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Research Article

Utility of Bronchoscopy in Patients with Tree in Bud Appearance on Computerized Tomography of Chest

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Abstract

Background: This is a retrospective study to determine the usefulness of bronchoscopy in diagnosis and management of patients who have tree in bud appearance on Computerized Tomography (CT) of the chest.

Methods: We performed a retrospective chart review of all the patients over last 10 years that had tree-in-bud (TIB) appearance on CT chest. We compared the patients who underwent bronchoscopy for the diagnosis of TIB (group 1) vs. patients who did not undergo bronchoscopy (group 2).

Results: Group 1 consisted of 19 patients, with a mean age of 55 years +/- 16. The mean follow-up was 4.6 years +/- 2.6. The diagnosis in group 1 included infection in 13/19 patients, consisting of *Mycobacterium avium* complex (MAC) in nine patients, Aspergillosis in one patient, and viral infection in two patients (Cytomegalovirus (CMV) and Rhinovirus) and oxacillin-sensitive *Staphylococcus aureus* infection in one patient. Additional findings of aspiration, sarcoidosis, primary ciliary dyskinesia, and obstructive bronchiolitis were observed in one each. Group 2 consisted of 21 patients. The mean age was 62 years +/- 14. The mean follow-up was 4.5 years +/- 2.3. In terms of diagnosis, 8/21 patients had infection (7 patients with MAC and 1 had *Coccidioidomycosis*) and 7/21 patients had recurrent aspiration pneumonia.

Conclusion: Patients with TIB appearance on the CT chest without associated CT findings do not require bronchoscopy for further diagnosis and management.

Keywords: *Tree in Bud; Chest CT; Bronchoscopy*

Background

The "tree-in-bud" pattern on thin-section computed tomography (CT) is characterized by small, centrilobular nodules of soft-tissue attenuation connected to multiple branching linear structures of similar caliber originating from a single stalk [1,2]. Initially described in cases of endobronchial spread of *Mycobacterium tuberculosis* [3], it has subsequently been reported as a manifestation of a variety of entities, including: peripheral airway diseases, such as infection (bacterial, fungal, viral, or parasitic) [4-6], congenital disorders, idiopathic disorders (obliterative bronchiolitis, panbronchiolitis) [7,8], aspiration, inhalation, immunologic disorders, connective tissue disorders [9,10] and peripheral pulmonary vascular diseases such as neoplastic pulmonary emboli [2,11].

Frequently TIB is found incidentally. These patients are then referred to pulmonary clinic for further evaluation. Historically, they are subjected to bronchoscopy to obtain an airway specimen for further analysis. Bronchoscopy is an invasive procedure that requires

multiple resources including: conscious sedation, trained nurses, bronchoscopy suite time, respiratory therapist, and a subspecialty trained physician. Additionally, bronchoscopy is an invasive procedure with associated risks. Most patients have other symptoms and/or concomitant findings on the chest CT that assist in the diagnosis and bronchoscopy could be avoided. However, bronchoscopy is still performed to confirm the diagnosis in a majority of cases.

Our hypothesis is that bronchoscopy in patients with TIB does not alter the clinical management and should be avoided. The intent of this study is to retrospectively look at these select patients to examine the utility of bronchoscopy and the impact of bronchoscopy on patient outcomes.

Methods

Setting

This was a single center study undertaken at University of North Carolina, a tertiary care teaching hospital located in Chapel Hill, North Carolina, USA.

Subjects

The study was designed as an observational retrospective analysis of cases from January 1, 2003 through December 31, 2013. Following an Institutional Review Board (IRB) approval, a retrospective medical record review was undertaken on all patients during this time frame. Patients who had CT chest during this time frame were screened. Each CT chest was independently reviewed by a chest radiologist (Katherine Birchard, MD). All studies with findings of TIB were included, with the exception of patients with a diagnosis of bronchiectasis or cystic fibrosis. Additionally, patients who had associated findings of: pulmonary nodule(s), mass(es), mediastinal/hilar lymphadenopathy, atelectasis or pleural effusion(s) were also excluded.

Study design

We performed a retrospective chart review of all the patients over a 10-year period that had TIB appearance on CT chest. We compared patients who had bronchoscopy for the assistance in diagnosis of TIB (group 1) vs. patients who had TIB appearance on CT chest who did not undergo bronchoscopy (group 2). We then looked at the outcomes and evaluated for potential benefits of bronchoscopy in patients with TIB on CT chest. Patients who underwent bronchoscopy had a combination of bronchoalveolar lavage, brushings, and/or transbronchial biopsy.

