Case Report

Laryngeal myofibroblastic tumor: case series and literature review

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Abstract

Inflammatory myofibroblastic tumor (IMT) or (plasma cell granuloma) of the larynx is a rare benign lesion that usually involves the lungs and broncopulmonary tree, as well as abdominal viscera. Overall this kind of tumor represents less than 1% of all tumors in the lung and respiratory tract with only 31 cases reported to date in the English language literature of laryngeal IMT. We report the first 2 cases in Saudia Arabia of IMT of the larynx treated at King Abdulaziz University Hospital (KAUH) with literature review.

Keywords: Inflammatory myofibroblastic tumor - plasma cell granuloma – laryngeal tumors

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Introduction

Inflammatory myofibroblastic tumor (IMT) or plasma cell granuloma of the larynx is a rare benign lesion that commonly affects lung and abdominal viscera.[1] The lesion was first described by keen et al in 1986. [2] Wenig et al[3] who proposed the term IMT for lesions that are predominantly fibroblastic rather than a mixture of inflammatory or reactive growth pattern in the larynx. These tumors tend to be locally aggressive, benign, may grow slowly or rapidly and usually manifest with progressive symptoms referable to mass effect. Head and neck IMTs account for 14%-18% of all lesions. Surgical excision is considered the main stay of treatment. [4] The purpose of this article is to report two cases of laryngeal IMT and to review the published literature.

Case report

Case 1

A 38-year-old male presented to Otorhinolaryngology clinic at King Abdulaziz University Hospital (KAUH), Riyadh, Saudi Arabia with 3 year history of dyspnea and stridor with exertion and globus sensation. His symptoms progressed to be obstructive in nature during sleep with progressive straining and change of voice. He did not report any history of dysphagia. He is a known case of hypertension and hyperlipidemia on treatment.

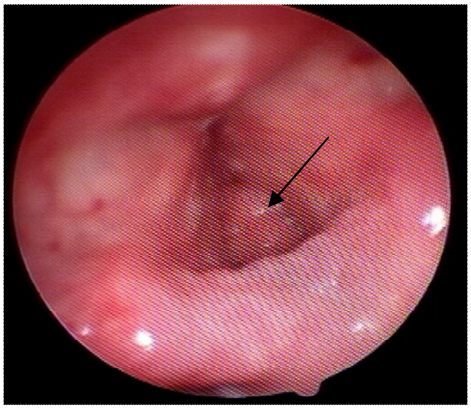

Figure 1: Axial CT scan with contrast media showing a mass originating from left lateral area of subglottis and extending to the trachea.

Physical examination showed an over weighted patient with short neck and moderate biphasic stridor at rest. Fiberoptic laryngostroscopy revealed bilaterally mobile vocal folds. Huge mobile polypoidal subglotti mass occlude 80-90% of laryngeal lumen was also noticed (figure 1). Oxygen saturation was above 95%.

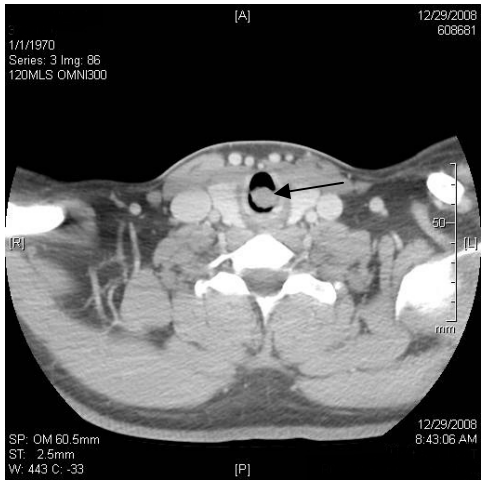

Figure 2: Histopathological examination of the tumor in case 1.Inflammatory myofibroblastic tumor consisting of several "staghorn" vessels with areas of hyalinized fibrosis and numerous aggregates of inflammatory cells. (Hematoxylin and eosin stain X 200).

The patient was admitted to the hospital where contrast-enhanced CT-scan of the neck was obtained. It revealed non-enhanced huge mass (1.2x1cm) in subglottic area at level of cricoid cartilage (C6-C7), from left lateral part, and extending to the trachea. There were no signs of infiltration or invasion to adjacent structure and no radiological lymphadenopathy (figure 2).

