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Benign Sinonasal Neoplasms: A Focus on Inverting Papilloma

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Benign tumors of the sinonasal tract are a histologically diverse group of neoplasms that may have similar clinical presentations. When symptomatic, they generally present because of a mass effect and perturbation of surrounding normal structures. Nasal airway obstruction, epistaxis, epiphora, rhinorrhea, and recurrent sinusitis are common presenting symptoms. Tumors also may be asymptomatic; these generally present as incidental findings on radiographic imaging performed for nonrhinologic purposes. Although the differential diagnosis of such a lesion may be narrowed by historical, endoscopic, and radiographic information at the time of presentation, the diagnosis rests on pathologic analysis of a biopsy specimen.

These tumors can be divided into several groups: fibro–osseous (osteoma, chondroma, ossifying fibroma, and fibrous dysplasia), neural-related (schwannoma, neurofibroma, and meningioma), hamartomatous (respiratory epithelial adenomatoid hamartoma) and odontogenic (ameloblastoma, and calcifying epithelial tumor of Pindborg), vascular (hemangioma, hemangiopericytoma, juvenile nasopharyngeal angiofibroma, and pyogenic granuloma), and inverted papilloma.

Fibro–osseous tumors

Osteoma is the most common benign sinonasal tumor, and it has been reported to be seen on 1% of routine sinus radiographs, most commonly localized to the frontal sinus [1]. These tumors are slow growing and well circumscribed, with symptoms generally attributable to obstruction of the drainage pathway of nearby sinuses. When symptoms are present, the symptom complex most commonly includes frontal pain and headache [2,3]. On

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endoscopy, they appear as firm masses with a smooth mucosal covering (Figs. 1,2). Their management has been documented, and it depends on their location, rate of growth, symptoms, and effect on surrounding structures [4]. Gardner's syndrome is an autosomal-dominant condition consisting of osteomas (usually multiple), soft tissue tumors (such as epidermal inclusion cysts or subcutaneous fibrous tumors), and polyposis of the colon. This triad of symptoms should be remembered by otolaryngologists, and should prompt gastroenterology referral if this is suspected, as malignant degeneration of these colonic polyps will occur in 40% of patients [3].

Differentiation between ossifying fibroma and fibrous dysplasia is important, as the management of these benign fibro–osseous tumors may differ. Radiographically, fibrous dysplasia characteristically has a ground glass appearance on CT images. It generally presents in younger patients (children and adolescents), and its growth rate may decrease or stop after puberty. Because of this, the management of fibrous dysplasia of the sinonasal cavity is generally expectant or conservative [5]. Again, familiarity with systemic syndromes is essential to the practice of rhinology. McCune-Albright's syndrome is a disseminated form of polyostotic fibrous dysplasia that also manifests with precocious puberty, early skeletal bone maturation, and abnormal skin pigmentation [6,7].

Ossifying fibroma, on the other hand, has a more aggressive growth pattern and can exhibit rapid bony erosion and become locally destructive. Although this tumor is found most commonly in the mandible, the sinonasal counterparts tend to be more destructive [8]. The management pattern of ossifying fibroma should reflect the nature of this tumor, and resection generally is recommended early in the disease process. Endoscopic resection of these tumors may be feasible but is associated with a higher recurrence rate than other benign tumors [5].

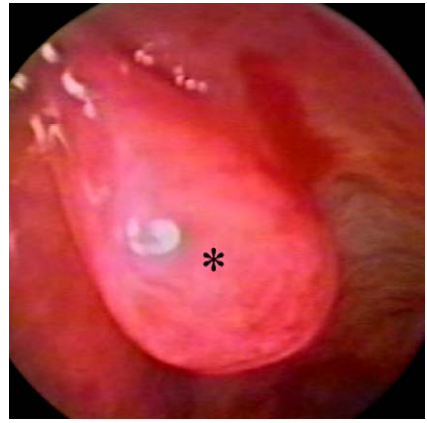

Fig. 1. An endoscopic, endonasal view of an osteoma reveals a firm lesion (*) with a normal mucosal covering.