Analysis

We used XLSTAT (version 2014) to analyze continuous and non-continuous variables. Measures of central tendency and measures of dispersion were calculated for the continuous data. The difference between two observed means were calculated using students t-test. All data were expressed as mean ± SD. A two-sided *p* value of less than 0.05 was considered statistically significant.

Results

A total of 40 patients in the 10-year period from January 1, 2003 to December 31, 2013 were included in this study. Patients were then divided into two groups. Group 1 included patients who had TIB appearance on CT chest and subsequently underwent bronchoscopy. Group 2 was comprised of the patients who had TIB appearance on CT chest bud did not undergo bronchoscopy. There were 19 patients in group 1, their mean age was 55 years +/- 16 (SD), with 12 females and 7 males. There were 14 Caucasians, 2 Asians, 2 African Americans and 1 Hispanic. Fourteen patients presented with cough, 3 with shortness of breath and 2 with others (hemoptysis, wheeze). Patients in group 1 had 63 CT scans among them with a mean of 3.3 per patient. The mean follow-up was 4.6 years +/- 2.6 SD. The mean Forced Expiratory Volume in 1st second (FEV1) in this group was 70% predicted +/- 21 SD. Infection was determined to be the primary etiology in a majority (13/19) patients in group 1 and included: MAC (9 patients), Aspergillosis (1 patient), the viral infections CMV and Rhinovirus (2 patients), and oxacillin-resistant *Staphylococcus aureus* (1 patient). Additional findings of aspiration, sarcoidosis, primary ciliary dyskinesia, and Obliterative bronchiolitis were found in one each. In 2/19 the etiology was unknown. In terms of comorbidity, 5/19 patients (26%) who underwent bronchoscopy had some form of malignancy. Three patients had leukemia (1 Acute lymphocytic leukemia (ALL) and 2 Acute myeloid Leukemia (AML)), one had non-Hodgkin's lymphoma, and another had breast cancer. One patient had

underlying asthma and one had allergic bronchopulmonary aspergillosis. The etiology was not determined in the patient with non- Hodgkin's lymphoma and one of the patients with AML; the other patient with AML had an associated diagnosis of obliterative bronchiolitis. In the patient with ALL, CMV was isolated. In patient with breast cancer, MAC was isolated.

There were 21 patients in group 2 (patients who had TIB appearance on CT chest bud did not undergo bronchoscopy). These patients had regular clinical follow up, sputum analysis and radiological follow up. The mean age was 62 years +/- 14 (SD). There were 12 females and 9 males. There were 17 Caucasians, 2 African Americans and 2 Asians. Thirteen patients presented with cough, seven with shortness of breath and one patient was asymptomatic. There were a total 57 CT scans with a mean of 2.7 scans per patient. The mean follow-up was 4.5 years +/- 2.3 SD. The mean FEV1 was 72% predicted +/- 22 SD. In terms of diagnosis, 8/21 patients had infection (7 patients with MAC and 1 had *Coccidioidomycosis*), 7/21 patients had recurrent aspiration pneumonia, and in 6 patients the etiology was unknown. In terms of comorbidity, one patient had underlying asthma and 6/21 patients (28.5%) had some form of malignancy (esophageal, ovarian, lung, pancreatic, head and neck, and carcinoid tumor). All patients with malignancy were treated; the patient with lung cancer had stage 1 disease and had a left upper lobe resection performed.

	Group 1 (bronchoscopy)	Group 2	p value*
Age (mean)	55 years +/- 16	62 years +/- 14	p = 0.14
Mean FEV1	70% +/- 21	72 % +/- 22	p = 0.29
Follow up (mean)	4.6 years +/- 2.6	4.5 years +/- 2.3	p = 0.8
History of malignancy	5 patients	6 patients	NA
CT scan (mean)	3.3 per patient	2.7 per patient	NA
Numbers	19	21	NA

Table 1: *Group comparison.*

**p >= 0.05 was considered not significant.*

	Group 1 (bronchoscopy)	Group 2
Age	55 years +/- 16	62 years +/-14
Sex	12 Females 09 Males	12 Females 09 Males
Race	14 Caucasian 02 Asian 02 African American 01 Hispanic	17 Caucasian 02 Asian 02 African American
Common presentation	Cough, shortness of breath	Cough, shortness of breath
History of cancer	02 AML 01 ALL 01 Non-Hodgkin lymphoma 01 Breast cancer	01 Esophageal cancer 01 Ovarian cancer 01 Lung cancer 01 Pancreatic cancer 01 Head and neck cancer 01 Carcinoid tumor
Diagnosis	09 MAC 01 CMV 01 Aspergillus 01 Rhinovirus 01 ORSA 01 Aspiration 01 Sarcoidosis 01 Primary ciliary dyskinesia 01 Obliterative bronchiolitis 02 Etiology unknown	07 MAC 07 Aspiration 01 Coccidioidomycosis 06 Etiology unknown
Total patients	19	21

