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Systematic Review

Ear, Nose and Throat Section

Pyogenic Granuloma of the Lower Airway- A Systematic Review

VM LAKSHANA DEVE[1], R SITHANANDA KUMAR @VENKATESAN[2], TC VIKRAM RAJ MOHANAM[3], RG ARTHY[4], JAYAPRIYA DJAMBOULINGAM[5], MARY KURIEN[6]

ABSTRACT

Introduction: Pyogenic granulomas (PGs) are benign lesions that are very common in the upper aerodigestive tract. These lesions occur due to hormonal imbalance or due to a predisposing traumatic factor. They are relatively rare in the lower respiratory tract. There are few published papers of PG involving the lower airway in the past 30 years.

Aim: A case of pyogenic granuloma of larynx mimicking malignancy has been presented along with the systematic review on methods of diagnosis, successful management, and prevention of pyogenic granuloma recurrence in the lower respiratory tract.

Materials and Methods: This systematic review of literature included reports from 1981 till date, where complete details of the records were available. These reports were collected from the search engines "PubMed" and "Google Scholar" using the MeSH terms "pyogenic granuloma" OR "lobular capillary haemangioma" AND "lower respiratory tract". The results were reviewed by three different authors independently with a main focus on methods of diagnosis and successful management and prevention of recurrence.

Results: A 59-year-old male patient presented to ENT Department with hoarseness of voice for the past six months. On examination with video laryngoscope, a pale pinkish polypoidal mass originating from the anterior commissure and extending into the subglottic wedge with normal vocal cord mobility was noted. Neck examination showed splaying of thyroid cartilage with tenderness and there were no palpable lymph nodes. Computed Tomography (CT) examination suggested a neoplastic etiology of thyroid cartilage erosion. The patient was managed by microlaryngeal excision of the mass and histopathological analysis revealed pyogenic granuloma with no evidence of malignancy. From the 25 papers reviewed, a predisposing trauma like a history of intubation/lower airway procedures like bronchoscopy or laryngoscopy is not a prerequisite for the occurrence of PG of the lower airway. The lesions can be excised via microlaryngoscopy or using the bronchoscope depending on the site of lesion. The various surgical modalities used for excision are cold steel dissection, laser excision and cryotherapy.

Conclusion: Meticulous dissection and removal of the lesion with postoperative measures to prevent additional trauma like antireflux measures and appropriate antibiotic therapy seems to be helpful in preventing recurrence. Role of steroids in the management of pyogenic granuloma has not been supported by adequate literature. Further studies are required to comment on the adequacy of duration of follow-up.

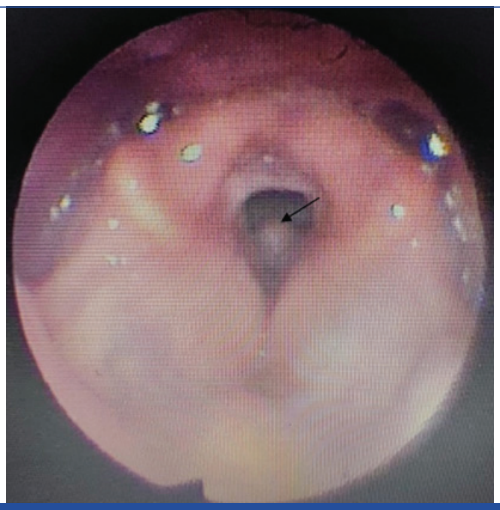
Keywords: Larynx, Lobular capillary haemangioma, Tracheobronchial tree

INTRODUCTION

Pyogenic granulomas or Lobular Capillary Haemangiomas (LCH) are common benign vascular lesions with rapid growth pattern. They are usually seen in the skin and upper aerodigestive tract. Pyogenic granulomas have a multifactorial etiology which include viral infections, chronic irritation, sudden hormonal variations, pre-existing arteriovenous malformations, and trauma [1,2]. Pyogenic granuloma of the larynx and the tracheobronchial tree is an exceedingly rare occurrence [3,4]. They are usually bound to recur and have been effectively managed by surgical excision, intralesional corticosteroids and laser therapy [5-7]. This article focuses on one such case and a systematic review of the current literature on the varying manifestations, diagnostic and treatment modalities, focussing on the incidence of recurrence and the role of steroids to prevent it.

