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PREDICTIVE FACTORS OF RECURRENCE AND MALIGNANT TRANSFORMATION IN VOCAL CORD LEUKOPLAKIA

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ABSTRACT

Objective: To identify antecedent risk factors for predicting vocal cord leukoplakia recurrence and malignant transformation. **Materials and methods:** The sample included 58 patients attending the Ear, Nose, and Throat Surgery Clinic at Tishreen University Hospital during the time period 2022-2023 with white lesions on the vocal cord and who met the inclusion criteria in the research. Their ages ranged from 35 to 77 years, with an average of 64.27 ± 6.8 years. All patients participating in the study were interviewed and the following information was recorded for each patient: name; Age, gender, habits and instincts (smoker, alcoholic); Then he took a comprehensive medical history from the patients, A comprehensive clinical examination of the head and neck was performed and the larynx was carefully examined with a laryngoscope. The morphological features of the lesion and its extension on the vocal cord were recorded. An initial clinical diagnosis was made. Then a tissue biopsy of the white lesion on the vocal cord was performed and sent to the pathological autopsy. After the results appeared, appropriate treatment), patients were monitored for 18 months, during which factors leading to leukoplakia recurrence and transformation into malignancy were identified. **Results:** The study showed that the smoking and the degree of dysplasia and the extent of the lesion extending over the vocal cord have a significant statistical significance in the recurrence of vocal cord leukoplakia and its transformation into malignancy. **Conclusions:** The patient should be informed of the possibility of leukoplakia reoccurring and becoming malignant if the patient is a smoker, and/or has vocal cord leukoplakia with a lesion of more than half of the vocal cord and/or moderate or severe dysplasia on histological biopsy result.

KEYWORDS: Pathology of laryngeal cancer, recurrence of vocal cord leukoplakia.

INTRODUCTION

Leucoplakia is a whitish plaque on the mucous membrane which lining the mouth, throat, and other areas. It is a benign lesion, but in less than 10% of cases it may develop into an intraepithelial dysplasia and a malignant neoplasm.[1]

Histologically, Leucoplakia of the vocal cords is a local intraepithelial hyperplasia that affect the upper surface of one or both of the vocal cords and is considered a part of the transformation spectrum of laryngeal epithelium into malignancy, so the histological biopsy is necessary to determine the final diagnosis of leukoplakia.[3,4]

Leucoplakia is a recurrent disease if the risk factors persist in the patient who aren't followed-up well and that may lead to a malignancy transformation, and that could be avoided by periodic follow –up.[8]

OBJECTIVES

- **Main objective**: identification of antecedent risk factors for recurrence of leucoplakia and malignant transformation.
- ***Secondary objectives***: early detection of malignancy as a result of periodic follow-up, early treatment and consequent better prognosis.

MATERIALS AND METHODS

- **Study design:** observational descriptive study (case series).
- **Study period and place**: The study was conducted in the department of otorhinolaryngology and Head and Neck Surgery, Tishreen university hospital, Lattakia, Syria from 2022 to 2023.
- **Study sample**: 70 patients.

- **Inclusion criteria:** All patients with white lesions on the vocal cord.

- **Exclusion criteria**

1. Patients who couldn't underwent surgical intervention (6 cases).
2. Patients with another laryngeal lesions (3 cases).
3. Patients who lost to follow-up (3 cases).

According to this we had to exclude 12 patients and it remained 58 who included in our study**.**

METHODOLOGY

- We have taken a full history including the main complaints with their severity and duration, and the past history of any chronic disease, surgery, allergic reaction, medical treatments.
- General examination with CXR, ECG and laboratory tests were done.
- Full ENT examination with laryngeal endoscopy to assess the lesion and its location (using rigid endoscope 90 ◌̊ or flexible endoscope).
- Excisional biopsies were taken under general anesthesia from the vocal cord lesions and sent for the histopathological examination.
- Patients were followed-up periodically every 3 months for 18 months.
- Patients were divided according to:

