Clinical Analysis and Risk Factors in Laryngeal Leukoplasia

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ABSTRACT

Objective: Leukoplasia requires careful clinical follow-up with recurrent biopsies, regardless of the histopathological grade of dysplasia, because it has a potential risk of malignant transformation. This study aimed to investigate the clinical features and risk factors of laryngeal leukoplasia.

Methods: Overall, 174 lesions of 97 patients who were diagnosed with vocal fold dysplasia between 2007 and 2013 at our clinic were retrospectively analyzed. Histopathological classification of laryngeal leukoplakia, gender, age, systemic diseases, smoking habits, initial symptoms, duration of symptoms, location, size and number of lesions, and recurrence of the lesion were recorded.

Results: Ten (10.30%) of the patients were females and 87 (89.70%) were males. The average age was 56.95 years. The initial sypmtom of all patients was hoarseness. Average cigarette use was 38.82 packets/year; smoking frequency was 93.8%; and reflux frequency was 16.6%. Indirect and direct laryngoscopic examinations revealed that 103 (59.53%) patients had leukoplasia and 70 (40.46%) patients had vocal cord irregularities. Mild dysplasia was the most common histopathological diagnosis. The lesion location was 45.1% in the anterior 1/3, 32.34% in the middle 1/3, and 22.55% in the posterior 1/3 of the vocal cord. The age distribution, sex ratio, duration of initial symptom, reflux rate, smoking rate, and localization were not statistically significant ($p>0.05$) in patients with and without recurrence. Leukoplasia recurrence rate was significantly higher ($p<0.05$) than irregularity rate.

Conclusion: In laryngeal leukoplasia, biopsy and histopathological examination are important for evaluating epithelial dysplasia and its degree. Histopathologically, factors such as presence and severity of dysplasia and smoking increase the risk of developing malignancy. Clinically homogeneous leukoplasia has a higher recurrence rate than nonhomogeneous irregularity. However, age distribution, sex, duration of initial symptom, reflux rate, smoking, and localization does not increase the recurrence rate, according to the results of this study.

Keywords: Leukoplasia, dysplasia, vocal cord, larynx

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INTRODUCTION

Leukoplakia is a clinical term describing white lesions in mucous membranes. Dysplasia is a pathological term showing cellular atypia and structural changes in the epithelium. Laryngeal leukoplakia is considered to be precancerous because of the possibility of transformation into squamous cell carcinoma (SCC). Smoking, alcohol, gastric reflux, viral infections, poor use of sound, and toxic gas inhalation are the main risk factors for leukoplakia.

Diagnosis is made by direct laryngoscopy. A white plaque that is not easily removed from the underlying mucosa is specific for diagnosis (1). A biopsy is performed to determine the presence of dysplasia during laryngoscopy. The most important parameter in pathological examination is the presence of dysplasia and its severity.

The coexistence of leukoplakia with irregularities increases the suspicion of carcinoma in preoperative evaluation. In such a case, there is a debate about the intervention that should be done during the operation. An excisional biopsy, stripping, and laser ablation may be the options for the surgical treatment.

With regard to histopathology, a careful clinical follow-up with recurrent biopsies is required regardless of the degree of dysplasia.

In this study, the risk factors that may help in making decisions about the surgical intervention in the preoperative examination in patients with vocal cord leukoplakia are evaluated.

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METHODS

Approval for the study was obtained from the Clinical Research Ethics Committee of Şişli Hamidiye Etfal Training and Research Hospital (22/10/2013-505). The files of the patients who underwent direct laryngoscopy between 2007 and 2013 were retrospectively reviewed. Patients with vocal cord leukoplakia were included in the study. Patients with an ulcerovegetan mass, polyps, nodules, and previously diagnosed laryngeal carcinoma were excluded from the study.

Gender, age, smoking, symptoms and symptom duration, examination findings, localization of the lesion, histopathological classification of leukoplakia, and recurrence were analyzed.

In regard to histopathology, the lesions were divided into four groups (2, 3):

Group I: Inflammatory changes, hyperkeratosis

Group II: Mild-to-moderate dysplasia

Group III: Severe dysplasia and carcinoma in situ (CIS)

Group IV: Micro invasive and invasive SCC

The presence of irregularities associated with leukoplakia and the location of the lesion were evaluated. The location of the lesion was evaluated in six groups according to the cord and level (Figure 1).

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences version 21.0 program (IBM Corp., Armonk, NY, USA). Data were expressed as the mean±standard deviation, minimum–maximum, ratio, and frequency in descriptive statistics. The Kolmogorov–Smirnov test was used for control of the distribution of the variables. An independent samples t-test and the Mann-Whitney U test were used for a quantitative data analysis; Chi-squared test was used for the analysis of qualitative data.