The patient was subsequently taken to operative room for microlaryngosopy and bronchosopy with possible tracheotomy. Tracheotomy under local anesthesia was done because of difficult intubation and exposure of the larynx. Microlaryngoscopy revealed large lingual tonsil, short epiglottis and firm 2cm polypoidal mass originated from left lateral subglottic area and trachea. The mucosa of the mass appeared to be normal. The remainder of upper airway was looking normal also. Multiple biopsies were taken using cupped forceps and sent for histopathology.

Using a laryngeal microdebrider size 4 and a 30 degree telescope, the stem of the mass was removed. Hemostasis was achieved by adrenaline and forceps diathermy. Intra-operatively, the patient received IV dexamethasone of 6mg and postoperatively he was started on oral corticosteroids and proton pump inhibitor 40 mg daily for 2 weeks. The patient was kept on tracheotomy tell final histopathology report was released.

Histopathology was consistent with squamous and respiratory epithelium infiltrated by inflammatory cells including numerous plasma cells and foamy macrophages and with dilated vessels and areas of hyalinized fibrosis. A panel of histochemical staining has been done and show strong positive staining to smooth muscle actin (SMA) and Vimentin. Desmin was also positive. This was suggestive of IMF tumor with rich histiocytes (Figure 3). No evidence of malignant cells was reported. Patient was decannulated successfully and discharged home after few days in a good condition. The patient had laryngostroboscopy examination one month post operatively (Figure 4) and it showed no recurrence or remnant of the disease, small vocal fold granuloma was noted which disappear after few months. The Patient remained free of symptoms with normal breathing and normal voice for 2 years following initial resection of the mass.

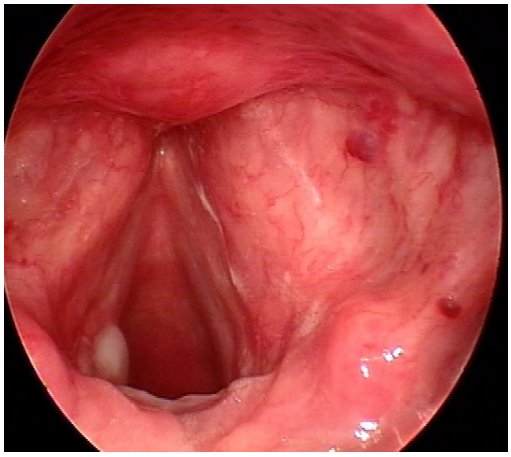

Figure 3: Laryngostroboscopic examination of case1 one month post-operatively showing completely removal of the mass. There is vocal fold granuloma which was disappeared after few months.

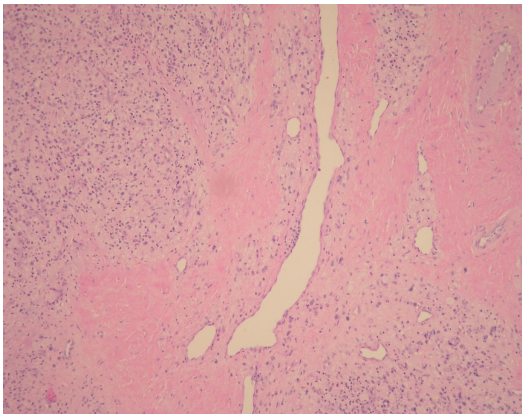

Figure 4: Histopathological staining of the tumor in case 2. Inflammatory myofibroblastic tumor consisting of foci of numerous plasma cells and lymphocyte which appear to be infiltrating between collagen fibers. (Haematoxylin and eosin stain X 400)

Case 2

A 54-year-old male presented to Otolaryngology clinic at king Abulaziz University Hospital (KAUH) complaining of 7 month history of gradually progressive change of voice. He did not report any breathing or swallowing difficulty. He is a heavy smoker (20 cigarettes per day for more than 20 years), with no history of alcohol abuse. He has diabetes mellitus on diet control. The patient's surgical history revealed microlaryngoscopy and biopsy of left true vocal fold mass at another hospital 2 month ago. Histopathology revealed non-significant inflammatory cells.

Auditory perceptual assessment showed severely strained and leaky dysphonic voice. Telescopic laryngostroboscopy revealed bilateral mobile vocal folds with large (1.5X1 cm) semispherical swelling arising from the under surface of the left true vocal fold and subglottic area, with absence of mucosal wave over the left vocal fold. Neck examination showed no lymphoadenopathy. Contrast-enhanced CT scan was obtained, which revealed mild enhanced mass at the left true vocal fold, with no invasion or infiltration and no radiological lymphadenopathy.

