



Jennifer Morrison

Persistent hoarseness

A case study

Keywords: hoarseness; pharynx; asthma; drug therapy

Case study

Marion, a university lecturer aged 48 years, presented to her general practitioner complaining of persistent hoarseness for 4–5 weeks. Over the preceding 5 months she had suffered two prolonged episodes of bacterial sinusitis and an infective exacerbation of her asthma, each requiring several weeks of various antibiotics and oral prednisone, and each associated with transient hoarseness. Marion has generally well controlled asthma and has used a medium dose inhaled corticosteroid (fluticasone/salmeterol via dry powder inhaler) for many years. She has also used an intranasal corticosteroid (budesonide 64 µg daily) on a daily basis for 2 years to help control symptoms of rhinosinusitis. She is a lifelong nonsmoker and is otherwise in good health. She rinses her mouth after each inhaled corticosteroid dose. She has no pets and does not live on a farm. The only travel she has done in the past few years is to the United Kingdom to attend a conference. During this trip she did not travel to any rural areas.

Marion's GP was concerned about the persistent hoarseness and referred her to an ear, nose and throat (ENT) surgeon who examined her lower pharynx and larynx with a fibre optic scope. In his letter back to the GP he described seeing 'a small red nodule' on her left vocal cord at laryngoscopy. There were no other abnormal findings and she was advised to watch and wait.

After several weeks she returned to the ENT surgeon with worsening hoarseness. This time he performed microlaryngoscopy which demonstrated an inflamed, bulky left vocal cord covered with white debris. A biopsy

was taken which was reported as growing both *Aspergillus* and *Cryptococcus* species. Marion was commenced on itraconazole 100 mg/day oral for 1 month. Despite several weeks of antifungal treatment, her symptoms did not improve. A microbiologist was consulted who suggested repeating the biopsy to reconfirm the pathogen. This second biopsy grew *Candida* species, and she was changed to fluconazole 200 mg/day oral for 2 weeks and referred to a speech therapist with gradual resolution of her hoarseness over the next 6 months. Marion had a chest X-ray (screening for lung cancer), which was unremarkable, and tests for human immunodeficiency virus (HIV) serology, full blood count and fasting blood glucose, which were all normal.

Marion's asthma had been well controlled for many years on a medium dose inhaled corticosteroid. She was referred to a respiratory physician for an opinion on ongoing management of her asthma and the decision was made to cease her inhaled and intranasal corticosteroids. She was temporarily changed to montelukast sodium 10 mg/day oral, however, this is not subsidised on the Pharmaceutical Benefits Scheme for adult asthma so she did not continue to use it. At the time of writing, she had ceased all her asthma medications and was doing surprisingly well.

Question 1

What are the causes of acute and persistent hoarseness?

Question 2

What are the indications for specialist referral in a patient with persistent hoarseness?

Question 3

What is the diagnosis in this case and what are the risk factors for this condition?

Question 4

What test is required for definitive diagnosis of this condition?

Answer 1

The most common causes for acute hoarseness are viral upper respiratory tract infections, acute tonsillitis and vocal abuse (shouting/screaming). In the patient with persistent hoarseness (more than 3 weeks), other more serious and sinister causes must be considered including malignancy, foreign body, motor neurone disease, myaesthesia gravis, leukoplakia, fungal infection, goitre, and pharyngolaryngitis due to gastro-oesophageal reflux.¹ Benign tumours of the vocal cords (eg. polyps, nodules, papillomas) may cause significant hoarseness but usually resolve with voice rest and speech therapy.

Answer 2

Any patient who has a persistent voice change for more than 3 weeks, despite adequate voice rest, or who has any 'red flags' such as a history of neck trauma or risk factors for, or symptoms of, malignancy, should be referred for specialist assessment.² Patients who rely on their voice for their profession (eg. singers or public speakers) should also receive prompt assessment. In this case, the patient was struggling to perform her role as a university lecturer and had to cancel several classes due to an inability to speak clearly, comfortably and audibly to students. Prompt referral to an appropriate specialist can reduce impact of the hoarseness on the patient's quality of life.

Answer 3

The diagnosis in this case is fungal laryngitis, which is a rare but significant cause of hoarseness. In order to make a diagnosis of fungal laryngitis, it is important to be aware of the risk factors for this condition and maintain a high index of clinical suspicion if risk factors are present.

Risk factors for fungal laryngitis include:

- impairment of the local mucosa barrier such as from previous radiotherapy, trauma (eg. intubation), infection, smoking, gastro-oesophageal reflux disease, and inhaled and oral corticosteroids³
- increased risk of developing an unusual fungal infection from contact with farm or domestic

animals. Travel to South America, Africa and South-East Asia is also a known risk factor for developing pulmonary fungal disease, however the literature is lacking as to whether laryngeal disease may also occur⁴

- immune compromise. Fungal laryngitis in immunocompetent patients is unusual, so it is important to consider the possibility of immune compromise from conditions including HIV, haematological malignancy, diabetes, severe nutritional deficiencies³ or other malignancies such as lung cancer (particularly in a smoker).

This patient's risk factors for fungal laryngitis included long term inhaled corticosteroid use (both oral and intranasal), recent upper and lower respiratory tract infections, as well as several weeks use of oral prednisone.

Answer 4

Definitive diagnosis of fungal laryngitis requires a tissue biopsy and culture.⁵ Fungal spores and inflammation may be visible at microscopy and special stains for fungi assist with identifying the organism.

Discussion

In 2006, 5.7% of the Australian adult population was prescribed an inhaled corticosteroid (alone or in combination with a long acting beta agonist).⁶ It is important that patients who require an inhaled corticosteroid are on the lowest possible steroid dose to control their symptoms and that they are taught to maintain good oral hygiene after using their device.⁷ Roland et al⁵ suggest six factors contributing to upper airway inflammation caused by inhaled corticosteroids (*Table 1*). They argue that these factors may predispose a patient to local side effects including hoarseness (also termed dysphonia in some papers), oropharyngeal candidiasis, cough, perioral dermatitis, thirst and tongue hypertrophy.

This case is unusual because of the fungi cultured on the initial biopsy. It is unclear whether these initial biopsy findings were accurate, despite the surgeon following correct collection and storage procedures. There is little published in the literature on fungal laryngitis. Of that in existence, none of the case studies described colonisation with anything other than *Candida* species, making this patient's second biopsy result more reassuring, and the initial finding likely to be incidental.

Table 1. Factors contributing to upper airway inflammation caused by inhaled corticosteroids⁵

The steroid itself (eg. dose, regimen)
The manner in which the steroid is propelled into the airways
Intrinsic inflammation of the upper airway in asthmatic patients
Mechanical irritation due to cough
Intercurrent inflammatory disease (eg. rhinitis)
Intercurrent inflammatory stimuli (eg. smoking)

Important points

- General practitioners should consider fungal laryngitis as a cause for hoarseness in patients with risk factors.
- It is important to organise early specialist referral if hoarseness is persistent.
- Patients on inhaled corticosteroids should be maintained on the lowest possible steroid dose to control their symptoms and taught to maintain good oral hygiene after using their device.

Author

Jennifer Morrison MBBS(Hons), MPH, DCH, is a general practice registrar, GPSynergy, Armidale, New South Wales. jenniferlmorrison@gmail.com.

Conflict of interest: none declared.

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correspondence afp@racgp.org.au