

Isolated Laryngeal *Coccidioidomycosis* - A Case Report and Review of the Literature

Antony N*

Texas Tech University Health Sciences Center, El Paso, Texas

*Corresponding author: Antony N, Texas Tech University Health Sciences Center, El Paso, Texas, United States, E-mail: nishaalantony@gmail.com

Citation: Antony N (2014) Isolated Laryngeal *Coccidioidomycosis* - A Case Report and Review of the Literature. J Immunol Infect Dis 2(1): 101. doi: 10.15744/2394-6512.1.201

Received Date: November 04, 2014 Accepted Date: January 02, 2015 Published Date: January 08, 2015

Introduction

Coccidioidomycosis involving the larynx is a rare occurrence which seems to present with non-specific upper airway symptoms. The diagnosis is made by tissue biopsy and the treatment is usually fluconazole for 6-12 months depending on the clinical presentation. In unusual presentations of laryngeal problems clinicians should consider *Coccidioidomycosis*, especially in endemic regions.

Case Presentation

We present a 59-year-old Hispanic female resident of West Texas who presented with symptoms of hoarseness, sore throat, and low-grade fevers for 2-3 months. She had been evaluated by her primary care physician who had treated her with several courses of antibiotics including quinolones, azithromycin, and cephalosporins. Because of the persistence of her symptoms she was sent to an otolaryngologist. On examination her temperature was 98.4 F, blood pressure was 124/78 mm Hg, and pulse 78 bpm. Laryngoscope revealed a soft tissue mass along the left side of the airway just above the vocal cords. No cervical lymphadenopathy was noted. The rest of the examination was unremarkable.

A biopsy of the lesion revealed spherules with endospores and accompanying granulomas; fungal cultures were consistent with *Coccidioides immitis*. Chest x-ray was unremarkable. Computed tomography (CT) scan of the chest revealed two pulmonary nodules at the superior segment of the left lower lobe. Other relevant labs included hemoglobin and hematocrit of 13.9 g/dL and 40.6% respectively, normal range 11.5-15 and 34-44. White blood count was 11,000 per μ L (4-10.5) with 58% neutrophils, 31% lymphocytes, 8% monocytes, 2% eosinophils, and 1% basophils. The *C. immitis* complement fixation titer (CFT) was negative at <1:1 and enzyme immunoassay (EIA) was unavailable. The patient was placed on fluconazole 400 mg per day for 6 months. Serial follow-ups revealed a decreasing size of the laryngeal mass with complete resolution of the lesion by the end of 3 months and repeat a chest x-ray demonstrated some resolution in the size of the lung nodules. Repeat serum *Coccidioidomycosis* CFT level remained negative.

Discussion

Coccidioidomycosis spp. is a dimorphic fungus endemic to the southwestern United States and Northern Mexico [1]. Infection occurs through inhalation of the *Coccidioidomycosis* arthroconidium from the soil. The areas with the highest endemic sources of infection are in California and Arizona which together make up more than 50% of all cases [2]. The incidences in high-risk locations have risen from 5.3 cases per 100,000 in 1998 to 42.6 per 100,000 cases in 2011 [3]. This rise in reported cases has been in part hypothesized to the increased sensitivity of *Coccidioidomycosis* serological tests and industrialization into endemic areas [3,4]. The most common presentation of *Coccidioidomycosis* includes symptoms of chronic fatigue, malaise, and productive cough. Episodes of occasional arthralgias are common with a primary pulmonary source as well [5]. The risk factors associated with severe disseminated infection are immunosuppression such as, AIDS, solid organ transplant recipients, lymphomas, or prolonged steroid use [6]. While the vast majority of *Coccidioidomycosis* infections have a primary pulmonary source, primary *Coccidioidomycosis* of the larynx is a very rare and unusual presentation.

A review of the literature was done using Medline and PubMed and was simplified into a table (Table 1). The following characteristics seemed consistent with patients with laryngeal *Coccidioidomycosis*. First, the most common complaint appeared to be vocal changes, primarily hoarseness of the voice in 50% of cases. Other presenting symptoms were cough, malaise, and a non-specific flu-like presentation. Secondly, 50% of the patients demonstrated evidence of possible pulmonary involvement with chest imaging, however only 23% of patients underwent bronchoscopies or pulmonary biopsies. In a majority of cases, the diagnosis was confirmed with a biopsy of the larynx or sputum cultures. And thirdly, in 58% of cases the CFTs were equal or greater than 1:16. Any positive CFT is considered clinically relevant; IgG will diminish over a period of 6 months after treatment. It is for this reason that it is used as a marker of successful therapy along with clinical resolution of the initial symptoms. In addition, PCR for *Coccidioidomycosis* spp has been developed which has shown very high sensitivity and specificity in infected patients [7]. As well,

use of enzyme immunoassay (EIA) for patients infected with *Coccidioidomycosis* can assist with a definite diagnosis in presence of an inconclusive or inconsistent CFT [8]. Sensitivity for patients with symptomatic infections is very high, however in immunocompromised or asymptomatic patients results should be interpreted with caution [8].

