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CASE REPORT

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Atypical pulmonary manifestations suggestive of lung cancer in behçet's disease with spontaneously regressing lymphadenopathy and a lung mass: a case report

So-yun Kim[1†], Min-kyung Yeo[2†], Subin Im[3] and Chaeuk Chung[1,4*]

Abstract

Background Behçet's disease (BD) is a multisystem inflammatory disorder that can affect various organs, including the lungs. Pulmonary manifestations are rare and typically present as pulmonary artery aneurysms.

Case presentation We report the case of a 56-year-old East Asian male with a 27-year history of BD, who had no respiratory symptoms, such as hemoptysis, cough, or fever. Chest imaging revealed lymph node enlargement and a lung mass, initially raising concerns of malignancy. Despite the suspicious radiological findings, three biopsies, including a surgical biopsy, were all negative for malignancy. Remarkably, over the course of 2 years, these pulmonary manifestations spontaneously regressed without any specific treatment for lung involvement, and the patient remained in a stable BD state.

Conclusions BD patients are at an increased risk for malignancy compared to healthy controls, making it crucial to differentiate between malignancy and BD-related pulmonary abnormalities. This case highlights that, in the absence of active BD symptoms, lymphadenopathy and lung masses can occur and may resolve spontaneously. Accurate diagnosis and vigilant monitoring are essential in BD patients but BD-related lung involvement should be considered in similar cases.

Keywords Behçet's disease, Lymphadenopathy, Lung mass, Pulmonary manifestation, Regression

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Introduction

Behçet's disease (BD) is a chronic inflammatory condition characterized by a wide range of systemic manifestations, including urogenital ulcers, arthritis, skin lesions, and inflammation of the eyes and vascular structures (1, 2). Although it can affect multiple organ systems, pulmonary involvement is relatively rare and generally manifests as pulmonary vascular lesions. Pulmonary manifestations occur in 1–7.7% of cases, with pulmonary artery aneurysms being the most common finding, often accompanied by thrombosis [3–6].

This report presents the case of a male with a 27-year history of BD who exhibited radiological features suggestive of lung cancer. Computed tomography (CT) and positron emission tomography (PET-CT) of his chest revealed peribronchial tissue thickening, bronchial narrowing, and multiple enlarged lymph nodes, raising concerns about a potential malignancy. Despite the rarity of such presentations in BD, these findings highlight the importance of including BD in the differential diagnosis when encountering similar radiological abnormalities.

Case report

A 56-year-old East Asian male with a 27-year history of BD, characterized by recurrent oral ulcers, skin lesions, joint pain, and ocular abnormalities, was referred to our hospital following the new identification of right hilum enlargement in a recent chest X-ray. Imaging studies, including chest X-ray and CT performed 18 months earlier, showed no evidence of right hilar enlargement (Fig. 1A and D). The patient, who had maintained a stable BD state on a consistent dose of 20 mg prednisolone for prior past 3 years, reported no respiratory symptoms, such as cough, sputum production, or dyspnea. His medical history included stage 3 A colon cancer diagnosed approximately 18 months before, for which he underwent surgery and chemotherapy, achieving complete remission.

Blood tests revealed that the patient did not carry the Human Leukocyte Antigen B27 allele, and the antinuclear antibody test was negative. His white blood cell (WBC) count, C-reactive protein (CRP) levels, and erythrocyte sedimentation rate (ESR) were all within normal ranges, with values of 7,220/μL, 0.8 mg/dL, and 2 mm/h, respectively, showing no laboratory abnormalities indicative of infection. Additionally, repeated interferon-gamma (IFN-γ) release assays were negative, reducing the likelihood of tuberculosis. Tumor markers were within normal ranges, with carcinoembryonic antigen at 4.64 ng/mL and carbohydrate antigen 19 – 9 at 16.86 U/mL, but lactate dehydrogenase was elevated at 609 U/L.