RESULTS

Ten (10.30%) of the patients were female and 87 (89.70%) were male. The mean age was 56.95. All patients presented with symptoms of hoarseness. The mean smoking rate was 38.82 packs/year, and the rate of smoking was 93.8%. The incidence of reflux was 16.6%.

In indirect and direct laryngoscopic examinations, 103 (59.53%) patients had leukoplakia, and 70 (40.46%) patients had vocal cord irregularities. The number of non-smokers was 6 (6.18%); 5 (83.33%) of these patients had mild dysplasia, and 1 (16.67%) had severe dysplasia. Mild dysplasia was the most common histopathological diagnosis. The distribution of histopathological examination results was found to be 8.67% in Group I, 52.02% in Group II, 30.06% in Group III, and 9.25% in Group IV (Table 1). The most common location of the lesions was the anterior one-third of the vocal cords, and posterior involvement was rare.

The age distribution, gender ratio, first symptom duration, reflux rate, smoking rate, and localization were not statistically significant ($p>0.05$) in the patients with and without recurrence. The leukoplakia recurrence rate was significantly higher when compared to irregularity ($p<0.05$) (Table 2). When the histopathological results were examined according to the age distribution of the patients, the mean age was found to be higher in cases with micro-invasive and invasive SCC; it was observed that as the severity of dysplasia increased, the average age increased.

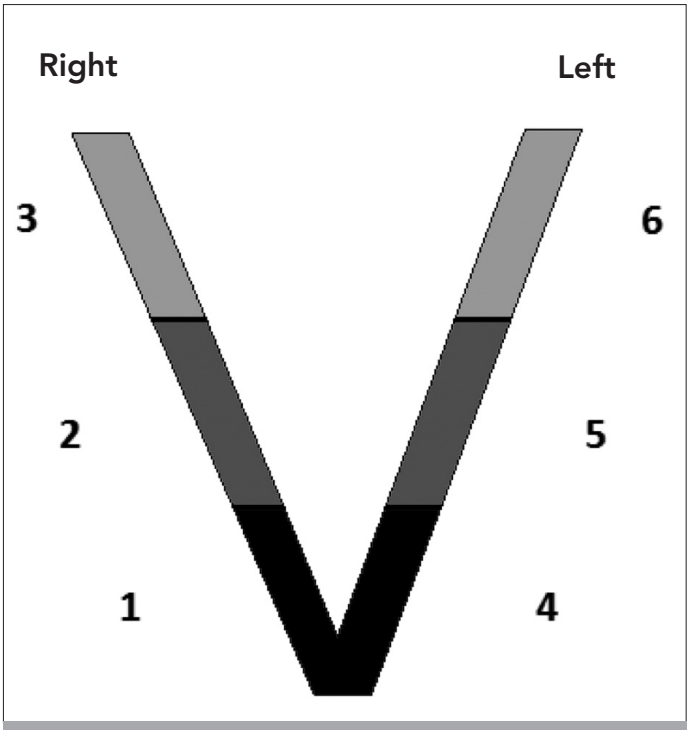

Figure 1. Lesion Location

DISCUSSION

In 1930 for the first time, Jackson et al. (4) showed in a study the development of SCC on the surface of laryngeal keratosis and proposed that laryngeal keratosis was a pre-neoplastic lesion. Gale et al. (5) found in the literature that the rate of conversion to carcinoma varied between 0% and 57%, and heavy dysplasia had a higher conversion rate. Weller et al. (6) found in the meta-analysis (9 studies, 940 patients) in 2010 the malignant transformation rate of laryngeal leukoplakia at 14%, and the mean duration of carcinoma development 5.8 years.

It was seen that as the degree of dysplasia increased, the rate of malignant transformation also increased (severe/CIS, 30.4%; mild to moderate, 10.6%) (1). Isenberg et al. (7), in their review, reported that 256 (8.2%) malignant transformations were observed in a 1–300 month follow-up of 3107 biopsies. They found that the severity of dysplasia in the first biopsy was proportional to the development of carcinoma.