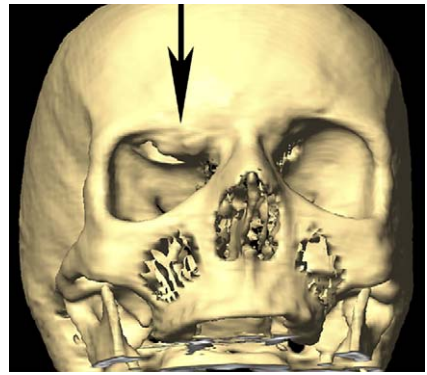

Fig. 2. Three-dimensional reconstruction of a sinus CT of a patient with an osteoma (*arrow*) of anterior table of the frontal sinus. This view demonstrates the effect of the tumor on the volume of the globe. This outward expansion caused vision changes and diplopia, and the internal growth of the osteoma resulted in a frontal sinus mucocele.

Other benign tumors

Neural-related tumors include meningiomas, schwannomas, and neurofibromas. Meningiomas are encountered infrequently in the nose and paranasal sinuses and arise from ectopic arachnoid tissue. Their growth is generally expansile in nature, and can be difficult at times to differentiate from intracranial meningioma. The skull base is generally intact in sinonasal cases, and the bowing of bone is generally in a direction toward the skull base [9]. Schwannomas generally present along the nasal septum as they arise from branches of the trigeminal nerve [10], but they can present along on peripheral nerves (Fig. 3). Similarly, neurofibromas can arise from peripheral nerves in the sinonasal cavity; differential diagnosis of these neoplasms relies on pathologic analysis of the tumor.

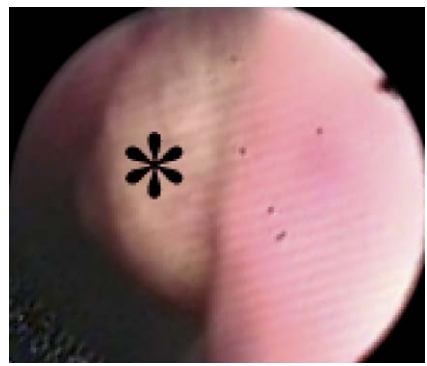

Fig. 3. Endoscopic view depicts a schwannoma (*) arising from the superior turbinate in the sphenoethmoidal recess.

Hamartomatous lesions of the sinonasal tract are tumors composed of cells that, at some point during development, were a normal part of the local anatomy. They include respiratory epithelial adenomatoid hamartoma (REAH) and odontogenic tumors. The two hamartomas of odontogenic origin primarily seen in this area are ameloblastoma and the calcifying epithelial tumor of Pindborg. Twenty percent of all ameloblastomas arise in the maxilla, and the sinuses generally are involved after secondary growth into these air-containing spaces (Fig. 4) [11]. Pindborg's tumors are much rarer and can present clinically in a fashion similar to ameloblastoma.

Juvenile nasopharyngeal angiofibroma (JNA) is seen in males and generally presents in the second decade of life with nasal airway obstruction and epistaxis. This is a firm, well-encapsulated tumor that usually arises near the sphenopalatine foramen near the posterior attachment of the middle turbinate. Its growth may lead to a dumbbell-shaped tumor with one lobe growing into the nasopharynx and the other toward the pterygopalatine fossa. Resection of this tumor may involve preoperative embolization, and endoscopic techniques frequently are employed [12]. Other vascular benign neoplasms of the sinonasal tract include hemangiomas, hemangiopericytomas, and pyogenic granulomas. A review of these and other tumors are beyond the scope of this article.

Inverted papilloma

Inverted papilloma (IP) is a distinct clinical and pathological entity with a long and rich history. It is characterized best by its local invasion, tendency for recurrence, and association with malignancy.

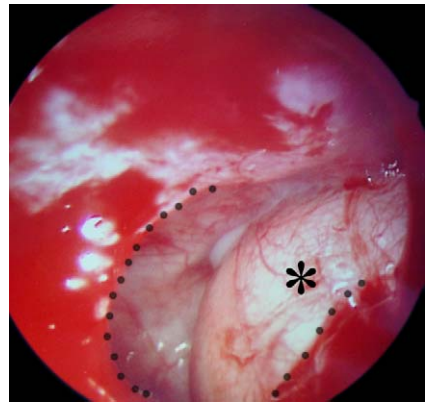

Fig. 4. Endoscopic view demonstrates an ameloblastoma that extended into the maxillary sinus. A large middle meatal antrostomy was made (*detailed with dotted line*), and a 70° endoscope was directed toward the inferior wall allowed exposure to the tumor (*).

