Rhinology, 44, 205-210, 2006

Inverted papilloma: feasibility of endonasal surgery and long-term results of 87 cases*

Amir Minovi, Malte Kollert, Wolfgang Draf, Ulrike Bockmühl

Department of Otorhinolaryngology, Head and Neck and Facial Plastic Surgery, Klinikum Fulda gAG, Teaching Hospital of the Philipps-University Marburg, Fulda, German

SUMMARY

Background. *The aim of this retrospective study was to assess the potentials and limitations of endonasal micro-endoscopic sinus surgery in the management of sinonasal inverted papilloma (IP) and to demonstrate long-term results.*

Methods. *Eighty-seven patients underwent resection of an IP either via an endonasal, an osteoplastic maxillary or frontal sinus or a combined approach. Charts were reviewed for presenting symptoms, tumour stage according to the Krouse classification, surgical management and follow-up status.*

Results. *Most tumours were staged as T2 or T3 (42.5% each). Sixty-eight (78.2%) patients were referred for primary surgery. Nineteen (21.8%) patients presented with recurrent disease. The majority of IP (70%) were removed via an endonasal micro-endoscopic procedure. In 20 (23%) patients a combined approach was performed. The overall recurrence rate was 10.3%. Referring to endonasal surgery the incidence of recurrent IP was 10% in contrast to 15% after a combined procedure.*

Conclusion. *Our data show that endonasal micro-endoscopic surgery offers an effective and safe treatment modality of IP with insignificant morbidity. Strict application of selection criteria, wide removal of the tumour origin along the subperiosteal plane as well as drilling the underlying bone and close follow-up of patients are mandatory for success.*

Key words: Inverted papilloma, paranasal sinuses, endonasal surgery, long-term follow-up

INTRODUCTION

In 1991 the World Health Organisation has classified three different histopathological types of sinonasal papillomas: exophytic or fungiform papilloma, columnar cell papilloma and inverted papilloma (IP) [1]. IP is the most common type and accounts for approximately 70% of all sinonasal papillomas and from 0.5% to 4% of all neoplasms of the sinonasal tract [2]. They are characterized by a high recurrence rate, a tendency for malignant transformation and multicentric involvement. Recurrence rates up to 50% are reported, with almost all tumours recurring at the site of the previous surgery [2-6]. Malignant transformation occurs in about 11% of cases with IP [3]. IP occur mostly in the fifth and sixth decades with a male to female distribution of 5:1 [2,6]. Although the etiology of IP is still unknown, it has been demonstrated by molecular-biological analysis that human papilloma virus is involved in IP formation being detected in up to 86% of these tumours. In particular, viral subtypes 6, 11, 16 and 18 were most frequently found [7].

The invasive capacity to surrounding structures and the propensity to be associated with squamous cell carcinoma, make the treatment of IP particularly challenging for the surgeon. The accepted treatment of choice is complete wide local resection, but controversy surrounds the surgical approach that should be used. Traditionally, lateral rhinotomy or midfacial degloving with en bloc tumour resection in combination with medial maxillectomy were used and are still standard approaches [6,8-11]. However, there is currently a growing body of evidence to support endonasal endoscopic and/or microscopic surgery in the resection of these tumours showing comparable rates of recurrence to an external approach [5,12-17]. When properly indicated and planned, endonasal procedures can favourably compete with traditional external techniques in the surgical treatment of IP. Nevertheless, long-term results are needed to establish the efficacy of a surgical approach in a disease presenting late recurrences.

This study presents a series of 87 patients with IP treated by endonasal and/or osteoplastic approaches at one institution. Based on tumour characteristics and long-term follow-up results it proposes indications for each of these techniques.