Author	Year	Age/ Sex	Presentation	Diagnosis	Pulmonary Cocci	Serology	Therapy	Outcome
Allen et al.	2011	52/F	1 year history of dysphonia and cough with prior history of treated pulmonary coccidioidomycosis	Videolaryngoscopy positive for erythema and pseudomembranous exudate over epiglottis and periform fossa. Chest CT demonstrated large pneumoceles and lung damage. Biopsy of vocal cords and sputum cultures grew <i>C. immitis</i> .	No	Complement fixation titer (CFT) was 1:32	Fluconazole	After 6 weeks of antifungal therapy, laryngoscopy noted complete resolution of infection.
Patel et al.	2009	28/M	1 week history of sore throat, hoarseness, dry cough, and dysphagia	Contrast computed tomography scan of neck and chest positive for abscess on false vocal cord with lymphadenopathy and pulmonary nodules; culture positive for <i>C. immitis</i> .	Yes	Undetectable IgG & IgM	I&D; oral fluconazole	Clinically improved
Crum et al.	2004	47/M	Hoarseness, neck adenopathy and increasing CF titer, history of pulmonary coccidioidomycosis	FNA of neck LN was negative, laryngoscopy noted 3 nodules on vocal cords which yielded a positive diagnosis	No	CFT was 1:8, increased from 1:2	Fluconazole 600mg QD for 2 months	Adenopathy and hoarseness resolved over 2 months. No relapses over 11 month follow-up period.
Rosen et al.	2001	14?M	3 week history of worsening hoarseness and dyspnea; history of disseminated coccio as a child	Chest X-ray noted calcified granulomas consistent with previously treated pulmonary coccidioidomycosis. Laryngoscopy with biopsy grew <i>C. immitis</i> .	No	IgG was positive, CFT was 1:16	IV fluconazole for 3 days, switched to PO 200mg Q6hr	Unknown
Boyle et al.	1991	40/F	6 week history of moderate hoarseness, lymphadenopathy of the rt side of the neck, fever, night sweats, moderate dry cough, and fatigue	Contrast computed tomography scan of neck positive for supraglottic edema and near total compromise of the airway as well as bilateral lymphadenopathy and a nodule on right perijugular lymph node; biopsy and histological examination positive for caseating granulomas and multinucleated giant cells, double walled spherules with endospores indicated <i>C. immitis</i> .	Yes	IgM; CFT was 1:32	Fluconazole	Clinically improved

