

# Oncocytic Schneiderian papillomas: Clinical behavior and outcomes of the endoscopic endonasal approach in 33 cases

Apostolos Karligkiotis, MD,<sup>1\*</sup> Maurizio Bignami, MD,<sup>2</sup> Paola Terranova, MD,<sup>2</sup> Stefania Gallo, MD,<sup>2</sup> Francesco Meloni, MD,<sup>1</sup> Giovanni Padoan, MD,<sup>2</sup> Davide Lombardi, MD,<sup>3</sup> Piero Nicolai, MD,<sup>3</sup> Paolo Castelnuovo, MD<sup>2</sup>

<sup>1</sup>Department of Otorhinolaryngology, University of Sassari, Sassari, Italy, <sup>2</sup>Department of Otorhinolaryngology, University of Insubria, Varese, Italy, <sup>3</sup>Department of Otorhinolaryngology, University of Brescia, Brescia, Italy.

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**ABSTRACT:** *Background.* The purpose of this study was to evaluate the clinical behavior of oncocytic Schneiderian papillomas in relation to the rate of malignant transformation and recurrences and to report the long-term results of the endoscopic endonasal treatment.

*Methods.* A retrospective analysis was carried out on patients with oncocytic papilloma, endoscopically managed over the past 20 years, at 2 university centers following a uniform policy.

*Results.* Thirty-three patients were treated between November 1991 and December 2010. The mean follow-up period was 62 months. We observed 2 cases of persistence (6%) at the maxillary sinus level. Both

of these patients underwent endoscopic surgical revision. Squamous cell carcinoma (SCC) was observed in 1 patient (3%).

*Conclusion.* The endonasal endoscopic technique proved to be a safe and effective approach for the treatment of oncocytic papillomas. An oncocytic papilloma is not to be considered a negative prognostic factor in terms of malignant transformation or recurrence. © 2013 Wiley Periodicals, Inc. *Head Neck* 00: 000–000, 2013

**KEY WORDS:** oncocytic Schneiderian papilloma, endoscopic endonasal approach, inverted papilloma, skull base, sinonasal benign tumors

## INTRODUCTION

Oncocytic Schneiderian papillomas (OSPs), also known in the literature as cylindrical cell papillomas, are rare sinonasal benign tumors arising from the Schneiderian membrane and represent the rarest (3% to 5%) of the 3 histologic entities of papillomas described by Hyams.<sup>1</sup> They show many features in common with the inverted papillomas (IPs) but microscopically they are characterized by tall, columnar epithelium composed of oncocytes.<sup>2</sup> OSPs are equally distributed between the sexes and occur mostly in patients over 50 years of age<sup>3</sup>; they arise typically from the lateral nasal wall or in the paranasal sinuses, usually in the maxillary or the ethmoid ones, as unilateral lesions (Figure 1) and may extend into contiguous areas such as the orbit and the skull base. Their clinical behavior is in parallel with IPs because of local recurrence and association with malignancy. Malignancies arising in OSPs are rare events, although their incidence seems to be higher (10% to 17%) than in IPs (5% to 10%),<sup>4</sup> with invasive squamous cell carcinoma (SCC) being the most frequently reported tumor. Mucoepidermoid, small cell, and undifferentiated carcinomas have also been described.<sup>5</sup> A systematic review of the literature supports endoscopic resection as a favorable

option for most cases of sinonasal papilloma, revealing a lower recurrence rate compared to external approaches.<sup>6</sup>

In this study, we analyzed all patients affected by OSP and treated at 2 university centers following a uniform policy for the management of Schneiderian papillomas. The purpose was to add our experience to the small amount of data currently available on this topic and to compare the clinical behavior of OSP and the outcomes of the endoscopic endonasal approach with the reports existing in the literature.