MATERIAL AND METHODS

Clinical Data

The charts and histology reports of all patients with IP treated

*Received: December 5, 2005; accepted: May 15, 2006. Footnotes: Dedicated to the 65th birthday of Professor Draf.
Partly presented at the 18th IFOS World Congress, Rom, Italy, June 2005.

between 1989 and 2004 at the Department of Otorhinolaryngology, Klinikum Fulda gAG, Teaching Hospital of the Philipps-University Marburg were retrospectively reviewed. The demographics, clinical symptoms, sinus involvement, surgical procedure performed and disease recurrence were recorded for each patient. The extent of sinus involvement was assessed from radiological findings based on computed tomography (CT) and magnetic resonance imaging (MRI) and the findings at surgery. Tumours were classified according to the Krouse staging system for IP [18].

Follow-up was carried out on an ambulant basis for at least 5 years. Mean follow-up was 73.9 months (range: 12 to 175 months). In the first year, the patients were seen at 3, 6 and 12 months, and subsequently yearly. They were examined with nasal endoscopy and yearly MRI scans. Biopsies were taken from any area suspicious for recurrent IP.

Surgical Technique

All surgical procedures were performed under general anaesthesia. Vasoconstriction was achieved by placing cotton swaps soaked in naphazolinhydrochlorid in the nasal cavity for 10 minutes followed by subsequent injection of lidocain with 1:200.000 adrenaline at the agar nasi and the uncinate process. In any case the microscope as well as endoscopes were used. The kind of the operation varied in relation to the site of origin and the extent of the lesion. Basically we used *a)* a completely endonasal resection, *b)* a combined approach, i.e. endonasal procedure complemented with an osteoplastic frontal (OFS) or maxillary sinus (OMS) technique as described by Weber [19] and Feldmann [20] or *c)* an exclusively osteoplastic approach. In general, whenever the lesion exceeded laterally of an imaginary line drawn through the lamina papyracea or originated far laterally in the maxillary sinus at least a combined approach was used. All medially localized tumours were resected via an endonasal procedure, which included the medial maxillectomy or enlarged maxillary sinus technique indicated as endonasal Denker operation [21]. IP that originated from the posterolateral, anterior or inferior wall of the maxillary sinus were managed by an osteoplastic maxillary sinus operation (OMS). Whenever possible the nasolacrimal duct should be kept intact. IP surrounding the lacrimal pathway may demand to sacrifice it just below the lacrimal sac that then should be opened in the way of an endonasal dacryocystorhinostomy. All procedures were performed under endoscopic and/or microscopic view. If feasible lesions were removed "en bloc", but in large tumours the nasal portion of the mass was first debulked to subsequently focus on the most critical lateral areas, where dissection was always carried out in the subperiosteal plane. Then drilling of the disease underlying bone was accomplished and frozen sections from surgical bed margins were taken to ensure surgical radicality and complete tumour removal. Exposured dura was covered with artificial fascia lata (Tutoplast®).

RESULTS

Clinical Data

A total of 87 patients with IP were treated surgically during the evaluation period. Of these were 29 female and 58 male patients (male to female ratio of 2:1). The mean age at diagnosis was 53.8 years (range, 15 to 83 years). Beyond it, there were 10 additional patients who showed squamous cell carcinoma associated with IP. These cases were excluded from further evaluation.

The most frequently reported symptoms were nasal obstruction (70.1%), headache (24.1%), hyposmia and rhinorrhea (19.5% each) and chronic sinusitis (17.3%). Twenty patients (23%) were asymptomatic.

There were 40 right-sided tumours and in 47 patients lesions were on the left side. Definition of the initial site of the IP was done by preoperative radiological diagnostics and intraoperative appearence. As summarized in Table 1, in 58 (66.7%) patients the IP originated from the lateral wall of the nasal cavity and involved the anterior ethmoid in 56 (64.4%), the posterior ethmoid in 37 (42.5%) and the maxillary sinus in 45 (51.7%) cases. The posterolateral, anterior or inferior wall of the maxillary sinus was infiltrated in 21 (24.1%) cases. Frontal and sphenoid sinuses were only rarely involved as well as the orbit. No patient presented with a bilateral lesion. Bony erosion of the medial wall of the maxillary sinus and the skull base was found in 15 cases (17.2%).

