

Glottic cancer in a non-smoking patient with laryngopharyngeal reflux

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Abstract

The onset of carcinoma of the larynx, especially of the glottis, is heralded mainly by a change of voice. It has a male preponderance and is almost exclusively common to smokers and patients with heavy alcohol consumption. We report a case of glottic carcinoma in a non-smoker female patient. The only possible risk factor for her is a history of laryngopharyngeal reflux.

Introduction

The incidence of laryngeal squamous cell carcinoma is low, comprising 1% of all the carcinomas in men, and much lesser in women.¹ In Malaysia, the most common type of laryngeal cancer is transglottic cancer. This is an extension of glottic carcinomas, which has extended to the adjacent areas. In comparison with the worldwide prevalence, the most common type of laryngeal cancer is glottic cancer. This signifies late presentation or detection of glottic carcinomas in Malaysia.² Early laryngeal cancers, especially those affecting the glottic subsite, are associated with a 5-year survival rate of >90%.³ It is more common in chronic smokers and alcoholics. Gastric reflux is believed to be a risk factor for the development of laryngeal carcinoma, although the literature is conflicting. It has been thought that laryngopharyngeal reflux can damage laryngeal epithelium through chronic inflammation, production of reactive oxygen and nitrogen species, intracellular acidification and activation of proliferative signalling pathways, all of which will finally lead to malignant transformation.⁴

Case report

A 67-year-old lady presented with hoarseness for 2 years, which is not progressive, and preceded by a history of prolonged cough. The symptom was associated with frequent throat clearing. She had no dysphagia, odynophagia, difficulty in breathing or aspiration symptoms. She was initially sought treatment from a private clinic and was subsequently referred to hospital. She initially treated by an ear, nose and throat surgeon (ENT) in another hospital

as laryngopharyngeal reflux for her prolonged cough and throat symptoms and was given follow-up to monitor the symptoms. She was referred to a general surgeon because she also complained of dyspepsia and heartburn. Esophagogastroduodenoscopy was done and she was diagnosed to have a peptic ulcer. However, she defaulted follow-up in the hospital and came to the private clinic again alternating with the government health clinic for follow-up for almost a year before she defaulted. She was referred to us by a cardiologist for persistent hoarseness when she came for her heart problem. She had mild difficulty in breathing; however, she did not have cough. She did not smoke or drink alcohol. She was not working and stayed with her daughter. There was no history of malignancies in the family.

On examination of the larynx, she had a swollen left true and false vocal cord with irregular border. There were phonation gaps, and the airway was slightly narrowed. She had no enlarged lymph node.

Biopsy of the swollen vocal cord and tracheostomy under general anaesthesia were done. Histopathological examination of the biopsy showed a few small clusters of malignant cells seen infiltrating the stroma. In other areas, atypical were seen admixed with fibrin and connective tissue. The cells were large with pleomorphic and hyperchromatic nuclei with eosinophilic cytoplasm. Some showed individual cell keratinisation. Abnormal mitoses were frequently seen. The diagnosis was squamous cell carcinoma (**Figure 1**).

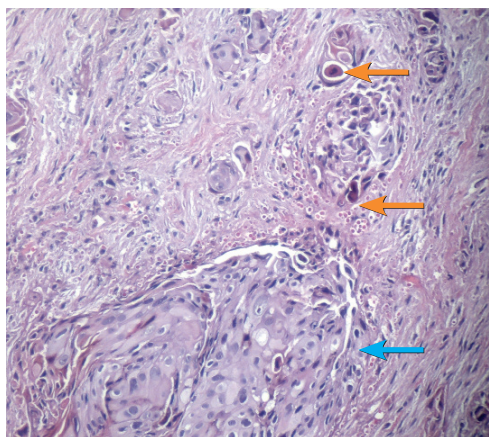


Figure 1. H&E stain $\times 20$: Tiny fragment of the tissue with areas of haemorrhage, focally infiltrated by solid sheets (blue arrow) and small clusters of malignant squamous cells. The cells are large and some have abundance eosinophilic cytoplasm with hyperchromatic nuclei. Individual cell keratinisation (yellow arrow) noted focally

She went for a computed tomography scan to determine the extent of the lesion and staging. There was a lesion over the left vocal cord extending to the anterior commissure, posterior commissure and strap muscle, especially the sternohyoid muscle. The thyroid cartilage was eroded. There was no distant metastasis seen. She was staged as $T_{1b}N_0M_0$. She was treated with radiotherapy. Currently, she was still under follow-up after oncology therapy without evidence of recurrence.

Discussion

Smoking and alcohol consumption are the main risk factors for laryngeal cancer.⁴ It is less common in non-smokers, as in our patient. She also did not drink alcohol. Other minor risk factors that have also been associated with laryngeal cancer are diet,⁵ environmental and occupational exposures,⁶ dentition and oral hygiene⁷ and gastroesophageal reflux.⁸ The only positive risk factor was acid reflux.

Reflux of gastric acid has been primarily and commonly associated with oesophageal adenocarcinoma, usually due to metaplastic transformation.⁹ Acid reflux can reach beyond the oesophagus into the laryngopharynx (known as laryngopharyngeal reflux). However, such transformation is not common in the pharynx and larynx.

A recent case-controlled study reported significant positive association between a history of frequent acid reflux and incidence of laryngeal squamous cell carcinoma among non-smokers and non-drinkers. They also reported an inverse association between antacid use and laryngeal squamous cell carcinoma, suggesting the efficacy of the treatment in reducing the risk of laryngeal carcinoma attributable to gastric reflux.⁴ Their finding is consistent with several published studies¹⁰⁻¹² on the relationship between gastric reflux and laryngeal cancer. Our patient was not compliant towards her treatment for gastric ulcer, and this probably predisposed her to the development of cancer.

The most common symptom for glottic carcinoma is hoarseness followed by stridor.² A cross-sectional survey was done in 2010 looking at the reasons and timing of referral for patients with hoarseness, for instance persistent symptoms >2 weeks, worsening of symptoms, associated symptoms, e.g., cough, dysphagia, shortness of breath and neurologic symptoms, risk factors like alcohol and tobacco users and if the patient is a professional voice user. The most common reasons given by primary care physicians for not evaluating patients with voice problems include patient not complaining of voice problem, unsure of the best method, more important problems, not comfortable evaluating patient's voice, not enough time, and unsure of treatment options. Less common reasons are the primary care physicians do not feel the voice problem is a priority and no ENT or speech pathologists.¹³ In our case, the reason for the delay in the diagnosis could be due to her non-progressive symptoms. She had been having the symptoms with similar severity for 2 years, and non-compliance was thought to be the reason as to why the patient was having having persistent symptoms. The fact that glottic cancer does not commonly present with cervical lymph node enlargement will make the clinical suspicious of malignancy more difficult. Most of the head and neck cancers usually cause progressive symptoms but not in this patient. The only way to confirm the diagnosis of malignancy is by histopathological examination. It is safer to have a high index of suspicion for malignancy in elderly patient even though the history is not suggestive.

Conclusion

Laryngopharyngeal reflux has been described as one of the minor risk factors for the development of laryngeal squamous cell carcinoma. It should be considered as a possible risk factor especially in a patient who is not

smoking and consuming alcohol. Suspicious of carcinoma should be higher especially in the elderly, to avoid misdiagnosis and continuously treating for acid reflux. Biopsy should be performed to get histopathological diagnosis to exclude malignancy.

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