

Endobronchial Nodules in a Patient With Rheumatoid Arthritis

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We report the case of a patient with rheumatoid arthritis who presented with endobronchial nodules. Endobronchial biopsy showed a large B cell lymphoma. Non-Hodgkin lymphoma rarely involves the endobronchial tree, and is typically treated with systemic chemotherapy, but in this case additional treatment with argon plasma coagulation was used for local control of the disease.

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Introduction

Rheumatoid arthritis affects the lungs in 30–40% of cases.¹ Among its pulmonary complications are benign rheumatoid nodules,² but clinicians should be aware of the higher risk of malignancy in such patients.

Case Summary

We report the case of a 58-year-old white female with a 40-year history of rheumatoid arthritis, who presented to the chest medicine clinic for persistent dyspnea, hypoxemia, and right-lower-lobe atelectasis. She had been treated with nonsteroidal anti-inflammatory drugs and had been on prednisone (10 mg/d) for 4 years.

Four weeks prior to presentation she was admitted to another facility with pneumonia. Her chest radiograph showed right-middle-lobe and lower-lobe consolidation and atelectasis, and diffuse chronic interstitial changes (Fig. 1). Clinically she improved after treatment with systemic antibiotics, but she continued to be dyspneic and to require

supplemental oxygen. Her right-middle lobe and lower-lobe atelectasis persisted. A pulmonary function test revealed mild restrictive defect. A chest computed tomogram revealed narrowing of the right main bronchus, with possible endobronchial tumor and right-lower-lobe collapse with diffuse parenchymal fibrosis and honeycomb changes (Fig. 2).

During that same hospitalization flexible bronchoscopy found multiple small tracheal nodules and a large nodule obstructing the right main bronchus. Endobronchial biopsy revealed intense chronic inflammation with intermixed histiocytes, lymphocytes, and eosinophils.

General physical examination showed arthritic deformities of both hands and rheumatoid nodules over the proximal interphalangeal joints and olecranon bursae. Chest auscultation revealed decreased air entry over the right side of the chest. Laboratory studies were unremarkable, except for the arterial blood gas sample, which showed a pH of 7.39, a P_{CO_2} of 47 mm Hg, and a P_{O_2} of 62 mm Hg while on supplemental oxygen at 4 L/min.

In view of the persistence of the right-middle-lobe and lower-lobe atelectasis, our high suspicion for malignancy with the patient's history of rheumatoid arthritis, and the nondiagnostic biopsy performed at the other facility, a repeat flexible bronchoscopy was done at our institution to rule out malignancy. During bronchoscopy, multiple smooth-looking nodules were seen (Fig. 3). Another nodule at the origin of the right main bronchus occluded about 70% of the lumen (Fig. 4). Distally the bronchus intermedius was completely occluded by more nodules. The orifice of the right-upper lobe was still patent, but the bronchoscope could not be advanced into its different segments. The left tracheobronchial tree was unremarkable.

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Fig. 1. The posteroanterior and lateral radiographs show a right-base consolidation, volume loss, and diffuse bilateral interstitial fibrosis.

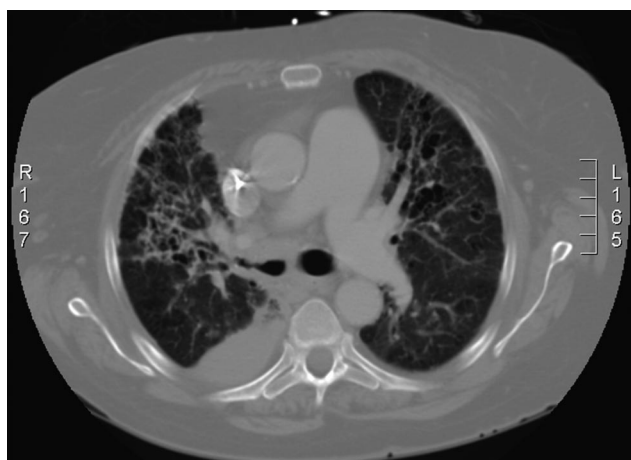


Fig. 2. Computed tomogram shows narrowing of the right main bronchus, possible endobronchial tumor, right-lower-lobe collapse, diffuse parenchymal fibrosis, and honeycombing changes.

