Is planned surgery important in sinonasal inverted papilloma?

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Key-words. Inverted papilloma; sinonasal; endoscope; recurrence

Abstract. Is planned surgery important in sinonasal inverted papilloma? Objective: To evaluate which clinical characteristics of inverted papilloma (IP) can result easily in misdiagnosis by clinicians and to determine the recurrence rate of inverted papilloma depending on diagnosis confirmation pre-operatively, intra-operatively or post-operatively.

Patients and methods: Fifty-one patients were treated for IP and 47 patients attended regular post-operative follow-up appointments for at least one year (mean: 54 months).

Results: The patients were assigned to 3 groups: group Ia, in which IP was not confirmed until the post-operative pathology findings; group Ib, in which IP was confirmed during the operation; and group II, in which IP was confirmed before the operation. There were nineteen (37%) patients in group Ia, nine patients (18%) in group Ib and twenty-three patients (45%) in group II. The recurrence rates for groups Ia, Ib and II were 33%, 11% and 5% respectively.

Conclusions: The initial presentation of bilateral sinonasal disease can easily lead the doctor into the misdiagnosis of IP. Bony erosion, remodelling, and a widening of the natural orifice of the sinuses on a CT scan are useful signs indicating IP. The correct diagnosis prior to surgery is a determinant of outcome. The use of frozen sections should, however, improve outcome as well. In this study we highlight the high prevalence and relatively low control rate of misdiagnosed IP (pathology undetermined pre-operatively) and hope to remind clinicians that early recognition of the tumour is most beneficial to patients.

Introduction

Sinonasal inverted papilloma (IP) is a rare tumour, owing its name to the fact that, histologically, its surface epithelium inverts into the underlying stroma. IP tends to appear as a lobulated, polyloid bulky mass, pale pink to grey in colour, and generally of a firmer consistency than a nasal polyp. Even so, IP is easily confused with inflammatory mucosa and polyps, and is sometimes found hiding between them. By contrast with its well-documented clinical behaviour, the aetiology of IP remains unclear. The presenting symptoms of IP may include nasal obstruction, rhinorrhea, epistaxis, facial pain and ear discomfort. Despite being a benign tumour, the well-known tendency to recur locally, the locally aggressive behaviour and the characteristics of squamous cell carcinoma (SCC) transformation mean that it has received a great deal of attention from clinicians. The two diseases are concomitantly diagnosed in 2% to 13% of patients. A further 1% to 1.5% of patients have been found to have a metachronous malignant lesion.1

More conservative procedures such as transnasal polypectomy used to be accompanied by high recurrence rates.2 Over the past 20 years therefore, lateral rhinotomy, medial maxillectomy, midface degloving or Denker’s approach have become the standard methods used to manage the majority of inverted papillomas. These external approaches, aimed at en bloc excision, did indeed reduce the recurrence rate (0-27%),24 but they also resulted in an increase in associated morbidity, including epiphora, dacryocystitis, diplopia, persistent crusting, vestibular stenosis, unacceptable scars or nasal deformity. In the same way, many otolaryngologists have tried to excise the inverted papilloma using endoscopic or endoscope-assisted procedures. The lower incidence of complications and the similar control rate to those seen when using external approaches have led to a widespread acceptance of endoscopic or endoscope-assisted procedures.3,5

Even though IP has received much attention in the literature, it is still easy to confuse it clinically with inflammatory mucosa and polyps, the reasons for this being the low incidence rate of IP and the fact that it often occurs in conjunction with polyp formation (22-49%).6-9 In this study, we retrospectively reviewed patients treated for sinonasal IP in order to
evaluate which clinical characteristics interfere with early recognition of IP and to compare the recurrence rates of IP depending on the timing of pathological confirmation.

Materials and methods

This study includes patients who were treated by all the surgeons of the otolaryngology department at Changhua Christian Hospital and received a diagnosis of sinonasal IP between 1995 and 2005. Charts of operation findings and CT images were reviewed and assessed retrospectively. The information they provided included age upon diagnosis, gender, presenting symptoms, timing of pathological confirmation, tumour origin, extension, grading, radiology findings, approach routes, number of months of follow-up, recurrence and associated malignancy. All of the patients were asked to attend regular follow-up appointments post-operatively. Sinonasal endoscopy was routinely performed; computed tomography (CT) scanning, magnetic resonance imaging (MRI) or biopsies were performed if needed. Chi-square testing, Fisher’s exact analyses, and Chi-square testing for trend were conducted to compare statistical differences and linear-by-linear association between groups.

