Medially originated inverted papilloma

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OBJECTIVES: The objective of this study was to determine the characteristics of medially originated inverted papilloma (MOIP) and compare them with laterally originated inverted papilloma (LOIP).

METHODS: A retrospective review of the charts for a total of 83 patients with sinonasal inverted papilloma (IP) was conducted. Tumors originating from the nasal septum or the turbinates were categorized as MOIP, whereas tumors originating from the four sinuses were categorized as LOIP.

RESULTS: Twenty-eight (34%) and 55 (66%) cases were categorized as MOIP and LOIP. MOIP from the middle turbinate behaved more aggressively than LOIP from the ethmoid sinus (P = 0.009), but less aggressively than LOIP from the maxillary medial wall (P < 0.05). Radical procedures were implemented in 14 patients with LOIP, but not in any patients with MOIP (P = 0.002). The recurrence rates were comparable in both groups (P = 0.472).

CONCLUSIONS: The categorization of IP on the basis of tumor origin enabled a better surgical design and more accurate excision of the tumor. Although in some cases MOIP may behave more aggressively, radical procedures were indicated in only the late Krouse stage LOIP without compromising the recurrence rate.

No sponsorships or competing interests have been disclosed for this article.

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Received July 23, 2008; revised October 7, 2008; accepted October 23, 2008.

Otolaryngology–Head and Neck Surgery (2009) 140, 324-329

doi:10.1016/j.otohns.2008.10.037

Sinonasal inverted papilloma (IP) arises primarily from the lateral nasal wall and often extends to the paranasal sinuses and the surrounding vital organs. An IP originating from the medial nasal cavity is considered very rare and is most often thought to be either a nasal septum lesion or an early staged tumor (i.e., T1 and T2 in the Krouse staging system or group A in the Cannady staging system). A medially originated inverted papilloma (MOIP) can extend far laterally, thus resembling an advanced stage tumor on CT scan or MRI. However, regardless of the extent of the tumor, MOIP may be easier to excise than laterally originated inverted papilloma (LOIP). Identification of the tumor’s origin therefore is important to improve control of the disease because recurrence always takes place at the tumor origin. There is no single surgical solution, but rather a range of procedures from which the best choice may be made to attain complete resection of the tumor, including its origin, according to each individual case.

Common staging systems have been proposed mainly on the basis of the extent of the tumor, rather than its origin. However, these staging systems and recommendations are not able to provide a definitive surgical scheme. In this study, IP was categorized according to the location of the tumor origin, namely MOIP or LOIP, and surgical approaches were chosen on the basis of this categorization. The objective was to provide a more precise prognosis, hence to formulate a better surgical strategy and minimize recurrence rate. The differences in tumor staging, surgical approach, associated malignancy, and postoperative recurrence rate between patients with MOIP and LOIP were studied.

The 83 patients in this study represented the largest series of sinonasal IP cases among the Chinese population to date. This was also the first article that clarified the characteristics of MOIP and illustrated the tumor origin in IP.

METHODS

Patients who had IP diagnosed in the sinonasal region between November 1991 and December 2007 were included in this study. Approval of the retrospective review was obtained from the Institutional Review Board in Chang Gung Medical Center. The origin of each tumor was classified into two groups: MOIP when the tumor originated from the nasal septum or the turbinates, and LOIP when the tumor originated from the ethmoid sinus, maxillary sinus walls, frontal sinus, or sphenoid sinus. The staging system devised by Krouse was adopted to grade the extent of the tumors and is elaborated here. Stage I disease is limited to the nasal cavity alone. Stage II disease is restricted to the ethmoid sinuses, and medial and superior portions of the maxillary sinuses. Stage III disease implicates the involvement of the lateral or inferior aspects of the maxillary sinuses, or extension into the frontal or sphenoid sinuses.
Stage IV disease indicates tumor spread outside the confines of the nose and sinuses, as well as any malignancy. Endoscopic surgery was carried out in all patients; then a refinement of the endoscopic technique, sequential segmental endoscopic surgery (SSES), was conducted, especially in patients with advanced stage tumors. The endoscopic approach for the surgical dissection was devised mainly on the basis of the tumor’s origin. The tumor mass was dissected and separated from the surrounding normal tissue along with the following procedures according to indications: ethmoidotomy or ethmoidectomy, maxillary sinusotomy, frontal sinusotomy, sphenoidotomy or sphenoidectomy. Radical procedures such as endoscopic medial maxillectomy (EMM) or the Caldwell-Luc operation were performed only when the tumor originated from the maxillary sinus antrum.