## MATERIALS AND METHODS

A total of 404 patients affected by sinonasal Schneiderian papilloma were treated in the Department of Otorhinolaryngology of the University Hospitals of Varese–Pavia and Brescia (Italy) between November 1991 and December 2011. In 33 of the patients, conclusive histology revealed the presence of OSP and this study focuses on this group. Three cases with features of both IP and OSP were also included in the study. In these latter patients, the lesion was defined as “mixed” and was ultimately classified as OSP because of the predominating oncocytic epithelium. The other 371 patients had a pathologic diagnosis of IP. All patients were fully informed about the method of treatment and gave their written consent to the therapy. A retrospective review was performed to evaluate age at diagnosis, sex, presenting symptoms, anatomic site of origin, rate of recurrence, and association with carcinoma. Inclusion in this study required a minimum follow-up of 12 months.

\*Corresponding author: A. Karligkiotis, Department of Otorhinolaryngology, University of Sassari, Azienda Ospedaliero Universitaria di Sassari, Viale San Pietro 43, 07100 Sassari, Italy. E-mail: alkis.karligkiotis@gmail.com

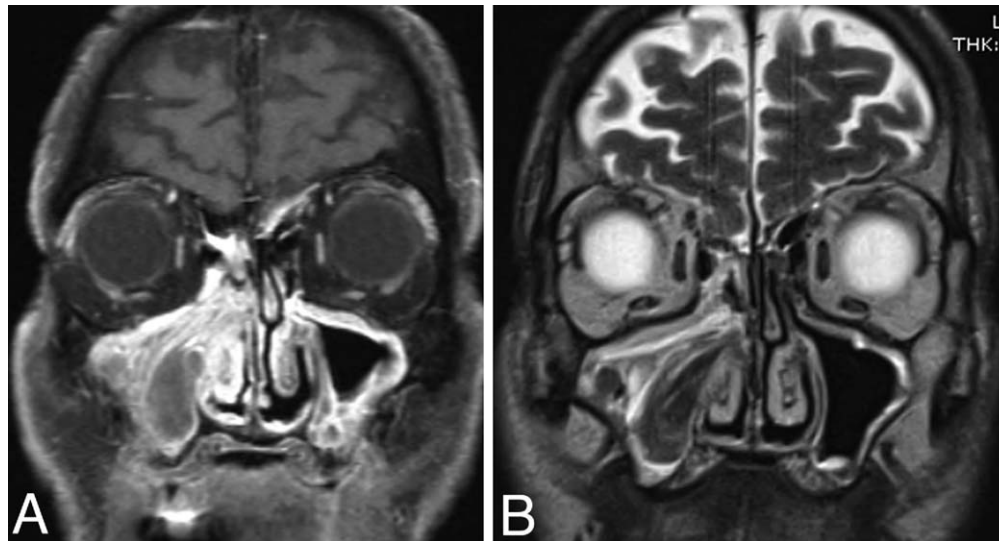


FIGURE 1. MR images of a right maxillary oncocyctic papilloma. T1-weighted image after gadolinium administration (A) and T2-weighted image (B) on the coronal plane.

The extension of the OSP was assessed preoperatively by nasal endoscopy and radiologic studies. All patients received radiological assessment by CT and/or MRI to better evaluate the tumor extension and to differentiate between inflammatory and tumoral involvement of the sinuses. After imaging evaluation, a biopsy under endoscopic control was performed in local anesthesia. All patients in the series were retrospectively staged using clinical, radiologic, and histopathological evaluations according to the Krouse<sup>7</sup> and Han et al<sup>8</sup> staging systems.

Endoscopic endonasal resection was the treatment of choice for all patients, and was performed with the patients under general anesthesia. Three different types of endoscopic resection were performed according to the classification used for IPs (Figure 2; Table 1).<sup>9</sup> Only 1 patient underwent a combined endoscopic approach with an osteoplastic flap because of massive frontal sinus involvement. One patient had an endoscopic duraplasty of the anterior skull base secondary to the intracranial intradural extension of the OSP; this case has been described previously.<sup>10</sup>

Postoperative follow-up was performed with nasal endoscopy every 2 months for the first year, every 3 months for the second year, every 6 months until the fifth year, and then once a year. Postoperative MRI was performed in the case of inadequate visualization of the primary sinus involved, because of scar tissue or when recurrence was suspected. Whenever suspicious tissue was observed, a biopsy was performed with the patient under local anesthesia. The study met the approval of the local board of medical ethics.