Results

Our study included 51 patients with a sinonasal inverted papilloma, 29 male and 22 female (male:female = 1.32:1). The mean age was 58 years (range, 22-80). All of these patients received a sinonasal endoscopy and CT scan with/without contrast evaluation prior to surgery. We performed biopsy pre-operatively where there was a clinical suspicion of tumour other than polyp. Four patients had undergone a previous nasal operation; two patients had received a nasal polypectomy; one patient had undergone the cauterisation of an inferior turbinate; and one patient had undergone two previous endoscopic sinus procedures for IP at another hospital. Twenty-eight patients had tumours in the left side of the nose, twenty-two in the right side, and one patient had tumours in both sides of the sphenoid sinus, possibly due to the tumour growing through or eroding the sphenoid septum.

Depending on the time of pathological confirmation, we divided the patients into three groups. Group Ia consisted of patients in whom IP was confirmed after the operation. Group Ib comprised patients in whom IP was diagnosed during the operation using frozen sections. Group II, the final group, consisted of patients in whom IP was diagnosed prior to the operation. There were 19 patients in group Ia, 9 in group Ib and 23 in group II.

In our series, most inverted papillomas were found to originate from the lateral nasal wall (84%) before spreading to involve the paranasal sinuses. The most commonly involved sinus in our series was the ethmoid sinus (79%), followed by the maxillary sinus (70%), the sphenoid sinus (16%) and the frontal sinus (6%). These tumours were staged and the results are shown in Table 1.

Most of the patients in group I (Ia+Ib, misdiagnosis pre-operatively) presented with nasal obstruction and discharge. One patient suffered from epistaxis (4%), one had headaches and the other complained of a loss of smell. Eighteen patients in group II suffered from nasal obstruction and discharge, and five patients experienced frequent epistaxis (22%). Seventeen (61%) patients in group I showed bilateral sinus disease initially, while only 2 (9%) patients in group II showed bilateral sinus disease.

The pre-operative CT scans of 45 of the 51 patients were available for use in this study; they included 24 patients in group I and 21 patients in group II. The CT scan images of twenty-three (51%) patients – 12 (50%) in group I and 11 (52%) in group II – mimicked the characteristics of a choanal polyp. Bone erosion or remodelling, especially in the natural orifice of the maxillary sinus, were noted on the images of 26 (58%) patients: 17 (79%) from group I and 9 (43%) from group II. These clinical characteristics and the CT findings of IP relating

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<td>Tumour stage using Krouse’s staging system</td>
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<td>Stage I</td>
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<tr>
<td>Group I (28)</td>
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<td>Ia (19)</td>
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<td>Ib (9)</td>
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<td>Group II (23)</td>
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to early recognition of the tumour or not are shown in Table 2.

After the diagnosis of IP, the extent of the surgery was based on the site of the tumour origin and extension, with the aim of the “en bloc” excision of the tumour. Maxillary sinus IP was treated with transnasal endoscopic medial maxillectomy or using a transantral Caldwell-Luc approach. Tumours involving the frontal recess or sinus were treated with Draf IIb frontal sinusotomy in our series. IP in the sphenoid sinus was treated with transnasal endoscopic sphenoidotomy, the orifice of the sphenoid sinus was enlarged and the tumour was removed delicately in the subperiosteal plane. Forty-seven patients in our series attended regular follow-up appointments for at least one year (range: 12 to 118 months; mean: 54 months). In group Ia, three patients stopped attending the follow-ups within one year, and one patient refused a biopsy and did not attend follow-ups 2 years later when abnormal MRI findings were noted. One patient in group II died of lung disease 6 months after surgery without obvious recurrence. All of the patients in Group Ia underwent functional endoscopic sinus surgery with removal of polyp-like tumours as much as possible, in accordance with the general consensus for polyp treatment. Recurrence was proved in five patients (33%), who then underwent another operation; two of these five recurrent cases needed a third operation. The patients in Group Ib were also initially scheduled to receive endoscopic surgery; two patients then underwent combined surgery with transantral Caldwell-Luc procedures after IP was proven by the examination of frozen sections. Tumour recurrence was noted in one (11%) patient in this group, who then accepted a second operation. Nineteen patients in group II were treated using endoscopic procedures, three with a combined endoscope and a transantral Caldwell-Luc approach, and one with a maxillary swing due to IP associated with malignancy. Tumour recurrence was noted in one (5%) patient in this group, who then accepted a second operation. Table 3 shows the operation methods and recurrence rates. Tumour recurrence rates in the three groups were significantly different (Fisher’s exact test, \( p = 0.041 \)) and there was a linear relationship (Chi-square test for trend, \( p = 0.021 \)).

