

# Inverted Nasal Papilloma: Retrospective Analysis of our Clinical Results

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## ABSTRACT

**Objective:** To evaluate our cases diagnosed with inverted nasal papilloma (INP) and to contribute to the literature on the future surgical and clinical approaches in the light of the results obtained.

**Methods:** In this study, 80 patients who underwent surgical treatment between 2010–2018 in our clinic were evaluated retrospectively. The patients were analysed according to demographic data, complaints, primary region, clinical stage, computed tomography (CT) scores, surgical methods, malign transformation and recurrence.

**Results:** Of the patients, 65 (81.25%) were male, and 15 (18.75%) were female. The mean age was 53±12 years. The most common complaint was unilateral nasal obstruction (96.2%). The most common primary site of INP was the lateral nasal wall (52.5%). Bone erosion was observed in 11 patients (13.7%). Of the 74 (92.5%) patients who underwent endoscopic sinus surgery (ESS), 23 (28.8%) of them underwent lateral rhinotomy to complete the tumor excision. 9 (11.3%) patients underwent revision surgery due to recurrence. In 4 (5%) of the cases, nonkeratinized squamous cell carcinoma was observed.

**Conclusion:** INPs have been investigated for both their diagnosis and treatment earlier with the introduction of endoscopy into the routine nasal examination. We think that close follow-up of cases is very important, especially because of the high rate of recurrence of these tumors and the transformation to malignancy.

## INTRODUCTION

Rhinosinusal papillomas are divided into three histological types, such as inverted, oncocyctic (columnar/cylindric) and exophytic (fungiform).<sup>[1]</sup> Inverted nasal papilloma (INP) is the most common type of rhinosinusal papilloma with a rate of 70% and constitutes approximately 0.5% to 4% of all sinonasal neoplasms.<sup>[2]</sup> INPs are benign epithelial tumors characterized by epithelial-stromal invagination, hyperplasia of the nose and paranasal sinus mucosal basal cells.<sup>[3]</sup>

INPs are usually derived from the lateral nasal wall and observed unilaterally. INPs are especially known as the disease of the 5<sup>th</sup> and 6<sup>th</sup> decades with male predominance.<sup>[3,4]</sup> Etiology is still unknown; however, human papillomavirus (especially types 6, 11, 16, 18) are a potential agent of the neoplasm.<sup>[5]</sup> In addition, bacterial and viral infections, chronic inflammation, allergens, smoking are thought to play a role in the development of INP.<sup>[6]</sup>

The first complaint of INP patients is usually nasal obstruction.<sup>[2]</sup> A multilobulated exophytic lesion in the physical examination may be confused with inflammatory nasal polyps. Therefore, INP should be considered and confirmed by histopathological examination in unilateral nasal polypoid masses.<sup>[7]</sup>

INP is considered as a local aggressive tumor in 2–10% of cases due to malignant transformation risk and recurrence rate of 12–20%.<sup>[8,9]</sup> The treatment of INP is surgical excision. Before the development of endoscopic sinus surgery (ESS) techniques, even if the approach methods, such as transnasal, lateral rhinotomy, midfacial degloving, are used, recently ESS are preferred instead of other surgical techniques.<sup>[6]</sup> In our study, we aimed to present the surgical methods and results of 80 surgically treated patients who were diagnosed with INP in our clinic with the literature.

## MATERIALS AND METHODS

In Health Science University Kartal Dr. Lutfi Kirdar Training and Research Hospital Otorhinolaryngology Clinic, information of 80 patients undergoing surgical treatment between the years of 2010–2018 with the diagnosis of INP were analyzed retrospectively. This study was approved by the Ethics Committee of our hospital (89513307/1009/406). Informed consent was obtained from all participants who enrolled in this study. Demographic data of the patients, such as age, gender, presenting symptoms, previously applied surgical interventions, the presence of additional disease, the anatomical region, stage, applied surgical techniques and recurrence information, were obtained by examining patient files retrospectively. Paranasal sinus CT was performed to evaluate the preoperative tumor prevalence in all patients. Clinical staging of the patients was performed according to Krause classification.<sup>[10]</sup> As a surgical method, lateral rhinotomy/medial maxillectomy, ESS and Caldwell-Luc operations were performed.

