Adult Inflammatory Myofibroblastic Tumor of the Trachea:

Case Report and Literature Review

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Running Title: Adult Tracheal Inflammatory Myofibroblastic Tumor

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ABSTRACT

Inflammatory myofibroblastic tumor of the trachea is a rare benign tumor of the adult. It is mostly seen before the age of 16. We describe a 20-year-old female patient who presented with stridor. She had a fixed obstruction on spirometry and a thorax computed tomography and bronchoscopy confirmed the presence of tracheal thickening and stenosis below the vocal cords and bronchial wall thickening at the level of carina. Bronchoscopic biopsies confirmed the lesion to be an inflammatory myofibroblastic tumor. After mechanical dilatation and resection by rigid bronchoscopy and corticosteroid therapy, the clinical status of the patient was relieved.

Key words: Inflammatory myofibroblastic tumor, trachea

INTRODUCTION

Inflammatory myofibroblastic tumor is a rare disease with the frequency of 0.04–0.07% of all respiratory tract tumors, generally and presents in pediatric and young children less than 16 years of age [1-3]. The lesion has been referred to as a plasma cell granuloma, inflammatory myofibroblastic tumor, inflammatory myofibrohistiocytic proliferation, fibroxanthoma, histiocytoma, fibrous histiocytoma, xanthomatous pseudotumor, postinflammatory pseudotumor, mast cell tumor, and plasma cell-histiocytoma [4, 5]. Inflammatory myofibroblastic tumors are frequently found in the lung but similar lesions have also been reported at almost every site in the body [3]. We reported an adult 20 year-old female patient with inflammatory myofibroblastic tumor of the trachea presenting with dyspnea and stridor.

CASE

A twenty year-old female patient with unremarkable past medical history was admitted to our hospital with the symptoms of hoarseness, cough and dyspnea. She had a cough without sputum and exertional dyspnea for one year. She had a recent wheezing attack in addition to

dyspnea and a cough. She was unresponsive to asthma medications which was started before the admission to our unit. The patient's physical examination was remarkable for the inspiratory stridor. Chest X-rays of the patient were normal. A pulmonary function test revealed a fixed obstruction with FEV1/FVC: 46%, FEV1: 62% (2.10 L), FVC: 119% (4.60 L) (Figure 1A). Reversibility of the pulmonary function test (FEV1) was negative. Computed tomography of the neck and thorax revealed tracheal thickening and stenosis below the vocal cords and bronchial wall thickening at the level of carina (Figure 2A and Figure 2B). Diagnostic flexible bronchoscopy showed tracheal stenosis approximately 2 cm below the vocal cords with an irregular mucosal appearance (Figure 3). Mechanical dilatation and resection was performed both for trachea and the bronchial system with rigid bronchoscopy. Histopathological examination of the biopsies from the lesion was reported as an inflammatory myofibroblastic tumor with S100 negativity, desmin positivity for smooth muscle cells and trichrom positivity for collagen tissue (Figure 4). After mechanical dilatation and resection by rigid bronchoscopy, 30 mg/day of deflazacort was started. Two weeks after the treatment the symptoms decreased. At the 6 month of the follow up, she was asymptomatic with a normal pulmonary function test and normal thorax computed tomography. The pulmonary function test showed FEV1/FVC: 79% , FEV:119% (4.02 L), FVC:132 (5.09 L) (Figure 1B)

DISCUSSION

Inflammatory myofibroblastic tumor has various names, including inflammatory pseudotumor, histiocytoma, fibrous histiocytoma, xanthoma, xanthofibroma, xantogranuloma, and plasma cell granuloma[6-8]. Barker et al reported first case of tracheal plasma cell granuloma in literature with conservative approach [9]. Inflammatory myofibroblastic tumors account for 0.04% to 0.7% of all lung neoplasms in previous reports [1, 2]. However, it is the most common