CT of the chest revealed marked lymph node enlargement and new peribronchial tissue thickening with bronchial narrowing in the anterior segment of the right upper lobe (RUL) (Fig. 1D). These findings were notably different from the previous CT (Fig. 1B) and raised the suspicion of lung cancer with metastatic lymphadenopathy. The patient was an ex-smoker with a 30-pack-year smoking history, having quit 1 year prior, further increasing the risk of malignancy. To differentiate malignancy, the patient underwent linear endobronchial ultrasound (EBUS) with biopsy of the 4R, 7, and 11R lymph nodes. EBUS-transbronchial needle aspiration (TBNA) was conducted using the Olympus BF-UC260FW system. A 22G needle was utilized to obtain samples from each lymph node, with three passes performed per node. However, all biopsy results were negative for malignant cells. Given the extent of lymph node enlargement and the possibility of false-negative results, a repeat linear EBUS of the 7R lymph node and the para-tracheal mass, as well as a RUL mucosal biopsy, were performed. However, no malignancy was detected.

Recognizing that small biopsies in cases of hematologic disorders, such as lymphoma, or granulomatous diseases, such as sarcoidosis, may not provide a definitive diagnosis, a surgical biopsy of the 4R lymph node (Fig. 2A and B) was conducted. Histopathological examination revealed acute suppurative and chronic inflammation with some eosinophils and leukocytoclastic vasculitis, suggesting the possibility of BD. (Figure 2C and D). Following surgery, PET-CT continued to suggest a potential diagnosis of lung cancer with lymph node metastasis (Fig. 3A–D). However, in light of multiple negative biopsy results and surgical findings, lung involvement by BD was considered the most likely diagnosis. After consultation with the rheumatology department, it was decided to monitor the patient without initiating additional immunosuppressive therapy, as the lung involvement was not rapidly progressive.

Subsequent follow-up over 10 months showed that the CT findings, including lymph node enlargement and peribronchial tissue thickening with bronchial narrowing, remained stable without significant changes (Fig. 4A and B). During this period, the patient's BD also remained stable, with continued treatment using 20 mg prednisolone.

Approximately 2 years later, on July 10, 2023, a non-contrast CT revealed a reduction in the size of the peribronchial soft tissue and lymph nodes in the RUL. Six months after this scan, the size of the lymph nodes continued to decrease, although the size of the peribronchial soft tissue remained stable. The most recent CT, performed 6 months later, confirmed a significant reduction in both the peribronchial soft tissue and lymph nodes (Fig. 4C, D).

