

## Video-assisted thoracic surgery for ambiguous lung or mediastinal masses in response assessments for hematological malignancies

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*To the Editor:* The morbidity of thoracic lesions is very high during the treatment of malignant hematological diseases, and tumor recurrence or invasion is common, in addition to infections. Percutaneous lung biopsy or bronchoscopy could result in severe hemoptysis, pneumothorax, or infection because of low platelets and hypoimmunity, and treatment is often ineffective due to the ambiguous diagnosis. Even when a patient is diagnosed with a fungal disease, it is difficult to eliminate the lesion with only antifungal medicine. Video-assisted thoracic surgery (VATS) is an important surgical procedure for major and minor lung resection with adequate pain relief and sedation in a minimally invasive setup, allowing thoracic procedures under spontaneous breathing.<sup>[1,2]</sup> We report here a series of cases to evaluate the feasibility and safety of VATS for making diagnoses by lung biopsy or pulmonary resections in the hematology department.

From December 2017 to July 2019, 12 patients with malignant hematological diseases underwent uniportal VATS (U-VATS) due to lung or mediastinal masses. Before deciding on the biopsy method, we compared interventional bronchoscopy, computerized-assisted transthoracic needle biopsy, and VATS, and chose VATS according to the location of the lesions, patients' conditions, and the risk of misdiagnosis. Patients' characteristics are shown in [Table 1]. Of the 12 patients, 83.33% (10/12) had complete remission after regular chemotherapy, 1 patient had partial remission, and 1 patient was diagnosed with hemophagocytic syndrome of unknown origin. During the treatments for hematological diseases, all patients received standard prophylactic treatment for pulmonary infection, which consisted of triazole antifungal agents and cotrimoxazole when the neutrophil count was  $<1 \times 10^9/L$ . No patient was confirmed to have fungal or *Pneumocystis carinii* infection before the mass lesions were found. For patients who underwent hematopoietic stem cell transplantation (HSCT), antimicrobial prophylaxis was used during HSCT

and lasted for 3 months posttransplantation. Patients with lung or mediastinal masses confirmed by computed tomography (CT) scans or positron emission tomography/computed tomography (PET/CT) received broad-spectrum antibacterial and empiric antifungal therapy for 1 month, but no improvement was observed. VATS-mediated lung and mediastinal mass biopsy were performed in five patients, VATS wedge resection was performed in six patients, and VATS radical resection was performed in one patient. The average blood loss was  $103.25 \pm 159.57$  mL. The length of hospital stay from post-operation to discharge was 2 to 10 days, with an average of  $4.25 \pm 2.16$  days. The time of VATS and the results of pathological assessment are shown in [Table 1]. Of the 12 patients, only 1 patient was confirmed to have a relapse of lymphoma, one had newly diagnosed lymphoma, six were diagnosed with pulmonary fungal infections, one was confirmed to have secondary cancer, and three patients who were suspected of having a relapse before VATS were found to have fibrous connective tissue hyperplasia. Patients were followed until death or the end of data collection on December 31, 2020, whichever came first. The 2-year cumulative survival rate was 66.7%.

The diagnosis of lung or mediastinal masses in patients with hematological malignancies is challenging during treatment due to low white blood cell counts, low platelet counts, coagulopathy, and immunodeficiency, which make conventional surgical resection impossible. Patients could be overtreated or miss the best time window for treatment without adequate evidence for making a diagnosis. Contrast-enhanced CT or PET/CT has limitations in making differential diagnoses between infection and malignancy in some cases because residual masses or new lesions after chemotherapy could be signs of relapse, infection, or secondary tumors. It has been reported that the standard uptake value (SUV) in cryptococcal pneumonia fluctuates between 0.93 and 11.6, and the average SUV<sub>max</sub> in tuberculosis (TB) is  $4.2 \pm 2.2$ , making them difficult to be distinguished from tumor relapse.<sup>[3]</sup>

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**Table 1: Patients' characteristics and the results of pathologic assessment by VATS.**