1. Sex: male\female
2. Age: younger than 60\ older than 60.
3. Smoking: current smoker\previous smoker\nonsmoker.
4. Alcoholism: alcoholic\nonalcoholic.
5. Symptoms: hoarseness\asymptomatic.
6. Presence of laryngopharyngeal reflex: present \ absent.
7. Lesion location: right vocal cord\ lift vocal cord\ both vocal cords.
8. Lesion extension: less than 50% of the cord\ more than 50% of the cord.
9. Morphologic changes: superficial\ ulcerative\ exophytic
10. Degree of histopathologic changes: hyperplasia\mild dysplasia\ moderate dysplasia\ severe dysplasia \carcinoma.

- Written Informed consent was taken from all the patients for the planned procedure in a perform approved by our institutional ethical committee.

Statistical Analysis

Data were entered, and analyzed using SPSS version 25.

- Description statistical: for qualitative variables we use frequencies, percentages, and graphics.

For quantitative variables we use mean, standard deviation, and range.

- Inferential statistical: we use chi-square test.

Odds ratio (OR) was calculated to study risk factors and it considered important if it was 2 or more.
p-value < 0,05 considered statistically important.

RESULTS

Table 1: Patients' distribution according to sex, age, smoking, & alcoholism.

		Number	%
Sex	**Male**	51	87,9%
	Female	7	12,1%
Age	**<60 years**	19	32,8%
	>60 years	39	67,2%
Smoking	**Current smoker**	40	68,9%
	Previous smoker	13	22,4%
	Non smoker	5	8,7%
Alcoholism	**Alcoholic**	32	55,2%
	Nonalcoholic	26	44,8%

This study was conducted on 58 patients, 51 were men(87,9%) and 7 were women (12,1%) with sex ratio (M:F)=(7:3). The age ranged from 35 to 77 years old with a mean of (65,27±6,8) years. 68% of patients were smokers and 55,2% were alcoholics.[table1]

Table 2: patients' distribution according to symptoms.

		Number	%
Presenting symptom	**Hoarseness**	52	89,7%
	asymptomatic	6	10,3%
Laryngo-pharyngeal reflux	**present**	23	39,7%
	Absent	35	60,3%

52 patients presented with hoarseness (89,7%) whereas 6 were diagnosed coincidently without laryngeal symptoms (10,3%). [table 2] 39,7 % of patients had laryngopharyngeal reflux.

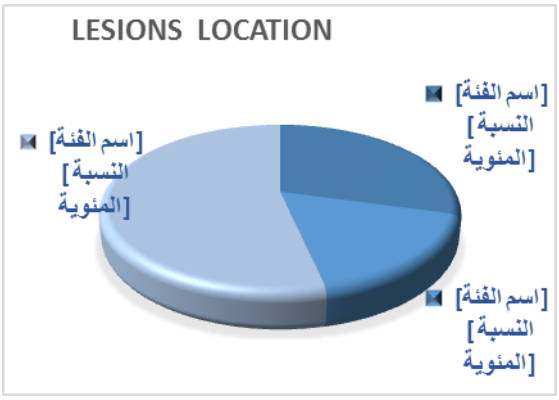

Figure 1: Patients' distribution according to the laryngeal lesions' location.

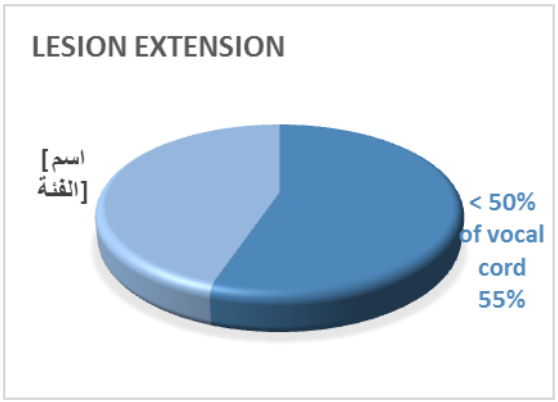

Figure 2: patients' distribution according to the laryngeal lesions' extension on the vocal cord.

