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CASE REPORT

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# A 47-Year-old Asian female with tracheobronchial space-occupying lesions caused by chronic lymphocytic leukemia

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**Case presentation**
A 47-year-old Asian woman was admitted with worsening chest tightness and dyspnea for 10 days. Computed tomography (CT) showed changes in the trachea and segmental bronchi. Pulmonary function results suggestive of severe obstructive ventilatory dysfunction. Bronchoscopic findings showed the presence of multiple nodular lesions in the patient's trachea and left and right main bronchi. Bronchoscopic biopsy, lymph node biopsy and bone marrow aspiration flow cytometry test results led to a definitive diagnosis of chronic lymphocytic leukemia (CLL), staged as Binet stage B and Rai stage 2.

**Keywords** Airway obstruction, Chronic lymphocytic leukemia, Bronchoscopy, Flow cytometry

## Introduction

Chronic lymphocytic leukemia (CLL) is a common leukemia in adults in Europe and the United States. The incidence of CLL in the United States is 4.5 cases per 100,000 people, and it is more common in men [1]. In Asia, however, the incidence of CLL is only one tenth of that in Europe and the United States, with an incidence rate of 0.2–0.6 cases per 100,000 people [2, 3]. Asian patients with CLL have a younger age of onset and a more variable clinical presentation, which may be closely related to genetic factors [4]. We report a rare case of a 47-year-old Chinese woman, in whom dyspnea and airway obstruction were important clinical manifestations, and the diagnosis of CLL was confirmed by hematological and pathological examination.

## Case report

A 47-year-old Asian female patient came to the hospital with worsening chest tightness and dyspnea, and painless cervical lymph node enlargement that occurred 2 months ago. Computed tomography (CT) scan revealed central airway obstruction (CAO) and physical examination also revealed several enlarged lymph nodes in the patient's submandibular and left supraclavicular fossa.

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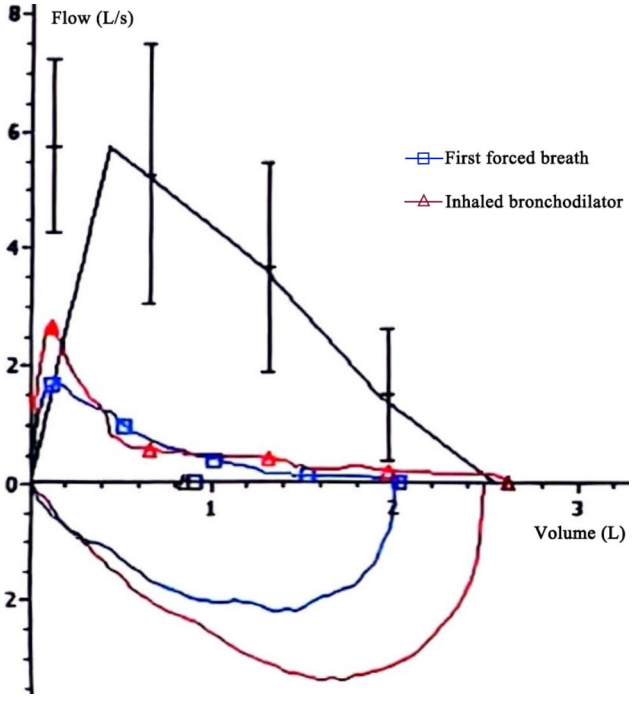


**Fig. 1** Pulmonary function tests. Results of the flow-volume loop for the first forced breath: $FEV_1 = 0.90$ L, FVC = 2.02 L, $FEV_1/FVC = 0.45$, PEF = 1.64 L/s, MEF75 = 0.95 L/s, MEF50 = 0.38 L/s, MEF25 = 0.11 L/s, MEF75/25 = 0.27 L/s

