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Research Article

Laryngeal Actinomycosis: A Case Report and Systematic Review of 32 Cases in the Literature

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Abstract

Objective

To report a case of vocal cord actinomycosis and provide a systematic review of the literature to provide a reference for its diagnosis and management.

Review methods

Relevant cases from a PubMed search were reviewed for age/gender, risk factors, clinical manifestations, and treatment.

Results

Thirty-two cases of laryngeal actinomycosis have been reported in the literature. Most (80%) cases presented in patient with known risk factors. The majority presented with dysphonia (61.5%). Thirteen (58.3%) involved the true vocal cords. Penicillin based therapy was treatment of choice.

Conclusion

A structured assessment revealed 32 cases of laryngeal actinomycosis in the literature. Actinomycosis should be considered on the differential, even in healthy individuals with symptoms of laryngeal impairment.

Keywords: Actinomycosis; Dysphonia; Larynx

Introduction

Actinomycosis is a chronic, granulomatous infection most commonly caused by the Gram-positive anaerobe *Actinomyces israelii*. Originally thought to be a fungus, this bacteria is a normal part of the normal oral flora in humans [1]. It can be easily identified by the aggregates of organisms on histopathological analysis. The most frequent sites of infection include the cervicofacial region, lung, pelvis, and genitourinary system in women especially those with intrauterine devices [2,3]. Aside from cervical involvement, the incidence of actinomycosis in humans is relatively uncommon with most major medical centers diagnosing around one case per year, with an overall incidence of one in 300,000 [4]. Predisposing factors for infection include poor local hygiene, local tissue damage, diabetes mellitus, immunosuppression, and malnutrition [5,6]. Infection classically presents as a slowly progressive mass that develops into multiple abscesses of soft tissue that can occasionally progress to bony invasion [3,7]. Diagnosis of laryngeal actinomycosis is exceedingly rare, especially in the absence of orofacial trauma or predisposing risk factors. An otherwise healthy patient in our clinic was diagnosed with primary vocal cord actinomycosis after presenting with dysphonia. A review of the literature for similar cases was performed to identify correlations in patient history and clinical presentation.

Case Report

A 50-year-old white female with a 34-pack-year smoking history and multiple recent bouts of atypical pneumonia presented for evaluation of dysphonia. She reported hoarseness for one year worsened by stress along with intermittent episodes of losing her voice completely. She also reported globus pharyngeus but denied dysphagia or any other complaints. Anti-reflux medication did not seem to provide symptomatic relief.

On exam the patient expressed mild dysphonia. No adenopathy, thyroid enlargement, or lesions on the inside of the mouth were noted. Laryngoscopy revealed a sessile whitish plaque-like lesion on the superior aspect of the middle-third right true vocal cord with asymmetric mobility but complete glottis closure (Figure 1). Additional nasopharyngeal and physical exam findings were otherwise unremarkable. The patient was taken to operating room for biopsy of lesion suspicious for vocal cord leukoplakia.

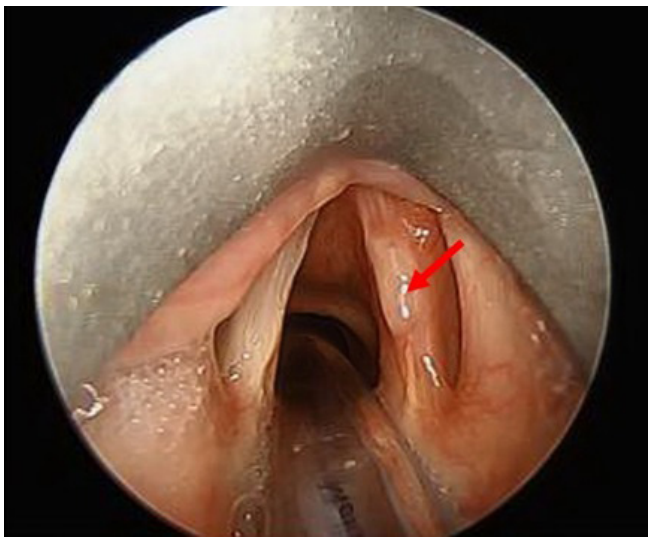

Figure 1: Nodule in middle third of right true vocal cord in our patient in clinic later diagnosed with laryngeal actinomycosis (arrow).