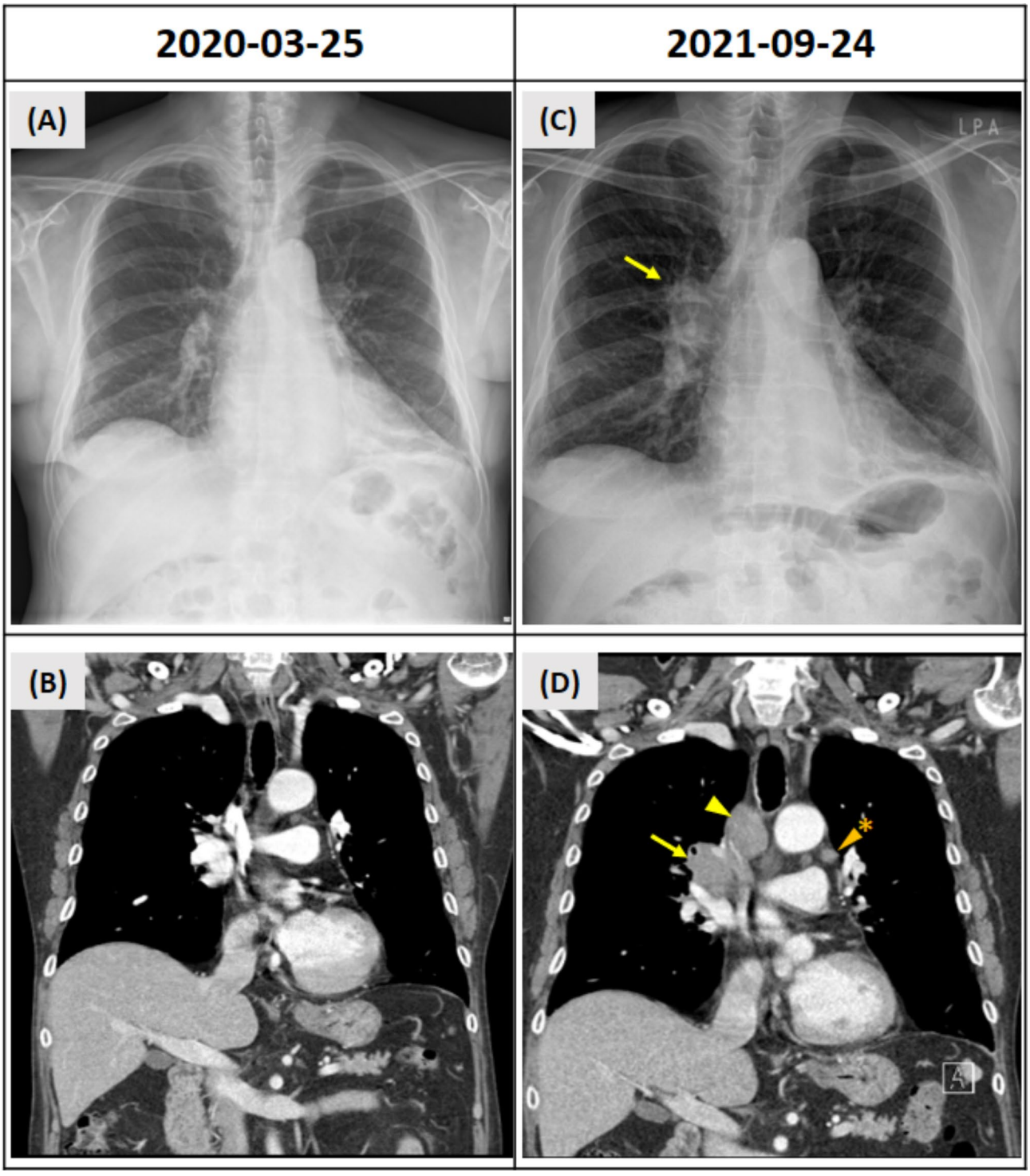

Fig. 1 Serial images of the patient's chest X-ray (CXR) and chest computed tomography (CT) illustrating changes in the size of the 4R lymph nodes. (**A**, **B**) The 2020 chest CT and CXR show no evidence of lymphadenopathy. (**C**, **D**) In the 2021 CXR and chest CT, hilar enlargement and increased lymph nodes are observed, with the 4R (yellow arrowhead) and 5R (orange arrowhead with star) lymph nodes noted, along with a mass-like lesion anterior to the right upper lung (yellow arrow)