The patient's pulmonary function test results on admission were 0.45 of forced expiratory volume in one second/forced vital capacity ($FEV_1/FVC$) (<0.70), the descending branch of the force-velocity curve was significantly indented. Pulmonary function tests showed that the patient had obstructive ventilatory dysfunction, which was associated with tracheobronchial space-occupying lesions (Fig. 1). The chest CT scan revealed tracheal and bronchial lesions (Fig. 2). The results of routine blood tests showed a leukocyte count of $28.3\times10^9$/L (3.5–$9.5\times10^9$/L), an absolute neutrophil value of $3.9\times10^9$/L (1.8–$6.3\times10^9$/L), and an absolute lymphocyte value of $24.0\times10^9$/L (1.1–$3.2\times10^9$/L), which was associated with a significant increase in the percentage of lymphocytes.

To further define the cause of airway obstruction, we performed video bronchoscopy on the patient, which revealed multiple nodular elevations in the trachea and the left and right main bronchi, suggesting severe central airway obstruction (Fig. 3). At the same time, we took tissue from the airways for biopsy with the aid of bronchoscopy. To clarify the cause of the patient's markedly elevated lymphocytes, we asked a hematologist for a consultation to discuss whether the patient had indications for a bone marrow aspiration test.

The patient's biopsy at the left main bronchus showed non-Hodgkin's B-cell lymphoma, and immunohistochemical results were CD20+, CD23+, CD43+, PAX5+,