### Statistical analysis

The mean, standard deviation and minimum-maximum values of the patients were calculated. In the analysis of the relationship between smoking, old surgery, recurrence and malignancy, Fisher's exact test and Pearson chi-square test were used. The significance of statistical results was accepted as  $p < 0.05$ . For statistical analysis, IBM SPSS Statistics for Macintosh, Version 20 (IBM Corp., New York, USA) program was used.

## RESULTS

The ages of 80 patients included in this study ranged from 20 to 83 years, with a mean age of 53 ( $\pm 12$ ) years. 65 (81.25%) of the cases were male and 15 (18.75%) were female (Table 1). The most common complaints were nasal obstruction (96.2%); rhinorrhea (41%), headache (36.2%), facial fullness (20%), hyposmia (18.7%), epistaxis (10%), epiphora (10%) and hearing loss (7.5%) followed this (Table 2). Twenty-four (30%) of the cases had a history of ESS and in 21 (26.25%) of them, pathological results of previous surgery were nasal polyps. The pathological result was reported as INP in three patients who had ESS applied before externally guided.

In this study, 54% of the patients had left side and 46% of the patients had right side lesion. There was no bilateral lesion in any of the cases (Fig. 1). When the primary anatomic localizations of the disease were evaluated, the lateral nasal wall was the most common site, with a rate of 68.7% (55 patients). In 26 (32.5%) patients, the disease taking his origin from middle meatus and its surroundings, five (6.25%) patients from the ethmoid sinus, four (5%) patients from the maxillary sinus, two (2.5%) patients from the inferior concha and one (1.25%) patients from the septum was detected (Table 3). Rhinosinusitis were present

**Table 1.** Distribution of the patients according to demographic and clinical parameters

	n=80	%
Gender		
Male	65	81.25
Female	15	18.75
Age groups (year)		
20–40	18	22.5
41–60	40	50
61–80	19	23.75
>80	3	3.75
Smoking habit		
Yes	31	38.75
No	49	61.25
Associated chronic rhinosinusitis		
Yes	7	8.75
No	73	91.25
Previous surgery		
Yes	24	30
No	56	70

**Table 2.** Distribution of the patients' complaints

Complaints	%
Nasal obstruction	96.2
Rhinorrhea	41
Headache	36.2
Fullness of the face	20
Hyposmia	18.7
Epistaxis	10

in 8.75%, nasal polyposis in 12.2%, antrochoanal polyp in 5.5% of the cases (Table 1).

According to the Krause staging system,<sup>[10]</sup> 4 (5%) of our cases were classified as stage 1, 27 (33.7%) were stage 2, 34 (42.5%) were stage 3 and 15 (18.75%) were classified as stage 4 (Table 4). On CT bone remodelling was detected in 33% of the cases and bone erosion was observed in 11 (13.75%) of our cases (Fig. 2).

The open technique with lateral rhinotomy was performed to complete the tumor excision in 23 (28.8%) of 74 (92.5%) cases that we started the operation with ESS. When we analyzed the distribution of these cases

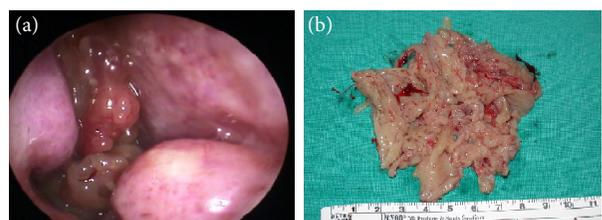


Figure 1. Clinical endoscopic view (a) of and endoscopically excised (b) inverted nasal papilloma.