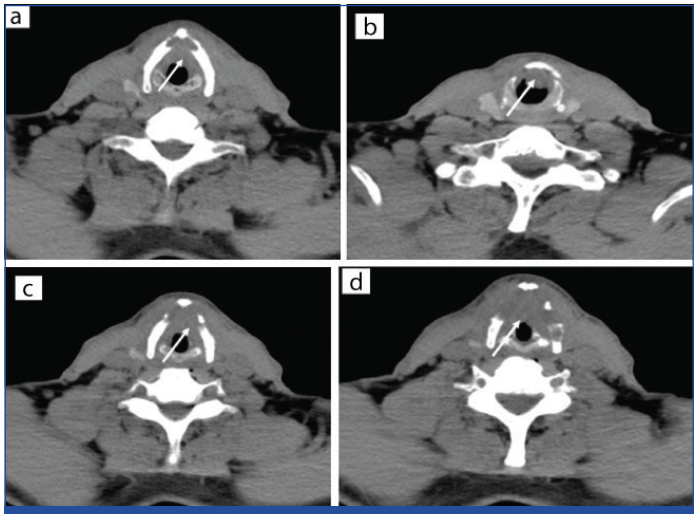
CASE REPORT

A 59-year-old male patient, farmer from Tamil Nadu, presented to ENT Department with persistent progressive hoarseness of voice for the past six months. There was no pain or difficulty in breathing or swallowing. He had no history of diabetes, hypertension, tuberculosis, or bronchial asthma, COPD. He did not give any history of consumption of alcohol or tobacco in any form. He denied any history of previous illness requiring hospital admission. A detailed ENT examination including video laryngoscopy [Table/Fig-1] showed a pale pinkish fleshy polypoidal mass arising from the anterior commissure and extending into the anterior subglottic wedge with normal vocal cord mobility. Airway was adequate posterior to the lesion and other areas of larynx appeared normal. Neck examination revealed splaying of thyroid cartilage with tenderness although there were no palpable lymph nodes. With the above history and clinical presentation, a provisional diagnosis of malignancy of the

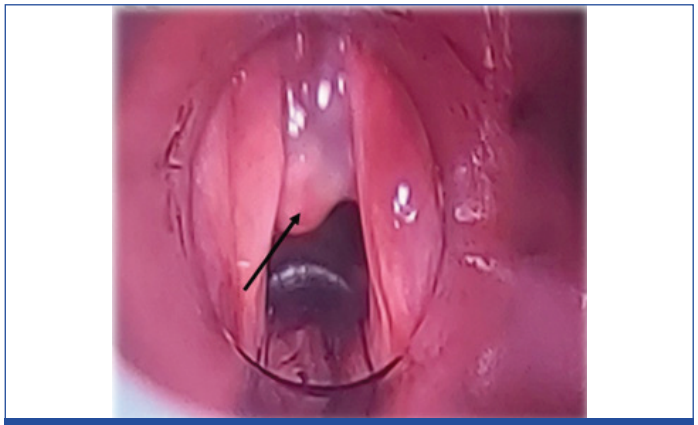


[Table/Fig-1]: Video laryngoscopy done in Out Patient Department (OPD) showing the mass in the anterior commissure.

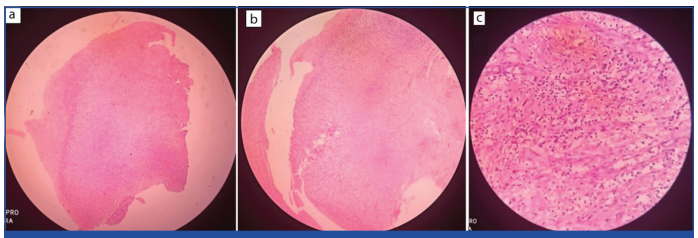
larynx was made and hence a CT [Table/Fig-2] was requested; which was also suggestive of a neoplastic aetiology with radiologic evidence of thyroid cartilage erosion. Hence, the patient underwent for a microlaryngeal excision of the mass and biopsy [Table/Fig-3] under general anaesthesia. The histopathological analysis of the specimen [Table/Fig-4a-c] showed polypoidal lesion with ulceration of overlying epithelium. The angiomatous tissue had numerous proliferations of thin-walled blood vessels arranged in lobules. There was a background of stroma with fibroblastic proliferation and mixed inflammatory infiltrates. This was reported to be polypoidal capillary haemangioma (pyogenic granuloma) with no evidence of malignancy.



[Table/Fig-2]: CT of neck sagittal and axial cuts (clockwise from left). a) Sagittal section showing the mass partially occluding the lumen of larynx; b-d) Axial cuts showing the mass and erosion of the body of thyroid cartilage.

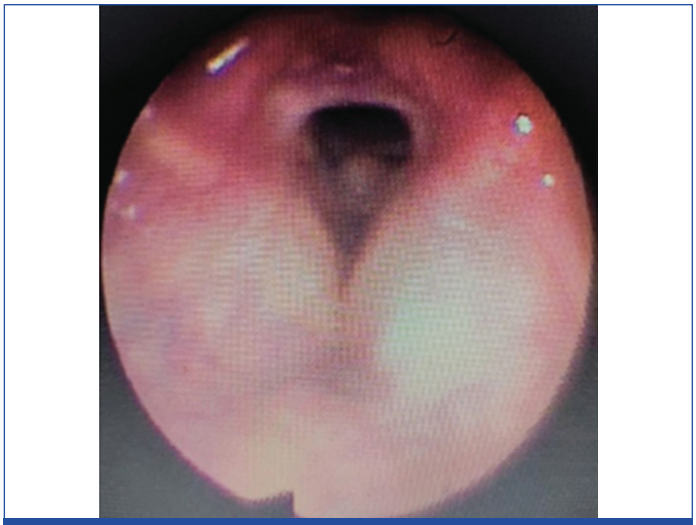


[Table/Fig-3]: Intra operative microlaryngoscopic picture showing pale pinkish fleshy polypoidal mass arising from the anterior commissure and extending into the anterior subglottic wedge.



[Table/Fig-4]: Histopathological images with haematoxylin and eosin staining. a, b) Image with 10X magnification showing polypoidal lesion with ulceration of overlying epithelium (extreme left and centre). The underlying stroma is cellular with fibroblastic proliferation and lobular arrangement of blood vessels; c) image with 40X magnification showing proliferating blood vessels and fibroblasts along with a mixed inflammatory infiltrate (extreme right).