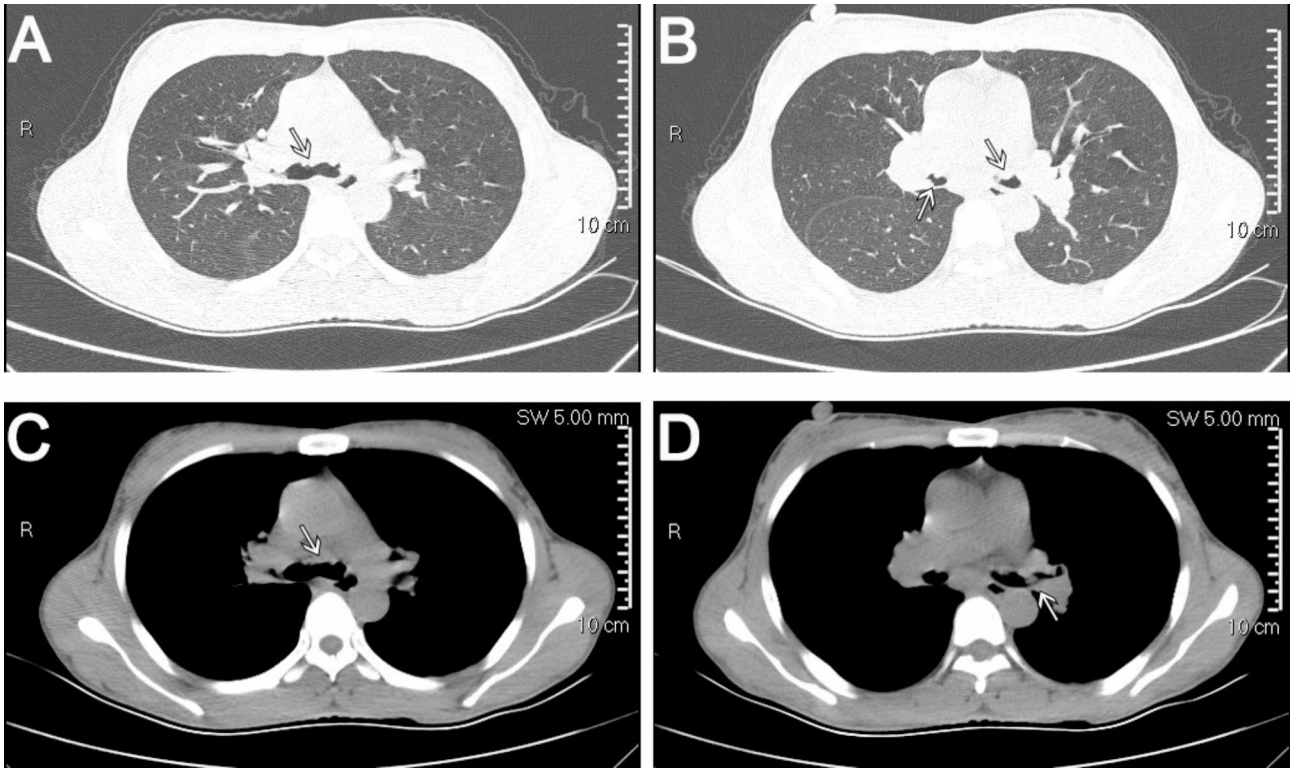


**Fig. 2** Computed tomography of the chest. A-D: Chest CT showed tracheal and bronchial lesions. (**A**, **B**: lung window; **C**, **D**: mediastinal window)

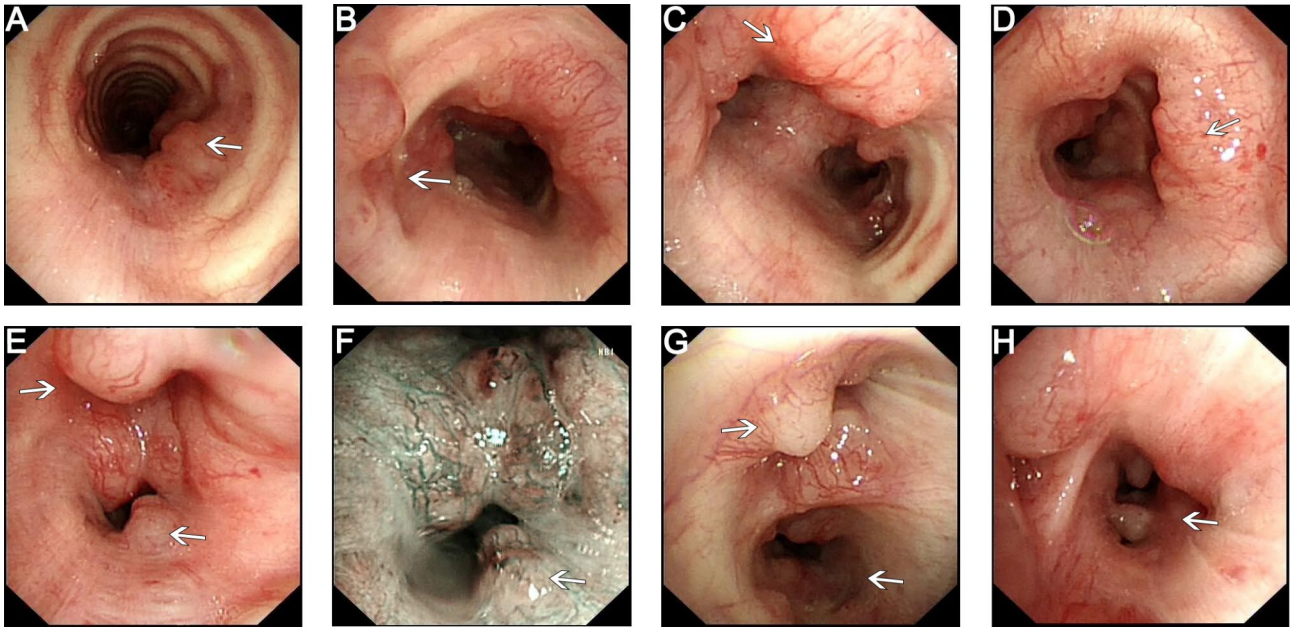


**Fig. 3** Video bronchoscope. **A**-**H**: Multiple nodular elevations in the trachea, carina of trachea, left main bronchus, and right main bronchus were seen microscopically (A-**B**: trachea; **C**: carina of trachea; **D**-**E**: left main bronchus; **F**: left main bronchus on narrow-band imaging endoscopy; **G**: right main bronchus; **H**: right intermediate lung segment). Bronchus