Endobronchial biopsy found large B cell non-Hodgkin lymphoma (Figs. 5 and 6). Flow cytometry revealed a monoclonal population of B cell lymphoma.

Because of the persistent symptoms, and to avoid complete atelectasis of the right lung, endobronchial ablation with argon plasma coagulation was performed via flexible bronchoscopy (argon flow of 0.4 L/min, at 30–35 watts). Two out-patient sessions were needed to ablate the nodules in the right main bronchus. There was no need for any additional mechanical debridement. The patient's symptoms improved, and a repeat bronchoscopy showed the right main bronchus to be more patent (Fig. 7), which allowed better ventilation of the right upper lobe.

Complete workup revealed a stage IVA diffuse large B cell non-Hodgkin lymphoma. The patient is being followed in the oncology clinic, where she is receiving systemic chemotherapy.

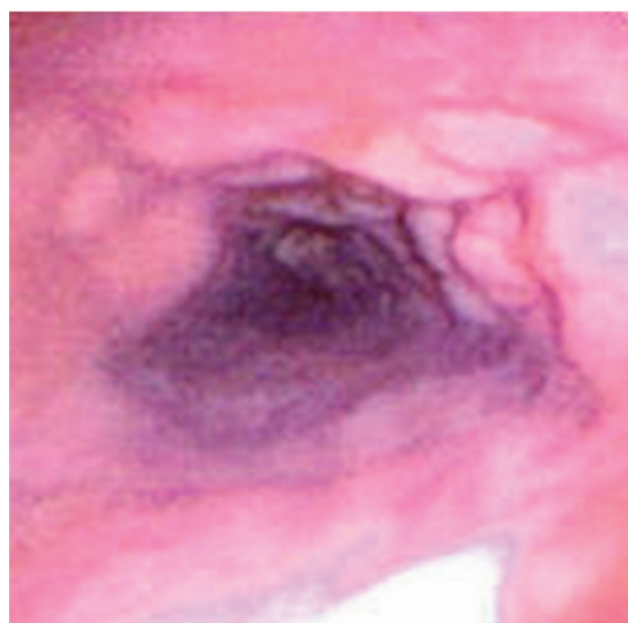


Fig. 3. Fiberoptic bronchoscopy shows multiple tracheal nodules.

Discussion

Rheumatoid arthritis affects the lungs in 30–40% of cases.¹ Pulmonary manifestations include the development of benign parenchymal nodules and diffuse interstitial, pleural, and vascular diseases.² Patients with rheumatoid arthritis may also develop obstructive airway disease¹ and drug-related pulmonary toxicities.³

The risk of cancer is increased in rheumatoid arthritis.⁴ The overall risk of lymphoma is about double that in the general population, but the risk in patients with the most severe arthritis is dramatically higher.⁴ Men with rheumatoid arthritis appear to have an extremely elevated risk of Hodgkin disease.

Endobronchial metastases of nonbronchogenic carcinoma are relatively rare.⁵ The most common tumors with a pro-

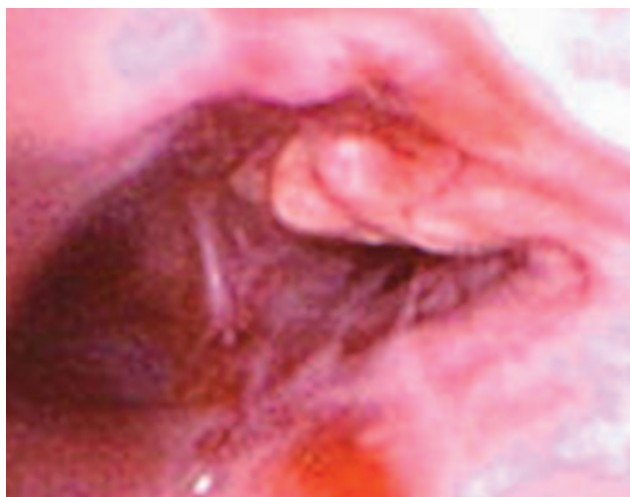


Fig. 4. Fiberoptic bronchoscopy shows a large nodule obstructing the right main bronchus.

