A 35-year-old lady was seen in the outpatient clinic owing to fever, cough with mucopurulent expectoration, and breathlessness for the duration of 1 month. She had history of similar episodes treated with antibiotics four times during last 2 years. There was no history of recurrent sinusitis, diarrhea, and skin or soft tissue infection. She had no history of diabetes mellitus or steroid intake. She denied any history of facial trauma or dental infection in the past. There was no history of tuberculosis in her or in the family. Radiograph and CT scan of the chest revealed right upper lobe consolidation. Flexible fibreoptic bronchoscopy revealed multiple nodules at opening of right upper lobe bronchus. This clinicopathological conference describes the details of differential diagnoses, difficulties in achieving the final diagnosis and management of such patient.

**KEY WORDS:** Clinicopathological conference, endobronchial nodules, recurrent pneumonia

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**PRESENTATION OF CASE**

Umasankar Kalai: A 35-year-old lady was seen in the outpatient clinic of this hospital owing to fever, cough with mucopurulent expectoration, and breathlessness for the duration of 1 month.

The patient had been well approximately 2 years before this presentation. In the past 2 years, she had four episodes of fever and cough with purulent expectoration at the interval of 4–6 months. Each time, she visited the physician and was diagnosed with pneumonia. She was empirically treated with broad spectrum antibiotics for a duration of 1–2 weeks during each episode. In between the episodes, she was asymptomatic. She had no history of chest pain or hemoptysis. Her appetite and weight were normal. There was no history of recurrent sinusitis, diarrhea, and skin or soft tissue infection. She had no history of diabetes mellitus or steroid intake. She denied any history of facial trauma or dental infection in the past. There was no history of tuberculosis in her or in the family. There was no family history of similar illness. She was not aware of her immunization status for influenza and pneumococcal infection. On examination, the vital signs and oxygen saturation were normal. The physical examination was normal, without wheezing, cyanosis, clubbing, or lymph-node enlargement. Her blood counts, renal and liver functions, and urine examination were normal. Her sputum was sent for gram stain, culture, potassium hydroxide (KOH) mount, acid-fast bacilli (AFB) smear, and Mycobacteria Growth Indicator Tube (MGIT) culture for *Mycobacterium* were sterile. Her human immunodeficiency virus (HIV) serology and tuberculin test were negative.

The initial chest radiographs done in December 2013 and May 2014 showed the presence of right mid zone and lower zone opacity [Figure 1a]. Computerized tomographic (CT) scan of the thorax was done for further evaluation that revealed right upper lobe consolidation [Figure 1b]. There was no hilar or mediastinal lymphadenopathy or pleural effusion.

With the diagnosis of nonresolving pneumonia, the patient was subjected to flexible fiberoptic bronchoscopy (FOB). FOB showed the presence of nodular growth [Figure 2] in the right upper lobe bronchus, causing nearly 90% luminal narrowing and giving the appearance of a mitotic process.
Differential diagnosis

Important features of the case
Vijay Hadda: This previously healthy, middle-aged-woman presented with recurrent episodes of pneumonia in the past 2 years now in addition to fever, cough, and expectoration; she also developed breathlessness. The presence of fever, cough with expectoration, and consolidation on radiograph with significant response to antibiotics points to an infective process. The consolidation during prior episodes and in the CT scan occurred in the right upper lobe that could have been due to persistent indolent infection or secondary to an anatomical abnormality of the airway leading to poor drainage and recurrent infection. The bronchoscopy performed to look for the cause of upper lobe preponderance of the lesion showed multiple endobronchial nodules causing complete occlusion of the right main bronchus. I assume that the endobronchial lesion was present for quite some time causing right upper lobe pneumonia. In this case, I would like to recall the causes of endobronchial lesion [Table 1] and narrow down on the differential diagnosis based on symptoms and radiology.

Benign endobronchial lesions
Hamartoma presents as a round endobronchial lesion with CT scan showing characteristic fat density and calcification. Lipoma appears as a pedunculated endobronchial lesion with CT scan showing fat density with absent calcification. Hamartoma and lipoma often grow quietly owing to frequent absence of hemoptysis. Fibroepithelial polyp is a rare cause of endobronchial lesion that presents as a well-defined endobronchial lesion.[41] In view of the long duration of symptoms, the possibility of benign etiology cannot be ruled out.

Malignant endobronchial lesions
Among the malignant causes bronchogenic small cell carcinoma, well-differentiated neuroendocrine tumor, bronchogenic squamous cell carcinoma and non-small cell carcinoma and endobronchial metastasis need to be considered.[42] In the absence of other organ involvement, endobronchial metastasis is less likely. Primary bronchogenic carcinoma without treatment would have led to a rapid downhill course. Bronchial neuroendocrine tumors can be considered a possibility since they are well-known to persist until they cause significant endobronchial symptoms requiring bronchoscopy, as in this case. Mucoepidermoid carcinoma (MEC) and adenoid cystic carcinoma should both be considered as they are slow-growing salivary gland type neoplasms, occurring mostly in young persons, with the appearance of a polyp in the central bronchial lumen up to the segmental bronchus level.[43]

Endobronchial lesion due to infection
Endobronchial tuberculosis (EBTB) continues to be a clinical challenge in endemic areas since it may mimic a variety of pulmonary diseases such as bronchogenic carcinoma, pneumonia, or bronchial asthma. The clinical course of EBTB is rather variable due to the interactions among the effects of Mycobacteria, host immunity, and antituberculosis drugs; any variation in these three factors may result in different clinical presentations.[44] EBTB sequelae such as bronchial stenosis can predispose to recurrent infections and therefore, cannot be ruled out in this case. Actinomycosis usually presents as multiple abscesses and sinuses involving the cervical, thoracic, or abdominal region. Rarely, it can present as endobronchial nodules. Endobronchial fungal infections due to *Aspergillus* species, *Coccidioides immitis*, Zygomycetes, and *Candida*