benign lung tumor in children under 16 years of age [2, 3]. Inflammatory myofibroblastic tumors can usually be seen at young ages more commonly below the 16 years old [10]. Inflammatory myofibroblastic tumors have been rarely reported at ages over 16 [11]. Tracheal involvement of an inflammatory myofibroblastic tumor has been rarely reported in the adult age group. A large series by Bahadori and Liebow reviewed 40 patients with inflammatory myofibroblastic tumor of the thorax. Among these patients, fifteen patients (38%) were children between 1 and 16 years of age (mean age, 8 years) and only one child had a tracheal tumor [12]. Adult tracheal inflammatory myofibroblastic tumors also are rare. To our knowledge, only 12 adult inflammatory myofibroblastic tumors with tracheal localization have been previously reported (Table 1). Apart from the table 1, Lee and et al. reported 15 patients who underwent surgical procedures owing to inflammatory myofibroblastic tumors. The mean age of these patients was 31.3 years (range, 7 months to 61 years). Four patients presented with the tumor located in the trachea [4]. However age of tracheal involvement was not defined. Because of the inconsistency in the pathologic diagnosis of the tumor and the limited number of patients typically seen with an inflammatory myofibroblastic tumor, the treatment of choice remains controversial. Inflammatory myofibroblastic tumors can be located in peritoneum, liver, spleen, breast, spinal cord and brain besides the respiratory system [13-18]. Inflammatory myofibroblastic tumors are more frequently seen in the lower lobe of the right lung and they are a solitary, oval and well defined lobulated mass that is peripherally located [19-21]. A mass lesion is located peripherally in 87% of the patients, centrally in 6% of the patients and the lesions can present radiologically as multiple nodular(5%), pleural based, cavitary lesions(5%) or the lesions can present with lobar atelectasis(8%) or hilar lymphadenopathy in 5% of the cases.[22, 23]. The definition of inflammatory myofibroblastic tumor proposed by the World Health Organization that is a lesion composed of a myofibroblastic spindle cell population accompanied by an inflammatory infiltrate of plasma cells, lymphocytes, and

eosinophils [24]. Myofibroblastic spindle cell populations account for the 70% of the total cell population in inflammatory myofibroblastic tumors similar to our case. The patients with inflammatory myofibroblastic tumors usually have nonspesific symptoms including dyspnea, stridor, chronic cough, hemoptysis and pleuritic chest pain. Some patients may be misdiagnosed as asthma and given asthma medication. In the small number of patients having endobronchial lesions, the clinical presentation may be acute and serious due to postobstructive pneumonia or symptoms associated to airway obstruction [11, 24]. Superior vena cava syndrome was reported as a serious associated condition in one case report of inflammatory myofibroblastic tumor of the mediastinum [25]. The etiology of inflammatory myofibroblastic tumor is unclear but trauma to the affected region secondary to inflammation has been thought as an possible etiology. Currently due to the existence of rare cases with a more aggressive clinical picture including local recurrence, malignant transformation or metastasis it was believed that inflammatory myofibroblastic tumor was a low-grade mesenchymal malignancy[24]. The findings about its recurrent chromosomal translocations involving 2p23, the anaplastic lymphoma kinase gene site, and the presence of other associated positive genetic fusions also led to the proposal that inflammatory myofibroblastic tumor was a malignant process rather than reactive lesion [24, 26-30]. Applebaum et al. proposed that COX2 and VEGF, as a mediator for angiogenesis, might play a role in the pathogenesis and growth of inflammatory myofibroblastic tumors [31]. Surgical resection has been known as the most relevant treatment modality of inflammatory myofibroblastic tumor with tracheal involvement. Surgical resection can be either intraluminal bronchoscopic removal with biopsy forceps or CO2 laser or open surgical intervention with segmental tracheal resection. A radical surgical approach and/or adjuvant radiotherapy and chemotherapy are not indicated and may be reserved for when the disease has an aggressive behavior [24]. Corticosteroids and non-steroidal agents have been reported as an alternative therapeutic strategy in rare selected

cases [32]. We performed intraluminal bronchoscopic removal and dilatation of the tumor by rigid bronchoscopy and started the corticosteroid treatment to the   patient.

The prognosis of an inflammatory myofibroblastic tumor is usually good but rarely it may involve a local invasion. Extrapulmonary inflammatory myofibroblastic tumors have a recurrence rate of 25%. Recurrence is related to the tumor's location, resectability and multinodularity. A metastatic rate for the tumor has been reported as <5% and is most often seen in children with intra-abdominal tumors [24, 33]. Fabre et al. followed 25 patients who had a complete resection for the tumor with a median follow-up of 80 months (range, 4–369 months), and found that both 5- and 10-year disease-free survivals were 89%. [34]. Recurrence rate information about the   trachea is limited due to the limited number of cases with inflammatory myofibroblastic tumors involving the trachea.

In conclusion, inflammatory myofibroblastic tumors, particularly tracheal involvement in adults is rarely seen and may present clinically as asthma or foreign body obstruction. Endobronchial involvement may show an acute presentation of respiratory distress. The most relevant therapy is open surgical resection or bronchoscopic resection. A follow –up is recommended for a potential recurrence.