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A 0.5 × 0.2 × 0.1 cm lesion was excised from the superior surface of the right true vocal cord. The patient was placed on voice rest two weeks following the procedure. Histopathology revealed a benign specimen consisting largely of a mass of fibrinopurulent exudate with granulation tissue with *Actinomyces* present. All findings were benign with no evidence of neoplasia or virocytes (Figure 2). The patient was started on amoxicillin 500 mg orally three times per day for one month with scheduled follow-up to monitor continued resolution of actinomycosis. The patient was seen in clinic at one month and two months following the procedure and achieved full resolution of her dysphonia. She denied any additional problems or complaints following the operation.

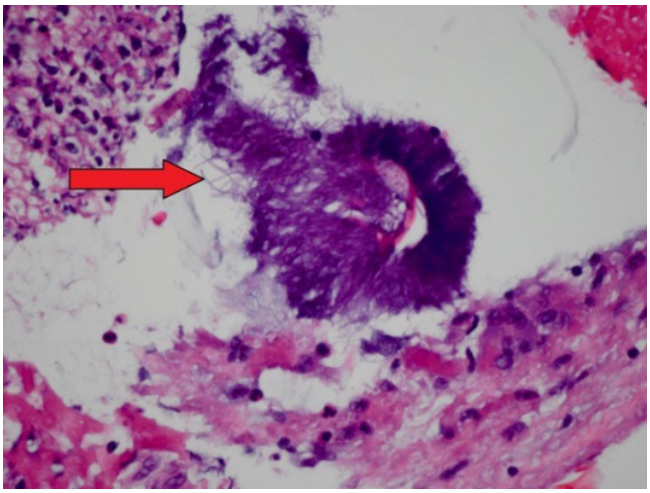

Figure 2: Histopathological image taken from our patient's vocal cord biopsy. The fibrinopurulent exudate in the vocal cords is centered somewhat on an aggregate of filamentous *Actinomyces* (arrow).

Systematic Review

Methods

A systematic search of PubMed and Scopus without time period or language restrictions was conducted. Variations of the words actinomycosis, laryngeal, and vocal cord found in the title, abstract, or keywords section of the publication were used as our search criteria. Articles were deemed relevant if they mentioned or alluded to report of actinomycosis diagnosed in the larynx or its substructures in the title or abstract. Google translate was used to gather relevant data from foreign publications. Articles were reviewed for age/sex of patient, risk factors, clinical presentation, and treatment.

Results

Our search revealed 259 articles, 30 of which were unique and relevant to our review of laryngeal actinomycosis. Most were individual case reports documenting the unusual presentation of clinical findings. Two articles described two cases of laryngeal actinomycosis yielding an overall count of 32 cases reported in the published literature. We were able to gather complete data for our analysis for 25 of the cases and partial data on 7 of the cases. Results are shown in tables 1 and 2 [4,8-36]. Percentages are based on *n* reports of search criteria.

