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Original article

RECURRENCE RISK OF INFERIOR SURFACE LEUKOPLAKIA OF THE VOCAL CORDS: A RETROSPECTIVE STUDY.

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Abstract

Background :

Vocal fold leukoplakia (VFL) remains a diagnostic and therapeutic challenge despite our knowledge of its etiopathogenetic factors and the development of laryngeal visualisation. This study sought to identify lesions on the inferior surface of the vocal folds as a recurrence risk factor.

Methods:

This was a retrospective study with two years of data collection. The study included 37 VFL patients, who were separated into nonrecurrent and recurrent categories. Each patient's clinicopathological characteristics and surgical procedures were scrutinised.

Results :

15 (40.5%) of the 37 patients exhibited residual (3) or recurrent (12) VFL. 8 of 12 (66.7%) patients with recurrence and 6 of 22 (27.3%) patients without recurrence had inferior surface lesions of the vocal fold at the time of the initial operation (P =.036). Significantly more recurrences occurred in patients with inferior surface lesions. Other evaluated factors were not associated with recurrence.

Conclusion :

The presence of VFL lesions on the inferior surface is a significant recurrence risk factor.

Keywords: leukoplakia, vocal cord, laryngeal lesions, laryngoscopy, microsurgery, recurrence,
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1. Introduction:

Vocal fold leukoplakia (VFL) is a frequently encountered precancerous lesion in the field of otolaryngology. The medical condition known as "vocal fold leukoplakia" pertains to the presence of thick, whitish or grey patches on the vocal folds, irrespective of their histological characteristics. This term does not connote any histological or prognostic implications, as per sources [1, 2, 3]. The pathological findings of clinically ascertained VFL encompass hyperplasia, mild to moderate dysplasia, severe dysplasia, or carcinoma [4]. As per the World Health Organization's classification system of 2017, laryngeal dysplasia is categorised into low-grade and high-grade dysplasia [5].

The cutaneous abnormalities may present as either exophytic or planar, contingent on the density of the keratinized stratum of the epithelial tissue [6]. The nonkeratinizing nature of the vocal fold epithelium renders leukoplakic change as a manifestation of epithelial modification [7]. The nomenclature and categorization of this range of pathological abnormalities have undergone significant modifications throughout history in the med-

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ical and academic fields. During preliminary research, the clinical term "keratosis" was utilised interchangeably with "leukoplakia". However, contemporary terminology restricts the use of "keratosis" solely to denote a histological observation of a keratin layer on the squamous epithelium [8].

The pathogenesis of leukoplakia patches or plaques is attributed to chronic tobacco smoking, alcohol misuse, inhalation of irritant substances, and viral infections, including human papillomavirus (HPV) [12]. Additional potential etiological factors include occupational exposures, inadequate nutrient intake, vocal overuse or misuse, persistent infections, endocrine dysfunctions, and laryngopharyngeal reflux disease [8, 13, 14]. The etiological significance of infectious agents, such as the human papillomavirus (HPV), remains a subject of academic debate [15]. Individuals diagnosed with vocal fold lesions (VFL) typically present with voice-related symptoms akin to other such lesions. Hoarseness of voice is the most prevalent symptom, frequently prompting a referral to an otolaryngologist (ENT doctor).

According to medical literature, VFL exhibits a malignancy transformation rate of approximately 8% [16]. Approximately 50% of patients who receive a clinical diagnosis of vocal cord leukoplakia exhibit no dysplasia upon histopathological examination. Nevertheless, a subset of these lesions may ultimately undergo malignant transformation [17]. A significant hurdle encountered in the realm of clinical practise pertains to the determination of leukoplakia cases that necessitate microlaryngoscopy with histological examination [18]. The primary objectives of treatment in the majority of cases involve the restoration of vocal capabilities and complete removal of the lesion [6]. In instances of vocal fold lesions (VFL) with a significant probability of malignancy, the primary objective is to eliminate the cancerous cells at the initial stage. This may necessitate a profound resection, while individuals with a low risk of malignancy may benefit from a conservative approach or a policy of watchful waiting [6].