Two of the patients included in our study had IP associated with malignant transformation; both were proved pre-operatively. A pathological study in one patient showed malignant change with carcinoma in situ; this patient underwent a maxillary swing approach to treatment to eradicate the tumour. The other patient had IP with severe atypia; an endoscopic procedure was performed and no recurrence of the tumour was noted after 5 years of follow-up. In addition, another patient was found to have a benign IP combined with laryngeal cancer. Endoscopic wide excision and a laryngectomy were performed at the same time, and the patient recovered well with no tumour recurrence.

**Discussion**

Sinonasal papilloma has been classified into three types: (1) cylindrical papilloma, (2) exophytic squamous papilloma and (3) inverted papilloma. Even though inverted papillomas account for the majority of sinonasal papillomas, they are still rare. Over the past ten years, we have performed sinonasal endoscopic procedures on 5,465 patients in our department and only 51 patients (1%) were found to have IP. Moreover, Orlandi et al.\(^9\) suggested that a unilateral inverted papilloma associated with contralateral sinus inflammation is more common than any other sinonasal tumour. Roh et al.\(^4\) suggested that inflammatory cell population including macrophages, lymphocytes, plasma cells, polymorphonuclear leukocytes and eosinophils was significantly greater in IP than in other sinonasal papilloma. These data further suggest that inflammation may be involved in the pathogenesis of IP. After reviewing the
histopathology of 191 sinonasal papillomas, Michaels and Young concluded that IP is in fact an inflammatory polyp with squamous metaplasia and not a true papilloma. Our series included a 46-year-old man who underwent three procedures for nasal polyps at our hospital over five years. His “benign” polyp transformed into an IP and he received another endoscopic procedure. A review of the literature reveals that IP is frequently found in conjunction with inflammatory polyps (22–49%). It is possible that otolaryngologists misdiagnose a tumour when it first presents as nasal polyp.

There is no significant difference between group I and group II in terms of tumour stage (p = 0.150). The major presenting symptoms of IP are nasal obstruction and discharge. Other nonspecific symptoms such as headache, hyposmia and facial pain are easily confused with sinusitis. Even though the difference between the clinical prevalence of epistaxis in group I and group II was statistically significant (p = 0.079), this may be due to the low number of patients. However, in patients with epistaxis, the clinician may suspect a tumour early and manage an exact diagnosis sooner. Some authors have claimed that epistaxis is a predictor for associated malignancy, but this phenomenon was not seen in our study. Although the hallmark of IP is a unilateral huge polypoid tumour (Figure A), it is not rare to find these patients suffering from bilateral sinus disease (Figure B) in the clinic. In our series, 19 patients (37%) had bilateral sinus disease at first diagnosis; 17 (89%) in group I and only 2 (11%) in group II. There is a significant difference (p = 0.000) between the two groups. This means that the patients with IP can easily mislead the doctor into a misdiagnosis if they present with bilateral sinus disease.

A review of the literature shows that the majority (68-94%) of IPs originate in the lateral wall of the nasal cavity. In 43 patients in our series (84%), IP was found to have originated in the lateral nasal wall. The osteomeatal complex is the most common site of occurrence. Tumours from this area may spread to the sinuses and obliterate the natural orifice of the sinuses or protrude into the nasal cavity or nasopharynx (Figure C). Fifty-one percent of the available pre-operative CT scan images in our study were found to mimic choanal polyps, but there are no obvious differences between groups I and II (p = 0.873).

Inverted papilloma is characterised by its ability to destroy bone. In our study, bony remodelling, including erosion (Figure A) or hyperplasia (Figure D), was found in 58% of patients. There were no obvious differences between groups I and II (p = 0.058). Higher incidences of uncinate process erosion and widening of the natural orifice of the maxillary sinus were observed on the images of large tumours extending into the maxillary sinus than in cases of nasal polyps. In our series, up to 79% of group I showed bone erosion or remodelling after precise reviews of CT images retrospectively. Surgeons may overlook the tiny point in their bustling outpatient practices and should always keep this possibility in mind.

