasis |
|-------------------|------|----------------|--------------------------------------|-------------------------------|--|--|-------------------------------|------------------------|-----------------------------|
| Gerogianni [6] | 2008 | 64 | Dyspnea, dry coughing | 5 years | Bilateral (main, upper lobe) | Chemothrapy | 88.35 | None | None |
| Shen [7] | 2008 | 72 | None | Synchronous presentation | Left superior lobe | Chemothrapy | 612.34 | Alive, 19 months | Bones |
| Garai [8] | 2010 | 84 | Weight loss, hemoptysis | Synchronous presentation | Right intermediate | Hormonal therapy, bilateral subcapsular orchidectomy | 2500 | a | Lung |
| Bonney [9] | 2017 | 67 | None | 3 years | Right intermediate | a | Elevated | а | None |
| Bonney [9] | 2017 | 77 | None | 10 years | Left upper lobe | а | Elevated | а | None |
| Hatakeyama [5] | 2019 | 78 | Coughing, chest pain, weight loss | 20 years | a | Hormonal therapy | 714 | а | а |
| Asghar [10] | 2019 | 80 | Dyspnea | а | Right main bronchus | Cryotherapy | а | а | а |
| Freund [11] | 1999 | 63 | Coughing, dyspnea, hemoptysis | 9 years | Bilateral (right middle lobe, left carina) | Hormonal therapy | 425.3 | Alive, 18 years | Bones |
| Lee# [12] | a | а | a | Synchronous presentation | a | Chemothrapy | а | Dead, 5 months | None |

^a No data available. #Lee reported two cases. Marchioni reported eight cases.

agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

None declares.

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