Patient was started on antibiotics (amoxicillin and potassium clavulanate 625 mg, twice a day), anti reflux measures and was kept on close follow-up. In the 6th postoperative week [Table/Fig-5], he again began to have hoarseness of voice and was found to have a recurrence at the same site. He was taken up for microlaryngeal excision and biopsy under



[Table/Fig-5]: Video laryngoscopy image showing recurrence at the 6th postoperative week follow-up.

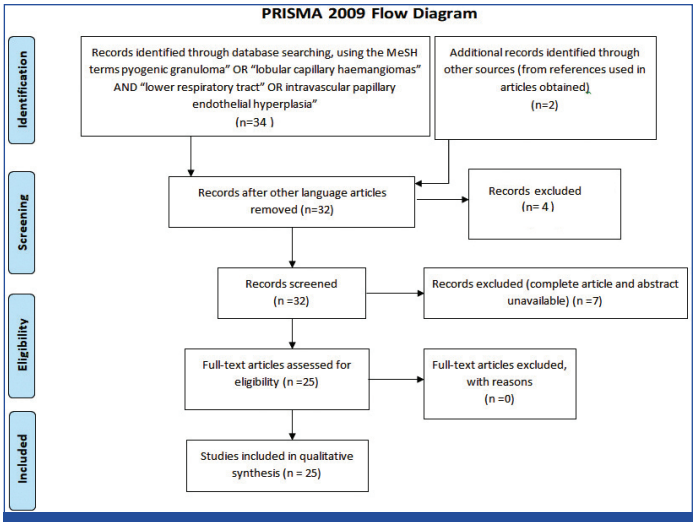
general anaesthesia, once again. Histopathological evaluation revealed features of pyogenic granuloma. Adjuvant measures like adequate voice rest, speech therapy and breathing exercises along with the anti-reflux measures were started. He was also given a short course of oral steroids at a dose of 1 mg/kg body weight, under antibiotic cover, which was then gradually tapered and stopped. He was found to be asymptomatic till six months postoperatively. Hence, a complete management of laryngeal pyogenic granuloma with meticulous excision, along with antireflux measures and oral steroid therapy under antibiotic- amoxicillin and potassium clavulanate 625 mg, twice a day cover helped in preventing recurrence of the lesion in this patient.

MATERIALS AND METHODS

A systematic review of literature was conducted according to PRISMA guidelines 2020 [8], with all published records available till date. Specific MeSh terms were used to search case reports/ series those involving the lower airway from the larynx till the tracheobronchial tree. The search engines "PubMed" and "Google Scholar" were searched to retrieve the published reports.

Search strategy: To search for relevant articles, MeSH terms with a combination of Boolean operators were used. The terms used were "pyogenic granuloma" OR "lobular capillary haemangioma" AND "lower respiratory tract".

Selection process: All articles published from the year 1980 till date were retrieved. Articles in English language with full text available were included. Those which were published in other language or those where full text was unavailable were excluded. Total 25 studies/case reports were included [Table/Fig-6].



[Table/Fig-6]: PRISMA flow diagram for selection process.

Data collection process: The authors screened each of the retrieved record independently. All data available from each of these records were tabulated and analysed.

Data items: Any data that went missing or any unclear information were noted as such. The data from the relevant articles like the varying manifestations of symptoms, details on the exact site of presentation of the lesion, treatment modalities, duration of follow-up, incidence of recurrence and morbidity were tabulated. The following calculations were performed with the available data: average and range of age of the patients, geographic distribution, relative frequency of the most common sites of occurrence of the lesion, presenting features, management options employed, complications, rate of recurrence.

Study risk of bias or certainty assessment: Two reviewers independently screened the complete published records of each article. Disagreements were resolved by consensus or by a third reviewer.

The tools proposed by Murad MH et al., Munn Z et al., and the JBI tool was used for quality assessment [9-11]. The JBI tool domains and their leading explanatory questions are:

Selection: 1. Does the patient(s) represent(s) the whole experience of the investigator (centre) or is the selection method unclear to the extent that other patients with similar presentation may not have been reported?

Ascertainment: 2. Was the exposure adequately ascertained?

3. Was the outcome adequately ascertained?

Causality: 4. Were other alternative causes that may explain the observation ruled out?

5. Was there a challenge/rechallenge phenomenon?

6. Was there a dose-response effect?

7. Was follow-up long enough for outcomes to occur?

Reporting: 8. Is the case(s) described with sufficient details to allow other investigators to replicate the research or to allow practitioners make inferences related to their own practice?

Questions 4, 5 and 6 are mostly relevant to cases of adverse drug events)

Effect measures/Synthesis methods: These are not applicable as most of the records were case reports. Hence no sensitivity analysis was conducted.

Ethical concerns: An informed written consent was obtained from the patient to publish his details. There are no other ethical concerns involved in this paper.