Historical perspective

In 1854, Ward was the first to document and detail the occurrence of papilloma in the sinonasal cavity [13]. Soon after this, Biliroth described two papillomatous growths within the nasal cavity and deemed them ''villiform cancers'' in 1855 [14]. Hoppman also gained experience with these tumors, and, in 1883, subcategorized these into hard and soft papillomas based on the texture of their epithelial lining [15]. It was Reingertz in 1935, however, who histologically described the epithelium of this tumor and noted that it inverted into the underlying connective tissue [16]. Since that time, this tumor, which shows histological inversion of the epithelium, has been called a myriad of descriptive terms, including: inverting papilloma, inverted papilloma, epithelial papilloma, papillary sinusitis, Schneiderian papilloma, inverted Schneiderian papilloma, soft papilloma, transitional cell papilloma, cylindrical cell carcinoma, polyp with inverting metaplasia, and benign transitional cell growth [17]. This, in part, reflects the initial lack of understanding of this tumor by clinicians and pathologists.

The efforts of Hyams served to remedy this issue. In 1971, Hyams reviewed 315 cases on papillomas from the nose and paranasal sinuses at the Armed Forces Institute of Pathology [18]. The report of these findings served to solidify the terminology and pathology of inverting papillomas, thus making clinicians and pathologists aware that this is a distinct and single clinicopathological entity. This report subdivided sinonasal papillomas into inverted, fungiform, and cylindrical cell types, which some feel simply reflects the local environment of the tumor [19].

Pathology

Grossly, the tumor appears exophytic and polypoid, yet it appears more vascular than an inflammatory polyp (Fig. 5). The tumor may be gray to pink and often has frond-like projections that extend from the main bulk of the specimen [17]. Although it may fill the nasal cavity to a variable degree, the site of localization to the native mucosa is often a discrete pedicle-like connection. Depending on its size and extent, the tumor may rest against other mucosa within the nasal cavity; similarly, it may occupy a sinus and rest against its mucosa. When IP occupies such an area without arising from it, the tumor bulk simply rests on the nearby mucosa, a mucosa that remains normal without evidence of invasion or any change caused by the nearby tumor.

IP gets the moniker inverted from the histologic appearance of the neoplastic epithelium. Microscopically, the epithelium of the IP is distinct from the respiratory (pseudostratified ciliated columnar) mucosa of the sinonasal cavity, and the epithelial cell may be squamous, transitional, or respiratory [17]. This epithelium is proliferative and is thickened compared with the surrounding normal epithelium and lacks mucus-secreting cells and eosinophils [20]. The nuclear to cytoplasm ratio is normal, and there are few (less than

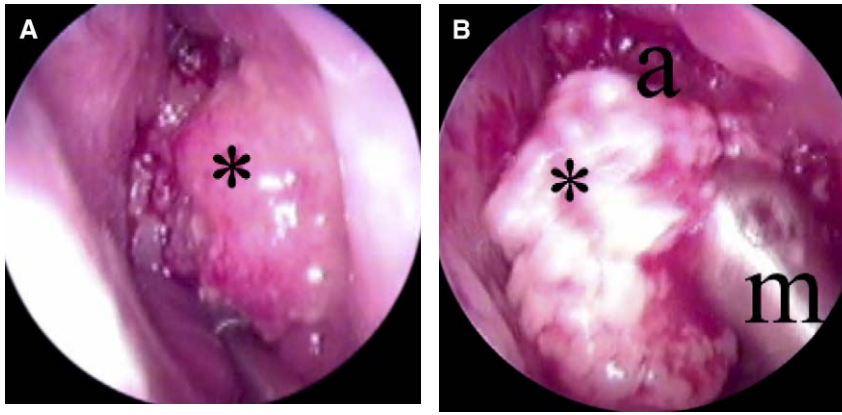

Fig. 5. (*A*) Intraoperative photographs of the right anterior nasal cavity reveal inverting papilloma (*), which at first inspection appears to emanate from the nasal septum. (*B*) A microdebrider (**m**) is used to manipulate the tumor and reveal normal underlying mucosa. The microdebrider is used to debulk tumor and helped to more clearly define the tumor attachment (**a**) to the lateral nasal wall in the middle meatus.

two) mitotic figures per high-powered field. Squamous metaplasia may occur, and the cells may become hyperkeratotic, with an overlying thin layer of keratin on the smooth surface of the tumor. The orderly maturation of cells from the basal layer outward is maintained. When viewed from low power, the inverting, endophytic nature of the epithelium is seen best and is markedly different from the histologically exophytic appearance of common papillomas. Also, there is no koilocytosis, which is present in common papillomas and would appear as vacuolization of cells near the surface.

