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Unique clinical and prognostic behavior of patients diagnosed with combined exophytic and inverted papilloma histologic subtype

Jakob L. Fischer MD[1,2] | Charles A. Riley MD[1,2] | Ashutosh Kacker MD[3]

[1]Department of Otolaryngology—Head and Neck Surgery, Walter Reed National Military Medical Center, Bethesda, Maryland, USA

[2]Department of Surgery, Uniformed Services University of the Health Sciences, Bethesda, Maryland, USA

[3]Department of Otorhinolaryngology, Weill Cornell Medical College, New York, New York, USA

Correspondence
Jakob L. Fischer, Department of Otolaryngology—Head & Neck Surgery, Walter Reed National Military medical Center, 8901 Wisconsin Ave, Building 19, Floor 5, Bethesda, MD 20889, USA.
Email: jakob.l.fischer.mil@health.mil

Abstract

Objectives: To evaluate the clinical and prognostic behaviors of sinonasal papillomas.

Methods: Patients diagnosed with sinonasal papilloma were reviewed between 2001 and 2016 at a tertiary rhinology practice. Using pathology-specific electronic medical record software, patients diagnosed with sinonasal papilloma were identified. Four subcategories of this lesion were identified: inverting (IP), exophytic (EP) oncocytic (OP) and inverting + exophytic (IP + EP) papillomas.

Results: A total of 107 patients were identified with unique sinonasal papilloma diagnoses. Of these, the majority were diagnosed with IP (87, 81.3%). The subpopulation of patients co-diagnosed with IP and EP (IP + EP) was unique with respect to clinical presentation and prognosis relative to both the IP and EP alone populations. IP + EP patients (5, 4.7%) were older with an average age of 75.25 years compared to 45 (EP) and 55.26 (IP), $p < .0001$. IP + EP patients more often presented with epistaxis (60%) compared to 33.3% (EP) and 4.6% (IP). Finally, all IP + EP patients had at least one recurrence of their disease, compared to 33.3% (EP) and 28.5% (IP).

Conclusions: Each histopathologic subtype of sinonasal papilloma has unique clinical characteristics and recurrence rates after surgical resection. The subpopulation of patients diagnosed with IP + EP tends to be older, more likely to present with epistaxis, and more likely to recur. Additional investigation and analysis of this subpopulation is warranted.

Level of Evidence: 4.

KEYWORDS

exophytic papilloma, inverting papilloma, oncocytic papillomas, Schneiderian papilloma, sinonasal mass, sinonasal neoplasm, sinonasal papilloma

1 | INTRODUCTION

In the most recent update of the World Health Organization classification of head and neck tumors in 2017, the term "Schneiderian papilloma" was eschewed in favor of the non-eponymous "sinonasal papilloma."[1]

This data were presented on May 2018 at the Combined Otolaryngology Sections Meeting in National Harbor, Maryland, USA as a poster presentation.

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These papillomas arise from ectodermally-derived respiratory mucosa and represent 0.5%–4% of all nasal tumors and demonstrate a propensity for recurrence, local invasion, and the potential for malignant transformation.[2,3] There are three distinct types of papillomas: inverted (IP), exophytic (EP), and oncocytic papillomas (OP). Histologically, IPs contain endophytic features, EPs demonstrate fungiform and squamous features, and OPs showing cylindrical cell and columnar features.[2] Previously these lesions were often confused with respiratory epithelial lesions such as respiratory epithelial adenomatoid hamartoma or seromucinous hamartomas.[4] In the last two decades, sinonasal papillomas have been more readily and easily differentiated from respiratory epithelial lesions.

Previous literature has shown that IP is the most common papilloma subtype, followed by EP, and with OP occurring rarely.[2] Within the last few years, multiple publications have noted a shift in the relative incidence of histological papilloma subtypes such that IP accounts for 80%–96% of sinonasal papilloma diagnoses.[5–7] Each histologic subtype has unique clinical characteristics which can be partially predicted by the anatomical subsite affected. Patients with EP tend to present most commonly with nasal septal lesions and are more likely to result in epistaxis compared to IP and OP which tend to present with nasal congestion and facial pressure given their tendency to arise within the paranasal sinuses, specifically the maxillary sinus.[8] There is a paucity of literature specifically examining mixed histologic subtypes and their specific clinical features.