Patients No.	Gender	Age (years)	Diagnosis	Disease status	Time of VATS	Pre-VATS	Post-VATS
1	Female	33	DLBCL	CR	Post-transplant	Suspicious infection	Relapse
2	Female	63	ALL	CR	Maintenance	Suspicious infection	TB
3	Female	24	ALL	CR	Post-transplant	Suspicious relapse	Thymic hyperplasia
4	Female	34	HD	CR	Post-transplant	Suspicious relapse	Thymic hyperplasia
5	Male	67	DLBCL	CR	Maintenance	Suspicious relapse	Thymic hyperplasia
6	Female	70	DLBCL	CR	Consolidation	Suspicious infection	Cryptococcal infection
7	Female	23	ALL	PR	Consolidation	Suspicious infection	<i>Aspergillus</i> infection
8	Female	44	AML	CR	Consolidation	Suspicious infection	<i>Aspergillus</i> infection
9	Female	45	HLH	PR	Consolidation	Suspicious lung cancer	Lymphoma
10	Male	53	AML	CR	Consolidation	Suspicious infection	<i>Aspergillus</i> infection
11	Male	76	CML	CR	Maintenance	Suspicious infection	Cancer
12	Male	46	MM	CR	Maintenance	Suspicious relapse	Cryptococcal infection

ALL: Acute lymphocyte leukemia; AML: Acute myeloid leukemia; CML: Chronic myelogenous leukemia; CR: Complete remission; DLBCL: Diffuse large B-cell lymphoma; HD: Hodgkin lymphoma; HLH: Hemophagocytic lymphohistiocytosis; MM: Multiple myeloma; PR: Partial remission; TB: Tuberculosis; VATS: Video-assisted thoracic surgery.

Moreover, contrast-enhanced CT or PET for remission assessment in many indolent lymphomas is not sufficient, and false-positives can occur.<sup>[4]</sup> It has been reported that thymic hyperplasia could occur in lymphoma patients after chemotherapy, especially for those who had adequate immune reconstruction.<sup>[4]</sup> The 2021 revised National Comprehensive Cancer Network (NCCN) guidelines for many types of lymphoma emphasized rebiopsy for residual lung or mediastinal masses to confirm the pathological diagnosis and prevent overtreatment for malignancy. Biopsy technologies, such as interventional bronchoscopy and computerized-assisted transthoracic needles, have limitations in obtaining enough samples. Moreover, NCCN guidelines indicate that excisional or incisional biopsy is preferred over core needle biopsy. Therefore, VATS has gradually been increasingly used to assist in pathological evaluation. In this report, 50% of patients were pathologically confirmed to be infected, and only one patient was confirmed to have a relapse, suggesting that infection, rather than a relapse of the tumor, was the main cause of the mass after regular treatment for hematological malignancy. Of the six patients who were confirmed to have infection, two had a cryptococcal infection, three had an *Aspergillus* infection, and one had TB. VATS helped make a reliable diagnosis so that antifungal treatment could be started.

VATS is an effective and safe option in the management of invasive pulmonary fungal infection in these patients, and it can also help remove lesions when necessary. VATS is superior to traditional surgery because it is less invasive, has fewer and smaller incisions, and has a shorter hospital stay.<sup>[1,2]</sup> Ma et al<sup>[5]</sup> reported that a total of 51 patients with hematological diseases underwent VATS for invasive pulmonary fungal infection, and no life-threatening complications or infection recurrences occurred at the 6- to 24-month follow-ups. Of the six patients who were confirmed to have infections, three patients who underwent VATS radical or wedge resection had very short hospital stays, and one of them had allogeneic HSCT only 14 days after VATS. VATS is associated with fast recovery and fewer complications, thus providing an opportunity for transplantation. Differential diagnosis of new pulmo-

nary lesions or residual mediastinal masses shown by contrast-enhanced CT or PET/CT for remission assessment of hematological diseases is of great importance. VATS is a safe and important procedure to make diagnoses and guide treatment.

#### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for all clinical information to be reported in the article. The patients understand that their names and initial will not be published and due efforts will be made to conceal the identity of the patients, although anonymity cannot be guaranteed.

#### Conflicts of interest

None.

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