Ages of the patient at the time of diagnosis ranged from 14 to 77 with a mean of 53.7 years. The sex of the patients was predominantly male (88.5%). Six (20%) of the patients had no predisposing risk factors reported. Immunocompromised status was present in six (20%) of the cases, most commonly as result of radiotherapy for previous laryngeal carcinoma. Other cases included chronic steroid

Variable	n	%
Age (n=30)		
Average age	53.7	
Oldest	77	
Youngest	14	
Sex (n=30)		
Males	26	86.70%
Females	4	13.30%
Risk factors (n=30)		
Radiotherapy	8	26.70%
None	6	20.00%
Immunocompromised	6	20.00%
Chronic steroid use	2	6.70%
Chemotherapy	2	6.70%
Leukemia	1	3.30%
HIV	1	3.30%
Oropharyngeal trauma	5	16.70%
Airway dilation	2	6.70%
Tooth extraction	1	3.30%
Prolonged intubation	1	3.30%
Recent laryngeal surgery	1	3.30%
Concurrent laryngeal carcinoma	3	10.00%
Concurrent secondary actinomycosis infection	2	6.70%
Diabetes	2	6.70%
Environmental exposure	1	3.30%
Site of involvement (n=27)		
Cricoid region	3	11.10%
Anterior commissure	4	16.70%
Aryepiglottal fold	4	16.70%
Epiglottis	3	12.50%
Posterior commissure	1	4.20%
Pyriform sinus	3	12.50%
Subglottic region	1	4.20%
Thyroid cartilage	1	4.20%
Vestibular fold	5	20.80%
Vocal cord	14	58.30%
Clinical presentation (n=29)		
Dyspnea	5	17.20%
Cough	3	11.50%
Dysphagia	9	34.60%
Dysphonia	16	61.50%
Edema of ear	1	3.80%
Fever	1	3.80%
Odynophagia	3	11.50%
Pharyngitis	5	19.20%
Stridor	3	11.50%
Weight loss	5	19.20%

Table 1: Results of laryngeal actinomycosis case review.