The purpose of this study was to evaluate the natural history of sinonasal papillomas and determine risk factors for recurrence and unique clinical and behavioral features that may aid in differentiating histological subtypes and to specifically evaluate those patients with mixed histologic subtypes and determine unique clinical features associated with this diagnosis.

2 | MATERIALS AND METHODS

This study was approved by the institutional review board of Weill Cornell Medical College. A comprehensive search of the electronic medical record was conducted for the years 2001–2016 to identify all patients treated for sinonasal papilloma by the senior author (AK). All adult patients presenting with a newly diagnosed sinonasal papilloma during this time were included. Patients with malignant pathology or those having undergone previous treatment for sinonasal papilloma or malignancy were excluded from review. Medical records were reviewed for demographics, clinical, and surgical details. Clinical notes were reviewed upon presentation to the otolaryngologist as well as all follow-up reports. Patient records without sufficient detail or those in which the subtype sinonasal papilloma were not characterized were excluded. Surgical pathology of all patients included in the database was reviewed by an experienced head and neck surgical pathologist. A tumor was defined as containing multiple subtypes if there was at least 10% presence of a second histologic subtype within the specimen.

3 | RESULTS

A total of 107 patients were identified with unique sinonasal papilloma diagnoses, of which 77 (72%) were male with a mean age of 55.9 (Table 1). The majority of patients were diagnosed with IP (87, 81.3%). Amongst those patients diagnosed with IP, 5 (4.7%) patients demonstrated synchronous diagnoses of IP and EP (IP + EP). The remainder of the patients were diagnosed with EP alone (9, 8.4%) and OP (6, 5.6%). Patients with IP + EP were older on average (75.3 years) than patients with other diagnoses, $p < .0001$. There were no differences among histologic subtypes based on tobacco use history, $p = .67$. The clinical presentation of the lesions varied by diagnosis. Patients diagnosed with IP and OP most commonly presented with nasal congestion. EP presented mostly commonly as a nasal mass or epistaxis, while patients with EP+ IP presented with epistaxis 60% of the time. The anatomical subsite of the sinonasal mass varied between specific pathologic diagnoses. All patients with OP presented with a mass within the maxillary sinus (9, 100%). Patients with IP + EP (2, 60%) and EP (6, 66.7%) most commonly presented with nasal septal lesions. IP demonstrated more variability in affected anatomical subsites but presented most commonly in the maxillary sinus

TABLE 1 Patient demographics.

	Total	OP	EP	IP	EP + IP	*p*-value
Total number	107	6	9	87	5	
Mean Age	55.87 ± 13.2	64.2 ± 5.8	45 ± 16.7	55.3 ± 11.7	75.3 ± 11.4	<.0001
Gender						
Male	77 (72%)	5 (83.3%)	7 (88.8%)	63 (72.4%)	2 (40%)	
Female	30 (28%)	1 (16.7%)	2 (22.2%)	24 (27.6%)	3 (60%)	.38
Tobacco use						
Current smoker	38 (35.5%)	0 (0%)	2 (22.2%)	6 (6.9%)	1 (20%)	
Ever smoker	37 (34.6%)	1 (16.7%)	2 (22.2%)	32 (36.8%)	2 (40%)	
Never smoker	16 (15%)	3 (50%)	5 (55.6%)	35 (40.2%)	2 (40%)	
Unknown	16 (15%)	2 (33.3%)	0 (0%)	14 (16.1%)	0 (0%)	.67

Abbreviations: EP, exophytic papilloma; IP, inverted papilloma; EP + IP, exophytic and inverted papilloma; OP, oncocytic papilloma.

TABLE 2 Presenting symptoms, primary tumor location, and local recurrence rates for each tumor histologic subtype.