Table 1. Distribution of paranasal sinus and extrasinus involvement.

Site of involvement	N° of cases (%)
Nasal cavity	58 (66.7)
Anterior ethmoid	56 (64.4)
Posterior ethmoid	37 (42.5)
Maxillary sinus	45 (51.7)
Frontal sinus	13 (14.4)
Sphenoid sinus	10 (11.5)
Orbit	2 (2.3)

Table 2. Tumour stage according to the Krouse [18] classification itemised on the surgical approach used.

Tumor stage	N° of cases (%)	N° of cases (%)	
		Endonasal surgery	External approaches
T1	11 (12.6)	11 (12.7)	-
T2	37 (42.5)	37 (42.5)	-
T3	37 (42.5)	13 (14.9)	24 (27.6)
T4	2 (2.3)	-	2 (2.3)

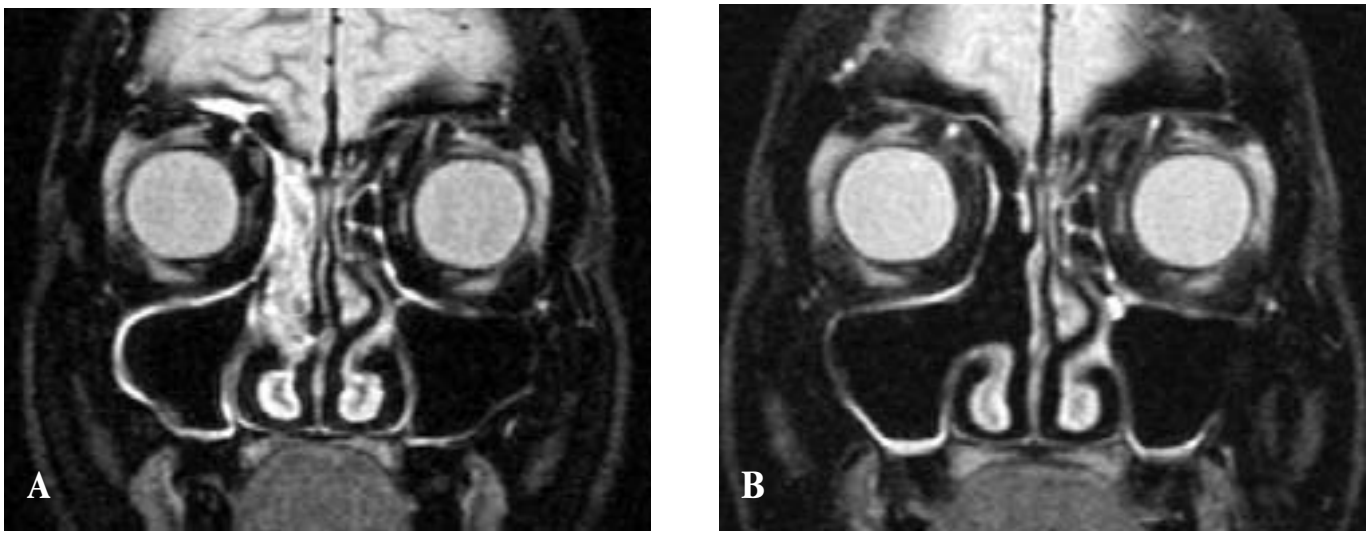

Figure 1. T1-weighted coronal magnetic resonance images enhanced with contrast medium showing IP arising from the right middle meatus. (A) Preoperative scan. (B) Postoperative appearance three years after resection by performing a Draf's type IIa drainage. This enlarged frontal sinus opening was necessary because of tumour growth within the frontal recess, which was proven by histology on frozen sections.