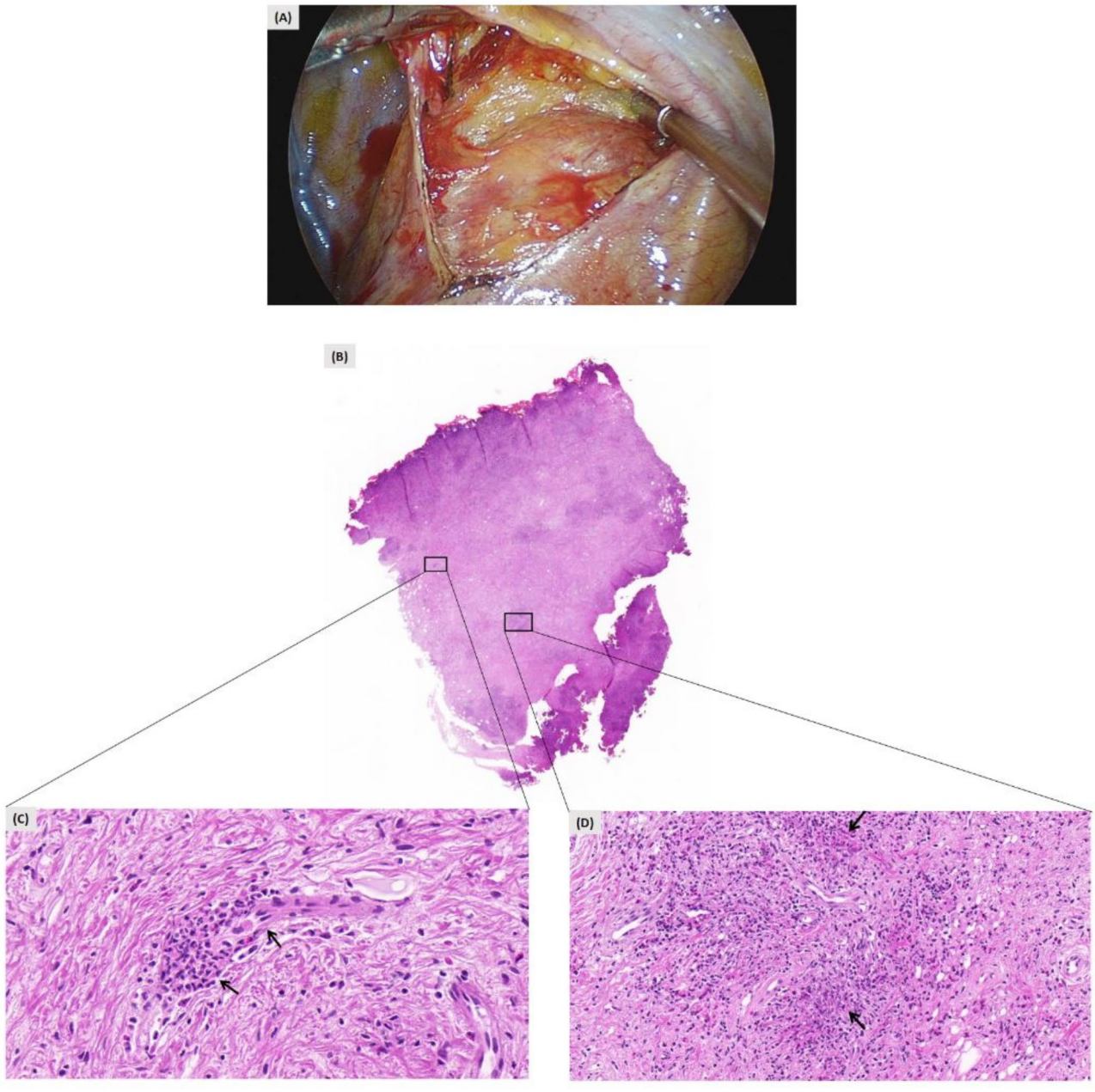

Fig. 2 Image and pathological findings from the surgical biopsy excision of the 4R lymph node. (**A**) Video-Assisted Thoracoscopic Surgery (VATS) biopsy of the 4R lymph node. (**B**) Hematoxylin and eosin staining of the lymph node. (**C**) Presence of leukocytoclastic vasculitis indicated by black arrows (×48). (**D**) Focal necrosis and mixed cell infiltration with eosinophils, along with leukocytoclastic vasculitis (black arrows) (magnification ×30)

Discussion

This case represents an exceptionally rare manifestation of BD involving the lungs, characterized by lymph node enlargement and peribronchial mass formation. To the best of our knowledge, this is the first reported case of BD with pulmonary involvement presenting with radiological features strongly suggestive of lung cancer. The patient's previous history of colon cancer and long-term smoking significantly raised the suspicion of malignancy, prompting extensive diagnostic investigations, including multiple biopsies and a PET-CT that suggested potential malignancy. However, all biopsy results confirmed benign findings.