The epithelium rests upon an intact basement membrane that is not invaded or interrupted by the overlying cells. It is not thickened and does not show any inflammatory changes. Microscopically, the epithelial layer invaginates into the underlying (subepithelial) stroma, which consists of a loose connective tissue without signs of desmoplasia [21] (Figs. 6, 7).

The diagnosis of IP depends on a tissue biopsy, which generally is taken in a clinical setting before definitive treatment. The cytologic appearance of the tumor (obtained by a touch preparation) has been shown to correlate with the histologic findings of IP, but its clinical use had not been adopted widely [22].

Etiology

There have been no widely accepted causative factors associated with IP. It is felt that the entire Schneiderian membrane (the embryologic origin of the mucous membranes of the sinonasal cavity) is at risk for the development of this epithelial neoplasm, and this eponym has persisted as a descriptor of IP [23]. The role of allergy has been discounted because of the lack of

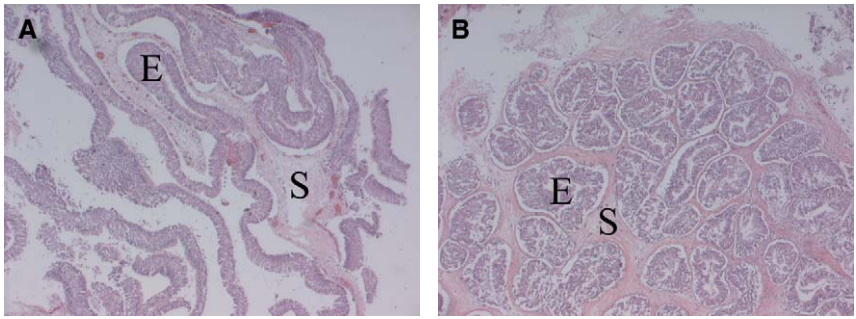

Fig. 6. (*A*) Tubular fronds of epithelium (*E*) invert into the underlying stroma (*S*). Hematoxylin and eosin stained sections of inverted papilloma are shown at low power. (*B*) The representative section was cut perpendicular to the long axis of these fronds, so multiple cross-sections of the epithelial fronds (*E*) are seen inverting into the stroma (*S*). Hematoxylin and eosin stained sections of inverted papilloma are shown at low power.

a personal history of allergic rhinitis in patients who develop IP. Chronic rhinosinusitis also has been presented as a possible etiologic factor, as this generally is associated temporally with IP [24]. It has been elucidated that the rhinosinusitis seen in patients with IP is secondary to alteration of the sinuses' natural drainage pathways by tumor. No association between tobacco products or alcohol use has been found. Although environmental exposures have been known to predispose individuals to sinonasal carcinomas, there has been no link established between this and IP.

A viral etiology for IP has been sought, likely because of the association between common papillomas and the human papillomavirus (HPV) [25]. Electron microscopy has failed to show ultrastructural evidence of viral particles in IP [26,27], and immunohistochemical techniques have not shown HPV antigens in IP [28,29]. Using in situ hybridization techniques, however,

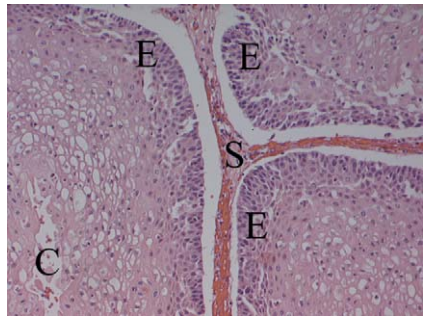

Fig. 7. Three epithelial fronds (*E*) are seen invaginating into the stroma (*S*). The core (*C*) of these fronds is fibrovascular. Note the orderly organization of the epithelial cells from the basal layer to the surface and the lack of mitotic figures. Hematoxylin and eosin stained sections of inverted papilloma are shown at high power.

HPV DNA has been found in IP specimens and is similar to that in HPV types 6 and 11 [30,31]. Still, the fact that HPV DNA has been found in these lesions is not enough to support a viral etiology for IP. Some, however, suggest HPV may be implicated in cases with multi-centric disease, dysplasia, malignancy, and the garden-variety tumor [32].