RESULTS

There were 25 studies with complete data from the year 1981. There were three case studies/reports, one with four neonates by Walner DL et al., and the other being a retrospective study by Fechner RE et al., comprising of the records of 46 patients [3,4]. There was also a retrospective study on receptors presented in these lesions with 22 patients [12]. The rest were all case reports. Most of the reports were from the USA followed by Turkey [Table/Fig-7] [1-7,12-29]. There was a total of 94 cases reported from all the available articles other than the present case. Although PGs are more common in pregnancy due to hormonal imbalance [9], these studies showed males and females to have been equally affected. They appear to present in varied age groups [4]. History of airway manipulation like an intubation were present in 75% of the study population. Tobacco and alcohol did not seem to have an additional influence according to this literature [5,13,15]. Hoarseness of voice, cough, and haemoptysis were the predominant presenting complaints. Patients with laryngeal PG manifested with voice change whereas those with tracheal or bronchial lesions manifested with cough and haemoptysis. Although laryngeal PG were more than the tracheal PG (10/94 cases), lesions in the trachea bronchial tree were more difficult as it was difficult to secure the airway prior to the surgery or for administration of anesthesia [14]. All these lesions were surgically removed using microlaryngoscopy with cold steel dissection or laser. Cryotherapy and brachytherapy were used in a few cases in an attempt to prevent recurrence [1,27]. There was one report [19], where botulinum toxin was given for a successful management and to prevent recurrence. All these lesions were confirmed histopathologically as PG. According to the data available, steroids where used in a total of five cases- both in adults as well as in children [3,5]. Topical application was done intraoperatively in neonates and multiple intralesional steroid injections were given in a young adolescent boy for recurrence [5]. Out of 94 patients that were reported, 11 cases showed recurrence. Presence of a laryngeal trauma like an intubation is not a primary entity determining the occurrence of pyogenic granulomas. Meticulous dissection and removal along with antireflux measures seem to be the important factors determining recurrence in these cases, however there are reports in which the cause of recurrence is unknown [20-22]. Administration of steroids may be helpful but is not proved to be the modality of choice to prevent recurrence.

Quality appraisal of the case reports and case series reviewed: The original articles which were three in number were methodologically analysed using the format used by Munn Z et al., and Murad MH et al., [9,10]. Each article was appraised for quality as tabulated in [Table/Fig-8] [1-7,12-18,20-29]. The validity was the average of subjective opinion of the three authors.

DISCUSSION

Pyogenic granulomas are most often seen in children and young adults. About 70% of PGs are seen in the head and neck region. They occur predominantly in the nasal cavity, oral cavity and oropharynx [1-3]. These benign tumors are known for recurrence as they have a rapid regrowth period of 18 months to 3 years. LCH or PG are pinkish friable masses that can be pedunculated or sessile, often arising from the upper aerodigestive tract [4,5]. The exact cause for PG is unknown but are often thought to be predisposed by prior insult to the local tissue in the form of trauma or instrumentation as they are often surrounded by inflammatory changes. This inference is supported by the few reports with a positive history of laryngeal manipulation prior to the occurrence of this lesion in present literature review [12,15]. Other factors seem to be hormonal shifts such as in pregnancy, effect of certain drugs, cytogenetic clonal deletion, production of angiogenetic caused by local irritation etc, VEGF, decorin, transcription factors pATF2 and pSTAT3, signal transduction pathways MPAK are factors overexpressed in PG. These are stimulated by local trauma. Their exact mechanism and roles in LCH or PGs remain unclear. In the lower airway, laryngopharyngeal reflux is an additional traumatic factor that can predispose to PGs [1,6].

According to Fechner RE et al., there are no pyogenic granulomas in the larynx or trachea [4], but according to current review of literature, these rare laryngo- tracheo-bronchial lesions generally present with hoarseness of voice, aphonia, decrease in voice quality, dyspnoea, wheezing, sensitivity in the throat, dry cough, haemoptysis, stridor, and dysphagia. Most patients do not complain of pain. In a laryngeal PG, the subglottis is the most common subsite to be involved. [7,12,14]. Tracheal and bronchial lesions are fewer in number and are diagnosed with fibreoptic bronchoscopy and high-resolution computer tomography [24-29].

Pyogenic granulomas were earlier used synonymous with granulomas that occur due to a pre-existing traumatic experience