This case was unique because the patient did not exhibit signs of an acute BD flare-up or any significant respiratory symptoms at the time of lymph node enlargement and RUL mass detection. The patient had been on a stable dose of prednisolone without a need for escalation, and remarkably, the pulmonary findings spontaneously

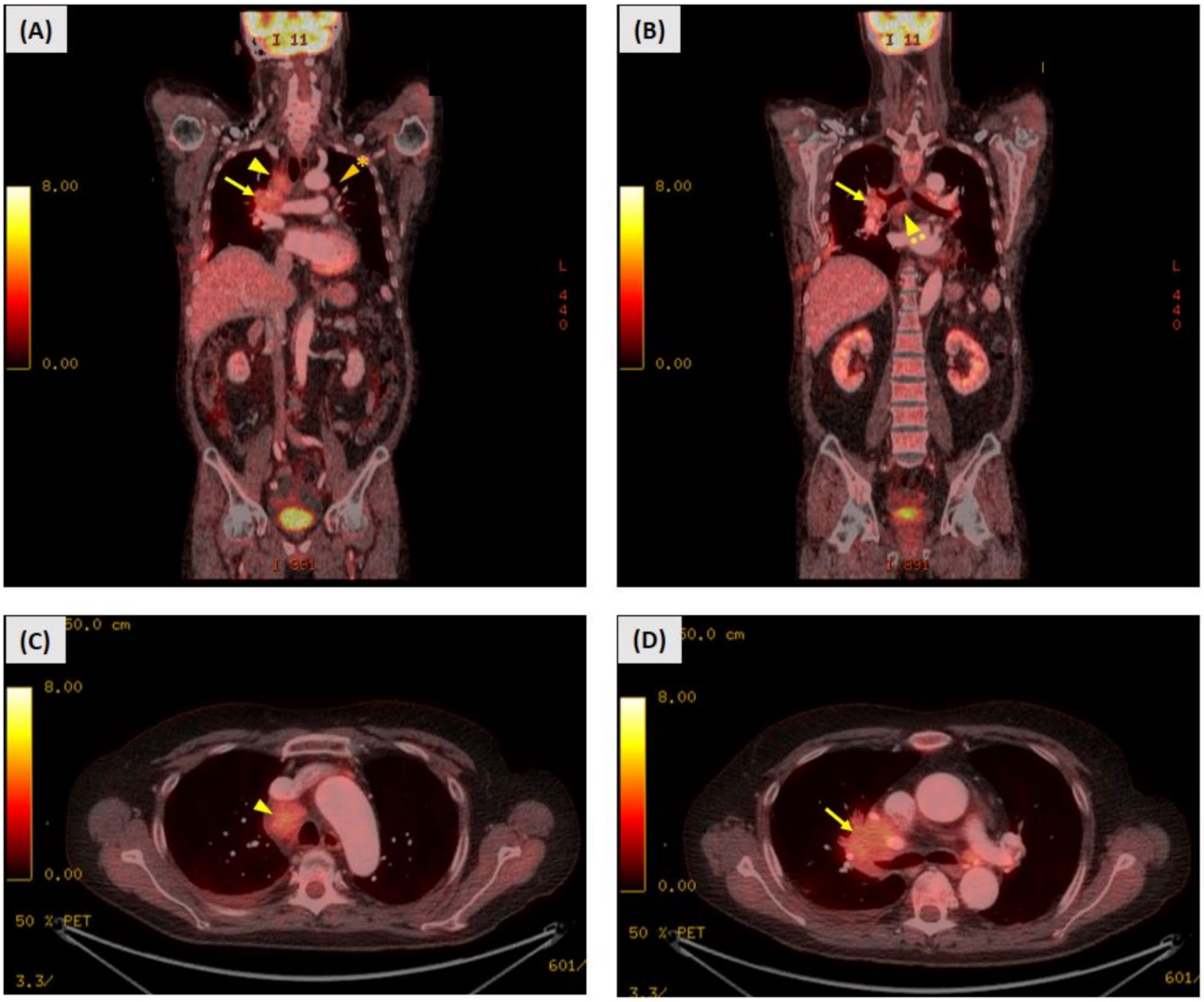

Fig. 3 Positron emission tomography-computed tomography (PET-CT) images of the patient. (**A**) Coronary image displaying the 4R lymph node (yellow arrowhead), 5 lymph node (orange arrowhead with star), and RUL tissue (yellow arrow). (**B**) Coronary image displaying 7 lymph node (yellow arrowhead with two stars), along with RUL tissue (yellow arrow). (**C**) Axial image of the 4R lymph node (yellow arrowhead). (**D**) Axial image of the RUL tissue (yellow arrow)

regressed over time without additional treatment. This highlights the rarity of such a presentation.