According to the classification of Krouse [18] the IP were stratified as follows (Table 2): 11 (12.6%) T1, 37 (42.5%) T2 and T3 each and 2 (2.3%) T4. There were no bilateral tumours. Sixty-eight (78.2%) patients presented with primary disease. Nineteen (21.8%) patients had previous surgery elsewhere before and were referred to our department for revision surgery. Of these, 12 patients suffered from recurrent lesions, and in 2 cases there was a history of 5 recurrences. In the previous surgery outwards 11 IP were removed endonasally, in 6 cases an osteoplastic maxillary sinus operation was carried out and in 2 cases a combination of both procedures was used.

Surgical Treatment

The majority of IP (n=61, 70%) were removed via an endonasal micro-endoscopic procedure. A typical example is shown in Figure 1. In 20 (23%) patients a combined approach and in six (6.9%) cases an osteoplastic maxillary sinus operation was performed (Table 3). All T1 (n=11) and T2 (n=37) tumours as well as 13 of the T3 lesions were resected exclusively endonasally (Table 2). In primary tumours an endonasal approach was chosen in 74% of the cases and a combined procedure in 21%. In revision surgery an endonasal removal was performed in 58% only and a combined approach in 32% of the cases. There were no major complications in our series.

Follow-up

During the follow-up period, ranging from 12 to 175 months (median 74 months) nine recurrences (10.3%) were observed. Three tumours had been operated via a combined approach and 6 endonasally. Hence, the recurrence rate for endonasal surgery was 10% compared to 15% after combined approach. None of the patients operated via an OMS approach showed recurrent disease. Of the 6 recurrent lesions that occurred after endonasal surgery two had been classified as T3, three as T2 and one as T1 tumours before the previous operation. When referred to us first time, the T1 and T2 tumours were primary lesions, whereas the T3 tumours already presented as recurrent diseases. Interestingly, one of the patients with a third recurrent tumour had a family history of IP involving the mother and

Table 3. Surgical approaches performed.

Surgical Approach	N° of cases (%)
Endonasal (EN)	61 (70%)
Combined	20 (23%)
EN + OMS	16 (18.4%)
EN + OFS	4 (4.6%)
OMS	6 (7%)

OMS = osteoplastic maxillary sinus approach,
OFS = osteoplastic frontal sinus approach

Table 4. Recurrence rates associated to surgical approaches.

Surgical approach	N° recurrences (%)	Mean recurrence interval (months)
Endonasal (EN)	6/61 (10%)	28 (3-87)
Combined	3/20 (15%)	102 (26-168)
Osteoplastic	0	0

three siblings. The mean recurrence interval after endonasal surgery was 28 months in contrast to 102 months after combined approach. These results are summarized in Table 4.

DISCUSSION

There is no doubt that surgery is the primary treatment of choice in IP. However, the best surgical approach and the extent of resection are still somewhat controversial, as is discussed in the literature [5,8,10,13,15,18]. During the last 5 years, several series have been published reporting on the endonasal endoscopic management of IP, and increasingly this has been accepted as the surgical modality of choice for most IP [5,12-17,22,23]. The present study supports the endonasal surgery of IP to be a very effective treatment strategy. A total tumour resection at the site of tumour attachment while preserving the healthy mucosa and the paranasal bony framework and also preventing damage to the patient's cosmetic appearance comprises our concept of minimally invasive surgery. Concerning the IP removal it is as radical as external approaches. As we have demonstrated the entity of dissection can be modulated in relation to the extent of disease to include a large spectrum of lesions, from those limited to the middle meatus to those involving the maxillary and the frontal sinus. In fact, an endonasal micro-endoscopic approach allows the dissection of a medial maxillectomy [24] or an endonasal Denker operation [21], which entirely exposes the maxillary sinus, and by performing a frontal sinusotomy type III according to Draf [25] large parts of the frontal sinus can be reached.