The treatment strategy differed between the three groups. In group Ia, although functional endoscopic sinus surgery (FESS) was the sole procedure, the recurrence rate was 33%. The reasons for the unexpectedly good result may be explained by (1) the irreversible mucosa change of a nasal polyp, leading to aggressive eradication during surgery or (2) the IP of some patients may account for only a small proportion and be hidden behind a nasal polyp. Recurrence occurred in five patients in this subgroup, who subsequently accepted further surgery. In all of these five recurrent cases, tumours were found to originate from, or spread into, the

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<th>Group</th>
<th>1st Operation</th>
<th>2nd Operation after recurrence</th>
<th>Recurrence rate</th>
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<tr>
<td>Ia (19)</td>
<td>FESS (19)</td>
<td>ES (4) ES + CL (1)</td>
<td>5/15 (33%) *</td>
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<td>Ib (9)</td>
<td>ES (7) ES + CL (2) ES (19) ES + CL (3) maxillary swing (1)</td>
<td>ES (1)</td>
<td>1/9 (11%)</td>
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<td>II (23)</td>
<td>ES (1)</td>
<td>1/22 (5%) **</td>
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*: number of patients; FESS: functional endoscope sinus surgery; ES: endoscope surgery with wide excision; CL: Caldwell-Luc approach

*: four patients were excluded: three patients were lost from follow-up within one year and one patient refused a biopsy and was lost from follow-up after 2 years

**: one patient died from lung disease 6 months after the operation.
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maxillary sinus or the sphenoid sinus. The second surgical procedure proved to be successful in three patients; another needed a third operation, and the final female patient needed five procedures to control her sphenoid tumour. By contrast, group Ib and group II patients were found to have relatively low recurrence rates of 11% and 5% respectively. The two patients in these groups who experienced a recurrence of the tumour were clear after their second surgery. Five patients in these two groups underwent combined endoscopic wide excision and Caldwell-Luc procedures, and one patient was treated using an external approach as the first-time surgery modality. The recurrence rates between the three groups differed significantly (Fisher’s exact test: p = 0.041). Group II had a better result than group Ib, and group Ib had a better result than group Ia (Chi-square test for trend: p = 0.021). In group Ib, even though doctors had changed their treatment strategy during the operation, many factors may have led to the poorer result compared to group II. These include the difficulty in achieving a safe margin after destruction, the impossibility of obtaining the agreement of the patient about informed consent re-writing, doctors’ willingness to engage in original approaches, even to difficult sinuses, operation time prolongation and so on. The advantage of the diagnosis of IP prior to the surgery is that the difficult sinuses can be addressed better. Higher magnification of the videoscope system, power instruments, and angle drills may also facilitate successful control in the operation.

In our study, maxillary sinus IP was treated with transnasal endoscopic medial maxillectomy or combined with a transantral Caldwell-Luc approach. The important factors affecting the choice of surgical approaches are the extension of the tumour and surgeon preference. The combined approach proved effective as a method for removing tumours affecting the anterior, lateral and inferior walls of the maxillary sinus. Thirty-five patients in our series had IP with maxillary sinus involvement. Five patients – four in group Ia and one in group II – had recurrent tumours after an initial endoscopic approach. Six patients treated with the combined approach in their first or second procedures and episodes subsequently recovered.

The incidence of frontal sinus involved ranges from 1% to 16%. Several methods have been used to treat IP of the frontal sinus; however, the number of cases is too small to determine their effectiveness. These included osteoplastic flap, lateral rhinotomy, external frontoethmoidectomy, endoscopic Lothrop procedure or a combined open/endoscopic

**Figure A-D**

A: The hallmark of IP is a unilateral huge polypoid tumour. Uncinate process erosion and widening of the natural orifice of the sinus were also noted. B: A patient with a right sinonasal IP showed bilateral sinonasal disease on CT scan. C: The tumour protruded into the nasopharynx and resembled a choanal polyp. D: Bony remodelling with hyperplasia and sclerosis change in IP.
approach. In our series, three cases with frontal recess or infundibulum involvement underwent a Draf IIb procedure. One patient in group Ib recurred and needed another endoscopic procedure before a cure was achieved.