Given the significant impact of disease stage on patient survival, it is imperative to prioritise early investigation of the pathogenesis of laryngeal carcinoma during the precancerous or leukoplakic stage, in order to initiate appropriate therapeutic interventions. The clinical diagnosis of laryngeal disorders is typically achieved through laryngeal imaging, followed by tissue sampling, which is commonly performed in an operative setting. Histopathology is a fundamental and customary diagnostic technique utilised to ascertain the existence and extent of dysplasia in biological specimens [19]. The objective of this initial investigation was to evaluate the correlation between inferior surface lesions and recurrent ventricular fibrillation.

2. Methods:

The present study received approval from the institutional review board at MGM Medical College Ethical Clearance Committee. This study was conducted in the Department of ENT, MGM Medical College, Jamshedpur, Jharkhand, India. A retrospective study was conducted to assess the data of 37 patients diagnosed with vesicoureteral reflux (VFL) who underwent treatment at our medical facility using cold instrument resection or in combination with a holmium yttrium aluminium garnet (Ho: YAG) laser (2100 nm, pulse energy 0.2 J, repetition rate 5 Hz, VersaPulse PowerSuite 100 W, Lumenis Ltd) over a period of two years from July 2020 to August 2022. Upon performing an initial laryngoscopy, the presence of white lesions on the vocal fold was clinically diagnosed as vocal fold leukoplakia (VFL). Surgical intervention was conducted on patients presenting with lesions characterised by irregularities in the vibratory patterns of the vocal folds, as evidenced by stroboscopic examination.

The study participants were stratified into two cohorts: those who experienced recurrence of symptoms (manifesting within 6 months post-treatment) and those who did not [12]. Subjects presenting with persistent pathology (manifesting within a timeframe of 180 days) were not included in the study. The study analysed various clinical factors, including sex, age, alcohol consumption, smoking, presence of laryngopharyngeal re-

flux disease (LPRD), site and size of the lesion (length of the lesion relative to the total length of the vocal fold membrane), the lesions of the inferior surface and anterior commissure, difficult laryngeal exposure (DLE), and pathological grade, to compare between groups.

2.1. Surgery:

All patients provided written informed consent in accordance with medical and academic standards. A preoperative laryngoscopy was conducted in the clinic utilising a digital strobe system. Visual recordings were conserved and analysed during every subsequent examination. Surgical interventions were executed under the administration of general anaesthesia, utilising a Saito direct laryngoscope manufactured by Nagashima Medical Instruments Co, Ltd, and a microscope.

Nine patients underwent microsurgical resection of the lesions using cold instruments during the primary surgical intervention. In a cohort of 28 subjects, a segment of the lesion was excised through microsurgery for biopsy utilising cold instruments. The remaining lesions were subjected to treatment with Ho: YAG laser, which caused vaporisation of the epithelium solely through non-contact irradiation. The laser fibre tip was positioned at a distance of 1 to 4 mm from the lesion. The inferior surfaces were observed via fiberoptic endoscopy during the surgical procedure and subsequently ablated utilising laser technology. The inferior surface lesions were identified intraoperatively by manipulating and inverting the superior surface of the vocal fold to expose the inferior surface.

The condition of difficult laryngeal exposure was determined when the complete lesion was not visualised using the smallest laryngoscope available. Lesions of the anterior commissure were visualised via fiberoptic endoscopy and subsequently subjected to laser ablation. Postoperative surveillance was conducted at intervals of 1 to 3 months for a minimum of 12 months. At each instance of postoperative follow-up, a comprehensive examination was conducted by closely scrutinising the lesions present on the inferior surface of the vocal folds using a fiberscope.

2.2. Statistical Analysis:

Fisher exact test was utilised for the statistical analysis. The odds ratio (OR) and 95% confidence intervals (CIs) for each risk factor were calculated using a two-tailed significance test. GraphPad Prism version 6.04 for Windows (GraphPad Software) was utilised to perform statistical analysis. Here are some descriptive statistics-analyzed data. The postoperative recurrence and potential significant clinical factors were evaluated using univariate analyses. Statistical significance was defined as P values less than 0.05 on both sides.

