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Laryngeal pyogenic granulomas do not express oestrogen or progesterone receptors

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Abstract

The objective of this study was to determine the presence of oestrogen and/or progesterone receptors in laryngeal pyogenic granulomas and the impact of these receptors on recurrence of pyogenic granulomas.

Twenty-two consecutive patients who underwent microlaryngoscopy and removal of pyogenic granulomas were studied retrospectively. The indications for surgery were airway compromise, failure of medical therapy and suspicion of malignancy. Twelve of these patients' granulomas were analysed for oestrogen and progesterone receptors.

Charts were analysed for age, sex, location of the lesion, history of trauma, intubation or gastroesophageal reflux disease (GORD), airway symptoms and recurrence. Oestrogen/progesterone receptors were analysed following deparaffinization of specimens and immunostaining with prediluted anti-oestrogen receptor monoclonal antibody and anti-progesterone receptor monoclonal antibody.

No sample expressed oestrogen or progesterone receptors. There were too few recurrences to detect if lack of these receptors played any role in determining outcome in this group. Most of the patients had a history of GORD, intubation or laryngeal surgery. There were 12 recurrences in four patients. All of the recurrences improved on prolonged courses of omeprazole.

Pyogenic granulomas do not possess oestrogen or progesterone receptors and are unlikely to respond to hormonal therapy. Patients who have, or are being operated on for, laryngeal pyogenic granulomas should be placed on proton pump inhibitors to decrease the likelihood of recurrence.

Key words: Larynx; Granuloma, Pyogenic; Receptors, Oestrogen; Receptors, Progesterone

Introduction

Hormone receptors in laryngeal tissue are a topic of interest because of the potential effects on treatment. Normal laryngeal tissues possess oestrogen and progesterone receptors to varying degrees.[1–3] Multiple studies have looked at the presence of steroid receptors in laryngeal cancer.[1,2,4]

Pyogenic granuloma is a benign vascular neoplasm often occurring on the skin and mucous membranes. The term lobular capillary haemangioma has been suggested as a more appropriate description based on the histology of the lesion.[5,6] An increased incidence of pyogenic granuloma occurs in pregnancy, which may suggest hormonal regulation.[7,8]

Pyogenic granuloma of the larynx is infrequently reported in the literature. We looked at the presence of oestrogen and progesterone receptors in a series of pyogenic granuloma of the larynx in order to determine whether hormonally-mediated treatment would be effective.

Materials and methods

Twenty-two patients with biopsy proven pyogenic granulomas of the larynx were identified at the Long Island Jewish Medical Centre between the years 1989 and 1998 (Table I). Patients with pyogenic granuloma of the trachea were excluded, as were patients who did not require direct laryngoscopy. Laryngoscopies were performed on patients whose laryngeal airway was compromised by the granuloma, had failed medical therapy or whose lesion was suspicious for malignancy. Charts were analysed for age, sex, symptomatology, smoking and drinking history, previous laryngeal surgery and/or intubation, gastroesophageal reflux (GORD) history, site of lesion, lesional morphology and recurrence (Table II).

Paraffin-embedded specimens were available from 12 patients (from Table I: patients' numbers 2–9, 12–15). Four to six micron sections were mounted on coated (poly-L-lysing) slides, deparaffinized and rehydrated. They were immersed in sodium citrate

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TABLE I
PATIENT CHARACTERISTICS

Patient no.	Age/sex	Tobacco/alcohol	Hx/O GORD	Symptoms	Recurrence
1	59/M	−/−	Y	H	No
2*	43/M	−/−	?	H, B	No
3*	69/F	−/−	N	H	No
4*	31/F	+/−	?	H, SOB	No
5*	65/F	+/−	N	H, SOB	No
6*	22/M	+/−	N	H	No
7*	34/F	−/−	N	H	No
8*	47/M	+/−	N	H	No
9*	39/M	−/−	N	H	No
10	28/F	−/−	N	H, OBST	No
11	58/M	+/+	?	H	No
12*	50/M	−/−	N	H	No
13*	28/M	−/−	N	H, OBST	× 8
14*	54/F	−/−	Y	H, SOB	No
15*	44/M	−/−	Y	H, B	× 1
16	57/F	−/−	N	H	No
17	44/F	−/−	N	H	× 1
18	47/F	−/−	N	H	× 1
19	46/F	−/−	N	H	No
20	61/F	+/+	N	H	No
21	45/M	−/−	N	H	No
22	40/M	−/−	Y	H	× 1

H = Hoarseness; B = Bleeding; SOB = Shortness of breath; OBST = Obstruction; GORD = Gastroesophageal reflux;
* = Oestrogen/Progesterone receptor assayed.

buffer (pH 6.0) and heated in a microwave oven for 30 minutes at a high setting. The sections were cooled for five minutes and stained as per protocol[9,10] on an automated immunostainer (Ventana Nexus, Ventana Medical Systems, Tucson, AZ) using prediluted anti-oestrogen receptor monoclonal antibody (clone 6F11) and anti-progesterone monoclonal antibody (Ventana Medical Systems). The slides were counterstained with one per cent methyl green control. These slides were run in parallel with positive controls for comparison. Additionally, no specimen revealed evidence of *Helicobacter pylori* when examined by light microscopy.

Results

Twenty-two patients were included in the study. Men and women were equally represented. The average age was 46 (range 22–69). The average age of the female patients was 49 (43 years for men). Tobacco and alcohol use were assessed. Six out of 22 patients had a history of tobacco use. Two out of 22 patients had a history of excessive alcohol use.