All segments of the tumor specimen were sent for pathological evaluation. The associated malignancy and postoperative recurrence rate were also elucidated.

Statistical analyses included the \( \chi^2 \) test with Fisher exact tests to compare the categorical presence or absence of pathological findings in cross tables. A \( P \) value less than 0.05 was regarded as statistically significant. SPSS for Windows 10.0 statistical packet program (SPSS Inc, Chicago, IL) was used for data analysis.

### RESULTS

The charts for a total of 83 patients with sinonasal IP were reviewed. There were 61 male and 22 female patients. The average age was 48 years with a range between 16 and 77 years. There were no cases of bilateral disease. IP was confirmed in all patients by pathological evaluation of the preoperative biopsy sample and thorough serial sectioning of the specimen segments.

Twenty-eight (34%) cases were classified as MOIP (Table 1). The results showed tumor origins located at the nasal septum (five patients), middle turbinate (21 patients), inferior turbinate (one patient), and superior turbinate (one patient). Among the patients with MOIPs, five patients were at Krouse stage I, 16 were at stage II, six were at stage III, and one patient was at stage IV (Table 1). Four of the five septal lesions and one lesion of the inferior turbinate that was confined to the nasal cavity were classified as stage I disease. The fifth septal lesion case and the superior turbinate lesion extending to the ethmoid sinus were classified as stage II disease. Among the cases of MOIP from the middle turbinate, there were 14 stage II tumors (involving the ethmoid sinus or maxillary medial wall), six stage III tumors (involving the frontal sinus, sphenoid sinus, or maxillary walls other than the medial wall), and one stage IV tumor (with orbital invasion).

Fifty-five (66%) cases were classified as LOIP. The origins of the LOIP tumors were located at the ethmoid sinus (19 patients), maxillary medial wall (20 patients), maxillary antrum (14 patients), and sphenoid sinus (two patients) (Table 1). Among the cases of LOIP, 25 tumors were at Krouse stage II, 24 tumors were at stage III, and six tumors were at stage IV. None of the LOIPs were of stage I classification (Table 1). Among the 25 stage II LOIPs, 19

<table>
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<th>Table 1 Characteristics of MOIP and LOIP</th>
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<tr>
<td><strong>MOIP</strong></td>
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<td><strong>Definition</strong></td>
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<td>Location and number</td>
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<tr>
<td>Total</td>
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<tr>
<td>Demographic data (Krouse stage)</td>
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<tr>
<td>I: 5 (18%)</td>
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<td>II: 16 (57%)</td>
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<tr>
<td>III: 6 (21%)</td>
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<td>IV: 1 (4%)</td>
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<td>Recurrence rate</td>
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<td>Referring to Krouse stage</td>
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<td>Associated malignancy rate</td>
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<td>(EMM or C-L operation)</td>
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<td>Total</td>
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<td>Referring to Krouse stage</td>
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* C-L operation, Caldwell-Luc operation. 
* \( P > 0.05; \) † \( P < 0.05. \)
cases originated from the ethmoid sinus, and six cases originated from the maxillary medial wall. Among the 24 cases of stage III LOIP, 14 tumors originated from the maxillary walls rather than the medial wall, two tumors originated from the sphenoid sinus, and eight tumors originated from the maxillary medial wall, and included four cases of squamous cell carcinomas (SCC), one case with orbital invasion, and one case with skull base involvement.

A total of 13 patients had frontal sinus involvement: two originated from the middle turbinate (MOIP), six originated from the maxillary medial wall (LOIP), and five originated from other maxillary walls (LOIP). The frontal sinus was involved via the attachment of a distal part of the tumor, and none of the 13 tumor cases originated from the frontal sinus.

Synchronous SCC occurred in four patients (5%) with primary cases of LOIP, whereas none of those with MOIP had associated malignancy. Malignant transformation or metachronous SCC has not occurred in any patients after surgery to date.

Endoscopic surgery was carried out in all 83 patients. Radical procedures (EMM or the Caldwell-Luc operation) were performed in 0 percent (0/28) of the MOIP cases and 25 percent (14/55) of the LOIP cases (P = 0.002). Among the 55 LOIP cases, EMM and the Caldwell-Luc operation were implemented in 11 and three cases, respectively. Among the late Krouse stage tumors (i.e., stages III and IV), none of the late-stage MOIPs required radical procedures (0/7) compared with the late-stage LOIPs (14/30) (P = 0.031). The recurrence rate at late Krouse stage was comparable between MOIP (1/7) and LOIP (6/30) (P = 1). In comparison with the late-stage tumors, none of the early-stage tumors (i.e., stages I and II) in our series received radical procedures (0/46 stages I and II IPs vs 14/37 stages III and IV IPs, P < 0.001) nor experienced recurrences (0/46 stages I and II IPs vs 7/37 stages III and IV IPs, P = 0.002) regardless of tumor origin (Table 1).