Author's name	Place of study	Year of publication	No. of patients	Age/range of age	Site of lesion	Tobacco smoking	Symptoms at presentation	Antireflux measures	Treatment modality	Adjuvant treatment modalities (given along with the main treatment or later to prevent recurrence)	Follow-up duration	Recurrence	Steroids	H/O intubation/ laryngeal trauma	Immunohistochemistry (IHC)
Qiu X et al [1]	China	2016	1 case report	39 years male	Multiple lesions- in the tracheobronchial tree	Not mentioned	Cough with hemoptysis	Not mentioned	Endoscopic excision	Cryotherapy-multiple times	2 years and still in progress	Ressidual lesions and recurrences	Not mentioned	No	Not done
Ozturk B et al., [6]	Turkey	2018	1	59 years male	Posterior 1/3 of vocal cord	Not mentioned	Hoarseness of voice	Not mentioned	Laryngoscopic excision	None	Not mentioned	Not mentioned	Not mentioned	No	Not done
Chawla M et al., [2]	Detroit, USA	2010	1	62 years male	Distal trachea	H/O smoking + about 40 years back	Hoarseness of voice	Not mentioned	Laser excision	Not mentioned	Short term follow-up-duration not mentioned	Cannot comment	Not mentioned	No	CD31, CD34 markers+
Marrinan MS et al., [12]	New York, USA	2001	22	22-61 years	Vocal folds and vestibular folds	6 patients were smokers-duration unknown	Hoarseness of voice ,shorteness of breath, obstruction	Given PPI for 6 weeks	Microlaryngoscopy	Not mentioned	Time not specified	5/22 had recurrence	NA	Positive in 15 patients	Not done
Garrett MM and Lee WT [13]	Cleveland, OH, USA	2007	1	20 years female	Supra glottis	Not mentioned	Hoarseness of voice , shortness of breath	Yes	Microlaryngoscopic excision	Not mentioned	1 year-good	Nil	Oral steroids were given prior to planning surgery	Yes- external sports injury to the neck	Not done
Walner DL et al., [3]	Chicago, USA	2008	4	neonates	Right-vocal and vestibular folds	NA	Respiratory distress and stridor	Yes	Microlaryngoscopic excision	Not mentioned	2 months	Nil	Steroid soaked pledget	No	Not done
Fechner RE et al., [4]	Virginia, USA	1981	46	10-77 years males and females	Anterior commissure, posterior commisure, vocal cords, subglottis	Not mentioned	Not mentioned	Not mentioned	Microlaryngoscopic excision	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Yes	Not done
Hanick AL et al., [7]	Cleveland, USA	2019	1	23 years pregnant lady	Right arytenoid	Not mentioned	Hoarseness of voice, hemoptysis, shortness of breath and globus sensation	Not mentioned	Microlaryngoscopic excision with KTP laser	Not mentioned	Not mentioned	None	Not mentioned	No	Not done
Liew YT et al., [14]	Malaysia	2018	1	56 years male	Right anterolateral wall of trachea at T1-T2- obstructing 90 % of the lumen (distal trachea)	Smoker for 20 years	Cough, wheeze and hemoptysis	Not mentioned	ECMO and bronchoscopic surgical excision	Not mentioned	3 years and still continuing yearly	None	not mentioned	NA	Not done
Egilmez O et al., [15]	Turkey	2015	1	47 years male	Left vocal process of arytenoid and posterior 1/3 of left vocal cord	Not mentioned	Hoarseness and dysphonia	Yes	Microlaryngoscopic excision	Not mentioned	Still on follow-up according to the article	Recurrence at 3 months post op	Not mentioned	Yes	Not done
Kalanjeri S et al., [16]	Louisiana, Ohio, USA	2016	1	57 years male	Mid trachea	Non-smoker	Cough and hemoptysis	Not mentioned	Electrocautery and snare	Not mentioned	Not mentioned	Not mentioned	Not mentioned	No	gene 8-for RCC

Acharya MN et al., [17]	Cottingham-UK	2016	1	56 years women	2 cm below the vocal cords on the right tracheal wall	Non-smoker, consumed alcohol within normal limits	Hemoptysis	Not mentioned	Rigid bronchoscopic removal	Not mentioned	1 year	No recurrence	Not mentioned	Not mentioned	Not done
Özgül MA et al., [18]	Turkey	2017	1	12 years male	Left lateral wall proximal 1/3 of trachea	Not mentioned	Hemoptysis, cough	Not mentioned	Rigid bronchoscopicremoval, electrocautery snare, argon plasmacoagulation	Not mentioned	6 months	No	Not mentioned	No	Not done
Galos D et al., [5]	Philadelphia, USA	2014	1	14 years male	Left vocal process of arytenoid and left vocal cord and extended to proximal 1/3rd of superior surface	Not mentioned	Dysphonia	Not mentioned	PPI, H2 blocker, microlaryngeal resection	Botulinum injections-multiple	9 months	Recurrence + multiple times	Multiple injections of steroid-dexamethasone	Not mentioned	Not done
Sataloff RT and Hawkshaw MJ [19]	Philadelphia, USA	2001	1	45 years male	Right vocal process filling the entire posterior glottis	Quit smoking 12 years back	Choking and gagging while talking, hoarseness	Yes	Microlaryngeal excision	Botulinum toxin	inadequate dt regarding follow-up	Yes	No	No	Not done
Drosnes DL and Zwillelberg DA [20]	Philadelphia, USA	1990	1	7 years male	Posterior part of left vocal cord	Not mentioned	Hoarseness, irregular respiration	No	Microlaryngeal excision	None	1 year follow-up	None	No	Yes	Not done
Tedla M et al., [21]	UK, Czechoslovakia, Singapore, czech republic	2014	1	48 years male	Inferior aspect of left vocal cord	Yes (history of smoking 25 years)	Hoarseness	No	Microlaryngeal excision	Not mentioned	8 months	Yes (once)	No	No	Factor VIII
Guvenc MG et al., [22]	Istanbul, turkey	2008	1	18 years female	Right pyriform sinus, aryepiglottic fold, protruding into laryngeal ventricle	No	Dysphagia	Not mentioned	Laryngopharyngotomy	Not mentioned	2 weeks	Not mentioned	No mentioned	Not mentioned	Not done
Irani S et al., [23]	Switzerland	2003	1	72 years female	3 cm below vocal cords	Not mentioned	Recurrent hemoptysis	Not mentioned	Microlaryngoscopy and excision	Not mentioned	1 year	Not mentioned	Not mentioned	None	Not done
Madhumita K et al., [24]	India	2004	1	40 years female	Right anterolateral wall of trachea upper third	Not mentioned	Hemoptysis and foreign body sensation	Not mentioned	Endoscopic excision	None	1 year	Not mentioned	Not mentioned	None	Not done
Porfyridis I et al., [25]	Greece	2007	1	17 years male	Left anterolateralwall of upper third of trachea	None	Cough and hemoptysis	None	Endoscopic excision	Electrocautery	12 months	None	Not mentioned	Not mentioned	CD31, CD34, CD56 markers
Udoji TN and Bechara RI [27]	Atlanta, USA	2011	1	55 years male	Left lateral wall of distal trachea	Yes 40 pack years	Cough, hemoptysis	not mentioned	Cryoprobe	None	3 months	None	Not mentioned	Not mentioned	None
Amy FT and Enrique DG [26]	Kentucky, USA	2012	1	22 years male	Left posterior wall, 3 cm above the carina	None	Cough, hemoptysis	Not mentioned	Electrocautery	Argon plasma coagulation	Yes (duration not mentioned)	Not mentioned	Not mentioned	Not mentioned	Not done
Jie S et al [28]	Beijing, China	2012	1	35 years male	Left lateral wall of proximal trachea	Not mentioned	Cough, bloody sputum	Not mentioned	Endoscopic excision and argon plasma coagulation	Brachy therapy	2 years	Yes (multiple times)	Not mentioned	None	Not done
Prakash S et al [29]	Australia	2014	1	23 years pregnant female	Posterior tracheal wall	Not mentioned	Hemoptysis, dyspnoea	Not mentioned	Surgical debulking	ECMO	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Yes (CD31)