Table 2: *Demographics/diagnosis.*

AML: Acute Myeloid Leukemia; ALL: Acute Lymphoid Leukemia; MAC: Mycobacterium avium Complex; CMV: Cytomegalovirus; ORSA: Oxacillin Resistant Staphylococcus aureus.

Discussion

Our study found that patients with TIB appearance on the CT chest without associated radiology findings (nodule, mass, lymphadenopathy) do not require bronchoscopy to determine the diagnosis. This is true even in patients with history of malignancy. The patients who underwent bronchoscopy had combination of bronchoalveolar lavage, brushings, and transbronchial biopsy, but the results were very similar to the non-bronchoscopy group.

In the group where bronchoscopy was not offered, diagnosis was achieved by the combination of clinical follow up, sputum examination, and follow up CT chest at regular intervals.

The most common cause of TIB appearance on CT chest in both groups was MAC. A diagnosis was obtained more often in the bronchoscopy group 89% vs. 71%. However, the outcome between the two groups was similar as there was no worsening of the TIB pattern appreciated on CT chest on follow-ups.

Li., *et al.* [12] looked at the presence of TIB pattern in patients with central lung cancer. They found that out of 652 consecutive patients, 147 patients (22.5%) had associated TIB pattern. They also found squamous cell carcinoma as being commonly associated with a localized TIB pattern. However, it is worth mentioning that in this study the patients had associated additional radiological findings consistent with central lung cancer. In our study, patients in group 1 and group 2 (26% and 28% respectively) had underlying malignancy and only one patient included in our study had comorbid lung cancer

Terhalle., *et al.* [11] recently published a case report citing noninfectious causes of TIB pattern. In their study a patient with chronic myeloid leukemia who presented with TIB appearance on CT chest was subsequently diagnosed with pulmonary infiltration from leukemia. In our study, three patients with leukemia who underwent bronchoscopy but the specimens obtained through bronchoalveolar lavage and transbronchial biopsy, revealed cytomegalovirus in one patient, obliterative bronchiolitis in another, while in one case the etiology was unknown.

Bronchiolar involvement of neoplasms resulting in TIB sign is rare. It can occur in patients with juvenile laryngotracheobronchial papillomatosis [11] and bronchoalveolar carcinoma [13]. More commonly, cancers of the breast, liver, kidney, stomach, prostate, and ovaries metastasize via vascular route and produce pulmonary nodule(s) and mass(es), but in a pattern that is distinct from a TIB pattern [14].

Our study finds that despite a history of malignancy, pure TIB appearance in the absence of other associated radiological findings are from benign causes, and do not warrant invasive procedures like bronchoscopy. Clinical follow up combined with sputum analysis and follow up CT chest as needed is sufficient.

We acknowledge our study has multiple limitations. First, this was a single center, retrospective study. The small patient population included in this study is an additional limitation. Further studies, preferably prospective, with larger patient cohorts will be needed to add to confirm the implications of our study findings. Additionally, there are, in rare instances, times where bronchoscopy may assist in the diagnosis of certain pathologies; importantly, juvenile laryngotracheobronchial papillomatosis and bronchoalveolar carcinoma [13,14]. The most common cause of TIB appearance within our study was MAC. Although, a formal diagnosis was achieved at a higher rate in the patient cohort that underwent bronchoscopy 89% vs. 71%, this did not translate to clinically relevant outcomes. It is imperative as clinicians to recognize that the path of an individual patient's care be determined by examining the cumulative evidence obtained by the history and physical, associated clinical findings, and follow-up, prior to subjecting patients to invasive procedures they may not be warranted.

Conclusion

Bronchoscopy may be avoided with TIB pattern in the absence of associated radiological findings (nodule, mass, lymphadenopathy) on CT chest

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Conflict of Interest Disclosure

The authors report no real or potential conflict of interest.

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None.

Author's Contribution

1. Vikas Pathak: Study design, conducted the study, data collection, manuscript preparation.
2. Jeremy Wininger: Manuscript preparation.
3. Anna Conterato: Data collection, manuscript preparation.

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