Seven patients (8%) had recurrences, including one patient with MOIP and six patients with LOIP. The recurrence rate was comparable between the patients with MOIP and those with LOIP, 4 percent and 11 percent, respectively (P = 0.472). The overall success rate was 92 percent (76/83). The follow-up period ranged between 3 and 161 months (mean 49 months).

DISCUSSION

In 2000, a cohort study of 20 series with sinonasal IP showed comparable recurrence rates from both radical external and endoscopic approaches. The author indicated that the extent of the disease, which primarily determines the optimum surgical approach, could be identified at only the time of surgery. In 1995, it was reported that only a single origin was found in each patient studied. Hence, surgery with a customized approach evolved on the basis of the determination of the tumor origin. The success rates increased considerably after more concerted attempts at the endoscopic approach had been made, resulting in an even lower recurrence rate compared with external approaches.

An IP originating from any one of the turbinates had not been separately studied and was likely to be generalized as a laterally originated disease in the literature. In the present study, IPs originating from the turbinates were separated from the “lateral nasal wall” and were categorized as MOIPs. Kamel et al proposed a grading method using tumor origin, in which tumors were divided into two types, with type I lesions originating from the septum or the lateral nasal wall and type II lesions originating from the maxillary sinus. In comparison, the categorization of patients in the present study into those with MOIP and LOIP provided a more distinct definition.

Few articles have focused on the medial origin of IP; most have reported on nasal septum lesions alone. The largest series of IPs to date were reported by Weissler et al in 1986 and Lawson et al in 2003. The incidence of nasal septum IP in these two articles was 17 percent (37/223) and 3 percent (5/160), respectively. In the present study, the proportion of nasal septum IPs (6%) was found to be consistent with the literature.

Regardless of the extent of the tumors in our patients, the entire bulk of all tumors originating from the turbinates or the septum in this present study could be excised with an ordinary endoscopic device, and none of the 28 MOIP cases required radical procedures, such as medial maxillectomy (Figs 1 and 2). On the other hand, only tumors originating from the maxillary antrum (14 cases) required radical procedures (Fig 3), whereas all other LOIP cases, regardless of their stage, could be treated without radical procedures (Table 1). In addition, although stage IV tumors are more aggressive than stage III tumors, radical operations were found to be more frequently required in stage III than in stage IV tumors. Stage III tumors also had a higher recurrence rate than those of other stages, including stage IV. In terms of preoperative evaluation and choice of surgical strategy, tumor extent or location may not be as important as tumor origin. Existing staging systems do not seem to necessarily provide prognostic information for the disease or imply a definitive surgical strategy.

In the present study, all the LOIPs from the ethmoid sinus were at stage II and were significantly less aggressive compared with those from the maxillary medial wall (P < 0.001). The LOIPs from the ethmoid sinus also tended to be less aggressive than the MOIPs from the middle turbinate (P = 0.009). These results signified that an IP from the ethmoid sinus may be regarded as a less aggressive lesion than one from the middle turbinate or maxillary sinus.

A majority of MOIPs originated from the middle turbinate, whereas most of the patients with LOIP had tumors that originated from the maxillary medial wall. The com-
parison of these two dominating structures provided valuable information about the differentiating characteristics of MOIP and LOIP. Patients with MOIP from the middle turbinate had a significantly lower incidence of stage IV tumors compared with patients with LOIP from the maxillary medial wall ($P = 0.045$), whereas the incidence of stage II tumors was significantly higher in patients with MOIP originating from the middle turbinate compared with LOIP originating from the maxillary medial wall ($P = 0.019$). These findings indicated that LOIP from the maxillary medial wall was more aggressive than MOIP from the middle turbinate. Furthermore, an LOIP from the maxillary medial wall may extend farther laterally and intrude into the surrounding vital structures or develop an associated malignancy (Table 1).