Author	Age	Gender	Risk Factors	Site of Involvement	Clinical Presentation	Treatment
Lensing F, et al. [8]	24	M	Oropharyngeal trauma: airway dilation	Cricoid cartilage and adjacent fat pad	Acute dyspnea and laryngeal pain 2 days after recent airway dilation	IV penicillin 6 weeks
Patel S, et al. [9]	74	M	Immunocompromised (neutropenia secondary to chemotherapy)	Vocal cord and Vestibular fold	Odynophagia and dysphagia	Ciprofloxacin and amoxicillin/clavulanic acid for 1° month
Sari M, et al. [10]	21	M	None	Vocal cord	Dysphonia for 6 months	Amoxicillin-clavulanate 625 mg TID for 8 weeks
Shaheen SO, et al. [11]	45	M	Hx of recent tooth extraction	Cricoid area and vocal cord	Recurrent pharyngitis	IV penicillin 1 mega unit 6 hours for 23 days, then PO 2 mega units daily for 10 days
Yoshihama K, et al. [12]	49	M	None	Vocal cord	Dysphonia 2 years	Amoxicillin-clavulanate 625 mg orally three times a day for 8 weeks
Syed MA, et al. [13]	74	M	Post radiotherapy for laryngeal carcinoma	Cricoid region	Dysphagia	Amoxicillin 500 mg three times daily
Sims HS, et al. [14]	47	M	Immunocompromised (post-transplant recipient, chronic steroid use for SLE)	Vocal cord	Dysphonia and dysphagia	IV penicillin for 2 wks. then PO penicillin for 3 months
Artesi L, et al. [15]	75	M	None (smoker)	Epiglottis and aryepiglottal fold	Dysphagia progressing to slight dyspnea over 2 months	IV penicillin for 15 days then PO clindamycin 600 mg TID for 4 months
Khademi B, et al. [16]	14	M	Hx of recent tooth extraction	Vocal cord	Dysphonia worsening over 2 months	IV penicillin for 2 wks. then PO penicillin for 3 months
Batur Çaliş A, et al. [17]	66	M	Concurrent cancer diagnosis (smoker)	Vocal cord and Vestibular fold	Dysphonia 4 months and dyspnea for 2 months	Surgical excision of lesion (for cancer)
Batur Çaliş A, et al. [17]	45	M	Concurrent cancer diagnosis (smoker)	Vestibular fold and Vocal cord	Dysphonia, dyspnea, dysphagia for 1 month	Surgical excision of lesion (for cancer)
Ferry T, et al. [18]	67	M	Hx of laryngeal carcinoma, chemotherapy and Radiotherapy (also smoker and previous MI)	Vocal cord and Vestibular fold	Dysphonia 2 yrs	Amoxicillin 6g/day for 4 months
Meidani M, et al. [19]	77	M	Prolonged intubation (from heart surgery) and Pulmonary actinomycosis		Fever, Cough, Weight loss	Penicillin
Menezes MC, et al. [20]	77	M	None (smoker)	Aryepiglottic fold	Dysphonia and pain worsening over 2 months	Antibiotics for 6 months
Moreno PJM, et al. [21]	52	F	Diabetes	Posterior commissure and Vocal cord	Cough 2 months	Cefuroxime-axetil 250 mg twice a day for 3 weeks
Wierzbicka M, et al. [22]	20	M	None	Epiglottis	Dysphagia and weight loss over several months	IV penicillin and clindamycin
Silvestri SB, et al. [23]	69	M	Concurrent cancer diagnosis (smoker)	Thyroid cartilage	Dysphonia, persistent cough, weight loss over 8 months	IV ampicillin 500 mg every 6 hours for 12 weeks, then PO for 6 to 12 months
Schumann R, et al. [24]	56	M	Environmental exposure	Aryepiglottic fold and pyriform sinus	Mild dysphagia and increased edema of ear	Surgical resection of abscess then amoxicillin and clavulanic acid for 3 weeks
Yasuda M [25]	53	M	Immunocompromised (adult T cell leukemia)	Anterior commissure	Dysphonia	Penicillin 20 million IU daily for 35 days
Fernandez SH [26]	30	F	Concurrent pulmonary actinomycosis infection	Vocal cord	Dysphonia 1 month	IV penicillin 6 wks.
Abed T, et al. [27]	35	F	Immunocompromised (chronic steroid use for SLE)	Anterior commissure	Dysphonia	Oral penicillin
Tsuji DH, et al. [28]	68	M	Post radiotherapy for laryngeal carcinoma	Vocal cord	Dysphonia, odynophagia, and pharyngitis for 3 weeks	Penicillin 10 million IU daily for 40 days
García Lozano MC, et al. [29]	53	M	None (smoker)	Vocal cord	Dysphonia	Penicillin 600,000 units orally q6 hours for 3 weeks
Brandenburg JH, et al. [32]	67	M	Post radiotherapy for laryngeal carcinoma	Subglottic	Dyspnea, stridor, dysphonia, weight loss over 7 months	Penicillin
Hughes RA Jr, et al. [33]	66	M	Diabetes	Pyriform sinus, aryepiglottic fold, hypopharyngeal wall	Pharyngitis and dysphagia over 5 days and weight loss, stridor	Cephalexin 4 months

Table 2: Articles included in systematic review of laryngeal actinomycosis with complete data.

*7 Cases with incomplete data that were reviewed are not depicted

use, chemotherapy, T-cell leukemia, and Human Immunodeficiency Virus (HIV). Five (16.7%) of the patents had a known history oropharyngeal trauma, two as a result of recent tooth extraction, one due to airway dilation, one due to recent surgery of the larynx and one due to prolonged intubation. Two (6.7%) patients had a secondary actinomycosis infection, both of the more common pulmonary subtype. Three (10%) of the cases were diagnosed in patients in addition to an initial diagnosis of laryngeal carcinoma. Two patients had a diagnosis of type II diabetes mellitus within the past three years. Finally, there was unusual case of suspected environmental exposure in which a patient inadvertently inhaled part of an ear of corn that formed a laryngeal abscess that was later found to be host to an actinomycosis infection.