IP originating in the sphenoid sinus is extremely rare. The surgical management of a sphenoid sinus tumour is especially challenging because of its deep-seated anatomic location and the inherent risks. The surrounding vital organs, including the internal carotid artery, optic nerve, pituitary gland and cavernous sinus, may lead to disastrous complications during sphenoid sinus surgery. Traditional external approaches to the treatment of massive sinonasal disease and disease extending outside the confines of the sinonasal cavity are notorious for their failure to address the problem properly. The endoscopic management of sphenoid IP allows maximum resection to the lateral compartment of the sphenoid sinus with minimal morbidity. Fakhri et al. suggested that, when treating a large erosive sphenoid IP, the surgical risks may be minimised with a staged resection and using computer-aided surgery. In our study, there were three patients whose IP originated in the sphenoid sinus. One patient belonged to group Ia, and the recurrent tumour was brought under control after four surgical procedures. The other two patients belonged to group II; their IPs were treated with transnasal endoscopic sphenoidotomy and cured after the first planned surgery.

IP is considered to be a premalignant condition. Progressive atypia and eventually squamous cell carcinoma were found in a three-year consecutive follow-up with biopsy specimens being found in a previously benign lesion. This presumed potential for malignant transformation has led to the view that extensive surgery is required. The extensive surgery is meant to eradicate IP completely as it can remain in bony invaginations and therefore recur on site; the second reason is the potential for malignant evolution. These are two separate reasons to perform the surgery necessary to prevent or lessen the incidence of recurrence. In the present series, only two patients (4%) were found to have IP associated with malignancy and both were in group II. The most appropriate method for managing these malignant tumours, either by endoscope or by an external approach, depends mainly on the size and extension of the tumour; the clinician’s personal experience is another important factor. The main limitation of the endoscopic approach is that that visualisation is not achieved of, for example, possible extensions to the lateral part of frontal sinus. Our first patient with carcinoma in situ (CIS) was treated using a maxillary swing approach; the second patient with severe atypia was managed using an endoscopic approach. Both patients attended regular follow-ups in our department without recurrence after periods of 6 and 5 years, respectively. Although there are no specific complications associated with the use of an external approach, the cosmetic advantage of endoscopic surgery over external approaches should not be ignored. Nasal IP associated with another anatomic site malignancy is seldom discussed in the literature. A 62-year-old male presented at our hospital with a nasal inverted papilloma combined with stage IV laryngeal cancer. An endoscopic approach and a laryngectomy were performed simultaneously. The patient has been free of recurrence for 2.5 years. It has been suggested that HPV (especially type 16) plays an active role in the carcinogenic pathway of IP and laryngeal carcinoma. Further studies in molecular biology should be designed in order to investigate their relationship. We suggest that a complete ear, nose and throat examination is indicated when IP is observed.

Concomitant inflammatory changes were a frequent finding in the patients with IP. The precision of tumour mapping in the contrasted/non-contrasted CT scans was reduced because of the difficulty of differentiating between tumour and inflammatory changes. MRI was better at differentiating IP from inflammation than CT, and should be ordered when there is a strong suspicion of IP. Five patients could not attend regular follow-up and the duration of three cases was less than two years, which might lead us underestimate the recurrence rate. The primary result supports the suggestion that clinicians should pay more attention to the features of IP in order to improve treatment results.

Conclusions

Endoscopic sinus surgery is a familiar technique to otolaryngologists and provides a powerful tool for treating an inverted papilloma. However, aggressive first surgery is important due to the higher recurrence rates in revision surgery. In patients with unilateral huge nasal polyps, and with or without contralateral sinus
disease, epistaxis, and bony erosion, remodelling, or widening of the natural orifice seen on the CT scan, the possibility of IP should be considered. Correct diagnosis prior to surgery is a determinant of outcome. The use of frozen sections, however, should also improve outcome. In this study we highlight the high prevalence and relatively low control rate of hidden IP and hope to remind clinicians that early recognition of the tumour is most beneficial to patients.

Take-home message: Even in cases of bilateral sinonasal disease, IP can be present. Asymmetry in clinical presentation, widening of the natural ostium, bony remodelling, calcification, and bleeding should rouse clinicians’ suspicions and lead to a complete pre-operative assessment. In such cases, MRIs must be ordered since this makes possible the correct diagnosis before surgery. IP requires radical surgery. FESS as described by Messerklinger has no place in the management of IP.

In cases of maxillary implantation, a truly radical Caldwell-Luc procedure must be conducted or a medial maxillectomy should be carried out by surgeons experienced in endonasal surgery. Strict follow-up is mandatory for at least 5 years. When IP is demonstrated post-operatively, a new evaluation is important and revision surgery should be planned.

References


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