[Table/Fig-7]: Systematic analysis of literature reports [1-7,12-29].

Name of the study	Were there clear criteria for inclusion in the study?	Was the condition measured in a standard, reliable way for all participants	Were valid methods used for identification of the condition for all	Did the case series/original article *have consecutive inclusion of participants?	Was there clear reporting of the demographics of the participants in the study?	Where the outcomes or follow-up measures reported adequately? (Good=1 year or more	Was there clear reporting of the presenting sites'/ clinics' demographic information	Was statistical analysis appropriate?	Selection	Ascertained	Causality	Reporting
Qiu X et al., [1]	NA	Yes	Yes	Not applicable	Not applicable	2 years (still in progress)	Yes	Not applicable	Yes	Yes	Yes	Yes
Ozturk B et al., [6]	Yes	Yes	Yes	Not applicable	Not applicable	Not mentioned	Yes	Not applicable	Yes	Yes	Yes	Yes
Chawla M et al., [2]	Yes	Yes	Yes	Not applicable	Not applicable	Short term (duration not mentioned)	Yes	Not applicable	Yes	Yes	Yes	Yes
Marrinan MS et al., [12]	Yes	Yes	Yes	Yes	Yes	Follow-up done (duration not mentioned)	Yes	Not applicable	Yes	Yes	Yes	Yes
Garrett MM and Lee WT [13]	Yes	Yes	Yes	Not applicable	Not applicable	1 year	Yes	Not applicable	Yes	Yes	Yes	Yes
Walner DL et al.,[3]	Yes	Yes	Yes	No	Yes	2 months	Yes	No statistical analysis were performed	Yes	Yes	Yes	Yes
Fechner RE et al.,[4]	Yes	Yes	Yes	Yes	Yes	Not mentioned	Yes	No statistical analysis were performed	Yes	Yes	Yes	Follow-up (details are missing)
Hanick AL et al., [7]	Yes	Yes	Yes	Not applicable	Not applicable	Not mentioned	Yes	Not applicable	Yes	Yes	Yes	Yes
Liew YTet al., [14]	Yes	Yes	Yes	Not applicable	Not applicable	3 years	Yes	Not applicable	Yes	Yes	Yes	Yes
Egilmez O et al., [15]	Yes	Yes	Yes	Not applicable	Not applicable	3 months later and till date	Yes	Not applicable	Yes	Yes	Yes	Yes
Kalanjeri S et al., [16]	Yes	Yes	Yes	Not applicable	Not applicable	Not mentioned	Yes	Not applicable	Yes	Yes	Na	Yes
Acharya MN et al., [17]	Yes	Yes	Yes	Not applicable	Not applicable	1 year (good)	Yes	Not applicable	Yes	Yes	Yes	Yes
Özgül MA et al., [18]	Yes	Yes	Yes	Not applicable	Not applicable	6 months	Yes	Not applicable	Yes	Yes	Yes	Yes
Galos D et al., [5]	Yes	Yes	Yes	Not applicable	Not applicable	9 months	Yes	Not applicable	Yes	Yes	Yes	Yes
Sataloff RT and Hawkshaw MJ [19]	Yes	Yes	Yes	Not applicable	Not applicable	Inadequate data of follow-up	Yes	Not applicable	Yes	Yes	Yes	Yes
Drosnes DL and Zwillenberg DA [20]	Yes	Yes	Yes	Not applicable	Not applicable	1 year follow-up	Yes	Not applicable	Yes	Yes	Yes	Yes
Tedla M et al., [21]	Yes	Yes	Yes	Not applicable	Not applicable	8 months	Yes	Not applicable	Yes	Yes	Yes	Yes
Guvenc MG et al., [22]	Yes	Yes	Yes	Not applicable	Not applicable	2 weeks	Yes	Not applicable	Yes	Yes	Yes	Yes
Irani S et al., [23]	Yes	Yes	Yes	Not applicable	Yes	1 year	Not applicable	Not applicable	Yes	Yes	Yes	Yes
Madhumita K et al., [24]	Yes	Yes	Yes	Not applicable	Yes	1 year	Not applicable	Not applicable	Yes	Yes	Yes	Yes
Porfyridis I et al., [25]	Yes	Yes	Yes	Not applicable	Yes	12 months	Not applicable	Not applicable	Yes	Yes	Yes	Yes
Udoji TN and Bechara RI [27]	Yes	Yes	Not applicable	Not applicable	Yes	3 months	Not applicable	Not applicable	Yes	Yes	Yes	Yes
Amy FT and Enrique DG [26]	Yes	Yes	Not applicable	Not applicable	Yes	Yes (duration not mentioned)	Not applicable	Not applicable	Yes	Yes	Follow-up (duration unavailable)	Yes
Jie et al., [28]	Yes	Yes	Not applicable	Not applicable	Yes	2 years	Not applicable	Not applicable	Yes	Yes	Yes	Yes
Prakash S et al., [29]	Yes	Yes	Not applicable	Not applicable	Yes	Not mentioned	Not applicable	Not applicable	Yes	Yes	Yes	Yes