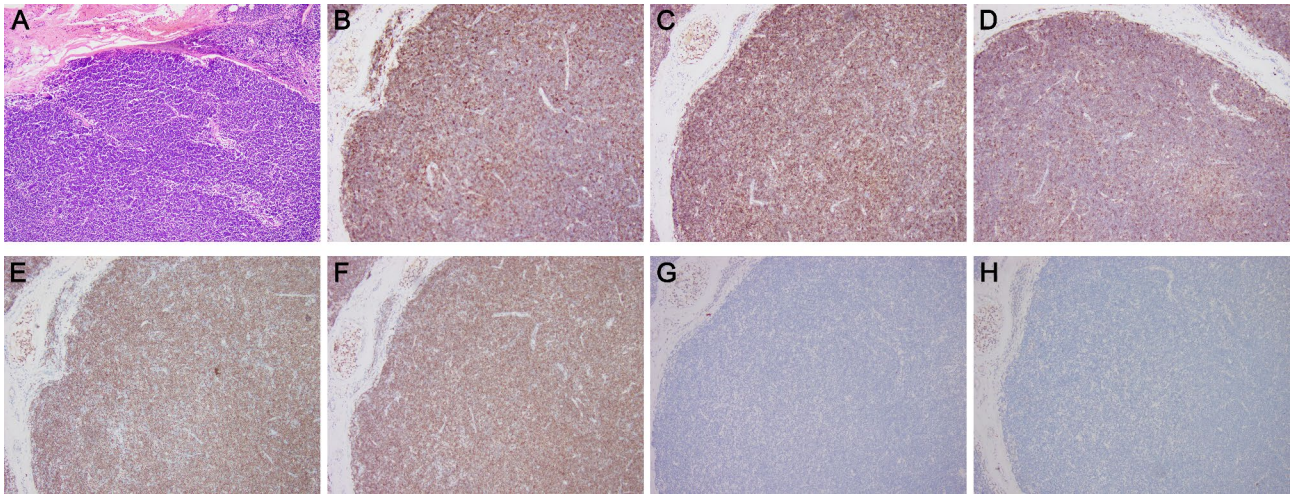


**Fig. 4** HE staining and immunohistochemical results of tracheal tissue biopsy. **A**: hematoxylin-eosin staining showed a large lymphocytic infiltration in the tissue. **B**-**D**: immunohistochemical results showed significant expression of human leukocyte differentiation antigens, CD20, CD23, and CD43. **E**: high expression of the B-cell surface specific transcription factor, PAX5. **F**-**H**: immunohistochemistry showed high expression of the proto-oncogene, BCL-2. BCL-6 was not expressed, and cyclinD1 was not expressed

CD5+, BCL-2+, BCL-6-, cyclinD1-, TTF-1- (Fig. 4), and immunohistochemical results of the tracheal biopsy were consistent with lymph node biopsy results in keeping with the chronic lymphocytic leukemia/small cell lymphoma diagnosis. Chromosome G-banding karyotype analysis of 20 mitotic metaphases resulted in 46, XX, add (18) (q21) [13] / 46, idem, add (13) (q12) [2] /46, XX [5], with 13 groups of 46, XX, add (18) (q21), 2 groups of 46, idem, add (13) (q12) [2], and 5 groups with normal 46, XX.