The most frequent sites of IP origin are the nasal fossa and the maxillary sinus whereas its exclusive localization within the frontal or sphenoid sinus is exceedingly rare [26,27]. Likewise, involvement of the orbit or intracranial invasion of IP are rare events [28,29]. The latter we have not found in our series but invasion of the anterior skull base at the level of the cribriform plate or the ethmoid roof was observed in 10 patients with recurrent diseases. Intraorbital growing was seen in 2 patients with extensive IP in the ethmoid. However, the tumours displaced the orbital content laterally without transgressing the periorbit. The presentation of IP is generally unilateral, but bilateral involvement of the sinonasal tract has been reported in a percentage of patients ranging from lower than 1% to 9% [6,12].

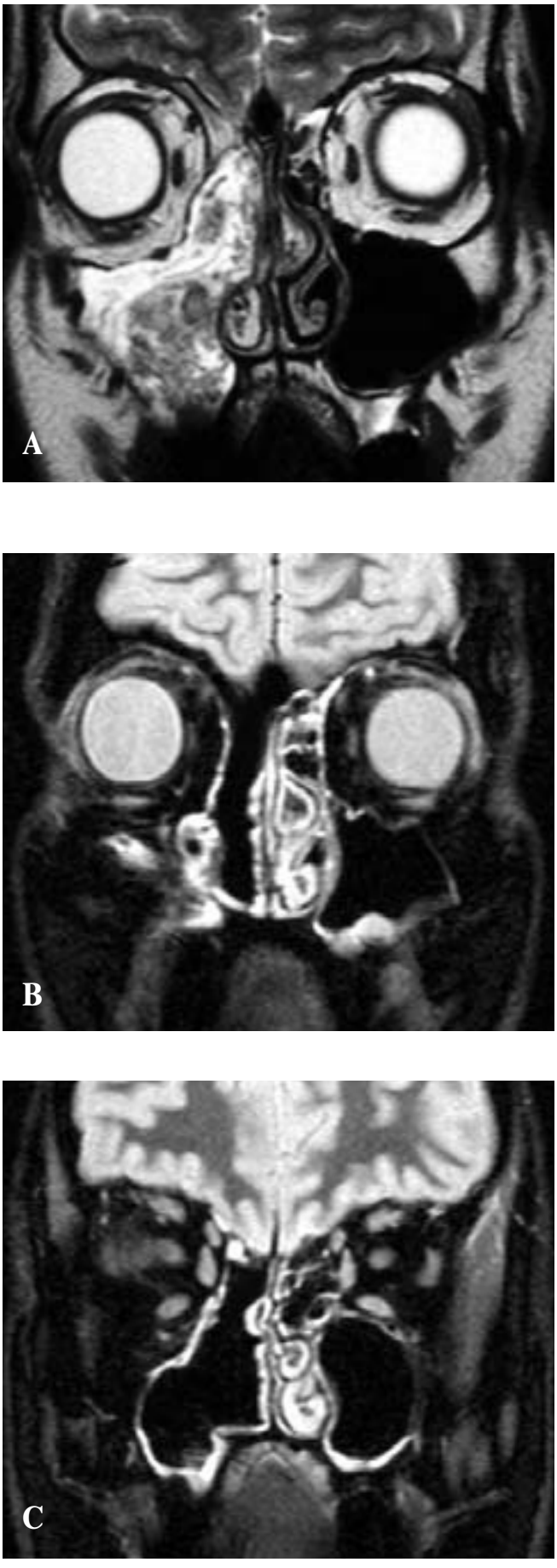

Figure 2. (A) Preoperative T2-weighted coronal magnetic resonance image presenting a large IP that originated from the anterior lateral wall of the right maxillary sinus as well as the ethmoid. (B+C) Postoperative short tau inversion recovery (STIR) sequences after tumour resection via a combined approach including an osteoplastic maxillary sinus approach and a modified Draf's type III drainage (5 years postoperatively). Modified type III drainage meant complete ethmoidectomy on the right side and after resection of the frontal sinus septum complete removal of both frontal sinus floors (but no ethmoidectomy on the left side). This was necessary to ensure complete removal of the IP that was infiltrating the very medial part of the frontal sinus infundibulum growing until the midline.

