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Letter to the editor

SINONASAL INVERTED PAPILLOMA: FACTORS AFFECTING RECURRENCE

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Summary

In this letter to the editor the authors would analyze some elements that could be risk factors for relapse of sinonasal inverted papilloma and search for an effective relationship between them and the representation of the tumor.
In this manuscript the authors updated our data, studying further 9 patients from 2012 until nowadays, taken into consideration age, sex, personal history of cigarette smoking and cancer staging, based on literature suggestion.

Introduction

The inverted papilloma (IP) is a benign neoplasm of epithelial nature of the respiratory mucosa of the nose and paranasal sinuses with a peculiar pattern of growth towards the stroma beneath the mucosa [1]. Its incidence is 0.6 to 1.5 cases per 100,000 inhabitants per year. It occurs most commonly between 40 and 70 years, with a mean age at diagnosis of 50 years, more frequently in males (M: F = 5.2: 1). Although a benign tumor, it has a peculiar behavior characterized by local aggression, risk of malignant degeneration (5-15%) and risk of recurrence (0-50%).

Objective to the study

The study aims to analyze, in a sample of 45 patients, some elements that we suspected to be risk factors for relapse and search for an effective relationship between them and the representation of the tumor. Two years later, we presented a study on the same population, analyzed until 2012, focusing on surgery technique as the main

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factor conditionig IP's relapses [2]. In this manuscript we updated our data, studying further 9 patients from 2012 until nowadays, taken into consideration age, sex, personal history of cigarette smoking and cancer staging, based on literature suggestion.

Material and Methods

In this letter to the editor we have examined and enriched a 45 record of patients treated over a period of time of 13 years (2002-2015) at the UO Otorhinolaryngology of the University Hospital "Paolo Giaccone" of Palermo. Of these patients, 32 to date have not relapsed (Group NR), while 13 have gone through at least one relapse (Group R). 7 patients of Group B had undergone the first surgery at a different hospital.
After surgery, patients were followed by endoscopic control every three months for the first year, every four / six months for at least five years and then annually.

Results

As for the age, in Group NR average age of patients is 59 years (12.98 ± SD; range 34-83 years). In Group R, however, the average age of patients at the time of first presentation is 51.7 years (SD ± 10.26; range 35-66 years). To compare the means is used a T test, bilateral to a confidence level a = 0.05. The p-value obtained was 0.051 (> 0.05), therefore it is not possible to state the statistical significance between the means of the age of the two groups. Considering the sex of all patients in the sample, men accounted for 80% (36 pcs), while women 20% (9 pcs). The distribution in the two groups according to sex is the following: Group NR: 29 males (91%), 3 females (9%); Group B: 7 males (54%), 6 females (46%). It was calculated the odds ratio (OR = 8.29) and 95% confidence interval for the odds ratio (95% CI: 1.65 to 41.58) that are statistical significant. Another data analyzed as a risk factor is cigarette smoking. Our sample included 15 smokers, 18 former smokers and 12 non-smokers, distributed in the two groups in the following way: Group NR: 11 smokers (34%), 13 former smokers (41%), 8 non-smokers (25%); Group R: 4 smokers (31%), 5 former smokers (38%), 4 non-smokers (31%). Given the distribution of the three categories of patients virtually comparable in the two groups, it was possible to conclude that cigarette smoking does not affect inverted papilloma' s recurrences, also without any statistical analysis. Of the 45 patients, 26 were subjected to CT and / or MRI at the UO Diagnostic Imaging our Polyclinic, the remaining came to our attention already equipped with radiological documentation. In none of the patients examined it was suspected the presence of malignancy after the analysis of radiological findings. The staging system employed was the Krouse's one (table 1),based on location and extention of the mass.[3] Patients taking into account the entire sample, as follows: 7 T1; 21 T2; 17 T3; 0 T4. The distribution in the two groups is the following: Group NR: 5 T1 (16%), 17 T2 (53%), 10 T3 (31%); Group R: 2 T1 (15%); 4 T2 (31%); 7 T3 (54%). The risk of recurrence according to the clinical stage was determined by calculating the odds ratio of T3 compared with T2 (OR = 2.98) and 95% confidence intervals (95% CI: 0.69 to 12, 76). Since the confidence interval contains the value 1, we can not say that a tumor at an early stage T3 has a greater risk of recurrence than T2.