	Tumor type *n* (%)			
	OP ($n = 6$)	EP ($n = 9$)	IP ($n = 87$)	EP + IP ($n = 5$)
Presenting symptoms				
Mass	0 (0%)	3 (33.3%)	9 (10.3%)	2 (40%)
Congestion	3 (50%)	2 (22.2%)	30 (34.5%)	1 (20%)
Hyposmia	0 (0%)	1 (11.1%)	5 (5.8%)	0 (0%)
Epistaxis	1 (16.7%)	3 (33.3%)	4 (4.6%)	3 (60%)
Crusting	1 (16.7%)	0 (0%)	0 (0%)	1 (20%)
Rhinorrhea	2 (33.3%)	0 (0%)	8 (9.2%)	0 (0%)
Headache	2 (33.3%)	0 (0%)	8 (9.2%)	0 (0%)
Imbalance	0 (0%)	0 (0%)	2 (2.3%)	0 (0%)
Cough	0 (0%)	0 (0%)	2 (2.3%)	0 (0%)
Primary tumor location				
Septum	0 (0%)	6 (66.7%)	2 (2.3%)	3 (60%)
Maxillary sinus	6 (100%)	1 (11.1%)	37 (42.5%)	1 (20%)
Ethmoid Sinus	2 (33.3%)	0 (0%)	27 (31.0%)	1 (20%)
Sphenoid sinus	1 (16.7%)	0 (0%)	9 (10.3%)	1 (20%)
Lateral nasal wall	0 (0%)	1 (11.1%)	17 (19.5%)	2 (40%)
Frontal sinus	0 (0%)	0 (0%)	7 (8.1%)	0 (0%)
Local recurrence rates	3 (50%)	3 (33.3%)	23 (26.4%)	5 (100%)

Abbreviations: EP, exophytic papilloma; IP, inverted papilloma; EP + IP, exophytic and inverted papilloma; OP, oncocytic papilloma.

(37, 42.5%) (Table 2). All patients underwent endoscopic surgical resection of their primary lesions with negative margins at the conclusion of surgery.

Recurrence rates of patients varied largely based on papilloma subtype. Three (50%) patients with OP developed a recurrence compared to 3 (33.3%) patients with EP and 23 (26.4%) patients with IP. In contrast, all patients (5, 100%) diagnosed with IP + EP developed recurrence of disease (Table 2).

4 | DISCUSSION

Sinonasal papillomas are benign lesions within the sinonasal tract that represent 0.5%–4% of all nasal tumors and demonstrate a propensity for recurrence, local invasion, and the potential for malignant transformation.[2,3] This study sought to evaluate the natural history of sinonasal papillomas and examine unique clinical and behavioral features based on histologic subtype. Our results support the hypothesis that different histological subtypes had different clinical presentations and different recurrence rates. Moreover, we identified a unique patient population with IP + EP that tended to present in older patients and demonstrated a higher propensity toward disease recurrence.

The specific pathogenesis of sinonasal papillomas remains unclear; however, the human papilloma virus (HPV) has been implicated as having a role in the development of sinonasal papillomas.[9] Several studies have postulated that chronic rhinosinusitis also plays a role in the development of sinonasal papillomas.[2,10] There are three distinct histopathological subtypes: IP, EP, and OP. Patients may also present with mixed tumors containing multiple histopathological subtypes, such as IP + EP in our patient population. IPs tend to appear as firm, gray lesions with multinodular and polypoid appearance on gross pathology.[9] Histologically, IPs have inverted or endophytic growth that is caused by squamous maturation of thickened epithelium inverting into the stroma with its own distinct basement membrane.[2] Grossly, EPs are gray-tan, "mushroom-shaped," verrucous papillary projections that arise from the anterior nasal septum. Although EPs have a similar cellular composition to IPs, they have branching exophytic proliferations with a fibrovascular core lined by well-differentiated squamous epithelium and formation of keratin. On gross analysis, OPs are soft, fleshy, pink papillary tissue that exhibit exophytic and endophytic growth patterns with pseudostratified columnar or cylindrical cells. The growth characteristics of mixed histology papillomas are less clear with a distinct paucity of literature specifically examining these histologic subtypes.

Current literature estimates that IP accounts for 80%–96% of sinonasal papilloma diagnoses.[5–7] Our patient population was consistent with this data, with IP accounting for 81.3% of tumors.

Patients diagnosed with IP, EP, and OP demonstrated a male predominance with an average age of presentation within the 6th decade of life, consistent with previously cited literature.[2]

Unique to our patient population was those diagnosed with IP + EP. These patients tended to be much older than those with IP or EP alone, presenting most commonly within the 8th decade.