## RESULTS

The age of these patients ranged from 32 to 80 years (mean, 60 years); 19 patients were men (57.6%) and 14 were women (42.4%). Seven patients (21.2%) had undergone 1 or more procedures of nasal polypectomy before

definitive surgical treatment. Unilateral nasal obstruction was the most frequent symptom observed in 81.8% of patients, whereas rhinorrhea, epistaxis, and anosmia were observed in 39.4%, 24.2%, and 12.1% of patients, respectively. Diagnosis of OSP was established at the initial biopsy in 21 of 33 patients (63.6%), whereas 11 of 33 patients (33.3%) had preoperative diagnosis of IP. The discrepancy between diagnosis of IP made on initial preoperative biopsy and final postoperative histology of OSP may be because of: (1) the small size of the sample to examine, which may have led to diagnostic difficulties, (2) the presence of “mixed” IP-OSP epithelium, (3) the possible inexperience of the pathologist with this histological variant, and (4) the rarity of OSP. One patient (1 of 33; 3.1%) with bilateral OSP in massive polyposis was not submitted to initial biopsy. The primary site of origin of the OSP was the lateral nasal wall in the region of the middle meatus in 11 cases (33.3%); 17 lesions were on the right side (51.5%), 15 were on the left side (45.5%), and 1 was bilateral (3%). Nineteen patients had involvement of the ethmoid sinus (57.6%), 26 of the maxillary sinus (78.8%), 1 of the sphenoid sinus (3%), and 1 of the frontal sinus (3%). A higher incidence of OSP arising from or involving the maxillary sinus was also noted in other series.<sup>1,11,12</sup> According to the Krouse<sup>7</sup> and Han et al<sup>8</sup> classification systems, the OSPs were stratified, as presented in Table 2.

The surgical resection performed was based on the site of origin and extension of the tumor within the paranasal sinuses and nasal cavity. Eight patients (24.2%) underwent a type 1 resection, 12 patients (36.4%) underwent a type 2 resection, and another 12 patients (36.4%) underwent type 3 resection. Only 1 patient (3%) underwent a combined endoscopic-osteoplastic flap approach.

No intraoperative complications were observed. One patient (3%) needed a concomitant endoscopic skull base duraplasty because of an intracranial intradural extension of the OSP,<sup>10</sup> but this issue was preoperatively estimated