Prior history of laryngeal trauma or manipulation was documented: six out of 22 patients had prior laryngeal surgery (laser arytenoidectomy, vocal polypectomy, ventricular cystectomy, and hemilaryngectomy). Nine patients reported prior intubation.

TABLE II
ASSOCIATED FACTORS WITH LARYNGEAL PYOGENIC GRANULOMAS

Patient no.	Trauma	Location	Peduncle v. Sessile	Recurrence
1	GORD	L midfold	unknown	No
2	none	R posterior	sessile	No
3	intubation	L posterior	peduncle	No
4	laser arytenoid	R posterior	peduncle	No
5	vocal polypectomy	L posterior	peduncle	No
6	hemi-laryngectomy	R anterior pseudofold	sessile	No
7	intubation	R posterior	peduncle	No
8	hemi-laryngectomy	L anterior pseudofold	sessile	No
9	none	R posterior	peduncle	No
10	intubation	R posterior	peduncle	No
11	intubation	R midfold	unknown	No
12	laser cordectomy	R midfold	unknown	No
13	none	R posterior	sessile	× 8
14	intubation	L posterior	peduncle	No
15	GORD	R posterior	sessile	× 1
16	intubation	L midfold	peduncle	No
17	none	L posterior	peduncle	× 1
18	intubation	bilateral	sessile	× 1
19	intubation	R posterior	sessile	No
20	ventricular cystectomy	R false fold	peduncle	No
21	intubation	R posterior	peduncle	No
22	GORD	R posterior	peduncle	× 1

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Four patients had no history of laryngeal trauma. Only four out of 22 patients reported a history of reflux disease.

All patients in this study were hoarse. Other presenting symptoms included bleeding (two patients), shortness of breath (three) and obstruction (two). Twelve out of 22 lesions were pedunculated. Eight lesions were sessile (two were not documented). The location of the lesion was also assessed. More lesions were right-sided (14) than left-sided (seven). One patient had bilateral pyogenic granuloma. Lesions were predominantly posterior (14), although two were anterior and four were mid-cord. Ten out of 14 posterior lesions were pedunculated.

Oestrogen and progesterone receptor status was assessed in a total of 12 specimens. None of the specimens contained these hormone receptors. No patient had evidence of *Helicobacter pylori* histologically in their pyogenic granuloma. There were 12 recurrences in a total of four patients. No factor predicted recurrence although the number of patients was small. All recurrences improved on a prolonged course of omeprazole.

Discussion

Pyogenic granuloma or lobular capillary haemangioma is infrequently reported in the otolaryngology literature. Histologically, the lesion is characterized by a lobular organization of capillaries. Fibrous stroma may be present. Secondary ulceration and granulation tissue often occurs.[5] Diagnosis is often controversial within the head and neck.[11] Early investigators denied the presence of these lesions in the larynx and trachea.[5] Contact ulcers of the larynx and pyogenic granuloma may be similar entities or may occur along a spectrum of disease.[12] This study documents the presence of pyogenic granuloma in the larynx and addresses some of their characteristics.

Our patients presented with a history of hoarseness. The patients included for analysis had airway obstruction leading to surgical excision of the lesion and represent the extreme of the disease process. A history of prior laryngeal manipulation from either laryngeal surgery or intubation was the most prominent defining characteristic of the study population. Age, sex and tobacco and alcohol use were not significant factors. Vocal fold lesions were predominantly posterior and pedunclated. The posterior laryngeal findings and history of intubation or laryngeal surgery point to a traumatic inciting factor. Laryngeal scarring and oedema are well known adverse responses to intubation.[13] This also suggests a relationship of laryngeal pyogenic granuloma to contact ulcers of the larynx.

An additional component of our study focused on the hormonal receptor status of pyogenic granuloma. The larynx is known to possess oestrogen and progesterone receptors.[1–4] Studies have also looked at this characteristic in pyogenic granuloma. The results have been inconclusive. Nichols *et al.* noted the absence of oestrogen and progesterone receptors of their study of 21 lobular capillary haemangiomas.[14] Whitaker *et al.* noted the presence of oestrogen and progesterone receptors in the endothelium and epithelium of lobular capillary haemangioma in their series of 30 lesions within the oral cavity.[7]

In our study of pyogenic granuloma within the larynx, all specimens tested were negative for oestrogen and progesterone receptors. The pathogenesis of pyogenic granuloma in the larynx is unlikely to be hormonally mediated. In addition, hormonal modulation is unlikely to work because of the lack of receptors on the target tissue. In many cases of pyogenic granuloma, the causative factor is trauma. It is probable that these granulomas are an acute and chronic attempt to repair the mucosal damage and do not represent intrinsic laryngeal pathology. This would explain the lack of receptors on these lesions.

Recent research has focused on the role of gastroesophageal reflux disease in the pathophysiology of multiple laryngeal disorders. Laryngitis, hoarseness, laryngospasm, dysphagia, globus sensation, and Zenker's diverticulum are only a few of the disorders thought to be caused or exacerbated by GORD.[15] Our evidence suggests that pyogenic granuloma is exacerbated by reflux disease. Patients improved on extended (six-week) trials of proton pump inhibitors and lifestyle modifications. Although our results are not conclusive, further research in this area is warranted.

Conclusion

Pyogenic granulomas of the larynx do not possess oestrogen or progesterone receptors and are unlikely to respond to hormonal therapy. Laryngeal trauma is an important although not exclusive factor in their development. Patients who have or are being operated on for laryngeal pyogenic granulomas should be placed on proton pump inhibitors to decrease the likelihood of recurrence. Reflux disease may play a role in the pathogenesis of these lesions and deserves further investigation.

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