Table 1:Review of adult inflammatory myofibroblastic tumors with tracheal localization

Case	Study(Date)	Age	Clinical picture	Localization	Histopathology	Treatment
1	Koch et al[35] (2011)	57	Hemoptysis, dyspnea	Trachea	inflammatory myofibroblastic tumor	Surgery
2	Filipe et al[11] (2010)	31	Dry cough, dyspnea	Trachea, LMB, RMB, carina	inflammatory myofibroblastic tumor	Bronchoscopic resection
3	Fabre et al[34] (2009)	19	undefined	Trachea	inflammatory pseudotumor	Surgery
4	He et al[36] (2009)	28	Dyspnea	Trachea	inflammatory myofibroblastic tumor	Surgery
5	Ono et al[37] (2006)	45	Dyspnea	Trachea	inflammatory myofibroblastic tumor	Bronchoscopic resection/ Nd-YAG) laser
6	Belák et al[38] (2006)	45	Dyspnea, stridor	Trachea	inflammatory myofibroblastic tumor	Surgery
7	Nikanne[39] (2004)	21	Dyspnea, cough	Trachea	inflammatory pseudotumor	Bronchoscopic resection
8	Restrepo et al[40] (2003)	20	Dyspnea, cough	Trachea	Inflammatory pseudotumor	Surgery
9	Amir et al[41] (2002)	21	Dyspnea, stridor	Trachea	Inflammatory pseudotumor	Surgery
10	Ishii et al[42] (1993)	61	Dypnea, wheezing	Trachea	inflammatory pseudotumor	Surgery
11	Satomi et al[43] (1991)	55	inspiratory stridor	Trachea	plasma cell granuloma	CO2 laser

LMB:Left main bronchus; RMB:Right main bronchus

Figure Legends

Figure 1: A. Flow-volume curves before treatment **B.** Flow-volume curves after treatment.

Figure 2: A. Tracheal thickening and stenosis below the vocal cords. **B.** Bronchial wall thickening and stenosis at the level of carina.

Figure 3: Bronchoscopic image of tracheal stenosis approximately 2 cm below the vocal cords with an irregular erythematous mucosal appearance

Figure 4: A. Hematoxylin-eosin staining at 10 magnitude. The polypoid tumor is made up of a proliferation of myofibroblastic cells with collagenous stroma cells with inflammatory infiltrate. **B.** Widespread cytoplasmic positivity with Vimentin immunohistochemical staining in tumor cells (Vimentin x 20)