3. Results:

There was a total of 37 patients (Table 1), with 35 men (94.6%), spanning in age from 32 to 84 years (mean age: 64.6 + 9.8 years). 27 patients (73%) drank alcohol, whereas 30 (82,4%) smoked cigarettes. Laryngopharyngeal reflux disease was prevalent among 15 patients (40.5%) [Table 1]. Thirteen (35.1%) of the patients had bilateral lesions, and fifteen (40.5%) had lesions that affected more than fifty percent of the vocal fold surface. Lesions of the inferior surfaces were observed in 16 patients (43.2%). Lesions of the anterior commissure were present in four (10.8%) patients, while DLE was present in five (13.5%). Mild dysplasia was the most prevalent histopathological finding at the initial biopsy (10 patients, 27.0%).

The clinical characteristics of sex (P =.16), age (P = 1.0), alcohol consumption (P = 1.0), smoking (P =.63), presence of LPRD (P =.45), site of the lesion (P = 1.0), lesion size (P =.71), anterior commissure (P =.6), DLE (P = 1.0), and pathological grade (P = 1.0) were not significant risk factors for recurrence [Table 1].

15 (40.5%) of the 37 patients had residual (3) or recurrent (12) VFL. Eight (66.7%) of the twelve patients with VFL recurrence had lesions on the inferior surface [Table 2]. Six (75%) of these eight patients had a recurrence of inferior surface lesions. One (25%) of the four VFL recurrences without lesions on the inferior surfaces had a recurrence of the lesion on the inferior surface. 27.3% of the patients in the nonrecurrent group

had lesions on the inferior surface. Thus, lesions of inferior surfaces were found to be a significant risk factor for recurrent VFL (P .036, OR: 5.3, 95% CI: 1.2-24).

12 to 104 months (mean: 34 + 26 months) and 35 to 123 months (mean: 68 + 24.5 months) after surgery for the nonrecurrent and recurrent groups, respectively. Recurrence was observed between 10 and 53 months (mean = 20 + 11 months) of follow-up. After 49 months, one patient developed carcinoma in situ (2.7%), and within 24 months, another patient developed invasive squamous cell carcinoma (2.7%).

4. Discussion:

Patients and surgeons are extremely concerned about the risk of recurrence following VFL surgery. The reported recurrence rates after surgery, including the results of our study, are high and vary widely (9.5%-46.4%) [4-6, 9, 11]. In addition, recurrence results in an increased malignant transformation rate, a reduced time interval to develop squamous cell carcinoma, scarring and dysphonia in the vocal folds due to repeated surgery, and a higher rate of malignant transformation [14]. Cold instrument resection, carbon dioxide laser, potassium-titanium-phosphate laser, and pulsed dye laser are among the different excisional and ablational options for VFL [15-20]. However, there are no significant distinctions between these methods in terms of recurrence prevention.

As risk factors for VFL recurrence, physicians have previously focused on the roles of gender, age, and lifestyle behaviours such as alcohol consumption and smoking [4, 7-10]. Alcohol consumption, smoking, LPRD, and lesion location and size were not identified as significant risk factors in this study. However, when interpreting the results, one must take into account the tiny sample size of the study. Moreover, these determinants are unrelated to physicians.

The rates of recurrence and malignant transformation in vocal fold lymphoma (VFL) have not changed as a result of the widespread use of in-office surgeries for vocal fold disorders today [21]. Hu et al. reported that two out of eleven patients had VFL recurrence on the inferior surfaces [20]. In our study, 6 (75%) of 8 patients had lesion recurrence on the inferior surface, while 1 (25%) of 4 patients had lesion recurrence on the inferior surface without primary inferior surface lesions.

Estimating the recurrence rate relied heavily on the duration of the follow-up. Mean recurrence duration is between 16 and 24 months, with a follow-up period of 32 to 109 months [7, 11, 14, 22-24]. In this study, the mean interval between recurrences was 20 months, and the duration of follow-up in the recurrent group was 68 months. Although the average follow-up time for nonrecurrent patients was 34 months, some cases lacked sufficient follow-up time to detect recurrence. Therefore, a minimum 2-year follow-up period appears necessary.

In addition to the tiny sample size, the retrospective nature of this study is also a limitation. Additionally, multiple surgeons performed the procedures, and variations in surgical techniques may have affected the outcomes. It is necessary to conduct a prospective investigation with a larger sample size.