**Table 3.** Inverted nasal papilloma's' origin of our cases

	n=80	%
Lateral nasal wall	42	52.5
Middle meatus	26	32.5
Ethmoid sinus	5	6.25
Maxillary sinus	4	5
Inferior concha	2	2.5
Nasal septum	1	1.25

**Table 4.** Distribution of our patients according to Krouse staging system

	n=80	%
Stage 1	4	5
Stage 2	27	33.75
Stage 3	34	42.5
Stage 4	15	18.75

according to the Krause staging system,<sup>[10]</sup> we identified 0 patients as stage 1, five patients as stage 2, nine patients as stage 3 and nine patients as stage 4. Stage 3 and four cases were statistically different from stage 1 and 2. Since maxillary sinus walls cannot be dominated endoscopically in 6 (7.5%) patients, Caldwell-Luc operations were performed in addition to ESS. Revision surgery was performed in nine (11.25%) cases due to recurrence. The mean recurrence time was 8.6 years in cases. None of the recurrent cases had undergone open surgery previously. All nine patients underwent ESS previously, but three of the patients undergoing revision ESS had a history of ESS performed previously. Pathological diagnosis of three patients was reported as a nasal polyp in the first ESS. According to the Krause staging system,<sup>[10]</sup> five of recurrent cases were classified as stage 2, four of recurrent cases were stage 3. There were not any stage 1



Figure 2. Coronal view of Paranasal Sinus CT: Soft tissue mass filling the right nasal cavity completely, bone erosion of the ethmoidal cells and bone defect in the lateral wall of the maxillary antrum.

and 4 in these cases. Stage 2 and 3 cases were statistically different from stage 1 and 4. There were no statistically significant differences between stage 2 and stage 3 in recurrent cases. Non-keratinized squamous cell carcinoma (SCC) was observed in four (5%) cases. While SCC was detected in 3 of these cases during the diagnosis of INP, the other patient was diagnosed as SCC by biopsy performed during the follow-up period 6 months after the first operation.

## DISCUSSION

INP are benign epithelial tumors that develop by stromal invagination of the mucosal epithelium in the nasal cavity and paranasal sinus; however, they are well-monitored lesions in the clinic due to their local aggressive course and the possibility of recurrence and malignant transformation.<sup>[3,11]</sup> Although INP can be seen at all ages, it is most commonly seen in the 5th and 6th decades. INP is observed more frequently in male patients.<sup>[3,4]</sup> The findings in our study were consistent with the previous data and the mean age was 53 and the M: F ratio was 4.33.<sup>[12-14]</sup>

The most common complaint in patients is the nasal obstruction. In addition, additional complaints, such as rhinorrhea, headache, epistaxis and anosmia, can be observed. The symptoms are not specific, but unilateral signs and symptoms should be considered for INP.<sup>[2,14]</sup> In our study, the most common symptom was a nasal obstruction, with a frequency of 96.2% similar to other studies. Rhinorrhea (41%), headache (36.2%), facial fullness (20%), hyposmia (18.7%), epistaxis (10%), epiphora (10%) and hearing loss (7.5%) followed this complaint.

In the endoscopic examination, the INP is more rigid and opaque than the inflammatory polyps. However, INP can be observed in the deep of inflammatory polyps. This may make it difficult to suspect INP in the endoscopic examination.<sup>[14]</sup> Although INP is often seen as a unilateral mass, the bilateral lesion has been defined between 4–9% in the studies.<sup>[7,14]</sup> It has been suggested that bilateral nasal involvement arises from the infiltration of the septum into the nasal meatus.<sup>[15,16]</sup> In our study, the bilateral lesion was not observed in any patient.

Imaging methods are important concerning the localization of the tumor; its prevalence, its relationship with adjacent structures and selection of the surgical intervention to be performed.<sup>[17]</sup> On the CT, INPs appear as heterogeneous intense contrast-enhancing masses in soft tissue density. Remodelling of the bone is characteristic and manifests itself with the calcification in the tumor, erosion and sclerotic changes in 43% of cases.<sup>[17,18]</sup> In our study, CT was routinely requested from all patients suspected of INP before the operation. In our series, bone remodelling was detected in 33% of the cases. We think that this particular image detection will be important in deciding the surgical method. Definitive diagnosis in INP is determined by biopsy, but in some cases, false negatives may occur because these lesions can be observed together with benign

polyps. However, the preoperative biopsy is considered important in the exclusion of malignancy.<sup>[19]</sup>

Although INP mostly originates from the lateral nasal wall and the maxillary medial wall, it may also originate from the frontal sinus, sphenoid sinus or nasal septum.<sup>[4,20]</sup> In our study, the lateral nasal wall was the most common localization, with 52.5% incidence.