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**Table 1: Etiology of endobronchial lesion**

| Benign | Malignant | Infective | Miscellaneous |
|--------|-----------|-----------|---------------|
| Fibroepithelial polyp | Bronchogenic carcinoma | Tuberculosis | Mucous plugs |
| Hamartoma | Bronchial carcinoid | Endobronchial metastasis | NTM* |
| Lipoma | Mucoepidermoid carcinoma | Nocardia | Foreign body |
| Adenoid cystic carcinoma | Actinomycosis | | |

*NTM: Nontuberculous Mycobacteria*
species, Cryptococcus neoformans and Histoplasma capsulatum are well-described in immunocompromised patients; however, in our case immunodeficiency state has been ruled out and therefore, fungal infection is less likely.[6]

**Miscellaneous causes**

Mucous plug and foreign body can both present as recurrent pneumonia. Foreign body, especially among adults, can be missed. However, bronchoscopy is usually diagnostic and therapeutic for both these conditions.

Considering all these possibilities I would suggest that the bronchoscopic samples, i.e., broncho-alveolar lavage (BAL) and biopsy be processed for staining and cultures for bacteria, Mycobacteria, and fungi, in addition to histopathology.

**Clinical diagnosis:** 1. Endobronchial tumor (benign etiology) 2. Endobronchial infection

**Anant Mohan:** With these clinical possibilities, can we have the histopathological evaluation of the biopsy?

**Firdaus Ali:** The endobronchial biopsy from the growth showed the presence of abundant necrosis with inflammatory infiltrate and bacterial colonies of Actinomycosis [Figure 3]. Actinomyces stains in tissue with Gomori methenamine silver and the Brown and Brenn modification of the Gram stain. “Sulfur granules” that are seen as round or oval basophilic masses with a radiating arrangement of eosinophilic clubs on the surface are the pathological hallmark of the disease. These sometimes can be seen with a magnifying glass.[6]

**Pathological diagnosis:** Endobronchial actinomycosis.

**Neetu Jain:** Endobronchial involvement is an uncommon manifestation of pulmonary actinomycosis. The common manifestations of pulmonary actinomycosis include nonresolving pneumonia with or without contiguous spread to pleura (effusion, thickening, empyema), chest wall (bone destruction and sinus formation), or mediastinum [superior vena cava syndrome (SVCS), tracheoesophageal fistula, pericarditis, and myocarditis].[6] The clinical features described among patients with endobronchial actinomycosis include cough, dyspnea, hemoptysis, and fever of variable severity that are similar to other respiratory diseases. Bronchoscopic appearance of endobronchial actinomycosis-like nodule or growth can easily be confused with other common diseases such as tuberculosis or malignancy.[8] In such a case, only microbiological evidence on either culture or biopsy can clinch the diagnosis as happened with the index case.

**Karan Madan:** The radiological findings in actinomycosis are nonspecific and share almost all features of other suppurative lung disease and/or malignancy. Pulmonary actinomycosis presents as nonsegmental consolidation (crossing fissures with low attention values due to either microabscesses or dilated bronchi), cavitating mass, nodules, and infiltrates while endobronchial involvement can cause bronchial thickening or endobronchial narrowing with distal collapse consolidation.[6,10]

**Sudheer Arava:** Diagnosis of actinomycosis is challenging and often delayed since most of the time, it is not suspected. Even when suspected, it is difficult to confirm the microbiological diagnosis. One of the reasons for this could be nonspecific features on chest radiograph which is usually first investigation among such patients. There are many factors that may be responsible for the inability to confirm the microbiological diagnosis such as inappropriate specimen collection (for anaerobic culture), prior usage of antibiotic therapy, and bacterial overgrowth. Overall bacterial confirmation is achieved in less than 50% of the cases.[11] The gold standard for diagnosing pulmonary actinomycosis is histological examination and bacterial culture of a lung biopsy, obtained by percutaneous biopsy guided by CT scan or by open surgical resection.

**Anant Mohan:** FOB is usually not diagnostic in pulmonary actinomycosis unless there is a clear endobronchial disease on which biopsy can be performed.[12] In our case, multiple endobronchial nodules were seen during FOB and biopsy from these showed colonies of actinomycosis. Actinomycosis is sensitive to multiple drugs; however, oral penicillin (500 mg to 1g at 6-h interval) or a penicillin-like beta lactum (amoxicillin or ampicillin) continues to be the drug of choice; the other alternatives include erythromycin (500 mg at 6-hour interval), tetracycline (500 mg at 6-hour interval), doxycycline (100 mg at 12-hour interval), and clindamycin (300–450 mg at 6-hour interval). For extensive disease, intravenous penicillin (18–24 million units per
day) for 2–6 weeks can be given prior to oral therapy. The duration of oral therapy is of 6–12 months based on clinical and radiological responses. This patient was treated successfully with clindamycin for 6 months.

Summary: Our case highlights the fact that the diagnosis of the thoracic form of actinomycosis (especially in the absence of sinuses or fistulae) is often delayed; FOB is useful to rule out other conditions and sometimes for definite diagnosis, as in our case and once diagnosed, it can be treated successfully.

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ICS-ATS-CDC workshop on research methodology

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