The success of papilloma surgery is judged mainly by the recurrence rate and the treatment morbidity. Incomplete tumour resection is regarded as the source of recurrent IP growth. Supportive evidence for this is that recurrent lesions appear at the primary site within a short follow-up period [8]. In our series we have found an overall recurrence rate of 10.3% within the mean observation interval of 73.9 months. Related to the endonasal approach the incidence of recurrent tumours was 10% compared to 15% after combined approaches. The latter higher percentage of recurrences may be due to the fact that all IP operated via external or combined approaches were of T3 or T4 stages. The recurrence rates of the most recent reports on endoscopic surgery of IP vary between 0% [13,24] and 27% [5,12,14-17,30,31]. Although, preoperative tumour assessment was comparable and staging was mostly performed according to the Krouse classification [18] IP dimension varied widely. Tomenzoli et al. [13] who reported 0% recurrences have treated mainly T1 and T2 tumours whereas our series included more T3 and T4 as well as recurrent lesions. In this regard, the results of the current study are intriguing, demonstrating again that precisely indicated endonasal surgery outclasses external approaches.

A criticism of the endonasal approach is the impossibility to obtain “en bloc” resection. Certainly, en bloc removal of these tumours is the ideal choice and it is often achieved in smaller lesions, but radical extirpation of the disease does not depend on it as shown by our long-term results. Instead, the primary purpose is to identify and widely remove the tumour origin along the subperiosteal plane and drilling the underlying bone. Therefore, it is acceptable to resect larger tumours segmentally [12,13,15].

In our experience there are two major limitations to the use of the endonasal micro-endoscopic approach, first is extensive involvement of the frontal sinus [12,13,15]. In our study cohort the frontal sinus was involved in 13 (14%) patients. Nine (69%) tumours have been managed endonasally by performing a Draf’s type II or III frontal sinusotomy [25] because the lesions were only growing marginally from the ethmoid into the frontal sinus (Figure 1). None of these patients developed a recurrent disease. We believe, that an exclusive endonasal approach is contraindicated if the disease largely involves the frontal sinus mucosa, especially in hyperpneumatized sinuses, because it is difficult to remove the diseased mucosa in the supraorbital region and to drill the underlying bone. The second major limition is a tumour origin from the posterolateral, anterior or inferior wall of the maxillary sinus [22] as shown in Figure 2. Other limitations that could be managed more properly by external approaches such as the osteoplastic frontal operation [19] or the osteoplastic maxillary sinus technique [20] are extensive intracranial and intraorbital infiltration and recurrent lesions associated with massive scar tissue. However, in any case, patients scheduled for an endonasal procedure should always be informed during the preoperative counselling of the possibility to intraoperatively revert to an external approach.

To choose the best surgical approach, i.e. to assess the endonasal endoscopic and/or microscopic resectability preoperative imaging is inalienable. Patient’s symptoms are more or less aspecific, and at time of clinical examination it is almost impossible to distinguish IP from inflammatory polyps, even in unilateral distribution of nasal polyps. In the assessment of sinonasal expansile lesions CT scan with contrast medium is generally considered the examination of choice. However, CT scanning cannot differentiate between retained secretion and inflamed mucosa from IP, and therefore is highly aspecific. According to Ojiri et al. [32] this limitation can be overcome by using MRI, which, apart from differentiating neoplastic tissue from inflammatory changes, identifies a convoluted cerebriform pattern suggestive for IP on T2 or enhanced T1-weighted sequences in about 80% of cases. Because the involvement of IP in the frontal and maxillary sinus may be limited to the region around the ostium, MRI is especially important for preoperative determination of the tumours’ origin. Guided by radiological findings we used the staging system according to Krouse [18] for disease classification and definition of the surgical approach required, although it lacks to map the frontal sinus involvement precisely.