In order to clarify the bone marrow involvement, the patient and her family chose to undergo bone marrow aspiration with informed consent. We performed flow cytometric analysis of the patient's bone marrow, and 77.7% of the bone marrow cells were abnormal mature B lymphocytes, with immunophenotypes of CD5+, CD19+, CD20+, CD22+, CD23+, CD200+, CD79b+, CD10-, CD38-, IgM-, FMC-7-, intracellular immunoglobulin Lambda light chain restricted expression, suggesting monoclonal B cells (Fig. 5). Flow analysis results were

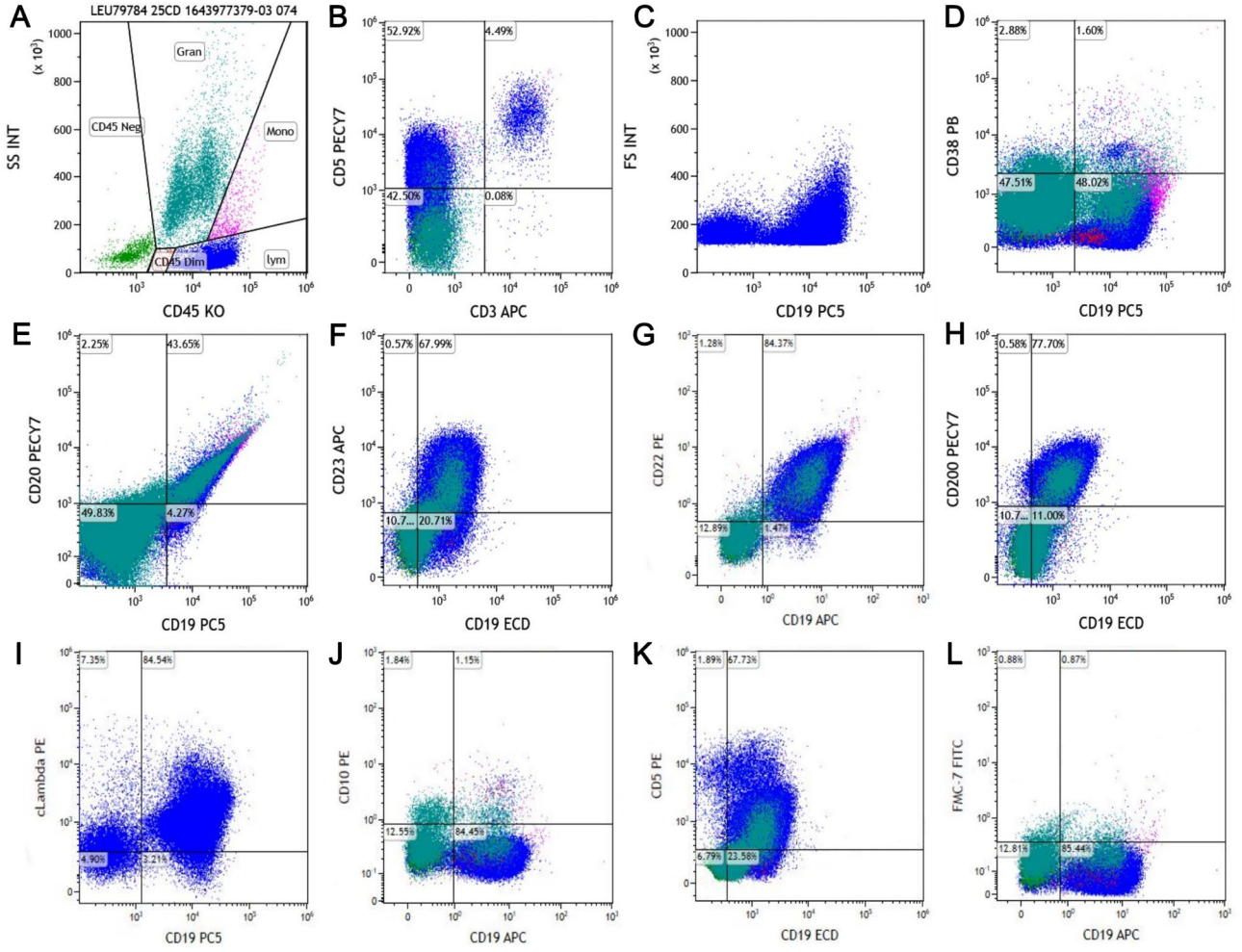


**Fig. 5** Immunophenotypic analysis of bone marrow specimens by flow cytometry. **A**: Sorting and proportion of leukocytes in bone marrow specimens. **B**-**L**: CD5+, CD19+, CD20+, CD22+, CD23+, CD200+, CD10-, CD38-, FMC-7-, intracellular immunoglobulin Lambda light chain restricted expression