Presenting symptoms varied substantially based on histologic subtype. IP + EP patients most commonly presented with epistaxis

followed by presence of nasal mass. This was similar in patients diagnosed with EP alone. Patients with IP and OP were more likely to present with nasal congestion, while rhinorrhea and headache were more commonly found in OP. This may at least be attributable to the location of these specific histologic subtypes. EP and IP + EP patients presented most commonly with septal lesions which would be more likely to cause epistaxis and identified as a nasal mass compared to IP and OP which tended to present in the paranasal sinuses most commonly. This may lend IP and OP toward presenting with nasal congestion and headache as these lesions may expand the medial wall of the maxillary sinuses and cause obstruction.[8]

Historically conservative surgical therapy for sinonasal papillomas consisted of endonasal polypectomies, which resulted in exceedingly high recurrence rates.[11] These procedures were then replaced by more invasive open approaches including medial maxillectomy via a lateral rhinotomy approach or midfacial degloving.[12] The complete removal of the lesion is paramount, and involves the removal of involved mucosa as well as mucoperiosteum. The advancements of endoscopic sinus surgery have revolutionized the treatment of this pathology over the last 2 decades, by providing a disease clearing surgery without the need for trans-facial incisions. A meta-analysis by Goudakos, et al.[12] examined surgical techniques for inverted papillomas and showed a lower recurrence rate with the endoscopic group at 13.8% compared to 18.7% in the open group. The main reason for recurrence is often inadequate resection at the site of origin.[11,13] Previously published recurrence rates were 12%–17% for IP, 22%–50% for EP, and 25%–35% for OP.[14] This was similar in our analysis: 26.4% with IP, 33.3% with EP, and 50% with OP developing recurrence.

Patients diagnosed with IP + EP were unique amongst our patient population as demonstrating a recurrence rate of 100% despite having a similar clinical presentation as EP, albeit with a small sample size. To date, no study has directly evaluated comparative rates of recurrence in patients with simultaneous diagnosis of multiple sinonasal papilloma subtypes. This is likely due to the rarity of these findings. Archang, et al. examined risk factors for recurrence in 118 sinonasal papilloma patients, 5 of which presented as mixed tumors with only one IP + EP patient. They found that younger age at presentation and previous sinonasal surgery were the greatest risk factors for recurrence but did not comment specifically on recurrence rates in patients with mixed histologic subtypes.[7] In our study population, patients with IP + EP were on average 10–20 years older than those with other sinonasal papillomas. Further study with larger populations of mixed histologic sinonasal papillomas would be necessary to further evaluate recurrence rates among this specific patient population.

As this study is a retrospective analysis, it is subject to several limitations. First, the sample size is small which introduces bias to the study and limits the ability to perform multivariate analysis that may provide more details regarding specific clinical factors for recurrence. This may be aided by future reviews with larger population sizes. Second, recurrence rates may be underreported, since sinonasal papillomas can be slow growing; some patients may develop a recurrence outside the range of this study. Data regarding clinical staging was also not available for review. Patients with more advanced papilloma may be at increased risk of recurrence and this should be further evaluated in future studies. Further analysis of these populations is warranted with future directions that may involve the genetics of those sinonasal papillomas that repeatedly recur, are particularly extensive, or have malignant potential. Additional evaluation is necessary to determine the specific role of HPV in the pathogenesis of sinonasal papillomas.

5 | CONCLUSIONS

Sinonasal papillomas are rare sinonasal masses that can present as distinct histopathologic subtypes or as mixed tumors. Each histopathologic subtype demonstrates differences in clinical presentation, anatomical sites of involvement, and recurrence rates. The subpopulation of patients diagnosed with IP + EP tends to be older, more likely to present with epistaxis and more likely to recur compared to diagnosis of EP or IP alone. Further evaluation of larger populations of mixed histologic sinonasal papillomas are necessary to further evaluate these findings.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

ORCID

Jakob L. Fischer https://orcid.org/0000-0002-8896-671X
Charles A. Riley https://orcid.org/0000-0002-1993-7018

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