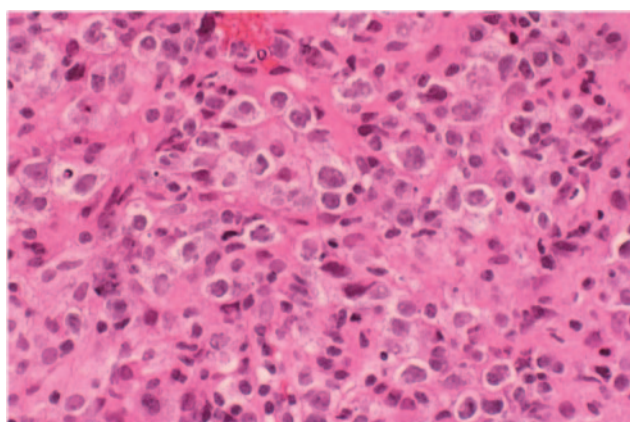


Fig. 5. Hematoxylin-and-eosin stained biopsy sample shows large, atypical cells with fine nuclear chromatin and moderate amounts of pale cytoplasm; some have distinct nucleoli. Note the absence of epithelial differentiation.

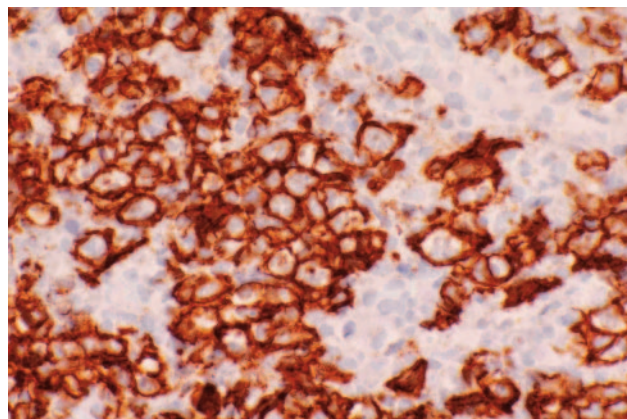


Fig. 6. High-power magnification image of a biopsy sample immunohistochemically stained for CD20 (B cells). The majority of positive cells are large cells.



Fig. 7. Bronchoscopy after argon plasma coagulation shows nearly complete ablation of the right main bronchus lesion.

pendency for endobronchial spread are colon, renal, breast, melanoma, and thyroid.^{5,6} Symptoms of such endobronchial metastasis include cough, hemoptysis, dyspnea, and wheezing.

Non-Hodgkin lymphoma is a heterogeneous group of lymphatic-system neoplasms with varying presentation, natural history, and response to therapy. It is associated with infections such as Epstein-Barr virus, *Helicobacter pylori*, and human herpes virus infections.^{7,8} In addition to rheumatoid arthritis, non-Hodgkin lymphoma is also associated with other autoimmune disorders such as Sjögren syndrome and systemic lupus erythematosus.⁹

Non-Hodgkin lymphoma involves thoracic structures in up to 43% of patients at some point in the course of the disease, and the mediastinum and lung parenchyma are particularly affected.¹⁰ However, endobronchial infiltration in non-Hodgkin lymphoma is extremely rare.

In 55 autopsies of patients with non-Hodgkin lymphoma, none showed endobronchial involvement.¹¹ In another autopsy study, only one of 93 patients with pulmonary lymphoma had an endobronchial lesion.¹²

The first case of endobronchial involvement was described in 1955 by Dawe et al.¹³ Kilgore, in a review,¹⁰ reported 4 cases of endobronchial lymphoma, all of which had disseminated disease at the time of their endobronchial involvement.