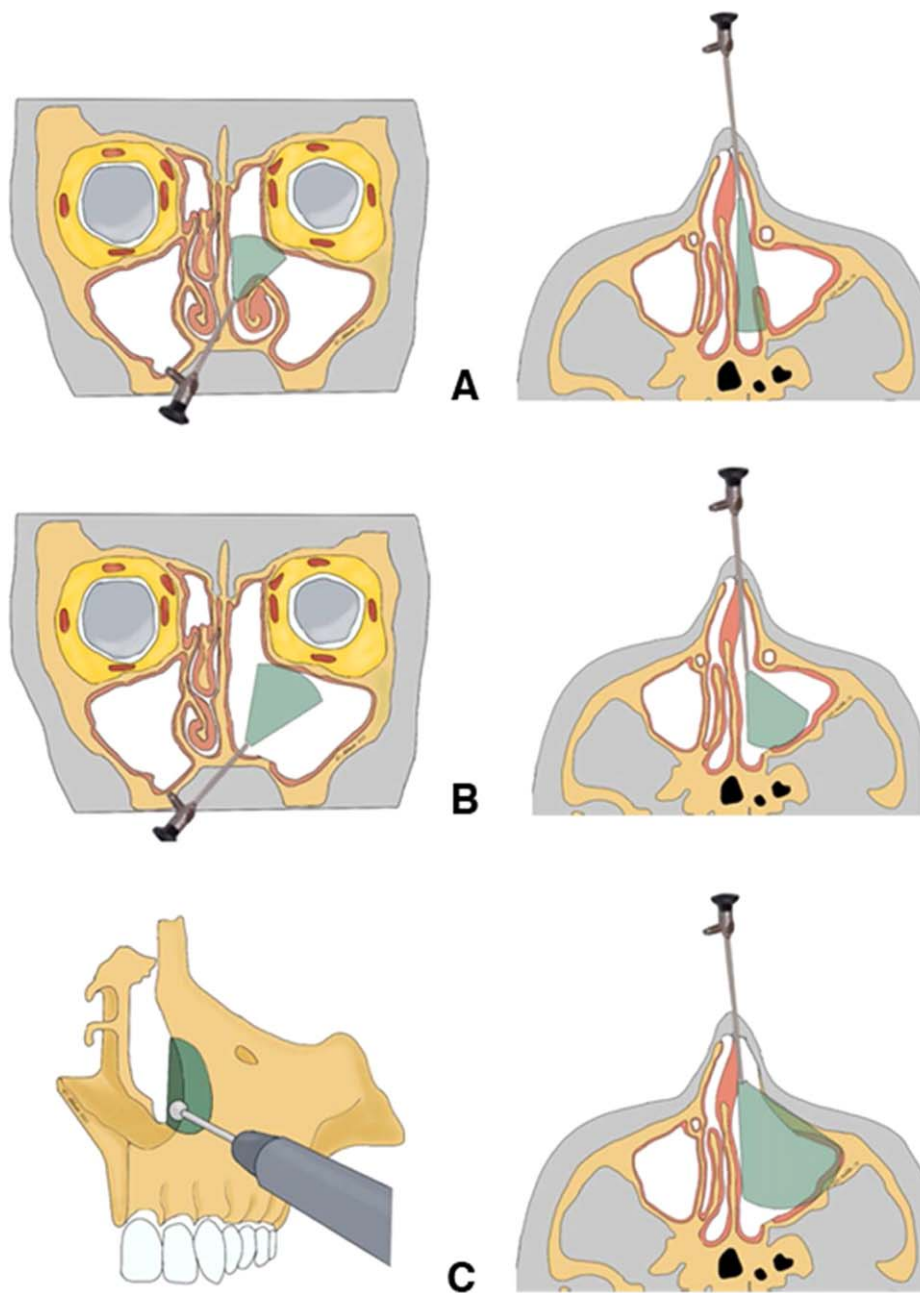


FIGURE 2. Endoscopic endonasal resections for oncocytic and inverted papillomas with ethmoidal and maxillary involvement (left nasal fossa). (A) Type 1 resection. (B) Type 2 resection. (C) Type 3 resection. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

and discussed with the patient. Delayed complications were identified in 3 patients (9.1%). In 2 patients, postoperative MRI showed the presence of a mucocele in the maxillary sinus; both patients underwent successful endoscopic marsupialization. In 1 case, postsaccal lacrimal pathway obstruction was treated by endonasal dacryocystorhinostomy with a lacrimal stent inserted for 2 months. In our experience, to avoid postsurgical stenosis of the lacrimal pathway, the duct must be transected 2 to 3 mm below the Bèraud–Krause valve with marsupialization of the upper part to prevent postoperative stenosis. The nasolacrimal duct transection has to be carried out with a

single cut. Multiple attempts with the scissors increase the risk of postoperative stenosis.<sup>13</sup>

The follow-up ranged from 138 to 12 months (mean, 62 months). No evidence of disease was observed in 94% of the patients (31 of 33 patients). Recurrence occurred in 2 cases (6%) after 20 and 46 months, respectively, from the first surgery. Both recurrences involved the maxillary sinus, which was the site of the primary lesion and were retreated endoscopically. One of these 2 patients initially presented a bilateral involvement of the nasal cavities and final histological analysis showed the presence of both OSP and IP patterns in nasal polyposis. During the

TABLE 1. Summary of surgical steps in the 3 types of endoscopic procedures.<sup>9</sup>