Recurrent IP is thought to be related to the development of malignancy [2]. Reported rates of associated squamous cell carcinoma vary from 2% to 53%, but most studies have stated the incidence between 5% and 15% [3,6,12]. Likewise and because tumour recurrence can occur even years after primary surgery it is recommendable to follow the patients prospectively for the rest of their life. During the first two years we propose endoscopic controls every 3 months, from the second to the fifth year every 6 months and thereafter yearly. If there is suspicion of tumour recurrence multiple biopsies have to be taken and a MRI examination should be performed. A ”recurrence” within the first year should be better estimated as residual tumour.

The results of this study support the concept that endonasal endoscopic or micro-endoscopic surgery is no longer an alternative but the treatment modality of choice in IP, especially in cases of T1 to T3 staged tumours. However larger tumours or lesions located laterally in the frontal or maxillary sinus should better be removed via a combined external and endonasal approach. The key to success is locating the origin of the tumour, defining its extent, completely removing all diseased tissue including a surrounding rim of normal mucosa and finally drilling the underlying bone. To achieve this via the endonasal minimal invasive approach the surgeon needs to be very experienced which requires a long training. Strict follow-up of these patients is mandatory because IP that recur may be harbouring a malignancy.

REFERENCES

1. Shanmugaratnam KSL. Histological typing of tumours of the upper respiratory tract and ear. World Health Organization. Berlin: Springer-Verlag, 1991: 20-21.
2. Hyams VJ. Papillomas of the nasal cavity and paranasal sinuses. A clinicopathological study of 315 cases. Ann Otol Rhinol Laryngol 1971; 80: 192–206.
3. Bielamowicz S, Calcaterra TC, Watson D. Inverting papilloma of the head and neck: the UCLA update. Otolaryngol Head Neck Surg 1993; 109: 71–76.
4. Calcaterra TC, Thompson JW, Paglia DE. Inverting papillomas of the nose and paranasal sinuses. Laryngoscope 1980; 90: 53–60.
5. Lund VJ. Optimum management of inverted papilloma. J Laryngol Otol 2000; 114: 194–197.
6. Phillips PP, Gustafson RO, Facer GW. The clinical behaviour of inverting papilloma of the nose and paranasal sinuses: report of 112 cases and review of the literature. Laryngoscope 1990; 100: 463–469.
7. Gaffey MJ, Frieson HF, Weiss LM, et al. Human papillomavirus and Epstein-Barr virus in sinonasal Schneiderian papillomas. An in situ hybridization and polymerase chain reaction study. Am J Clin Pathol 1996; 106: 475-482.
8. Lawson W, Kaufman MR, Biller HF. Treatment outcomes in the management of inverted papilloma: an analysis of 160 cases. Laryngoscope 2003; 113: 1548-1556.
9. Raveh E, Feinmesser R, Shpitzer T, et al. Inverted papilloma of the nose and paranasal sinuses: a study of 56 cases and review of the literature. Isr J Med Sci 1996; 32: 1163-1167.
10. Thorp MA, Oyarzabal-Amigo MF, du Plessis JH, et al. Inverted papilloma: a review of 53 cases. Laryngoscope 2001; 111: 1401-1405.
11. Myers EN, Fernau JL, Johnson JT, et al. Management of inverted papilloma. Laryngoscope 1990; 100: 481-490.