Patient underwent microlaryngoscopy, which revealed firm intrafolder mass involving the whole length of the left true vocal fold. The mucosal covering of the mass appeared mildly erythematous. The remainder of upper and lower airway appeared normal.

Biopsies of the mass were taken using a cup forceps. Histopathological assessment was consistent with chronic inflammation. One month later, the patient underwent another microlaryngoscopy, where microflap and laser excision of the mass with multiple deep biopsies were performed.

The histopathological result and immuno-histochemical stain came as dense and sclerotic fibrous connective tissue infiltrated by mix inflammatory cells consisting of a large number of plasma cell, lymphocyte and histocyte (Figure 5). The specimen showed scattered connective tissue cell within inflammatory mass using SMA and vimentin stain. Desmin stain was also positive for some myofibroblastic cells and infiltrated skeletal muscle fibers. This feature was suggestive of inflammatory myofibroblastic tumor. The patient had recurrence after one year and another endoscopic procedure with laser excision done and he is free from the disease for 6 month.

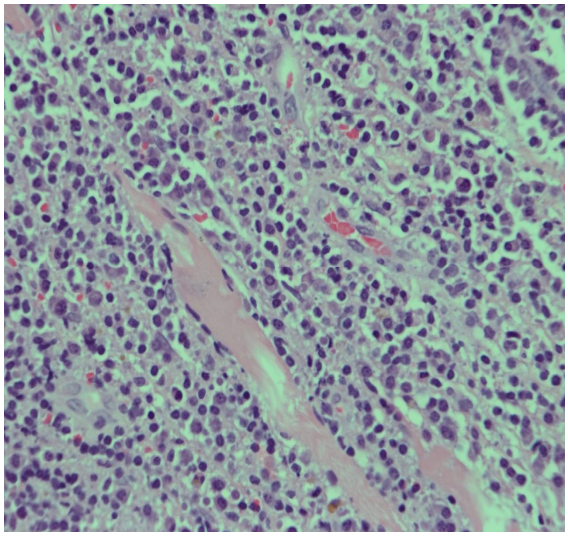

Figure 5: Histopathological staining of the tumor in case 2. Inflammatory myofibroblastic tumor consisting of foci of numerous plasma cells and lymphocyte which appear to be infiltrating between collagen fibers. (Haematoxylin and eosin stain X 400)

Discussion

Inflammatory myofibroblastic tumor is a newly described entity of neoplasm that usually involves the lungs and broncopulmonary tree, as well as abdominal viscera.[1] Overall, this kind of tumor represents less than 1% of all tumors in the lung and respiratory tract.[5]These tumors were originally reported in the lungs but also were described in other sites, like orbit, spleen, genitourinary tract, mesentery, cardio esophageal junction, breast, central nervous system and larynx.[6] Currently, IMT is considered as an intermediate locally recurrent neoplasm that rarely metastasizes and they usually follow a benign course and they have distinct histological appearance.[7]

Up to date, 31 cases of laryngeal IMT have been reported in literature (Table 1). The origin of this tumor is still unclear. Several theories have been proposed, including infectious, reactive (post-surgical or foreign body) and immunologic factors.[1] It may be reasonable to assume, based on the diversity of presentation and suggested etiologies, that these tumors represent a family of neoplasm's rather than a single clinical entity.[8]

Wenig et al first report case series on 1995 in Larynx.[3] He reported 8 cases, age ranging from19-69 years. Six cases presented in the glottis. Only one case was post-intubation. Out of the reported 31 cases, 2 cases had post-intubation trauma and excision of vocal fold cyst [1,3] and one case had a previous resection of thyrolglossal cyst. [9] However, trauma is difficult to prove as an etiology because these are few cases. Smoking had been suggested as a causative agent, as 7 cases (22.6%) of the 31 patients with IMT were smokers.[1] Alcohol abuse was not established as a causative agent as well as radiation exposure. Epstein-Barr virus has been associated with IMT at extralaryngeal lesions but not in the larynx. [1,10]