consistent with the immunophenotype of CLL. Combined with the clinical manifestations and laboratory tests we finally diagnosed the patient with CLL, with a clinical stage of Binet stage B and Rai stage 2.

Currently, in response to the patient's clinical presentation, the clinician continues to give symptomatic treatment such as cough relief, phlegm reduction, and asthma. As chronic lymphocytic leukemia is still an incurable disease, and patients who met the inclusion and exclusion criteria were encouraged to participate in the clinical trials [5]. The patient met al.l the inclusion criteria and none of the exclusion criteria. After providing informed consent, the patient participated in the clinical trial. The patient's symptoms of dyspnea have significantly improved, her condition is stable, and she is being followed up.

## Discussion

CAO is a very rare complication in patients with CLL. We report an Asian female patient who presented with chest tightness and dyspnea due to CAO and was diagnosed with CLL based on a comprehensive assessment that incorporated hematological parameters and other relevant clinical information.

In previous studies, we found case reports of CLL patients with combined upper airway obstruction, including extra-tracheal compression, subglottic intrinsic mass and tonsillar enlargement [6–8]. Berkman reported three cases of CLL with combined pulmonary infiltrates, where clinical evidence and imaging confirmed leukemic infiltration resulting in lung parenchymal injury [9]. Adrian reported a case of a patient with CLL combined with enlarged lymph nodes in the base of the tongue, resulting in upper airway obstruction and dyspnea [10]. Miranda found bronchial polyps in the bronchi of a patient with a 7-year history of CLL, but that case presented with focal polyp deposits, whereas the patient in

this study had multiple endobronchial elevations [11]. Bashoura explained that the pulmonary manifestations of leukemia patients involve multiple structures in the chest, and it is necessary to identify other malignant tumors and flow cytometry to confirm the diagnosis [12]. All of the above reports suggest that patients with CLL or lymphoma develop respiratory symptoms, however, these respiratory symptoms typically present as comorbidities after a patient is diagnosed with CLL.

Clinical manifestations of combined lung disease in CLL are often difficult to distinguish from primary lung disease, which presents diagnostic and therapeutic difficulties. Chernoff reported a case of a patient with CLL who developed bronchial stenosis at a later stage of the disease, which led to recurrent pneumonia and pulmonary fibrosis [13]. Notably, Christiansen found a reliable safety profile for endoscopic ultrasound-biopsy as an alternative to bronchoscopic biopsy in patients with respiratory impairment [14]. With suspected deep-seated lymphoma or CLL, a biopsy is always indicated to clarify the exact diagnosis at the most precise level possible. In this case, the patient presented with dyspnea, and the results of bronchial biopsy and flow cytometry helped confirm the diagnosis of CLL. Flow cytometry and genetic testing enable doctors to better understand the biological characteristics of tumors and formulate more precise treatment strategies.

In conclusion, this case describes tracheobronchial space-occupying lesions caused by CLL in a 47-year-old young Asian woman. Of note, CLL rarely involves the tracheobronchial tree, while confirming a diagnosis of CLL required a combination of the patient's other investigations. This reminds clinicians of the need for a multisystem approach to the diagnosis and differential diagnosis of CLL, as well as the requirement for early treatment of the disease.