According to our experience, the tumor origin usually appeared as an area of mucosal lesion that could not be identified until debulking of the tumor mass was performed (Figure 3). Unlike tumor attachments that could be more easily separated from the contiguous tissues, the tumor origin often invaded the submucosal or subperiosteal plane and was more difficult to detach. Because the middle turbinate is closely related to the middle meatus and ethmoid sinus, it is not uncommon for an IP to have attachment to both areas (middle turbinate and middle meatus/ethmoid). It is of the utmost importance to differentiate between tumor origin and attachment in our classification. Scrutiny during dissection of the tumor in search of the tumor origin is prerequisite for correct tumor categorization. There are some radiographic predictors of tumor origin or attachment, for example, focal hyperostosis, osteitis, or bony remodeling observed on CT; however, they do not provide a definitive location of the tumor origin nor enable a precise prognosis.

Inaccurate estimation of the extent of the tumor may result in an inadequate excision or attempt at an unnecessary procedure. In our experience, resection of a bulky tumor mass may not be sufficient, and the excision of a safety margin of the surrounding mucoperiosteum or bony structure should be mandatory. On the other hand, because the frontal sinus was not found to be an origin of IP in any of our patients or in most of the literature, tumors with frontal sinus involvement could be excised completely without further radical operations, such as the modified Lothrop procedure. En bloc removal of an extensive lesion may be both technically difficult and time-consuming when an endoscope is used. A meta-analysis indicated that the lack of an en bloc resection does not appear to compromise the tumor control rate. By using a refined endoscopic technique, SSES, even a large lesion could be removed completely with proper safety margins in our patients. A combination with EMM or the Caldwell-Luc operation is sometimes necessary to help improve the control rate of LOIP. The purpose is to enable an accurate identification of the tumor origin and complete excision of the main tumor within the maxillary antrum.

With endoscopic surgery chosen on the basis of tumor origin, an overall recurrence rate in our patients was comparable to or lower than that reported in the literature. The difference in recurrence rates was not statistically significant between the patients with MOIP and those with LOIP, despite the fact that radical procedures were not performed in any MOIP patients. If we look into our data and further analyze late Krouse stage tumors, none of the late-stage MOIPs required radical procedures compared with the late-stage LOIPs ($P = 0.031$). The surgical process involved a combination with EMM or the Caldwell-Luc operation to help improve the control rate of LOIP. The purpose is to enable an accurate identification of the tumor origin and complete excision of the main tumor within the maxillary antrum.
approach required for MOIP, regardless of Krouse stage, is nonradical, while resulting in a comparable recurrence rate even for late-stage tumors ($P = 1$). When compared with the late-stage tumors, none of the patients with early Krouse stage tumors in our series required radical procedures ($P \leq 0.001$) nor experienced recurrences ($P = 0.002$) regardless of tumor origin. Therefore, it seemed that radical procedures may not be required for early Krouse stage tumor. With the classification system by tumor origin as used in this study, we are able to further suggest that radical procedure is required in only late Krouse stage tumors with lateral origin (Fig 4). In addition, a nonradical procedure is effective and does not increase recurrence rate, even in late-stage tumors as long as they have a medial origin.

The association of IP with malignancy has been reported to vary considerably, ranging from zero percent to 53 percent. Benninger et al described SCC as being a synchronous lesion in most cases. As determined in a systematic literature review, the overall rates of synchronous and metachronous carcinoma transformation of IP were 7.1 percent and 3.6 percent, respectively. In the present study, SCC was also the most prevalent among IP patients. There were a total of four cases of synchronous SCC, whereas none of the cases were noted with metachronous carcinoma or malignant transformation to date.

**CONCLUSION**

Preoperative radiographic studies and endoscopic examinations are useful for planning an appropriate surgical approach. However, they are restricted in their ability to detect the location of the tumor origin, which may result in an inadequate excision or unnecessary procedures. In terms of characteristics, MOIP may behave more aggressively than
LOIP in certain cases. Radical procedures were necessary in only cases of late Krouse stage LOIP that originated from the maxillary antrum. Nonradical procedures were effective and did not increase the recurrence rate, even in late Krouse stage MOIP. The categorization of IPs based on tumor origin can enable better formulation of surgical strategies, a more accurate excision of the tumor, and a considerably reduced recurrence rate.

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Po-Hung Chang, study design, modifying; Ta-Jen Lee, writer, study design; Chi-Che Huang, data collection; Yi-Wei Chen, data collection; Kai-Ping Chang: data collection; Chia-Hsiang Fu, data collection.

**FINANCIAL DISCLOSURE**

None.

**REFERENCES**