Specific sub-site of laryngeal involvement was reported in 27 cases. Laryngeal actinomycosis was most commonly reported on or around the substructures of the glottis, the most common being the vocal folds (58.3%). Other common sites included the vestibular folds (20.8%), cricoid (11.1%), anterior/posterior commissures (20.8%), aryepiglottal fold (16.7%), epiglottis (12.5%), and pyriform sinus (12.5%). One case each of invasion into the thyroid cartilage and subglottic region was reported.

Laryngeal actinomycosis presents in a non-specific manner similar to other mass lesions in the larynx or oropharynx. After reviewing the cases, the most common clinical presentation was dysphonia (61.5%), reported in 16 of 29 cases. Nine (34.6%) presented with dysphagia and five (17.2%) with dyspnea. Other presentations included cough, odynophagia, pharyngitis, weight loss, stridor and fever.

Treatment involved excisional biopsy followed by penicillin based therapy in almost all cases. Therapeutic dose, timeframe, and method of administration varied from case to case. Earlier cases usually involved short term IV antibiotics followed by long-term oral administration for prophylaxis against secondary involvement. No cases reported seeding of disease to new site when the primary lesion was restricted only to the larynx. Cases with involvement limited to the larynx were treated with a shorter term dose of oral only antibiotics: 500-625 mg oral penicillin based therapy three times a day for up to 8 weeks following excisional biopsy [10,12,13,21].

Discussion

Despite the rarity of actinomycosis, and the even rarer reports of laryngeal actinomycosis, the disease should not be overlooked. Lesions identified early, can be easily treated and cured with oral antibiotics. Fortunately, due to its similar presentation to other dangerous diseases processes, such as laryngeal carcinoma, it is usually identified on initial biopsy.

Although our patient was female, a male predominance of laryngeal actinomycosis exists in the literature (86.7%) [8-30,32-36]. This is not different that the prevalence of pulmonary actinomycosis. A 94 patient, 10-year retrospective study on pulmonary actinomycosis identified a 70.2% male majority [37]. Similarly, the mean age was 52.1 years, just under the 53.7 years in our laryngeal actinomycosis review [37]. The exact causation of these factors has not been definitively established. Due to the retrospective nature of the study, all predisposing factors cannot be known, but aspiration of oral substances has been suggested as previous studies have demonstrated a higher incidence of pulmonary actinomycosis in alcoholics [37].

Known risk factors including immunodeficiency, oropharyngeal trauma, and diabetes, accounted for most patients in our study. Around one fourth of the patients did not have a known risk factor.

Clinical manifestations of the disease are variable, though analogous to other lesions in or around the glottis. Lesions can present both symptomatically and physically as laryngeal tumors. Considering the age of the population and risk factors, the exclusion of laryngeal carcinoma cannot be over emphasized. Patients should be followed in clinic to insure a carcinoma is not present in addition to the actinomycosis. Ongoing symptomology following adequate antibiotic therapy for actinomycosis should warrant prompt swift laryngoscopic evaluation and biopsy for suspected laryngeal carcinoma as 10% of patients with laryngeal actinomycosis have been found to have a current malignancy in our review of the literature [17,23].

Treatment of laryngeal actinomycosis very much depends on extent of involvement. Our case and analysis of similar cases shows that primary infection of the larynx restricted only to the glottis or its substructures, has been successfully treated and suppressed with excision of the lesion and eight weeks of oral penicillin based therapy [10,12,13,21]. More involved lesions, such as those with concurrent pulmonary involvement require more invasive therapy, including a course of intravenous antibiotic therapy.

Conclusion

Actinomycosis is an exceedingly rare disease with laryngeal involvement in a small minority of cases. A high level of clinical suspicion from patient history and exam is required for timely diagnosis and treatment, but should be accomplished following the guidelines of more common ailments such as laryngeal carcinoma. Due to similar gross presentation as neoplasia, the diagnosis of laryngeal actinomycosis should only be made from histological analysis at the time of ruling out laryngeal carcinoma. Excisional biopsy with penicillin based therapy seems to be the definitive course of treatment.

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