Type of endoscopic procedure	Surgical steps
1	Anterior and posterior ethmoidectomy, sphenoidotomy, large middle antrostomy, partial or complete middle turbinectomy, frontal sinusotomy (type I, IIA, IIB, or III according to Draf in relation to the extent of disease).
2	Anterior and posterior ethmoidectomy, sphenoidotomy, medial maxillectomy, partial or complete middle turbinectomy, frontal sinusotomy (type I, IIA, IIB, or III according to Draf in relation to the extent of the disease; $\pm$ nasolacrimal duct section).
3	Anterior and posterior ethmoidectomy, sphenoidotomy, endonasal Denker operation with nasolacrimal duct section, complete inferior and middle turbinectomy, frontal sinusotomy (type I, IIA, IIB, or III according to Draf in relation to the extent of disease).

follow-up, recurrence of the nasal polyposis was observed and biopsies performed during the polypectomy with the patient under local anesthesia revealed the presence of pure OSP. This patient underwent a second endoscopic resection under general anesthesia and, after 35 months of follow-up, is free of disease. Only 1 case (3%) of OSP associated with SCC was observed in our series, without evidence of disease after a follow-up of 27 months. In 1 patient, there was mild dysplasia and in another patient there was metaplasia.

## DISCUSSION

The classification of sinonasal papillomas has been controversial. The histomorphologically based classification formulated by Hyams<sup>1</sup> is the most accepted one, in which papillomas of the sinonasal tract are classified as IP, fungiform papilloma, and cylindrical cell papilloma. IP is the most common histological variant of papilloma of the sinonasal tract (Figure 3), whereas OSP is an uncommon, distinct variant, gaining its name by the onco-cytic nature of this lesion (Figure 4), which helped to replace the old term of cylindrical cell papilloma in 1984.<sup>2</sup>

In 1993, Kapadia et al<sup>5</sup> reported the largest series published to date, dealing with 150 cases of OSP in 800 sinonasal papillomas. Some smaller series (Table 3) and other single case reports have also been published in the literature.<sup>1,2,5,11,12,14-16</sup> We have treated a total of 404 patients with sinonasal papillomas; IP was present in 371 patients whereas 33 patients presented OSP. To our knowledge, this is the second largest case series of OSP presented in the literature and the first one to focus on the role of endoscopic endonasal resection in the treatment of this disease.

The clinical behavior of OSP is similar to that seen in IP with regard to local aggressiveness, malignancy coexistence, and a high recurrence rate. A study reviewing the literature in 2002 reported a recurrence rate in OSP ranging from 33% to 40% and malignant transformation in

10% to 17%.<sup>12</sup> In our series, malignant association was observed in 3%, which is in accordance with the largest series produced by Kapadia et al,<sup>5</sup> and only 2 cases (6%) needed revision surgery for persistent disease in the maxillary sinus. The only case of OSP with concomitant endocranial and orbital extension ever reported in literature is part of this series.<sup>10</sup>

The evolution of the endoscopic endonasal surgery over the last 2 decades has confirmed the efficacy of the