Clinical aspects of inverting papilloma

The incidence of IP has been documented at 0.2 [33] to 0.6 [34] cases per 100,000 people per year. It comprises 0.5% to 4% of primary nasal tumors [20] and is 1/25 as frequent as inflammatory polyps [35]. Weissler and colleagues [19] have reported the largest single report on their 35-year experience with IP that included 223 cases. The symptom complex reported by this group parallels that of other investigators and includes unilateral nasal obstruction (58%), epistaxis (17%), nasal drainage (14%), bilateral nasal obstruction (12%), nasal mass (9%), and sinusitis (9%). Other common presenting symptoms include headache, diplopia, facial numbness, facial swelling, and anosmia [20,36]. In a review of several large case series, the average time patients experienced these symptoms ranged from 27 to 66 months [20,37]. This surprising number is a reflection of the relatively innocuous and very nonspecific symptom complex experienced by this patient group. These symptoms overlap with a myriad of other conditions including allergy, chronic rhinosinusitis, and migraine.

Classically, IP has a predilection for males with a male:female ratio of 3:1. There is no side predilection, and cases are usually unilateral. Bilateral lesions are seen in 4.9% of patients [14]. There is no notable race predilection, as the rates mimic that of the standard population [19]. In a collection of 522 patients from five different studies, the average age was 54.3 years at the time of treatment [19,20,36,37,38], and it generally is reported to be most common in the fifth and sixth decades of life [39].

Krouse reviewed and summarized the published experiences with IP from 1967 to 1997. The primary sites of IP origin were documented including the lateral nasal wall (82%), maxillary sinus (53.9%), ethmoid sinus (31.6%), septum (9.9%), frontal sinus (6.5%), and the sphenoid sinus (3.9%) [14,40].

Radiographic findings

Although there are classic radiographic findings associated with IP, there are no pathognomonic findings of IP on imaging [41,42]. There is, however, still information to be obtained from these studies that can assist in the diagnosis and operative management [43]. CT and MRI are the common modalities used to evaluate IP. In a review of the literature, CT is the most widely performed study, and this better details bony anatomy. From a diagnostic standpoint, inverted papilloma is associated with bony changes. The most common bony finding is bowing of the bones near

the soft tissue mass. Tumors that extend into the maxillary sinus cause widening of the infundibulum on CT and make the uncinate process difficult to discern [41].

There is a classic association of IP with the term bony erosion. From a clinical perspective, this term connotes aggressive invasion of normal structures and usually is reserved for describing malignancies. The mass effect from IP is a slow and constant force on the surrounding mucosal and bony structures that can cause the affected bone to remodel. This bony remodeling is a better descriptor of the bony changes seen on CT [41], and it most commonly is seen at the medial wall of the maxillary sinus followed by the lamina papyracea [20]. Published series show a wide range of this finding, from 7% to 50% [17].

It has been postulated that the skull base has a different radiographic appearance in response to IP than that of other sinonasal bones. In the setting of IP near the floor of the anterior or middle cranial fossa, the bones of the skull base tend to resemble bone destruction. Unlike the relatively plastic facial bones, it is proposed that the skull base has a limited response to pressure; instead of remodeling, they just appear to erode and radiologically mimic malignancy [41,44] Also, because of the thin and sieve-like nature of the cribriform plate, intracranial extension can occur even without dramatic bony changes on imaging [45].

The association of CT evidence of bony erosion with malignancy in IP is also debated; one study [46] reports this finding in 100% of malignant specimen, while another shows 0% [47]. A similar scenario is seen with MRI and the detection of an IP-associated malignancy; there are no features present on MRI that differentiate IP from IP with malignancy or squamous cell carcinoma alone [45].

Sukenik et al [48] compared CT imaging with intraoperative nasal endoscopy to discern the ability of each to evaluate tumor extent. The sensitivity of each was identical at 69%, but the specificity of endoscopy exceeded that of CT (68% versus 20%). Endoscopy also had a better positive predictive value (55% versus 36%) and negative predictive value (91% versus 64%). Although both modalities seem to exaggerate the extent of disease, the presence of a normal intraoperative endoscopy is superior to CT in determining the extent of mucosa removal.

Contrasted CT may show slight enhancement of IP, and calcifications may be present. This is a nonspecific finding, but IP and esthesioneuroblastomas are the two most common nasal tumors associated with intralesional calcification [41].