BD is a chronic, multisystem inflammatory condition of unknown etiology with vasculopathy as its hallmark, affecting both small and large vessels. The disease typically follows a chronic, relapsing-remitting course, presenting with diverse clinical manifestations [2, 7]. There is no definitive serological marker for BD. The International Criteria for BD scoring system is commonly used, with ocular lesion, genital aphthosis, and oral aphthosis contributing 2 points, and skin lesions, neurologic manifestations, vascular manifestations, and a positive pathergy test contributing 1 point each to the total score. A score of 3 indicates a probable diagnosis and a score of 4 or higher indicates a definitive diagnosis of BD [1]. In our patient, the diagnosis was supported by a history of ocular lesions, oral aphthosis, skin lesions, and arthritis. He was maintained on long-term steroid therapy due to repeated exacerbations of symptoms during attempts to taper steroids while using other immune-suppressants before. Specifically, efforts to reduce the steroid dosage while on azathioprine and cyclosporine led to symptom worsening, necessitating an increase in steroid dosage. These findings suggest that the patient's condition was predominantly responsive to steroids, with insufficient control achieved using other agents. Furthermore, the use of Tumor Necrosis Factor-alpha inhibitors was avoided in this case due to the patient's history of colon cancer, as these agents are associated with an increased risk of solid tumor recurrence, which was a significant concern.