In another series of 27 patients with non-Hodgkin lymphoma,¹⁴ 10 patients had parenchymal pulmonary infiltrates without either hilar or mediastinal adenopathy. Endobronchial involvement occurred in only one patient.

There have been 3 reported cases of endobronchial non-Hodgkin lymphoma associated with human immunodeficiency virus.¹⁵⁻¹⁷ In 2 cases^{16,17} the lesions were solitary

and localized to the trachea. Flexible bronchoscopy failed to provide the diagnosis, and rigid bronchoscopy was required to obtain adequate tissue samples. In the other case the lesion was in the left main bronchus.¹⁵

The most common bronchoscopic finding in non-Hodgkin lymphoma patients with airway involvement is displacement or narrowing of the tracheobronchial tree by extrinsic compression from enlarged adjacent lymph nodes.¹⁰ As seen in our case, endobronchial lesions are usually associated with widely disseminated disease.¹⁰

The most common mechanisms of endobronchial involvement in non-Hodgkin lymphoma are direct bronchial invasion by a mediastinal mass and lymphatic spread to peribronchial connective tissues.^{18,19}

When non-Hodgkin lymphoma involves the bronchial tree, it should be differentiated from adenoma or primary bronchogenic carcinoma.²⁰ The inability to reach a diagnosis with flexible bronchoscopy in some cases could be attributable to the high propensity of these tumors to develop necrosis, notably the high-grade cell type.

As illustrated by our case, a nondiagnostic biopsy in the presence of highly suspicious endobronchial lesions should not be considered as proof of benignancy. Repeating the bronchoscopy is indicated. The second bronchoscopy may yield a diagnosis.²⁰

Argon plasma coagulation is a form of noncontact electrocoagulation that allows rapid coagulation with minimal manipulation of and mechanical trauma to the target tissue.²¹ The term "plasma" describes an electrically conducting medium produced when the atoms of a gas become ionized. The argon plasma coagulation probe is passed through the working channel of a flexible bronchoscope. A high-voltage spark delivered at the tip of the probe ionizes the argon gas as it is sprayed from the probe tip in the direction of the target tissue. When the probe is properly oriented, the current produced seeks any conductive surface, following the path of least resistance, spreading out uniformly over a wide surface area. The ionized gas (plasma) then seeks a ground in the nearest tissue, delivering the thermal energy with a penetration depth of 2–3 mm. Because argon plasma coagulation produces a homogeneous current, its effects are more uniform and precise than laser or electrocautery, and there is less tissue carbonization and smoke, which allows better visualization of the operative field.²¹

Argon plasma coagulation is effective in the treatment of hemoptysis and airway obstruction due to bronchogenic carcinoma. In a study of 60 patients (43 with bronchogenic carcinoma), argon plasma coagulation resulted in resolution of hemoptysis in all patients and symptom control due to decreased obstruction.²¹ Argon plasma coagulation has also been used in the management of carcinoids and occult lung cancer.^{22,23}

Chemotherapy remains the treatment of choice for non-Hodgkin lymphoma, but it cannot provide immediate relief of airway obstruction. Our case highlights the value of endobronchial intervention in providing palliation while awaiting the systemic effect of chemotherapy.

In summary, our case is the first report of an endobronchial large B cell non-Hodgkin lymphoma associated with rheumatoid arthritis. Endobronchial non-Hodgkin lymphoma is an extremely rare intrathoracic manifestation, usually occurring in the clinical setting of widely disseminated disease. It should be included in the differential diagnosis of endobronchial lesions, especially in patients with diseases associated with non-Hodgkin lymphoma, such as rheumatoid arthritis. Our case illustrates the possible difficulty of establishing the diagnosis. It is also the first to describe the use of argon plasma coagulation as an adjunctive measure to systemic chemotherapy.

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