The neoplastic theory had been proposed because of tumor recurrence in some reports and malignant progression. [11] Chromosomal rearrangement at chromosome 2p23 and expression of anaplastic lymphoma kinase 1 (ALK1) and p80 had been suggested. [12] Furthermore, loss of heterozygosity favors the neoplastic origin.[13]

Considering those 31 cases that have been reviewed from 1995 to 2010, including these two cases presented, age varied from 19 months to 74 years. [13,14] These tumors usually affect males (22/31 (71%), more than females (9/31 (29%). Seven patients of the 31 were children under the age of 13y (22.5%). [9,2,14-17]

IMT can affect any subdivision of larynx, but the true vocal folds are the most common laryngeal site in 51% of the cases,(16 cases include case 2) and then the subglottic area was affected by IMT in 22.5% of the cases (7 cases). There were 2 cases that occurred in right lateral wall of subglottis [9,18] and 2 cases occurred in left lateral wall (case1). [19] One case occurred at cricotracheal area, and 2 reported cases by the authors were in the subglottic region. The supraglottic area represents 9.6%, as 3 cases have been reported, one case was of a 7 years child at right laryngeal ventricle, one was of a 30-month child at right aryepiglottic fold, and one adult at right ventricular fold. [15,16,20] Anterior commissure represent 10% of the cases (3cases). [1,3,21] Adjacent laryngeal area was involved in 7% of the cases [3,14] (Table 1).

Presentations of these tumors vary but according to the case series which have been studied, the most common presentation was voice change 74%, (23 cases). Stridor represents 29% of the presentations (9 cases), dyspnea and shortness of breath occurred in 22.5% (7 cases). Globus sensation appeared in 16% (5 cases). (Table 2)

Radiological investigation including chest x-ray, CT-scan of the neck with contrast and laryngobronchoscopy with multiple biopsies and immuno-histochemical staining is essential in the diagnosis of these tumors. The differential diagnosis includes squamus cell carcinoma in adult, while in pediatric age group, it should be differentiated from inflammatory changes secondary to foreign body, and pediatric spindle cell tumor (fibromatosis,myofibromatosis).[13]

Table 1: Reported laryngeal IMT cases in literature.

Site	Age(years)/sex	Location
Supraglottic:		
1.Hanna et al[16]	7/M	Right laryngeal ventricle.
2.Rodrigues et al[15]	30mo/M	Right aryepiglottic fold.
3.Suh et al [20]	52/F	Right false cord.
Glottis:		
1.Wenig et al[3]	19/M	Right anterior vocal cord, 1cm.
2.Wenig et al[3]	65/M	Left true vocal cord and anterior commisure, 3cm.
3.Wenig et al[3]	64/M	Right true vocal cord 0.7x0.5x0.3cm.
4.Wenig et al[3]	26/F	Right true vocal cord 1x0.5cm.
5.Wenig et al[3]	67/M	Right anterior true vocal cord, 0.4cm.
6.Wenig et al[3]	22/F	Vocal cord.
7.Corsi et al[21]	57/M	Anterior commisure, 0.8cm, recurrent mass 0.6cm.
8.Kendall et al[23]	51/M	Right vocal cord, 0.4cm.
9.Matsumoto et al[26]	53/M	Anterior lift vocal cord, 0.5cm.
10.Martinez et al[27]	72/M	Left true vocal cord, 1.5cm.
11.Ereno et al[24]	74/M	Left vocal cord, 3.5cm.
12.Guilemany et al[28]	62/M	Right vocal cord.
13.Volker et a[29]l	32/F	Right vocal cord polyp, 0.8cm.
14.Belleza et al[30]	23/M	Right vocal cord, 0.5cm.
15.Zitsch et al[19]	57/F	Left true vocal cord.
16.Idrees et al[1]	56/M	Anterior commisure.
17.Idrees et al[1]	28/M	Right vocal cord.
18.Kumar et al[17]	10/M	Right vocal cord.
19. Present case 2	54/M	Left vocal cord.

Subglottic:		
1.Wenig et al[3]	54/F	Subglottic 1.5cm.
2.Munoz et al[9]	5/M	Right lateral wall of subglottic, 1.8x0.5cm.
3.Alaani et al[18]	49/F	Right subglottic
4.Zitsch et al[19]	33/F	Left subglottic, 1.3x1.2cm
5.Zapatero et a[22]	6/M	Cricotracheal , 1x1.5cm.
6.Keen et al[2]	11/F	Subglottic
7.Present case 1	38/M	Left lateral wall of subglottic.
Other:		
1.Wenig et al[3]	69/M	Pyriform sinus.
2.Das-purkayastha et al[14]	19mon/M	Immediate upper trachea.