5. Conclusion:

Leukoplakia of the vocal folds can be categorised based on the morphology of the plaque, which can be classified into three distinct types: flat and smooth, elevated and smooth, and rough. This categorization, although a subjective approach to evaluation, appears to exhibit reliability among impartial assessors. Lesions of the inferior surface of the vocal fold were a significant risk factor for recurrent VFL in this study.

6. Limitations:

In addition to the tiny sample size, the retrospective nature of this study is also a limitation.

7. Recommendations:

It is recommended to conduct a prospective investigation with a larger sample size.

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Original article

Clinicopathological characteristics	Case no, n (%)
Sex	
Male	35 (94.6%)
Female	2 (5.4%)
Age (years), mean ± SD = 64.6 ± 9.8	
≥65	20 (54.1%)
<65	17 (45.9%)
Alcohol consumption	
Yes	27 (73.0%)
No	6 (16.2%)
Unknown	4 (10.8%)
Smoking	
Yes	30 (82.4%)
No	4 (10.8%)
Unknown	3 (8.1%)
Presence of laryngopharyngeal reflux disease	
Yes	15 (40.5%)
No	19 (51.4%)
Unknown	3 (8.1%)
Site of lesion	
Bilateral	13 (35.1%)
Unilateral	24 (64.9%)
Size of lesion	
≥50%	15 (40.5%)
<50%	22 (59.5%)
Inferior surface	
Yes	16 (43.2%)
No	21 (56.8%)
Anterior commissure	
Yes	4 (10.8%)
No	33 (89.2%)
Difficult laryngeal exposure	
Yes	5 (13.5%)
No	32 (86.5%)
Pathology	
No dysplasia	24 (64.9%)
Mild dysplasia	10 (27.0%)
Moderate dysplasia	1 (2.7%)
Sever dysplasia	2 (5.4%)
Postoperative residual disease (n = 3) and recurrence (n = 12)	
Yes	15 (40.5%)
No	22 (59.5%)

Figure 1: Candidate Risk Factors Associate5d With Recurrent Vocal Fold Leukoplakia

Variables	Case no, (n)	Postoperative recurrence		Odds ratio (95% CI)	*P* value[a]
		No	Yes		
Sex					.16
Male	32	22	10	0.12 (0.0053-2.7)	
Female	2	0	2	1.00	
Age					1.0
≥65	19	12	7	1.2 (0.28-4.8)	
<65	15	10	5	1.00	
Alcohol consumption					1.0
Yes	26	17	9	0.79 (0.11-5.7)	
No	5	3	2	1.00	
Smoking					.63
Yes	27	17	10	0.59 (0.71-4.9)	
No	4	2	2	1.00	
Presence of laryngopharyngeal reflux disease					.45
Yes	13	10	3	0.47 (0.095-2.3)	
No	18	11	7	1.00	
Site of lesion					1.0
Bilateral	11	7	4	1.1 (0.24-4.8)	
Unilateral	23	15	8	1.00	
Size of lesion					.71
≥50%	12	7	5	1.5 (0.36-6.6)	
<50%	22	15	7	1.00	
Inferior surface					.036
Yes	14	6	8	5.3 (1.2-24)	
No	20	16	4	1.00	
Anterior commissure					.60
Yes	4	2	2	2.0 (0.24-16)	
No	30	20	10	1.00	
Difficult laryngeal exposure					1.0
Yes	5	3	2	0.58 (0.053-6.2)	
No	32	19	13	1.00	
Pathology					1.0
Moderate, severe dysplasia	2	1	1	1.9 (0.11-34)	
No dysplasia, mild dysplasia	32	21	11	1.00	

[a]Fisher exact test: *P* values <.05.

Figure 2: Candidate Risk Factors Associated With RecurrentVocal Fold Leukoplakia

8. Acknowledgement:

None

9. List of abbreviations:

VFL- Vocal fold leukoplakia
HPV- Human papillomavirus
CI- Confidence interval
OR- Odds ratio
LRPD- Laryngopharyngeal reflux disease
DLE- Difficult laryngeal exposure

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