17 patients(29,3%) had the lesion on the right vocal cord, 10 patients(17,3%) on their left vocal cord, and 31 patients (53,4%) on both vocal cords. [Figure1]

Lesions extension was <50% of the vocal cord in 32 patients (55,2%), and >50% of vocal cord in 26 patients (44,8%). [Figure 2]

Table 3: patients' distribution according to morphologic and histopathologic changes in the lesions.

		number	%
Morphologic classification	**Superficial**	48	82,8%
	Exophytic	9	15,5%
	Ulcerative	1	1,7%
Histopathologic Classification	**hyperplasia**	27	46,6%
	Mild dysplasia	11	18,9%
	Moderate dysplasia	3	5,2%
	Severe dysplasia	9	15,5%
	Carcinoma	8	13,8%

Study of leucoplakia recurrence after 18 months of surgery

Patients were divided into two groups : Recurrence and nonrecurrence.

3 patients have been excluded from our study because of the need of laryngectomy for their advanced disease and thus remained 55 patients.

- No statistically significant differences were found in recurrence rate between the groups according to sex and age.[table4]

Table 4: Recurrence rate of leucoplakia according to sex and age.

	Recurrence	Nonrecurrence	P=value	OR
Male	20(83,3%)	29(93,5%)	0,2	0,3[0,05-2,06]
female	4(16,7%)	2(6,5%)		
>60 years	13(54,2%)	23(74,2%)	0,07	0,4[0,1-1,2]
< 60 years	11(45,8%)	8(25,8%)		

- Significant differences were found in recurrence rate according to smoking, 83,3% of recurrence cases were smokers. current smoker had more recurrence rate than nonsmokers with an odds ratio =4,7.
- No significant differences were found in recurrence rate according to alcoholism. [Table 5].

Table 5: Recurrence Rate of Leucoplakia According to Smoking and Alcoholism.

		Recurrence	Nonrecurrence	P-Value	OR
Smoking	**Current smoker**	**20(83,3%)**	**17(54,8%)**	**0,0001**	**4,7[1,9-10,3]**
	Previous smoker	**3(12,5%)**	**10(32,3%)**		
	Non smoker	**1(4,2%)**	**4(12,9%)**		
alcoholism	**Alcoholic**	**15(62,5%)**	**15(48,4%)**	**0,2**	**1,7[0,6-5,2]**
	Non alcoholic	**9(37,5%)**	**16(51,6%)**		

- No significant differences were found in recurrence rate according to the lesions location.
- Significant differences were found in recurrence rate according to the lesion extension, 58,3% of recurrent cases had a lesion extension more than 50% of the vocal cord with an odds ratio 3.4. [table 6]

Table 6: recurrence rate according to lesion location and extension.

		Recurrence	Nonrecurrence	p-value	OR
Leucoplakia location	**R vocal cord**	6(25%)	10(32,3%)	0,8	1,3[0,09-4,5]
	L vocal cord	5(20,8%)	5(16,1%)		
	Both vocal cords	13(54,2%)	16(51,6%)		
Leucoplakia extension	**< 50% of vocal cord**	10 (41,7%)	22(71%)	0,02	3,4[1,1-10,5]
	>50% of vocal cord	14(58,3%)	9(29%)		

- No significant differences were found in recurrence rate according to morphologic changes of the lesions.
- Significant changes were found in recurrence rate according to histopathologic changes in the biopsy, 54,2% of recurrent cases had moderate or severe dysplasia or carcinoma in their biopsy results with an odds ratio 7,9. [table7]

Table 7: recurrence rate according to morphologic and pathophysiologic changes.