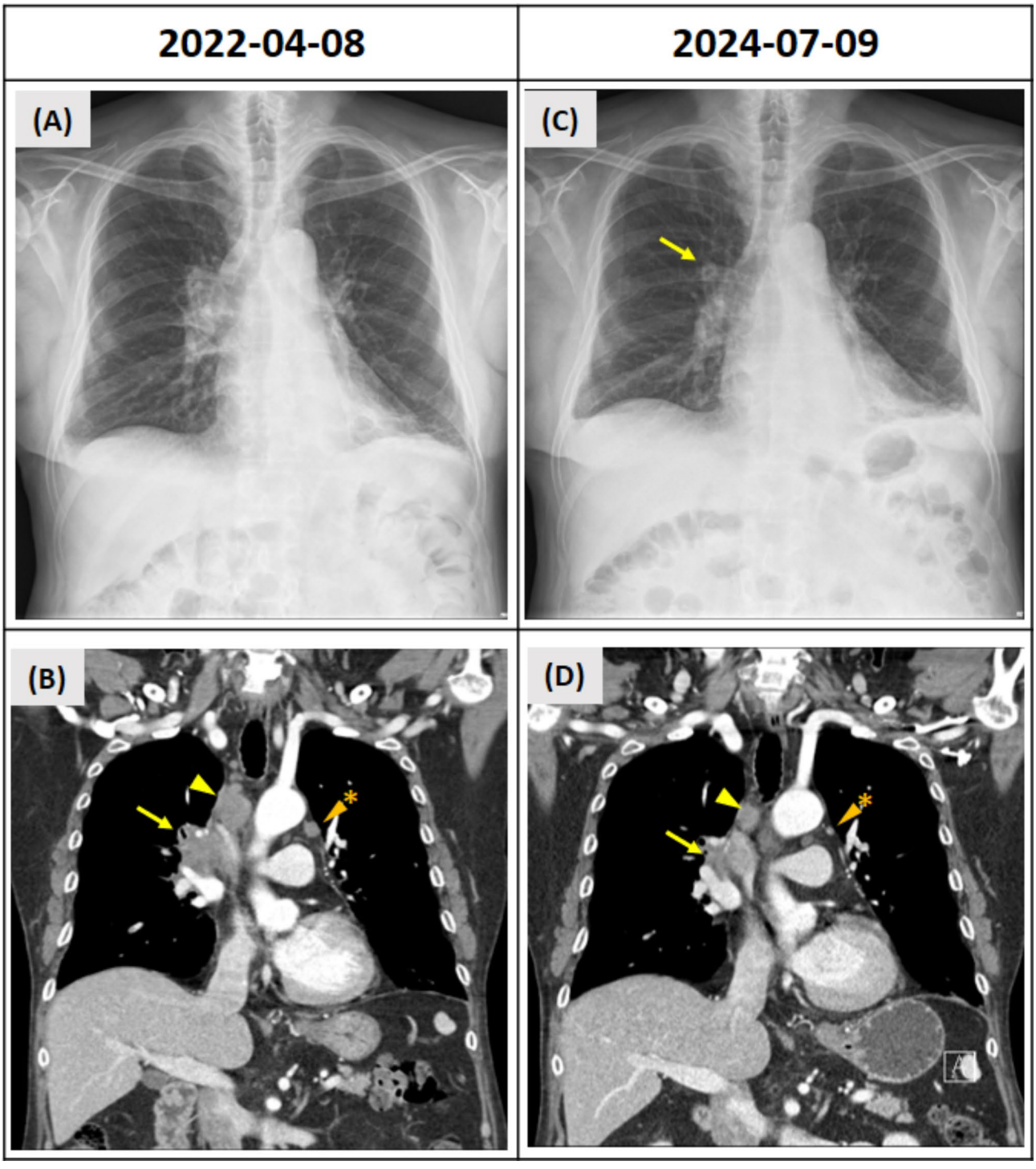

Fig. 4 Serial images of the patient's chest X-ray (CXR) and chest computed tomography (CT). (**A**, **B**) The 2022 CXR and chest CT continue to show same findings compared to 2021, with the enlarged 4R (yellow arrowhead) and 5R (orange arrowhead with star) lymph nodes, along with a mass-like lesion anterior to the right upper lung (yellow arrow). (**C**, **D**) The 2024 CXR and chest CT demonstrate significant improvement in the peribronchial soft tissue and lymph node size

BD can manifest in various forms, including pulmonary involvement, with pulmonary artery aneurysms being the most frequently reported pulmonary manifestation. Other pulmonary manifestations include arterial and venous thrombosis, recurrent pneumonia, cryptogenic organizing pneumonia, and pleurisy [5, 8, 9]. Hemoptysis is the most frequent symptom associated with pulmonary involvement [7–9], with other common