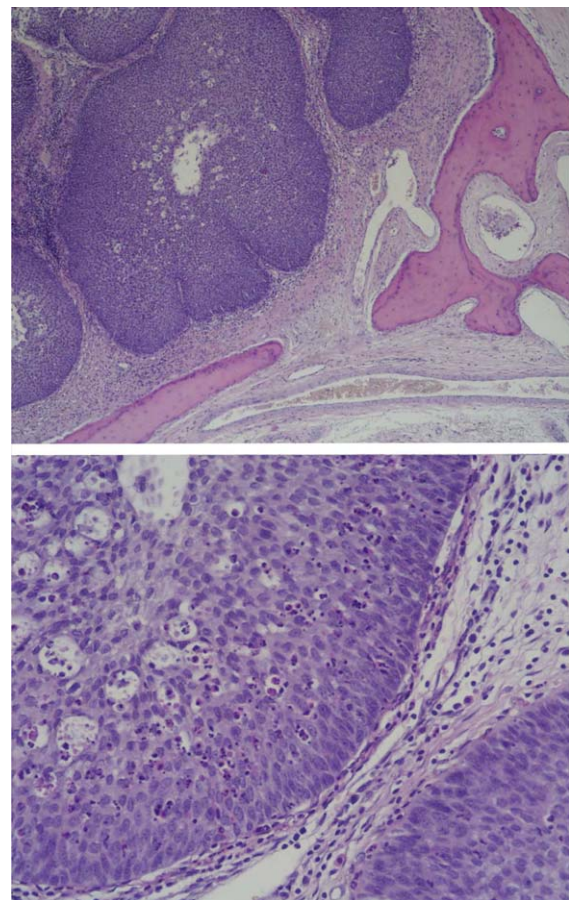
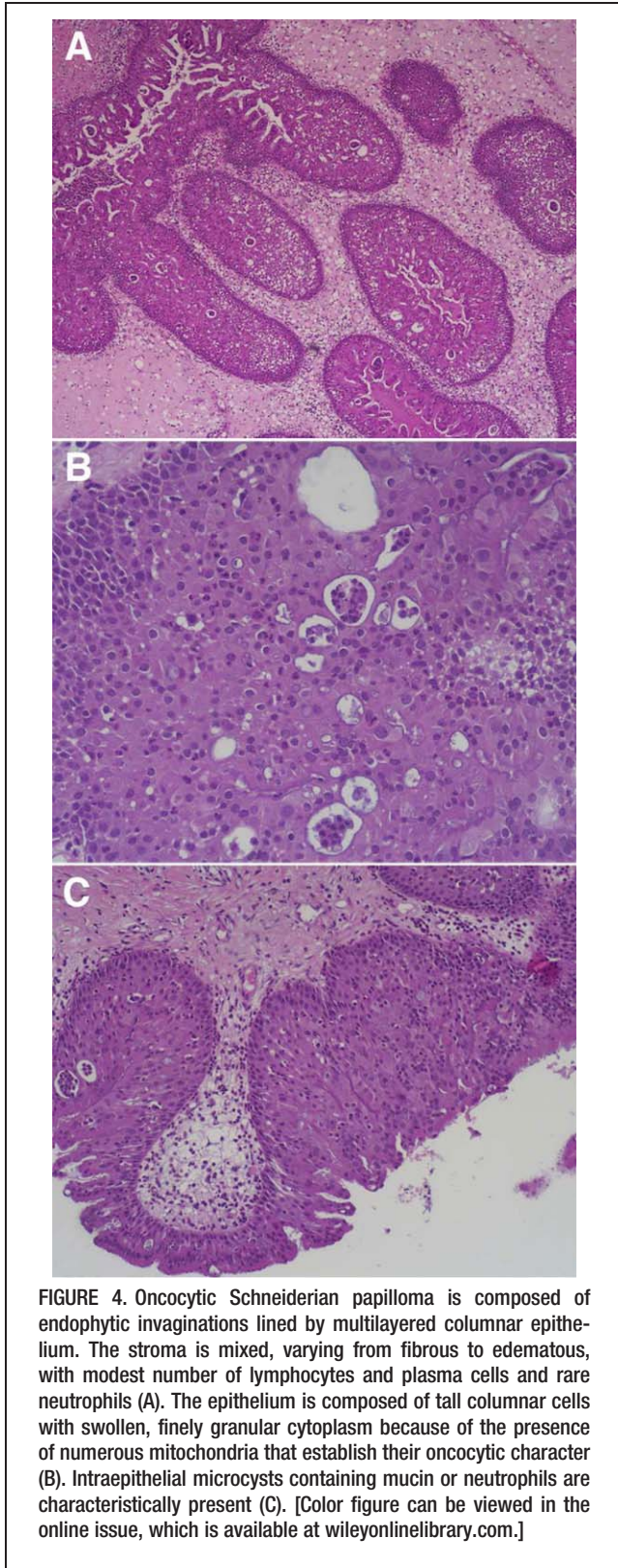


FIGURE 3. Inverted papilloma is characterized by ribbons of epithelium that grow endophytically into the underlying stroma. The multilayered non-keratinizing squamous epithelium alternates with columnar ciliated or transitional epithelium. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

TABLE 2. Distribution of patients ( $n = 33$ ) according to the Krouse<sup>7</sup> and Han et al<sup>8</sup> staging systems.