Author	Year	Age/ Sex	Presentation	Diagnosis	Pulmonary Cocci	Serology	Therapy	Outcome
Hajare et al.	1989	31 mo/M	2 day history of respiratory distress and stridor, history of steroid-dependent nephrotic syndrome	Chest X-ray was unremarkable. Laryngoscope revealed epiglottic and subglottic edema. Tracheal aspirate grew <i>C. immitis</i> .	No	CFT was 1:32	Amphotericin B for 4 weeks however d/c due to worsening renal function. Switched to fluconazole PO 6.6mg/kg/day for 1 year	Compliment fixation was negative 6 months after hospital discharge
Dudley	1987	21F	3 month history of gradually increasing neck mass and reports of not feeling "up to par"	Mass excised and histologic evidence of caseating granulomas.	No	CFT was 1:2	Excised; no antbx	3 year follow up showed no evidence of infection
Dudley	1987	13/F	Neck mass and lethargy; 1 year later neck nodes developed again, bilaterally	Biopsy/ histology confirmation; Biopsy showed caseating granulomas with endospore-packed spherules	No	CFT 1:2; CFT 1:32	Ketoconazole 6mo; ketoconazole (600mg) daily for 3mo.	Cervical adenopathy disappeared; Cervical adenopathy disappeared with no signs of return over 3 year follow up
Benitz et al.	1983	5/M	5 week history of right-sided pleuritic chest pain, cough, fever, occasional night sweats; increasing stridor and intercostal retractions.	Chest X-ray showed infiltrates in the middle and lower lobes of the right lung as well as mediastinal lymphadenopathy on the right. Coccidioidin skin test positive. Laryngoscopy and biopsy was performed and histologic examination showed granulomatous lymphadenitis and spherules consistent with <i>C. immitis</i> .	No	CFT 1:8 initially, but up to 1:32	Amphotericin B for 10 wk (total dose of 60mg/kg)	After 14 month there was no further recurrence of respiratory distress or stridor
Gardner et al.	1980	1/M	3 month history of rhinitis, stridor, and cough. Also noted were lethargy and dysphonia.	Bronchoscopy/ biopsy; sample obtained showed histologic evidence of granulomas and spherules suggestive of endospores consistent with <i>C. immitis</i> . The pathogen was also isolated from the sample; a skin <i>C. immitis</i> skin test showed 5mm of induration and erythema.	Yes	CFT was 1:8	Amphotericin B (IV) for 4 mo (total dose 65mg/kg) and tracheostomy	Although CFT remained unchanged and skin test positive, no symptoms or growth recorded at 5 month follow up
Ward et al.	1977	4.5 mo/M	3 month history of upper respiratory tract infection associated with wheezes and cough; subglottic stenosis with granular lesions	Laryngoscope and biopsy were taken; upon histopathologic examination fibrous stroma and spherules consistent with <i>C. immitis</i> were found.	No	CFT ranged from 1:32 to 1:128	Amphotericin B until CFT returned to 1:32 (total dose 271mg)	At 6 month post-treatment follow up, patient had no signs of infection and healthy

Author	Year	Age/ Sex	Presentation	Diagnosis	Pulmonary Cocci	Serology	Therapy	Outcome
Platt	1977	45/M	Hoarseness for 1 year with associated fever, malaise, hemoptysis and weight loss; history of pulmonary coccidioidomycosis s/p lobectomy	Chest X-ray showed extensive bilateral infiltration with cavitation. <i>C. immitis</i> was isolated in the sputum cultures.	No	CFT was 1:28-1:256	Amphotericin B for 2 year intermittently, however sputum was still positive. Switched to micronazole nitrate for 10 weeks for resolution.	Acute infection was resolved however bone marrow aspirate to assess anemia noted spherules of <i>C. immitis</i> .
Singh et al.	1956	34/M	Productive cough for 3 month with dysphagia and hoarseness for 1 month	Tracheostomy with biopsy of tracheal cartilage grew <i>C. immitis</i> . Biopsies from cutaneous lesions also grew the fungus.	No	CFT was positive	Dihydroxystilbamidine (IV) Q4hrs, total of 20 doses.	3 month after therapy, cutaneous lesions were healing and patient no longer required tracheostomy

Table 1: Review Literature of *Coccidioidomycosis*

The current treatment of laryngeal *Coccidioidomycosis* is amphotericin B or fluconazole, however the drug of choice is fluconazole [1,9-19]. To date, there have been no cases of laryngeal *Coccidioidomycosis* being treated with the newer azoles such as voriconazole or posaconazole. Relapse rates in isolated laryngeal infections are not known due to the scarcity of documented cases.

In this case, the usual features included multiple repeat negative CFT's, no definite evidence of pulmonary disease, and an isolated infection in an otherwise healthy female. At this point it would be difficult to speculate as to whether she would have had a positive EIA in the presence of a localized infection. However, given the laboratory and clinical data available, it would indicate the primary source of the patient's *Coccidioidomycosis* infection was limited only to her larynx. Due to her lack of pulmonary symptoms and negative CFT, a bronchoalveolar lavage was unnecessary and would add unneeded risks to the patient. There have been many proposed hypotheses of isolated laryngeal involvement however no proven theory has emerged as yet [20]. The most likely etiology of laryngeal involvement is from hematogenous spread of a primary pulmonary focus or dissemination from a high fungal burden in the host [20]. However, the etiology of our patient's laryngeal *Coccidioidomycosis* is not clear.

Due to the sporadicity of cases of laryngeal involvement of *Coccidioidomycosis*, morbidity and mortality is difficult to determine. With ease and mobility of travel it is very feasible for patients who live outside the expected area of infectivity to develop this illness. While cases of isolated laryngeal *C. immitis* are exceedingly rare, one should consider uncommon fungal etiologies like *Coccidioidomycosis* in patients with difficult to treat upper respiratory tract or pneumonia-like symptoms.