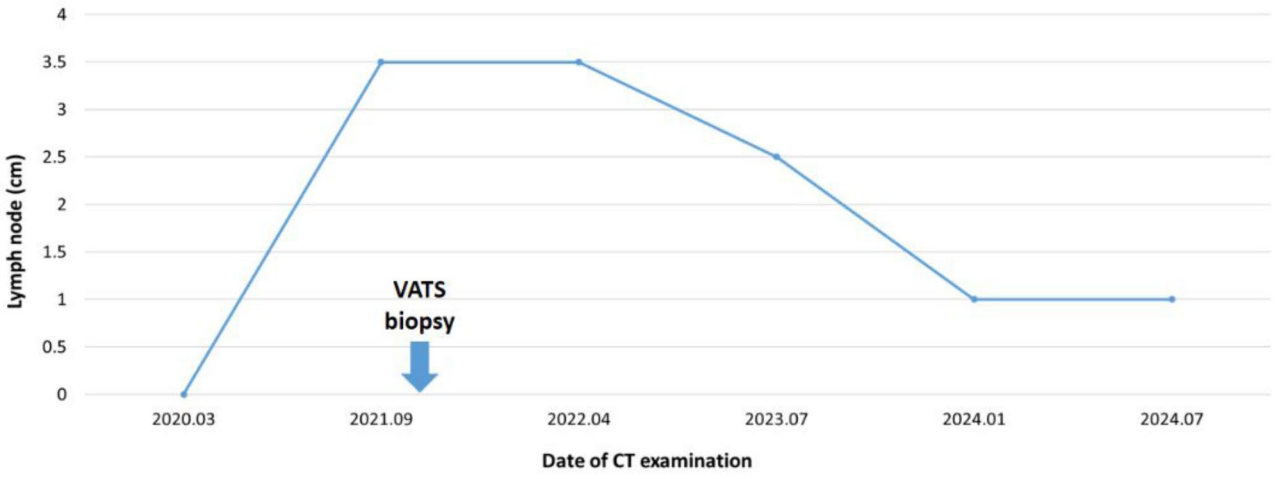

Fig. 5 Graph depicting longitudinal changes in 4R lymph node size over time

symptoms including dyspnea, pleuritic pain, cough, and fever. Cyclophosphamide and corticosteroids are effective in managing pulmonary manifestations and achieving radiological remission [5, 8]. Pulmonary parenchymal involvement in BD is often related to pulmonary infections [7, 10], and subpleural nodules and consolidations are frequently observed during disease exacerbations or at disease onset [4, 11].

Our patient did not exhibit any of the symptoms typically associated with pulmonary involvement in BD and laboratory findings such as WBC count, CRP levels, and ESR were all within normal limits, ruling out active infection. A negative IFN-γ release assay further decreased the likelihood of tuberculosis. The pulmonary manifestations observed in this case, including lymph node enlargement and bronchial narrowing due to a peribronchial mass, are extremely rare. Remarkably, these findings occurred in a stable disease state and regressed spontaneously without the need for additional medication (Fig. 5). The presence of enlarged lymph nodes on CT imaging, in the context of an absence of clinical symptoms and stable overall disease status, did not warrant immediate therapeutic escalation. Following a comprehensive evaluation of the patient's condition, including consultation with a rheumatology specialist, it was determined that additional treatment was unnecessary at this time. This decision aimed to balance effective disease management with minimizing potential treatment-related risks. Regular follow-up and monitoring were planned to ensure timely intervention in the event of any changes in the patient's clinical status.

BD patients are at an increased risk for developing cancer [12–14] and have higher cancer-related mortality [15]. Therefore, it is crucial to perform careful monitoring and not overlook cancer evaluations in BD patients. However, this case demonstrates that BD can present with unusual pulmonary findings, such as lymphadenopathy and lung masses. If lymphadenopathy or lung masses are detected in BD patients and biopsy results are negative for malignancy, the possibility of BD-related lung involvement should be considered. Furthermore, BD-related pulmonary manifestations, such as lymphadenopathy and lung masses, can occur even in the absence of active BD symptoms and may spontaneously regress. Therefore, in patients with BD, if symptoms are not severe and lung involvement progresses slowly, careful observation may serve as a viable management strategy.

Conclusion

This case highlights the importance of considering BD a potential cause of lymphadenopathy and lung masses in patients with a history of the disease, even in the absence of active BD symptoms or evidence of malignancy. It demonstrates that BD can present with atypical pulmonary manifestations that may spontaneously regress without specific treatment for lung involvement. Therefore, in BD patients with similar findings, a careful differential diagnosis is essential. In cases with mild symptoms and slow disease progression, close observation may be an appropriate management strategy.

Abbreviations

BD	Behçet's disease
CT	Computed tomography
PET-CT	Positron emission tomography
WBC	White blood cell
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
IFN-γ	Interferon-gamma
RUL	Right upper lobe
EBUS	Endobronchial ultrasound

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Not applicable.

Author contributions
SY Kim organized the clinical information of the patients and wrote the manuscript, while CU Chung provided in-depth analysis of the patient cases. MK Yeo took the pathology pictures and CU Chung supervised the case report writing. SB Im supported the writing of the manuscript.

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Data availability
All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Declarations

Ethics approval and consent to participate
This study was approved by the Clinical Research Ethics Committee of the Chungnam National University Hospital (approval number: CNUH 2020-11-043) and was therefore performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. At enrollment, written informed consent was obtained from each patient or from an authorized surrogate.

Consent for publication
Written informed consent was obtained from the patient for the publication of their personal and clinical information, along with any identifying images, included in this study.

Competing interests
The authors declare no competing interests.

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