Krouse <sup>7</sup>	T1	T2	T3	T4
	1	6	24	2
Han et al <sup>8</sup>	Group I	Group II	Group III	Group IV
	9	22	1	1



technique in obtaining excellent control and is now considered the first choice in the treatment of IP.<sup>17</sup> Because OSP shares the same biological features with IP, we applied the same surgical treatment in this kind of tumor as well. It is mandatory to underline that, as for IP, recurrence is considered to be the fault of the surgeon and not

because of the characteristics of the tumor, so great care has to be taken in its complete removal through a subperiosteal dissection and drilling out the bone underlying the pedicle of the neoplasm, which guarantees the oncological radicality independently of the approach used.<sup>9,18,19</sup> The extension of the tumor and its relationship with the surrounding structures are very important for the surgical assessment and can be achieved preoperatively by MRI investigation.<sup>20</sup> Nevertheless, recent studies suggest that osteitis and focal hyperostosis on CT scan predict the site of attachment of the lesion.<sup>21,22</sup> In our experience, imaging before any kind of surgical procedure is fundamental when approaching a unilateral sinonasal lesion, including IPs as well as OSPs, in order to make a preliminary distinction based on their radiological features. CT and enhanced MRI scans are both necessary because of their complementarity; the first allows the evaluation of the bony boundaries and the detection of calcification spots and bone sclerosis and the second adds details on the extent of the tumor toward adjacent structures and the distinction among different kinds of tissues (tumor tissue vs inflammatory tissue). In our series, patients who presented major or minor contraindication to CT or MRI scans underwent only 1 of these studies; otherwise both of them were performed. In case of MRI contraindications, an enhanced CT scan was obtained. Moreover, these radiological investigations represent an important guiding-instrument for surgery. Image guidance has always been a crucial point for endoscopic endonasal approaches. The advent of neuronavigation systems with real-time tracking images, the opportunity for 3D reconstructions using the preoperative CT data, and the possibility to obtain fusion images CT/MRI improved the accuracy of the surgical procedure and their use should always be promoted when possible. Since 2009, intraoperative image guidance navigation has been used at our departments in all cases of tumor surgery, revision surgery, and skull base surgery.

Endoscopic approaches cannot always obtain an en bloc resection. However, it is not the concept of an en bloc resection itself that has to be fulfilled to achieve complete removal, because what really matters when dealing with tumors is the radical effect obtained at the end of the procedure. It is crucial to achieve a complete resection of the lesion with histologically clear margins. Endoscopes providing a magnified view and the possibility to explore around corners — thanks to their angled lenses — offer the possibility of obtaining an efficacious radical effect in a piecemeal fashion.<sup>23</sup>

In our recent paper<sup>17</sup> on the endoscopic treatment of 212 IPs, we reported the feasibility of the technique tailored to the extent of the disease to be resected, proposing 3 different types of endonasal approaches (Figure 2; Table 1). A limitation for a purely endoscopic approach is encountered when the disease extensively involves the mucosa of the frontal sinus or of a supraorbital cell. In these cases, a combined endoscopic-osteoplastic flap approach is indicated. The results obtained (5.7% of recurrence for IP) demonstrated that complete removal of the lesion is possible when certain principles are followed: preoperative imaging assessment, attachment-oriented surgery, subperiosteal dissection of the tissues and

TABLE 3. Incidence of the histologic subtypes of sinonasal papillomas and distribution of clinical behavior by histologic type.