In our study, the presence of dysplasia was found in 82% of the biopsies conducted. Isenberg et al. (7) in their review reported that 47.1% of the biopsies conducted in their own clinic and

Table 1. General features

		Min.	Max.	Mean±SD / n-%	
Age		30	86	56.96±11.36	
Gender	Female			10	10.3%
	Male			87	89.7%
Smoking	No			6	6.2%
	Yes			91	93.8%
First symptom duration (month)		15 Days	240	18.5±32.5	
Number of applications	I			60	61.9%
	II			24	24.7%
	III ≤			13	13.4%
Examination	Leukoplakia (homogenous)			103	59.5%
	Irregularity (non-homogenous)			70	40.5%
Localization	Right			77	44.5%
	Left			87	50.3%
	Bilateral			12	6.9%
Localization	Anterior			146	84.4%
	Middle			107	61.8%
	Posterior			72	41.6%
Pathology	Inflammatory change			15	8.7%
	Mild dysplasia			76	43.9%
	Moderate dysplasia			14	8.1%
	Severe dysplasia			19	11.0%
	Carcinoma in situ			33	19.1%
	Micro-invasive carcinoma			6	3.5%
	Invasive SCC			10	5.8%
Reflux	No			82	84.5%
	Yes			15	15.5%

SD: standard deviation

48.2% in other studies revealed dysplasia. Ma et al. (8) stated that 72.5% of the biopsies revealed pre-cancerous lesion (mild, moderate, and severe dysplasia).

The most common pathological finding in our study was mild dysplasia (44%). Carcinoma was diagnosed in 9% of the cases. In the study by Kizil et al. (9), pathology findings showed mild dysplasia to be the most common pathology seen in 25.8% of the patients, and 18.2% of the patients had carcinoma. Isenberg et al. (5) in his review of 2007 stated that 2188 biopsies showed no dysplasia in 53.6% of cases, 33.5% showed mild-to-moderate dysplasia, and 15.2% showed severe dysplasia/carcinoma in situ.

In terms of localization, in our study, it was observed that the anterior part of the vocal cords was involved more frequently (84%). In 2012, Kızıl et al. (9) showed that the anterior and middle parts of the vocal cord were more involved, and the posterior involvement was less. Kalter et al. (10) in a study including 200 patients showed that the lesions with different degrees of dysplasia were mostly located in the anterior two-thirds, and only 11% of the patients had posterior one-third involvement.

In our study, it was found that leukoplakia, which had a clinically homogenous feature, had a higher recurrence rate than non-homogenous irregularity (46.6%/23.1%). On the other hand, the age distribution, sex ratio, first symptom duration, reflux rate, smoking rate, and localization did not increase the recurrence rate.

Table 2. Relapse values

		Relapse				
		No		Yes		
		Mean±SD/n-%		Mean±SD /n-%		p
Age		58.1±11.4		55.0	±11.3	0.200[t]
Gender	Female	5	50.0	5	50.0	0.373[χ²]
	Male	56	64.4	31	35.6	
	First symptom duration (month)	20.5±38.1		15.2±19.9		0.615[m]
Examination	Leukoplakia (homogenous)	31	53.4	27	46.6	0.019[χ²]
	Irregularity (non-homogenous)	30	76.9	9	23.1	
Reflux	No	51	62.2	31	37.8	0.742[χ²]
	Yes	10	66.7	5	33.3	
Smoking	No	4	66.7	2	33.3	0.843[χ²]
	Yes	57	62.6	34	37.4	
Localization	Right	25	56.8	19	43.2	0.277[χ²]
	Left	32	71.1	13	28.9	
	Bilateral	4	50.0	4	50.0	
Localization	Anterior	50	61.0	32	39.0	
	Middle	43	65.2	23	34.8	
	Posterior	27	64.3	15	35.7	
Pathology	Inflammatory change	5	62.5	3	37.5	
	Mild dysplasia	30	63.8	17	36.2	
	Moderate dysplasia	3	60.0	2	40.0	
	Severe dysplasia	9	100.0	0	0.0	
	Carcinoma in situ	5	29.4	12	70.6	
	Micro-invasive carcinoma	2	50.0	2	50.0	
	Invasive SCC	7	100.0	0	0.0	

t: Independent sample t test; m Mann–Whitney U test; χ^2 Chi-squared test; SD: standard deviation

CONCLUSION

In laryngeal leukoplakia, histopathological examination with biopsy is important for the evaluation of epithelial dysplasia and the grade. Factors such as the presence and the severity of dysplasia with regard to histopathology and smoking increase the risk of malignancy. It has been found that leukoplakia, which has a clinically homogenous feature, has a higher recurrence rate than non-homogenous irregularity. On the other hand, the age distribution, sex ratio, first symptom duration, reflux rate, smoking rate, and localization did not increase the recurrence rate.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Health Sciences University Şişli Hamidiye Etfal Training and Reseacrh Hospital. (Approval No.: 505; Approval Date: 22.10.2013).

Informed Consent: Informed consent was not taken from patients due to the retrospective nature of the study.

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