Compared with CT, MRI better characterizes soft tissue structures. In MRI, IP is hypodense to isodense on T1-weighted images and isodense to hyperdense on T2-weighted images. The mass slightly enhances with contrast and appears nonhomogeneous. The biggest advantage of MRI in the radiographic analysis of IP is differentiating tumor soft tissue from inspissated mucus, as these are hyperintense on T2-weighted images [41,45].

Association with carcinoma

An association between IP and squamous cell carcinoma (SCCa) exists; however, the exact details of this relationship are the matter of some controversy. In addition to the propensity of IP to cause local destruction, it is the association with malignancy that has driven therapy for these tumors. In his analysis of 30 years of published reports, Krouse documents the finding of carcinoma in 9.1% of all patients [14].

SCCa may present in the setting of IP in three different scenarios. First, a patient may have an inverting papilloma with small foci of SCCa within it. Also, some patients present with discrete and separate sinonasal tumors—both IP and SCCa at the same time—without evidence that the malignancy arose from the IP. Both of these scenarios are deemed synchronous, but it is not clear how these are related. The third entity is the metachronous malignancy, one that manifests in the area of a prior IP resection well after the time of primary tumor removal [17]. In many reports of malignancy in the setting of IP, these details are not included in the discussion of the tumor, which hinders better characterization.

It has been postulated that synchronous IP and SCCa share a common cellular lineage. Lawson suggests a common unstable or metaplastic epithelium gives rise to these two distinct pathologic entities that are related but remain separate [49]. The true relation is not known.

Metachronous carcinoma is much less common that its synchronous counterparts. Of the 233 patients, Weissler and colleagues [19] reported 11 malignancies, four of which were metachronous. Of 87 patients, Lawson reported five malignancies, one of which was metachronous [17]. Many authors consider IP to be a premalignant tumor because of these findings [14]. There have been case series and isolated presentations to solidify this thought. Vrabec followed an individual for 3 years with repeated biopsy of an initially benign IP. Over this time period, atypia developed and progressed to the point of SCCa, a finding reaffirmed by other studies [50,51].

There are no documented pathologic or clinical findings in IP associated with the future development of SCCa. Wormald suggests malignant disease is associated with bilateral IP, hyperkeratosis, greater than two mitotic figures per high-powered field, and presence of plasma cells [52]. In contrast, Suh and colleagues reported that atypical features in benign IP do not predict future development of carcinoma or recurrence of IP [53]. Also, the number of recurrences of IP does not correlate with the propensity for malignancy.

The malignancy issue (along with local destruction and recurrence) drives the treatment paradigm of standard IP. Whether IP is a true premalignant lesion remains a matter of debate.

Treatment regimens and rates of recurrence

Since the publication of Hyams in 1971, there has been an increased understanding and awareness of inverting papilloma. With the standardization

of reporting and increasing communication between clinicians, the management algorithm for IP has evolved.

Early surgical experiences with IP were fraught with high recurrence rates. These procedures, which had a curative intent, generally used the transnasal (closed) approach. Illumination was provided by a headlight (at best), and local tumor removal was attempted by local, simple resections that mimicked polypectomies [52]. An outcome analysis dealing with this type of procedure was published in 1971 and revealed a staggering recurrence rate of 71% [54].

As the understanding of IP progressed, the standard surgical approach became more aggressive. External procedures such as the Caldwell-Luc and external ethmoidectomy provided increase access to the sinonasal cavity. Open procedures with a lateral rhinotomy or midface degloving approaches allowed for increased visualization of the tumor bed and more complete resections than any of the prior methods, and most resections involved some form of maxillectomy.

In Weissler's 35-year review [19], treatment was subdivided into transnasal, external, and open. They noted the recurrence rate varied inversely with the extent of the procedure and was 71% for intranasal procedures, 56% for external procedures (Caldwell-Luc or some variation of external ethmoidectomy), and 29% for open procedures (lateral rhinotomy or midface degloving). In light of these recurrence rates, this study proposed the lateral rhinotomy approach as the standard of care for surgical treatment of inverting papilloma.

These recommendations were accepted widely by the surgical community, and open exposure, coupled with en bloc resections (usually involving some sort of maxillectomy), was performed routinely for extirpation of disease. The complication rate was acceptable and included ozena, diplopia, epiphora, nasal stenosis, bleeding, and death. As proposed, open management of IP had become the accepted and widely practiced standard of care. Numerous presentations of case series documented its effectiveness [51].