Table 2: Symptoms of IMT

Symptoms	No of cases	%
1. Voice change	23	74
2. Stridor.	9	29
3. Dyspnea and SOB.	7	22.5
4. Globus sensation.	5	16
5. Cough.	2	6
6. Apnea.	1	3.2
7. Respiratory failure.	1	3.2

The classical histopathological feature includes spindle or satellite cells distributed in chronic inflammatory back ground. [(1)] The mucosa show non-specific ulceration with granulation tissue. The submucosa show plump to ovoid spindle cells with focally collagen stroma. No cellular atypia. Inflammatory infiltration is variable and mostly consists of plasma cells, lymphocyte, esinophils and histocytes.

Based on histopathological pattern, long list of differential diagnoses mimicking these finding include: IMT, inflamed/infected leiomyosarcoma, nodular fasciitis, fibromatosis, myofibroblastoma, fibrous histocytoma, inflammatory malignant fibrous histocytoma, sarcomatoid carcinoma and benign and malignant smooth muscle tumor.[21]

IMT must be differentiated from spindle cell squamus carcinoma. The absence of atypical mitosis despite presence of mitotic figure is key feature of IMT that distinguishes it from spindle cell squamus carcinoma. [(3)] The typical immuno-staining pattern is reactivity for vimentin with muscle-specific actin and smooth muscle actin. [(1,12,21,17)] Other immunohistochemical stain is S-100 which is usually positive for large epithelioid cells. [(8)] Anaplastic lymphoma kinase 1 (ALK 1) can be found and considered as a favorable prognostic marker. [(12)] Negativity for cytokeratin, CD34 helps to make the diagnosis of IMT.[(17)]

The management of this disease is best achieved by microlaryngoscopies (with or without laser) and complete excision with or without steroid therapy.[(8)] Three out of the 31 patients were treated by open surgical excision

as initial management all of them were pediatric. [2,14,22]

Recurrence appeared in 9 cases including case 2. Eight cases treated initially by endoscopic excision. Wenig et al [3] reported a case treated by cordectomy, two occasion of recurrence in 2 years treated by laser & radiation therapy followed by laryngectomy with no evidence of disease (NED) for 6 months. Corsi et al [21] reported a case treated initially by endoscopic excision followed by another endoscopic excision, with NED for 12 months. Kendall et al [23] report an IMT case treated by endoscopic excision followed by hemilaryngectomy, with NED after 12 months. Ereno et al[24] reported a case of an old man who had IMT that was managed by several partial endoscopic excision. Alanni et al [18] reported a case with twice endoscopic excision, with NED 15 months. Rodrigues et al [15] reported a case in which partial excision by endoscopy was done, however, recurrence was found after 7 months. Zitsch et al [19] managed a patient with high dose of steroid with no response, followed by radiotherapy with no improvement also, then open excision was decided, and there was NED after 14 months. Hanna et al [16] report IMT in a child treated initially with endoscopic removal via laser and another three procedure was done due to incomplete exesion. Our case number two had recurrence after initial endoscopic procedure with laser, another endoscopic procedure done NED after 6 month. The recurrence rate of laryngeal IMT 8 to 18%. [4,17] The recurrence occurs within 2 month to 12 month. The factors that can lead to recurrence may include partial excision, incomplete excision, or steroid therapy alone. Coffin et al reported 84 patients with extra- pulmonary IMT, who were all children and adolescents. Adult cases are even rare in this study. Of the 53 patients under follow-up, 13 (25%) had one or more recurrences at 1–24 months after initial excision, and distant metastases were not documented.[25]

Conclusion:

IMT rarely involve the larynx, but should be considered in the differential diagnosis of lesions involving the larynx. IMT can mimic malignant lesions or recurrent respiratory papillomatosis. It can be differentiated by histopathological and immuno-histochemical assessment. The best treatment option is complete endoscopic excision, with or without laser, which gives good results with less morbidities. Recurrence among laryngeal IMT can occur from 8 to 18% to of patients and it depends on the option of management and usually occurs within one year postoperatively. The current study does not show the long term follow up and whether these patients will have recurrence or not.

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