12. Kraft M, Simmen D, Kaufmann T, et al. Long-term results of endonasal sinus surgery in sinonasal papillomas. Laryngoscope 2003; 113: 1541-1547.
13. Tomenzoli D, Castelnuovo P, Pagella F, et al. Different endoscopic surgical strategies in the management of inverted papilloma of the sinonasal tract: experience with 47 patients. Laryngoscope 2004; 114: 193-200.
14. Von Buchwald C, Larsen AS. Endoscopic surgery of inverted papillomas under image guidance--a prospective study of 42 consecutive cases at a Danish university clinic. Otolaryngol Head Neck Surg 2005; 132: 602-607.
15. Wormald PJ, Ooi E, van Hasselt CA, Nair S. Endoscopic removal of sinonasal inverted papilloma including endoscopic medial maxillectomy. Laryngoscope 2003; 113: 867-873.
16. Llorente JL, Deleyiannis F, Rodriog JP, et al. Minimally invasive treatment of the nasal inverted papilloma. Am J Rhinol 2003; 17: 335-341.
17. Winter M, Rauer RA, Goede U, et al. Invertierte Papillome der Nase und ihrer Nebenhöhlen. Langzeitergebnisse nach endoskopischer Resektion. HNO 2000; 48: 568-572.
18. Krouse JH. Development of a staging system for inverted papilloma. Laryngoscope 2000; 110: 965–968.
19. Weber R, Draf W, Kratzsch B, et al. Modern concepts of frontal sinus surgery. Laryngoscope 2001; 111: 137-146.
20. Feldmann H. Osteoplastic operation of maxillary sinus. Laryngol Rhinol Otol 1978; 57: 373-378.
21. Brors D, Draf W. The treatment of inverted papilloma. Curr Opin Otolaryngol Head Neck Surg 1999; 7: 33–38.
22. Sadeghi N, Al-Dhahri S, Manoukian JJ. Transnasal endoscopic medial maxillectomy for inverting papilloma. Laryngoscope 2003; 113: 749-753.
23. Waitz G, Wigand ME. Endoskopische, endonasale Abtragung invertierter Papillome der Nase und ihrer Nebenhöhlen. HNO 1990; 38: 242-246.
24. Kamel RH. Transnasal endoscopic medial maxillectomy in inverted papilloma. Laryngoscope 1995; 105: 847-853.
25. Draf W. Endonasal frontal sinus drainage type I-III according to Draf. In: Kountakis SE, Senior BA, Draf W, eds. The frontal sinus. Heidelberg Berlin New York: Springer, 2005; 219-232.
26. Chee LW, Sethi DS. The endoscopic management of sinonasal inverted papillomas. Clin Otolaryngol Allied Sci. 1999; 24: 61-66.
27. Lee JT, Bhuta S, Lufkin R, et al. Isolated inverting papilloma of the sphenoid sinus. Laryngoscope 2003; 113: 41-44.
28. Vural E, Suen JY, Hanna E. Intracranial extension of inverted papilloma: An unusual and potentially fatal complication. Head Neck 1999; 21: 703-706.
29. Elner VM, Burnstine MA, Goodman ML, et al. Inverted papillomas that invade the orbit. Arch Ophthalmol 1995; 113: 1178-1183.
30. Tufano RP, Thaler ER, Lanza DC, et al. Endoscopic management of sinonasal inverted papilloma. Am J Rhinol 1999; 13: 423–426.
31. Wolfe SG, Schlosser RJ, Bolger WE, et al. Endoscopic and endoscope-assisted resections of inverted sinonasal papillomas. Otolaryngol Head Neck Surg 2004; 131: 174-179.
32. Ojiri H, Ujita M, Tada S,et al. Potentially distinctive features of sinonasal inverted papilloma on MR imaging. AJR Am J Roentgenol 2000; 175: 465-468.

Ulrike Bockmühl, MD, PhD
Department of Otorhinolaryngology, Head and Neck and Facial Plastic Surgery
Klinikum Fulda gAG
Teaching Hospital of the Philipps-University Marburg
Pacelliallee 4
36043 Fulda
Germany

Tel: +49-661-846003
Fax: +49-661-846010
E-mail: u.bockmuehl.hno@klinikum-fulda.de