While investigating their experiences over a 15 year period, Lawson and colleagues [17] had a special patient population treated without an open approach that had recurrence rates similar to their standard resections. Ten patients with tumors limited to the inferior or middle meatus with minimal maxillary and ethmoid sinus involvement were treated by transnasal or transantral sphenoethmoidectomy. This procedure was chosen over the classic lateral rhinotomy and midface degloving approaches, as these patients were either not candidates for general anesthesia or had an initial erroneous biopsy specimen. The recurrence rate for these patients (10%) mirrored that of the 75 patients they treated with the classic open approach (9%). This and other studies suggested that, in certain clinical situations where tumor extent is limited, a more conservative approach to resection is a viable option for managing IP [17].

This concept was extrapolated into the endoscopic realm. In the mid-1980s, endoscopic sinus surgery was popularized, and the initial experience was to diagnose and treat inflammatory disorders of the nose and paranasal sinuses. As the familiarity with this new technique grew, so did the applications of endoscopic endonasal surgery. Its use in the surgical management of IP began as an extension of the ideals of Lawson and colleagues; certain tumors with limited extent could be treated successfully by a modality that was conservative and avoided an open approach. Endoscopic management fit this tenet, and Waitz and Wigand were the first to detail a case series on endoscopically treated patients. They noted a recurrence rate of this method similar to the more classic open approach (17% versus 19%) [55], and this was reaffirmed by other investigators also [56,57].

In all of the studies, it was detailed explicitly that endoscopic management was reserved for treating limited and easily accessible tumors. These generally were confined to the lateral nasal wall with possible minimal extension into the anterior ethmoid sinus. Because of this, the comparison of results of endoscopic versus open management was confounded by selection bias. The recurrence rates of endoscopic management of straightforward tumors were being compared with that of open management of more extensive and complex tumors. No widely accepted staging system could be used to standardize reporting [58].

As the experience with endoscopic sinus surgery for managing inflammatory conditions extended to tumor resection, surgeons had greater confidence in the management of more complex benign sinonasal tumors. First, more bulky tumors were addressed endoscopically. In situations where a large nasal IP fills the nasal cavity but is only physically associated with a small mucosal area, debulking of most the tumor with a microdebrider while retaining its site of attachment is of import (Fig. 5). This allows a better survey of the sinonasal cavity and allows better characterization of the attachment of the IP to the native nasal mucosa. It also serves to direct therapy to the specific area of pathology.

The endoscopic management of the bony architecture surrounding IP also evolved as more extensive tumors were addressed. Groups have discussed the resection of underlying bone when possible [38] and drilling the surface of the bone when not possible. As more extensive tumors were addressed in more sites than just the lateral nasal wall and the anterior ethmoid sinus, however, more invasive endoscopic procedures have been characterized. The goal of these procedures is to provide adequate exposure for resection and postoperative surveillance of the tumor bed.

Endoscopic techniques also have been applied to management of IP of the maxillary sinus. One distinct advantage of endoscopic approaches is that they also may incorporate adjunctive open procedures such as trephination and Caldwell-Luc to improve access or exposure [38]. Endoscopic management of IP of the maxillary sinus necessitates improved visualization of the sinus cavity, as even a 70° scope can fail to allow visualization of the

entire cavity. Therefore, a maxillary canine fossa puncture is essential to the use of endoscopy to manage maxillary sinus IP. This puncture site allows the introduction of the endoscope to allow total visualization when working transnasally and allows the passage of instrumentation while the endoscope is transnasal.

For tumors of the posterior wall of the maxillary sinus, a wide middle meatal antrostomy with removal of bone and mucosa flush to the posterior wall and roof of the maxillary sinus allows excellent exposure. Instrumentation introduced from a canine fossa puncture increases access. For involvement of the floor, anterior, lateral, or medial walls of the maxillary sinus, a form of endoscopic medial maxillectomy is needed. Wormald and colleagues [52] and Sadeghi and colleagues [59] give excellent detailed descriptions of the procedure, the end result of which removes the medial portion of the maxillary sinus and lateral nasal wall while retaining the medial buttress of the maxilla. Sadeghi and colleagues emphasized that the transnasal endoscopic medial maxillectomy is minimally invasive and allows the resection of tumor as an en bloc specimen. They feel this is more oncologically sound than endoscopic piecemeal removal, which they tout as ''basically a form of extended sinus surgery, not a medial maxillectomy'' [59].