In summary, laryngeal *Coccidioidomycosis* is an unusual presentation of a common illness endemic to the southwestern United States. The diagnosis is made on the biopsy of the larynx and treatment is with fluconazole for 6-12 months.

Acknowledgement

Dr. Suresh J. Antony for his input and assistance in developing this manuscript.

References

- Boyle JO, Coulthard SW, Mandel RM (1991) Laryngeal involvement in disseminated coccidioidomycosis. *Arc Otolaryngol Head Neck Surg* 117: 433-8.
- Pappagianis D (1980) Epidemiology of coccidioidomycosis. *Coccidioidomycosis*, Springer US, 63-85.
- Centers for Disease Control and Prevention (CDC) (2013) Increase in reported coccidioidomycosis--United States, 1998-2011. *MMWR Morb mortal wklly rep* 62: 217-21.
- Hector RF, Rutherford GW, Tsang CA, Erhart LM, McCotter O, et al. (2011) The public health impact of coccidioidomycosis in Arizona and California. *Int J Environ Res Public Health* 8: 1150-73.
- Smith CE (1940) Epidemiology of Acute Coccidioidomycosis with Erythema Nodosum. *Am J Public Health Nations Health* 30: 600-11.
- Antony SJ, Dummer SJ, McNeil KK, Salas I (2005) Coccidioidomycosis in renal transplant recipients. *Infect Dis Clin Prac* 13: 250-4.
- Gago S, Buitrago MJ, Clemons KV, Cuenca-Estrella M, Mirels LF, et al. (2014) Development and validation of a quantitative real-time PCR assay for the early diagnosis of coccidioidomycosis. *Diagn microbiol Infect Dis* 79: 214-21.
- Blair JE, Mendoza N, Force S, Chang YH, Grys TE (2013) Clinical specificity of the enzyme immunoassay test for coccidioidomycosis varies according to the reason for its performance. *Clin Vaccine Immunol* 20: 95-8.
- Patel S, Snyder L (2009) A Sore Throat in the Southwest. *Am J Med* 122: 233-5.
- Allen JE, Belafsky PC (2011) Laryngeal coccidioidomycosis with vocal fold paralysis. *Ear, nose, throat j* 90: E1-5.
- Crum NF, Lederman ED, Stafford CM, Parrish JS, Wallace MR (2004) Coccidioidomycosis: a descriptive survey of a reemerging disease. Clinical characteristics and current controversies. *Medicine* 83: 149-75.
- Rosen EJ, Newlands SD, Patel J, Kalia A, Friendman, NR (2001) Reactivated laryngeal coccidioidomycosis. *Otolaryngol Head Neck Surg* 125: 120-1.
- Hajare S, Rakusan TA, Kalia A, Gibson FB, Strunk CL (1989) Laryngeal coccidioidomycosis causing airway obstruction. *Pediatr Infect Dis J* 8: 54-6.
- Dudley JE (1987) Coccidioidomycosis and neck mass 'single lesion' disseminated disease. *Arc Otolaryngo Head Neck Surg* 113: 553-5.
- Benitz WE, Bradley JS, Fee WE, Loomis JC (1983) Upper airway obstruction due to laryngeal coccidioidomycosis in a 5-year-old child. *Am J Otolaryngo* 4: 367-70.

16. Gardner S, Seilheimer D, Catlin F, Anderson DC, Hernried L (1980) Supraglottic coccidioidomycosis presenting with persistent stridor. *Pediatrics* 66: 623-5.
17. Ward PH, Berci G, Morledge D, Schwartz H (1976) Coccidioidomycosis of the larynx in infants and adults. *Ann Otol Rhinol Laryngol* 86: 655-60.
18. Galgiani JN, Ampel NM, Blair JE, Catanzaro A, Johnson RH, et al. (2005) Coccidioidomycosis. *Clin Infect Dis* 41: 1217-23.
19. Singh H, Yast CJ, Gladney JH (1956) Coccidioidomycosis with endolaryngeal involvement. *AMA Arch Otolaryngol* 63: 244-7.
20. Platt MA (1977) Laryngeal coccidioidomycosis. *JAMA* 237: 1234-5.

Submit your next manuscript to Annex Publishers and benefit from:

- ▶ Easy online submission process
- ▶ Rapid peer review process
- ▶ Online article availability soon after acceptance for Publication
- ▶ Open access: articles available free online
- ▶ More accessibility of the articles to the readers/researchers within the field
- ▶ Better discount on subsequent article submission

Submit your manuscript at

<http://www.annexpublishers.com/paper-submission.php>