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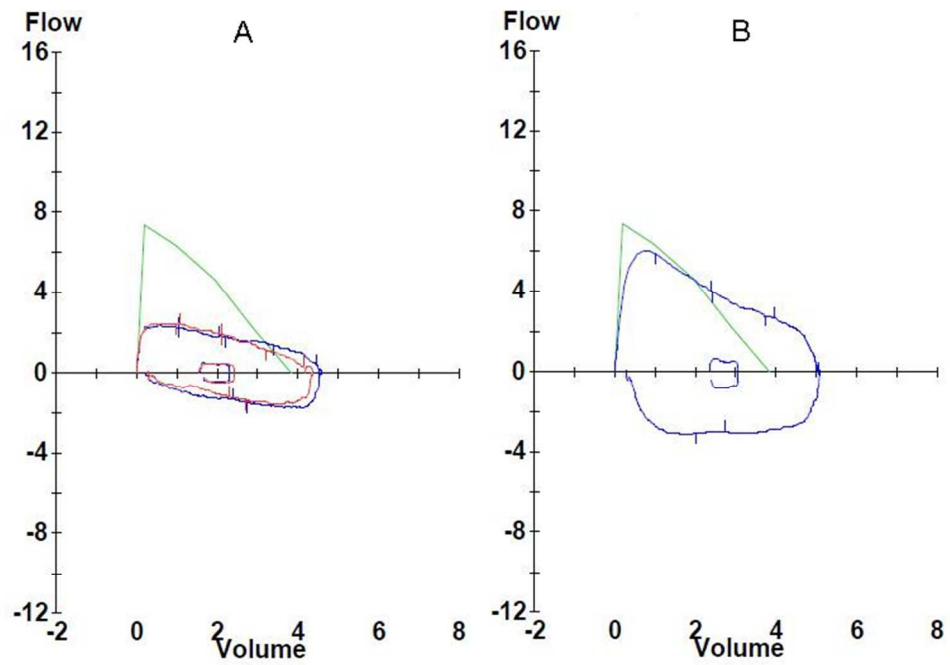
A. Flow-volume curves before treatment B. Flow-volume curves after treatment.
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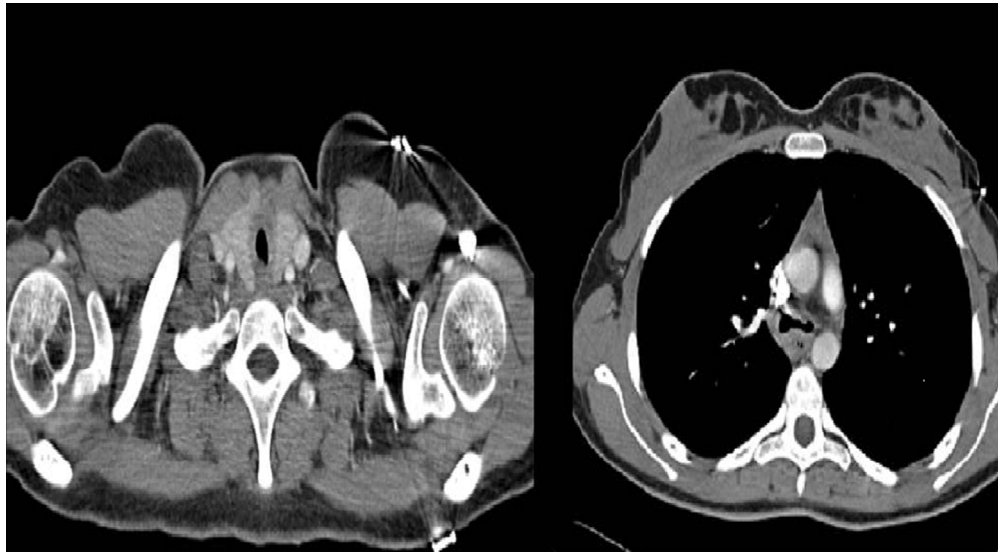
A.Tracheal thickening and stenosis below the vocal cords. B. Bronchial wall thickening and stenosis at the level of carina.
278x152mm (96 x 96 DPI)
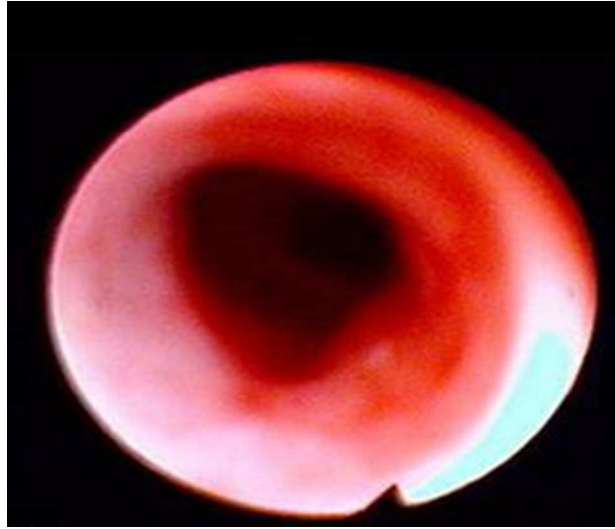
Bronchoscopic image of tracheal stenosis approximately 2 cm below the vocal cords with an irregular erythematous mucosal appearance
93x86mm (84 x 77 DPI)
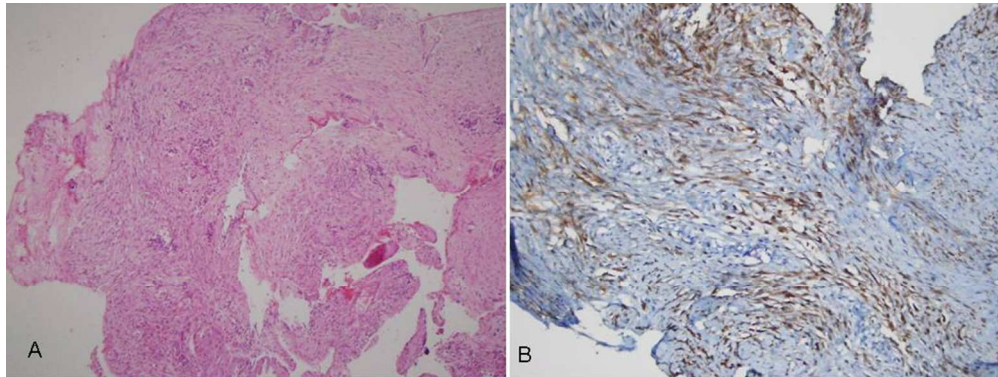
A. Hematoxylin-eosin staining at 10 magnitude. The polypoid tumor is made up of a proliferation of myofibroblastic cells with collagenous stroma cells with inflammatory infiltrate. B. Widespread cytoplasmic positivity with Vimentin immunohistochemical staining in tumor cells (Vimentin x 20)
286x107mm (96 x 96 DPI)