IP of the frontal sinus and frontal recess has the potential to be managed endoscopically; however, careful patient and case selection is key to success. At best, nasal endoscopy provides limited access to the frontal sinus, and management of a neoplasm in this area is difficult [4]. The endoscopic modified Lothrop procedure [60] has been implemented successfully in selected cases of IP of the frontal sinus and frontal recess. In unilateral disease, operating on the uninvolved frontal sinus predisposes the patient to the morbidity of the surgery; however, this is acceptable, as it allows margins to be assessed better intraoperatively and allows improved tumor surveillance postoperatively [52]. In IP involving the lateral frontal sinus, endoscopic resection is not encouraged if the anatomy precludes adequate access. In these cases, osteoplastic flap without obliteration is encouraged. No obliteration is recommended so the primary site may be followed better radiographically and endoscopically. Creating a wide frontal sinusotomy at the time of tumor removal increases visualization for surveillance in the postoperative period [56].

In Krouse's review of 30 years of published data on 1426 patients, the recurrence rates of IP in multiple types of procedures were analyzed. For the analysis of recurrence data, he categorized the surgical approaches of this period into four groups: nonendoscopic intranasal, conservative (Caldwell-Luc, transnasal, and transantral procedures short of an en bloc resection), aggressive (en bloc resection of tumor by means of midface degloving, lateral rhinotomy, or Weber-Ferguson incision), and endoscopic (including all endoscopic approaches). The recurrence rates for these groups were 67.3%, 44.0%, 18.0%, and 11.8%, respectively (Table 1). There was no statistical difference between the recurrence rates of the aggressive and endoscopic groups [14].

Table 1
Recurrence rates [14]

Treatment type	Percent recurrence
Intranasal (without endoscopy)	67.3
Conservative (Caldwell-Luc, external ethmoidectomy procedures)	44.0
Aggressive (lateral rhinotomy, midface degloving, maxillectomy)	18.0
Endoscopic and extended endoscopic	11.8

As previously stated, there is a selection bias that confounds these data. In the current era, only certain tumors are treated endoscopically, and a comparison of the recurrence rate of this group must take this into account. In an effort to standardize disease reporting and communication between investigators, Krouse has developed a staging system for IP. This is not the first staging system proposed for IP, but it does take into account salient clinical factors that are germane to the description of the disease process. The factors that determine a patient's stage are also important factors in the selection of a surgical approach, and they include extent of disease, location of disease, and the presence of malignancy. This four-stage system (Box 1) mimics that of the T staging system of the American Joint Committee on Cancer [58]. T1 lesions can be treated with endoscopic techniques without much resection of bone; T2 tumors are also accessible with endoscopic techniques but require some removal of bony structures. T3 lesions have the potential to be managed endoscopically if adequate visualization can be achieved; similarly, an open procedure with medial maxillectomy could be used to manage this type of IP. Lastly, an open surgical approach is recommended for T4 tumors to provide maximal exposure [14].

The management algorithm of IP has come full-circle and has returned to transnasal approaches, although current transnasal techniques are performed under endoscopic visualization. Endoscopy and powered instrumentation allow more extensive transnasal surgery to be done with better tumor identification and localization. As the sites of tumor involvement are visualized better, a more directed resection is possible, incurring less trauma to the

Box 1. Krouse staging system for inverting papilloma [58]

T1—Tumor isolated to one area of the nasal cavity without extension to paranasal sinuses.
T2—Tumor involves medial wall of maxillary sinus, ethmoid sinuses, and/or osteomeatal complex
T3—Tumor involves the superior, inferior, posterior, anterior, or lateral walls of the maxillary sinus; frontal sinus; or sphenoid sinus.
T4—Tumor with extrasinonasal extent or malignancy

surrounding mucosa and anatomic structures. These concepts apply some principles of functional endoscopic sinus surgery to the management of IP.

Summary

Benign sinonasal neoplasms are a pathologic and clinically varied group of tumors. Inverting papilloma is a notable member of this group, and it is renowned for its high rate of recurrence, its ability to cause local destruction, and its association with malignancy. This article aimed to familiarize the clinician with all the practical aspects of inverting papilloma and its management. The treatment algorithm for this tumor has undergone a complex evolution that continues today.

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