Discussion

The propose of our study is not limited exclusively to the research of the risk factors for recurrence, but also wants to identify a personalized follow-up based on the individual characteristics of each patients.
In our sample, recurrence occurred in 13 of 45 patients analyzed (29% of cases), as literature data (5-30%).[4,5] Relapses, in most cases, arise within the first five years, although they have been observed up to 20 years after the first presentation. In our sample of 13 cases of recurrences, 9 pcs (69.2%) were detected in the first 5 years, while the others (30.8%) in a period between 6 and 13 years.
As for the age, it was noted a slight difference between the average age of pa-

tients in group NR (59 years) and that of patients of Group R(52 years old) at the time of the first operation .
Hence, patients who have relapsed, at the time of first presentation, were younger than those in which the tumor occurred only once.
However, the result of the statistical test (T test) did not yield the expected results, and so we could not confirm the hypothesis that younger age predisposes to recurrence. It is however to be noted that the value of p was greater than the expected value of only 0.001. For this reason we believe that, despite our inability to confirm a relation between age and the risk of recurrence, this is a parameter to be explored in other studies with larger samples.
Another factor considered is the sex. In the whole sample we have 31 males and 9 females, with a ratio of 4: 1. As it might be expected given that it is a cancer that affects mostly men. Looking at sex of patients in the two groups separately, we observe a prevalence of women in Group R compared to Group NR. The statistical analysis (OR and 95% CI) has confirmed the suspicion, allowing us to declare that in our sample, the women had a eight times greater risk of relapse than men. We can therefore say that female sex is a risk factor for recurrence.
We have put interest in the attitude to cigarette smoke, since has been shown a correlation between smoking and the malignant transformation of inverted papilloma.
We have analyzed the data, dividing the patients in smokers, former smokers and nonsmokers, and evaluating them separately in the two groups. Data analysis allowed us to rule out effects of cigarette smoking on recurrence of inverted papilloma. Based on Krouse's staging system we analyzed our patients and calculated the risk of relapse in case of T3 patients in comparison with T2. In our sample, in case of T3 tumor, there was a probability of recurrence nearly three times higher than patients in T2. However, due to small sample, this result was not statistically significant. For this reason, according to the available data there is not a correlation between clinical stage and recurrence.
It should be noted, also in this population, that we could get more meaningful results expanding our case series. This situation, it is reasonable under the same criteria of staging. It is clear, in fact, that a tumor stage T3, which can also be extended to the sphenoid or frontal, it is more difficult to be attacked from the

Staging System for Inverted Papilloma	
T1	Tumor totally confined to the nasal cavity, without extension into the si-nuses. The tumor can be localized to one wall or region of the nasal cavity, or can be bulky and extensive within the nasal cavity, but must not extend into the sinuses or into any extranasal compartment. There must be no con-current malignancy
T2	Tumor involving the ostiomeatal complex, and ethmoid si-nuses, and/or the medial portion of the maxillary sinus, with or without involvement of the na-sal cavity. There must be no concurrent malignancy
T3	Tumor involving the lateral, inferior, superior, anterior, or pos-terior walls of the maxillary sinus, the sphenoid sinus, and/or the frontal sinus, with or without involvement of the medial portion of the maxillary sinus, the ethmoid sinuses, or the nasalcavity. There must be no concurrent malignancy
T4	All tumors with any extranasal/extrasinus exension to invol-ve adjacent, con-tiguous structures such as the orbit, the intracranial compartment, or the pterygomaxillary space. All tumors associated with malignancy

Table 1: The Krouse staging system (reproduced from: Krouse et al.,Laryngoscope.2000)

surgical point of view, with increased risk of tumor persistence. The last diagnostic test performed is histological examination. A feature that is immediately evident is the absolute absence of malignancy in inverted papillomas examined in our sample. This is in contrast with literature data, in which the percentage are different[6].

Conclusions

Among the factors that we analyzed cigarette smoking does not affect the appearance of recurrence; the female increases the risk of relapse; there was a correlation between clinical stage and age, but this was not statistically significant. In conclusion, it is worth recalling that, given the wide possibility of recurrence even after many years, the data obtained from this evolution of the study published in 2013 need to be validated by a long-term follow-up in which our patients are still subjected.

References

1. Hyams VJ. Papillomas of the nasal cavity and paranasal sinuses. A clinicopathological study of 315 cases. Ann Otol Rhinol Laryngol 1971;80(2):192-206.
2. Marchese D, Aleo G, Gallina S, Dispenza F, Speciale R. Personal experience on inverted papilloma surgical treatment. Euromediterranean Biomedical Journal, 2013 8(17):85-90.
3. Krouse JH. Development of a staging system for inverted papilloma. Laryngoscope. 2000 Jun;110(6):965-8.
4. Lane AP, Bolger WE. Endoscopic management of inverted papilloma. Curr Opin Otolaryngol Head Neck Surg 2006;14 (1):14-8.
5. Wolmard PJ, Ooi E, van Hasselt CA, Nair S. Endoscopic removal of sinonasal inverted papilloma including endoscopic medial maxillectomy. Laryngoscope. 2003;113(5):867-873.
6. Busquets JM, Hwang PH. Endoscopic resection of sinonasal in-verted papilloma: a meta-analysis. Otolaryngol Head Neck Surg. 2006;134(3):476-482