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# Laryngeal cryptococcosis; a condition reported in renal transplant recipients and other immunosuppressed patients

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## ARTICLE INFO

### Article Type:

Letter to Editor

### Article History:

Received: 17 March 2017

Accepted: 12 April 2017

ePublished: 6 May 2017

### Keywords:

*Cryptococcus neoformans*

HIV infection

Laryngeal cryptococcosis

### Implication for health policy/practice/research/medical education:

*Cryptococcus neoformans* is ubiquitous fungus commonly found in the environment, particularly in soil, usually in association with pigeon and other bird droppings. Its clinical impact depends mostly on the immune state of the host.

**Please cite this paper as:** Rodriguez-Morales AJ, Ramirez-Jaramillo V. Laryngeal cryptococcosis; a condition reported in renal transplant recipients and other immunosuppressed patients. J Nephroarmacol. 2017;6(2):119-121. DOI: 10.15171/npj.2017.17.

**C***ryptococcus neoformans* is ubiquitous fungus commonly found in the environment, particularly in soil, usually in association with pigeon and other bird droppings (1,2). Its clinical impact depends mostly on the immune state of the host (1,2). In AIDS, cancers and transplant recipients, this pathogen can cause primary pulmonary infections or disseminated, including the central nervous system (CNS), among other locations, which can include the larynx (1,2). In this setting, we have read with interesting the recent case report by Sandhu et al (2), where they described a case of cryptococcosis in a renal allograft recipient that clinically presented with hoarseness of voice and mimicked laryngeal carcinoma on examination. Although we congratulate on the observation, correct diagnosis and management, we would like further discuss its implications, but particularly a more thoughtful review of previously reported cases of laryngeal cryptococcosis.

Whilst we concord that *Cryptococcus neoformans* laryngitis is “uncommon”, at least 21 cases, since 1975, have been reported in the scientific literature, located using Medline and Scopus (2-5). Then, we have reviewed and synthesized them (Table 1). Of them, the median age was 64 years-old (range 30-87 years-old), 57% were male, 90% presented hoarseness, only one was a renal transplant recipient, but six were receiving corticosteroids, five

had chronic obstructive pulmonary disease, five with asthma, three with HIV infection/AIDS and two with diabetes. Four of them were exposed to birds, particularly pigeons (Table 1). In 18 out of the 21 cases, diagnosis was based mostly in biopsy including other complementary diagnostic tools. Regarding the treatment, 71% received fluconazole (in 4 of them by 6 months), 14% itraconazole and 10% amphotericin B. In 4 cases (19%) no antifungal pharmacological treatment was used (Table 1).

Then, the case reported by Sandhu et al (2), was very young, with similar risk factors to those reported before (e.g. use of corticosteroids and the transplant), being diagnosed by the biopsy from laryngeal mass lesion and treated with fluconazole. As they, we agree of the utmost need for biopsy confirmation in these cases, but particularly also the call for more research on therapeutic options on these types of cryptococcosis, as e.g. there are no randomized, prospective trials of antifungal treatment of solid organ transplant recipients. In these and other immunosuppressed patients (e.g. HIV/AIDS), therapy would be difficult to choose, especially when dissemination to the CNS occurs (6).

### Authors' contribution

AJRM conceived the idea and worked the first draft. VRJ reviewed literature and collected data. All authors revised

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**Table 1.** Reported cases of laryngeal cryptococcosis, 1975-2017