Author, y, reference	No. of patients	IP cases	Malignancy	Recurrence	OSP cases	Malignancy	Recurrence
Hyams, 1971 <sup>1</sup>	315	149	13%	46%	10	10%	40%
Barnes and Bedetti, 1984 <sup>2</sup>	122	61	13%	—	6	17%	33%
Weissler et al, 1986 <sup>14</sup>	139	131	—	—	8	—	—
Kapadia et al 1993 <sup>5</sup>	800	560	9%	—	150	4%	—
Buchwald et al, 1995 <sup>15</sup>	82	58	—	—	5	—	—
Michaels and Young, 1995 <sup>11</sup>	191	139	—	—	16	—	—
Nachtigal et al, 1998 <sup>16</sup>	72	56	—	—	4	—	—
Kaufman et al, 2002 <sup>12</sup>	40	34	9%	15%	6	17%	33%
Lombardi et al, 2011 <sup>17</sup>	212	212	5.2%	5.7%	NR	—	—
Present study, 2013	404	371	—	—	33	3%	6%

Abbreviations: IP, inverted papilloma; OSP, oncocytic Schneiderian papilloma; NR, not reported.

drilling out the bone underlying the neoplasm, and multiple frozen sections. An exclusively endoscopic approach may be contraindicated in the following situations: (1) massive involvement of the mucosa of the frontal sinus and/or of a supraorbital cell, (2) concomitant presence of a malignancy involving critical areas, and (3) presence of abundant scar tissue from previous surgery.<sup>17</sup> Intracranial extension is not considered a contraindication because the surgical experience acquired in recent years has demonstrated that endoscopic skull base duraplasty of large defects can be performed with a multilayer technique using free grafts such as fascia lata, cartilage, bone, mucoperichondrium, and mucoperiosteum, after drilling the bone around the defect in order to obtain a smooth and regular surface and undermining the dura from the intracranial skull base bone.<sup>10,24</sup> However, these patients should be informed regarding the possibility of the surgeon having to switch to a combined approach during the operation. In our series, we never had cause to switch to the surgical procedure, and, in our opinion, this was because of correct preoperative surgical planning with both CT and MRI investigations.

We believe that following these principles and contraindications in the endoscopic resection of OSP as well, is the key to successful management of these tumors and is justified because we observed only 2 recurrences (6%) in the 33 cases treated, compared with the previously reported recurrence rate that ranged from 33% to 40%.<sup>12</sup> Because 1 of the 2 recurrences was diagnosed after 46 months, at least 5 years of follow-up are recommended. Because of the rarity of this tumor, 2 patients with minimum follow-up of 12 months were included in the present series in order to have a bigger cohort of patients. One patient with a minimum follow-up of 17 months and 2 patients with 22 months were also included for the same reason. All other patients (28 of 33; 84.8%) had a minimum follow-up of 24 or more months (mean, 62 months).

According to our experience, OSPs represent 8.2% of sinonasal papillomas (33 of 404 patients), they have a lower malignancy association (3%), and the same rate of recurrence (6%) as IPs. In our previous article regarding the treatment of IP, we reported that the rates in 212 IPs were 5.2% for malignancy association and 5.7% for recurrence.<sup>17</sup> It is our suggestion that histological findings that are positive for OSP must no longer be considered a

negative prognostic factor in terms of malignant transformation or rate of recurrence. If endoscopic endonasal surgery is performed by experienced hands, this tumor can be considered curable and, in our opinion, the technique can be considered the gold standard for the treatment, although larger series dealing with this topic are needed.

## CONCLUSIONS

Currently, the transnasal endoscopic approach proves to be the first choice in the treatment of most cases of Schneiderian papillomas. Although our series of OSPs includes a limited number of patients ( $n = 33$ ), but with an overall mean follow-up of 62 months, the analysis of the outcomes suggests that endoscopic surgery may be considered the gold standard in the treatment of the vast majority of OSPs. Moreover, the endoscopic technique with the introduction of multiangled scopes and drills, decreases hospitalization time and morbidity compared to external procedures, despite the longer surgical training and great experience required. However, patients with extensive involvement of the frontal sinus may require a combined approach. Because we observed 1 recurrence after 46 months, a minimum follow-up of at least 5 years is advisable. Finally, on the basis of the analysis carried out, we conclude that OSP is not to be considered a negative prognostic factor in terms of malignant transformation or recurrence.

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