#### Abbreviations

| | |
|---|---|
| CLL | Chronic lymphocytic leukemia |
| CAO | Central airway obstruction |
| CT | Computed tomography |
| $FEV_1$/FVC | Forced expiratory volume in one second/forced vital capacity |
| PEF | Peak expiratory flow |
| MEF | Maximal expiratory flow |

#### Author contributions

JW.Z and GH.C conducted the case analysis. FQ.G, Z.C, Y.F and HK.S conducted the Data collection.JW.Z and L.L wrote the original manuscript text. P.X and L.P provided funding acquisition. CJ.L and L.P reviewed and edited.

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#### Data availability

No datasets were generated or analysed during the current study.

## Declarations

#### Ethics approval and consent to participate

No applicable. Ethical approval to report this case was not required due to its retrospective nature.

#### Competing interests

The authors declare no competing interests.

#### Clinical trial number

Not applicable.

#### Consent to Publish

Written informed consent were obtained from the patient for publication of this case report.

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#### References

1. Fabbri G, Dalla-Favera R. The molecular pathogenesis of chronic lymphocytic leukaemia. Nat Rev Cancer. 2016;16(3):145–62.
2. Mak V, Ip D, Mang O, Dalal C, Huang S, Gerrie A, Gillan T, Ramadan KM, Toze C, Au WY. Preservation of lower incidence of chronic lymphocytic leukemia in Chinese residents in British Columbia: a 26-year survey from 1983 to 2008. Leuk Lymphoma. 2014;55(4):824–7.
3. Gale RP. Chronic lymphocytic leukemia in China. Chin Med J (Engl). 2022;135(8):883–6.
4. Yi S, Yan Y, Jin M, Xiong W, Yu Z, Yu Y, Cui R, Wang J, Wang Y, Lin Y, et al. High incidence of MYD88 and KMT2D mutations in Chinese with chronic lymphocytic leukemia. Leukemia. 2021;35(8):2412–5.
5. Hematological Oncology Committee of China Anti-Cancer A, Chinese Working Group for Chronic Lymphocytic L. The guidelines for diagnosis and treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma in China(2022). Zhonghua Xue Ye Xue Za Zhi. 2022;43(5):353–8.
6. Winkler CF, Corpus R. Tracheal obstruction in chronic lymphocytic leukemia. Chest. 1980;77(2):244–5.
7. Firestone FN, Robinson MJ. Upper airway obstruction: a rare presentation of chronic lymphocytic leukemia. Chest. 1972;61(5):505–7.
8. Dean MG, Cunningham I, Dao LP, Cole I, Mulligan SP. Chronic lymphocytic leukaemia with upper airway obstruction. Leuk Lymphoma. 1996;20(5–6):505–7.
9. Berkman N, Polliack A, Breuer R, Okon E, Kramer M. Pulmonary involvement as the major manifestation of chronic lymphocytic leukemia. Leuk Lymphoma. 1992;8(6):495–9.
10. Bersabe AR, Romain JT, Ezzell EE, Renshaw JS. Chronic lymphocytic leukemia as an unusual cause of Rapid Airway Compromise. Case Rep Oncol Med. 2017;2017:8247353.
11. Maw M, Harvey M, Harrington Z, Baraket M, Montgomery R, Williamson J. Endobronchial deposits of chronic lymphocytic leukemia - an unusual cause of central airway obstruction. Respirol Case Rep. 2015;3(2):41–3.
12. Bashoura L, Eapen GA, Faiz SA. Pulmonary manifestations of Lymphoma and Leukemia. Clin Chest Med. 2017;38(2):187–200.
13. Chernoff A, Rymuza J, Lippmann ML. Endobronchial lymphocytic infiltration. Unusual manifestation of chronic lymphocytic leukemia. Am J Med. 1984;77(4):755–9.
14. Christiansen IS, Bodtger U, Nessar R, Salih GN, Kolekar S, Sidhu JS, Hoegholm A, Laursen CB, Arshad A, Clementsen PF. Safety and feasibility of oesophageal ultrasound for the work-up of thoracic malignancy in patients with respiratory impairment. J Thorac Dis. 2023;15(7):3965–73.

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