No	Age	Sex	Clinical manifestations	Comorbidity/risk factors	Confirmatory diagnosis	Treatment	References
1	30	M	Hoarseness	Immunosuppression after renal transplantation	Biopsy, histology, PAS and H-E stain	Oral fluconazole 400 mg day per 6 months	(2)
2	82	F	Hoarseness and Stridor	COPD and CAD.	Biopsy, fungal culture, GMS stain.	6 weeks Itraconazol, 10 weeks fluconazol, PDL therapy for persistent lesions, 2 months fluconazole post PDL.	(3)
3	78	F	Hoarseness	Mild Asthma treated with budesonide	Direct visualization first, then biopsy. 1 year later: alcian blue and mucicarmine stain + Fontana-mason stain. PCR assay.	First cycle fluconazole 100 mg day per 3 weeks, no response, repeated cycle. 1 year later: 15 weeks fluconazole 400 mg day.	(4)
4	71	F	Cough and Hoarseness	COPD + corticosteroids and nystatine. Exposure to bird droppings.	Biopsy + Grocott-Gomori methenamine silver stain and mucicarmine. Serum criptococcus antigen.	KTP laser, photoablation, fluconazole 400 mg 6 months.	(5)
5	58	M	Husky voice	Asthma with budesonide and formoterol	Biopsy, histology, acid Schiff stain, Grocott methenamine silver fungal and Alcian Blue stain.	Fluconazole 400 mg/d for eight weeks.	(7)
6	65	F	Hoarseness	HIV +. Meningitis and pulmonary localisation. Asthma, allergic fungal sinusitis, poliomyelitis.	Biopsy	Amphotericin B followed by fluconazole during 6 months	(8)
7	55	M	Hoarseness and cough	Albuterol, flunisolide, last year prednisone therapy cycle twice.	Biopsy, histopathology, Gomori's methenamine silver stain	Itraconazole 200 mg twice daily for 6 weeks followed by fluconazole 400 mg a day for 10 weeks.	(9)
8	NR	M	Failure of tracheoesophageal voice prosthesis	Pigeon fancier	Incubation of the membrane on Sabouraud glucose agar, + Microscopic examination of with India Ink. PCR.	Remove prosthesis.	(10)
9	42	M	NR	AIDS, pulmonary tuberculosis and hydropneumothorax.	NR	Oral fluconazole for 8 weeks	(11)
10	61	M	Hoarseness	Glucocorticosteroid-dependent. COPD, insulin-dependent diabetes. TI: 35-pack-year.	Biopsy, Capsular staining with mucicarmine.	Single 400-mg dose of oral fluconazole and then prescribed 200 mg/d per 6 weeks.	(12)
11	47	M	Hoarseness and dyspnea	Works with soil and chicken manure.	Bronchial washings culture, biopsy, Alcian blue stain.	Amphotericin B 2 g in 30 days.	(13)
12	73	M	Hoarseness	Insulin-dependent diabetes. Chirurgical remove of "growth"	Histopathology, Gomori methenamine silver stain and mucicarmine stains.	Laryngoscopy and local excision.	(14)
13	64	M	Hoarseness	Inhaled corticosteroids for asthma.	Histopathological examination with methenamine silver and mucicarmine staining	Fluconazole 400 mg daily for 10 months.	(15)
14	44	M	Hoarseness	HIV, Hepatitis C and smoking.	Biopsy and staining.	Fluconazole for 3 months.	(15)
15	79	F	Hoarseness	Inhaled corticosteroids.	Biopsy, no reactive serum antigen	Fluconazole for 6 months.	(15)
16	87	M	Dry cough and Hoarseness	COPD	Biopsy, Gomori's methenamine silver, acid-Schiff and mucicarmine stains.	Fluconazole 400 mg every day for 2 months.	(16)
17	68	F	Hoarseness	Cigarette smoking	Excision, Grocott stain.	Excision.	(17)
18	31	F	Hoarseness	Works in a chemist's shop.	Biopsy, mucicarmine and Alcian blue stains.	No treatment.	(18)
19	53	M	Hoarseness	Exposition to pigeons	Biopsy, Gomori's methenamine silver and mucicarmine stain.	Fluconazole 400 mg daily for 6 weeks.	(19)
20	82	F	Hoarseness	COPD requiring home oxygen, systemic and topically inhaled steroids.	Biopsy and fungal culture.	Itraconazole for 6 weeks, followed by ten week fluconazol, PDL, two months of fluconazole.	(20)
21	66	F	Cough and Hoarseness	Asthma, albuterol use	Bronchoscopy, PCR analysis.	Oral fluconazole 400 mg daily.	(21)

Abbreviations: M=Male; F=Female; COPD=Chronic obstructive pulmonary disease; AIDS=Acquired immunodeficiency syndrome; HIV=Human immunodeficiency virus; NR=not reported; CAD: coronary artery disease.

and approved the submitted version.

### Conflicts of interest

The authors declared no competing interests.

### Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

### Funding/Support

None.

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