[Table/Fig-8]: Quality appraisal for case reports and case series [1-7,12-18,20-29].

like intubation granuloma that occur in the arytenoids. According to Fechner RE et al., LCH have diagnostic lobular arrangement of capillaries that clearly distinguish them from granulomas [4]. They also claim that, LCH occurred spontaneously whereas granulomas occurred due to pre-existing trauma and that, they should not be used as pathological misnomers for each other [4-7].

The histopathology is the gold standard of diagnosis. Microscopically, although they are similar to granulation tissue in early stages, there is a background of mixed inflammatory infiltrates with oedematous stroma. The prominent finding is supposed to be numerous capillaries and venules arranged in a radial lobular pattern. As the lesion matures, the stroma becomes more fibromyxoid and there is less inflammatory infiltrate. There are surroundings of acute and chronic inflammatory cells forming granulomas. Surface erosion or ulceration which may occur initially may re-epithiliase. The differential diagnosis for these lesions includes granulation tissue, lipoma, papilloma, angiofibroma, histiocytoma, haemangiopericytoma, angioendothelioma, angiosarcoma, tuften haemangioma, intravascular angiomatosis granulomatous infections, hyperplasia, and varicosities [11-15].

Treatment options include surgical excision using cold steel dissection, laser photocoagulation, electrocautery snare, liquid nitrogen freezing, micro irradiation, brachytherapy, intralesional injection of ethanol or corticosteroids and sodium tetradecyl sulphate sclerotherapy. All modalities of treatment seem to give satisfying results although, recurrences have been observed in a few cases [19-28]. Although there is one report with usage of botulinum toxin to prevent recurrence, there is no strong evidence to support this finding [19]. There is dearth of studies in this literature comparing the treatment modalities to prove the superiority of any single technique and chances of reducing recurrences. Adequate long term follow-up for atleast three years is required according to the current data. Many studies have been reported without following-up the patient and hence the status of recurrence cannot be commented upon. There are number of studies that had less than three months or no follow-up of the patients [2,6,12,16,22]. Whilst there are reports where the lesion was successfully managed without recurrence with a follow-up of at least one year [1,13,20]. There were two studies in which patients had multiple recurrence which was treated using multiple injections of steroids and brachytherapy respectively [5, 28]. An additional therapy with anti reflux measures is proven to be beneficial. Proton pump inhibitors and H2 blockers given for a period of 12 weeks postoperatively reduces laryngopharyngeal reflux and aids in preventing recurrence as seen in the present case [6].

Limitation(s)

There are several limitations in this study. Since most studies are case reports, a publication bias is possible. The results in this study depend on the quality of literature search. Completeness of the search was maximised by having two reviewers perform this task independently. Some articles were not able to be retrieved in full text and in English language and thus were not included in the study.

CONCLUSION(S)

Pyogenic granulomas or lobular capillary haemangiomas occur very rarely in the lower airway. Prior trauma is not a prerequisite for these lesions. These lesions present with progressive voice change and breathing difficulty. They can be successfully managed by thorough surgical excision, intralesional or postoperative steroid therapy along with long term anti reflux measures to prevent recurrence. Although there is not adequate literature to optimise the duration for follow-up in these cases, a period of one to three years following the procedure seem to be the usual teething period for recurrence, based on this systematic review. Hence, a close follow-up one year and a yearly visit till three years postoperatively is suggested.