		recurrence	nonrecurrence	p-value	OR
Morphologic changes	**Superficial**	20(83,3%)	27(87,1%)	0,6	0,7[0,1-3,3]
	Exophytic	4(16,7%)	4(12,9%)		
Histopathologic changes	**Moderate and Severe dysplasia+ carcinoma**	13(54,2%)	4(12,9%)	0,001	7,9[2,1-29,9]
	Hyperplasia+ mild dysplasia	11(45,8%)	27(87,1%)		

DISCUSSION

- Our study was conducted on 58 patients who presented to otorhinolaryngology department and diagnosed with vocal cord leucoplakia.
- In our study, the majority of patients were males (87,9%), whereas females represent 12,1% of patients, and that may because of the biologic changes between men and women, since the size and the shape of the vocal cord affect its vibration and ability to produce sound, and vocal cords in men are longer and thicker than in women which allow more tense and vibration.
- The age ranged between 35 and 77 years with a mean=64,27±6,8 years, and 67,2% of patients were more than 60 years old, and that may depends on many factors, one of them is the lost of strength and flexibility of tissues and muscles with age, in addition to the prolonged use of voice and frequent exposure to the pollution and environmental factors which damage the epithelium of vocal cord, and we can't forget the hormonic changes which result in mucosal dryness and histologic changes in the epithelium.
- Our study showed that chronic exposure to external factors such as smoking, alcohol and the presence of laryngopharyngeal reflex leads to molecular changes in the body, irritation and redness of the mucous, which leads over time to abnormal proliferation of cells, which in turn leads to leucoplakia of the vocal cord.
- Significant differences were found in the study groups according to smoking, 83,3% of leucoplakia recurrent cases were smokers, and current smokers had more risk to recurrence with an odds ratio 4,7 time more than nonrecurrent cases, no significant differences were found according to the alcoholism and the presence of laryngopharyngeal reflex.
- Hoarseness was the most presenting symptom (89,7%), since the histologic changes in the vocal cord epithelium with the mucosal irritation cause the voice changes.
- Significant differences were found in the recurrence rate according to the lesion extension, 58,3% of recurrent cases had a lesion that extend over more than 50% of the vocal cord with an odds ratio 3,4% time more than nonrecurrent cases.
- No significant differences were found in recurrence rate according to the morphologic changes.
- We have analyzed the relationship between the histopathologic results and the vocal cord leucoplakia, 46,6% of biopsies were hyperplasia, 39,6% were dysplasia, 18,9% of dysplasia were mild and 13,8% were carcinoma. After 18 months, results showed significant differences according histopathologic results. 54,2% of leucoplakia recurrent cases have had moderate or severe dysplasia or carcinoma and those had more risk of

recurrence with an odds ratio7,9 time more than nonrecurrent cases. As many studies have showed that the malignant transformation of leucoplakia was directly related to the degree of histopathologic changes, and thus the presence of moderate and severe dysplasia considered the strongest prognostic factor in the recurrence and malignant transformation of leucoplakia.

- In a study conducted by Xu.J et al(2021)[11], neither leucoplakia location nor extension were found to be related to the histopathologic changes' degree. however, Significant differences were found in the relation between morphologic and histopathologic changes(p value<0,01). Their study was correlated with our study as the histopathologic changes play a prognostic role in the malignant transformation of leucoplakia. Jabarin et al (2018)[14] found that smoking and severe dysplasia in the first biopsy result are significant prognostic factors for squamous cell carcinoma. Chi. W et al in their study (2016)[12] found that bilateral vocal cords lesions have more tendency for recurrent and malignant transformation and that wasn't correlated with our study, the reason might be our relatively small sample size. Moreover, they found that Histopathologic changes degree had a significant role in increasing recurrence and malignant transformation rate and that was correlated with our study.

CONCLUSION

The patient should be informed of the possibility of leukoplakia reoccurring and becoming malignant if the patient is a smoker, and/or has vocal cord leukoplakia with a lesion of more than half of the vocal cord and/or moderate or severe dysplasia on histological biopsy result, as they all prognostic factors in the recurrence and malignant transformation.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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