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REFERENCES

[1] Qiu X, Dong Z, Zhang J, Yu J. Lobular capillary haemangioma of the tracheobronchial tree: A case report and literature review. Medicine. 2016;95(48):e5499.
[2] Chawla M, Stone C, Simoff MJ. Lobular capillary haemangioma of the trachea: The second case. J Bronchology Interv Pulmonol. 2010;17(3):238-40.
[3] Walner DL, Parker NP, Kim OS, Angeles RM, Stich DD. Lobular capillary haemangioma of the neonatal larynx. Archives of Otolaryngology-Head & Neck Surgery. 2008;134(3):272-77.
[4] Fechner RE, Cooper PH, Mills SE. Pyogenic granuloma of the larynx and trachea: A causal and pathologic misnomer for granulation tissue. Archives of Otolaryngology. 1981;107(1):30-32.
[5] Galos D, Chowdhury FR, Gupta R, Heman-Ackah YD, Sataloff RT. Recurrent pyogenic granuloma in a noncompliant patient. Ear, Nose & Throat Journal. 2014;93(1):E32-33.
[6] Ozturk B, Gunduz FK, Altun E. Lobular capillary haemangioma of vocal cord in an adult. Clin Surg. 2018;3:1966.
[7] Hanick AL, Meleca JB, Billings SD, Bryson PC. Pyogenic granuloma of the larynx: A rare cause of hemoptysis. American Journal of Otolaryngology. 2019;40(2):331-33.
[8] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. International Journal of Surgery. 2021;372:n71.
[9] Murad MH, Sultan S, Haffar S, Bazerbachi F. Methodological quality and synthesis of case series and case reports. BMJ Evid Based Med. 2018;23(2):60-63.
[10] Munn Z, Barker TH, Moola S, Tufanaru C, Stern C, McArthur A, et al. Methodological quality of case series studies: An introduction to the JBI critical appraisal tool. JBI evidence synthesis. 2020;18(10):2127-33.
[11] Moola SZ, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, et al. Chapter 7: Systematic reviews of etiology and risk. Joanna briggs institute reviewer's manual. The Joanna Briggs Institute. 2017.
[12] Marrinan MS, Myssiorek D, Fuchs A, Wasserman P. Laryngeal pyogenic granulomas do not express oestrogen or progesterone receptors. J Laryngol Otol. 2001;115(10):798-801.
[13] Garrett MM, Lee WT. Obstructing pyogenic granuloma as a result of blunt laryngeal trauma. Otolaryngol Head Neck Surg. 2007;136(3):489-90.
[14] Liew YT, Ting KN, Zulkiflee AB, Prepageran N. Different Perspective in Managing Airway Obstruction Secondary to Giant Tracheal Pyogenic Granuloma. Int J Respir Pulm Med. 2018;5(1):01-04.
[15] Egilmez O, Uzun L, Ozkanli S, Kalcioglu M, Tekin M. A troublesome lesion of the larynx: Lobular capillary haemangioma. Scripta Scientifica Medica. 2015;47(4):56-60.
[16] Kalanjeri S, Kumar A, Mukhopadhyay S, Mehta AC. Lobular capillary haemangioma ("pyogenic granuloma") of the trachea. Am J Respir Crit Care Med. 2016;193(12):1429-30.
[17] Acharya MN, Kotidis K, Loubani M. Tracheal lobular capillary haemangioma: A rare benign cause of recurrent haemoptysis. Case Reports in Surgery. 2016;2016:01-04.
[18] Özgül MA, Tanrıverdi E, Gül Ş, Asuk ZY, Acat M, Abbaslı K, et al. A Rare Cause of Hemoptysis in Childhood: Tracheal Capillary Haemangioma. Turkish Thoracic Journal. 2017;18(4):131.
[19] Sataloff RT, Hawkshaw MJ. Multiple bilateral vocal fold cysts and recurrent pyogenic 'granuloma'. Ear, Nose & Throat Journal. 2001;80(2):72.
[20] Drosnes DL, Zwillenberg DA. Laryngeal granulomatous polyp after short-term intubation of a child. Annals of Otology, Rhinology & Laryngology. 1990;99(3):183-86.
[21] Tedla M, Bežová M, Biró C, Tedlová E, Eng CY, Zeleník K. Intravascular papillary endothelial hyperplasia of larynx: Case report and literature review of all head and neck cases. Otolaryngologia Polska. 2014;68(4):200-03.
[22] Güvenç MG, Dereköylü L, Korkut N, Öz F, Öz B. Intravascular papillary endothelial hyperplasia (Masson lesion) of the hypopharynx and larynx. Ear, Nose & Throat Journal. 2008;87(12):700-04.
[23] Irani S, Brack T, Pfaltz M, Russi EW. Tracheal lobular capillary haemangioma: A rare cause of recurrent hemoptysis. Chest. 2003;123(6):2148-49.
[24] Madhumita K, Sreekumar KP, Malini H, Indudharan R. Tracheal haemangioma: Case report. J Laryngol Otol. 2004;118(8):655-58.
[25] Porfyridis I, Zisis C, Glinos K, Stavrakaki K, Rontogianni D, Zakynthinos S, et al. Recurrent cough and hemoptysis associated with tracheal capillary haemangioma in an adolescent boy: A case report. J Thorac Cardiovasc Surg. 2007;134(5):1366-67.
[26] Amy FT, Enrique DG. Lobular capillary haemangioma in the posterior trachea: A rare cause of hemoptysis. Case Rep Pulmonol. 2012;2012:592524.

[27] Udoji TN, Bechara RI. Pyogenic granuloma of the distal trachea: A case report. J Bronchology Interv Pulmonol. 2011;18(3):281-84.
[28] Jie S, Hong-Rui L, Fu-Quan Z. Brachytherapy for tracheal lobular capillary haemangioma (LCH). Journal of Thoracic Oncology. 2012;7(5):939-40.
[29] Prakash S, Bihari S, Wiersema U. A rare case of rapidly enlarging tracheal lobular capillary haemangioma presenting as difficult to ventilate acute asthma during pregnancy. BMC Pulmonary Medicine. 2014;14(1):01-04.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of ENT, Pondicherry Institute of Medical Sciences, Puducherry, India.
2. Associate Professor, Department of ENT, Pondicherry Institute of Medical Sciences, Puducherry, India.
3. Associate Professor, Department of ENT, Pondicherry Institute of Medical Sciences, Puducherry, India.
4. Postgraduate Resident, Department of ENT, Pondicherry Institute of Medical Sciences, Puducherry, India.
5. Senior Resident, Department of ENT, Pondicherry Institute of Medical Sciences, Puducherry, India.
6. Professor and Head, Department of ENT, Pondicherry Institute of Medical Sciences, Puducherry, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
TC Vikram Raj Mohanam,
Associate Professor, Department of ENT, Pondicherry Institute of Medical Sciences,
Ganapathichettikulam, Kalapet-605014, Puducherry, India.
E-mail: drtcvikram@gmail.com

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