The classification system described by Krause in 2000 is accepted in INP staging.<sup>[10]</sup> In the study performed by Çomoğlu et al.,<sup>[13]</sup> the majority of the patients (78.8%) were staged as T3. Krause et al. and in the articles published by Lawson et al.,<sup>[12]</sup> 91% and 88% were staged as T3 and T4, respectively. In our study, four (5%) of our cases were classified as stage 1, 27 (33.75%) were stage 2, 34 (42.5%) were stage 3 and 15 (18.75%) were classified as stage 4. Unlike other studies, stage 2 intensity of the patients was more. This situation can be explained by the increasing importance of ESS in the unilateral sinus pathologies and the possibility of early diagnosis with the developing technological parameters.

The gold standard in treatment is surgical resection of the tumor. Although various methods, such as lateral rhinotomy, medial maxillectomy, and Caldwell-Luc, have been applied, ESSs are generally used with the development of technical facilities.<sup>[16,20]</sup> In our study, the open technique with lateral rhinotomy was performed to complete the tumor excision in 23 (28.75%) of 74 (92.5%) cases that we started the operation with the ESS. Stage 3 and 4 groups were statistically significant in the Krause staging of 23 patients who underwent open technique lateral rhinotomy. In our opinion, it may be more meaningful to start operation with open technique in advanced stages. In the anterior and lateral wall involvement of the maxillary sinus, ESS can be performed in combination with Caldwell-Luc.<sup>[21]</sup> In our study, Caldwell-Luc intervention was added to ESS in six cases (7.5%).

Localized recurrence of INP is 0–24%.<sup>[22]</sup> In our study, revision surgery was performed in nine (11.25%) patients due to recurrence. All nine patients underwent ESS previously, but three of the patients undergoing revision ESS had a history of ESS performed previously. Stage 2 and 3 cases were statistically different from stage 1 and 4.

The rate of conversion to INP malignancy was reported as 9.1%.<sup>[8,9]</sup> In our study, non-keratinized SCC was observed in four (5%) of the cases. While SCC was detected in three of these cases at the time of diagnosis of INP, one of them was observed in the follow-up period of six months after the first operation.

## CONCLUSION

As a result, although the INP is a benign epithelial tumor, it should be closely monitored considering the risk of malignant transformation and recurrence. Endoscopic endonasal surgery has improved the treatment rates of INP as new surgical instruments and devices are developed.

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The authors declared that this study had received no financial support.

## Ethics Committee Approval

Approved by the local ethics committee.

## Informed Consent

Retrospective study.

## Peer-review

Internally peer-reviewed.

## Authorship Contributions

Concept: S.A., M.G.D., H.B., E.U.; Design: S.A., M.G.D., H.B., E.U.; Supervision: S.A., M.G.D., H.B., E.U.; Data: S.A., E.U.; Analysis: S.A.; Literature search: S.A.; Writing: S.A., E.U.; Critical revision: S.A.

## Conflict of Interest

None declared.

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### İnverted Nazal Papillomalı Hastalarımızın Klinik Sonuçlarının Geriye Dönük Analizi

**Amaç:** Kliniğimizde inverted nazal papilloma (İNP) tanısı almış olguların retrospektif olarak değerlendirilmesi, elde edilen sonuçlar ışığında sonraki cerrahi ve klinik yaklaşımlar konusunda literatüre katkıda bulunmaktır.

**Gereç ve Yöntem:** Kliniğimizde 2010–2018 arasında İNP tanısı alarak cerrahi tedavi uygulanan 80 hasta geriye dönük olarak değerlendirildi. Hastalar demografik verileri, başvuru şikayeti, kaynaklandığı primer bölge, klinik evresi, bilgisayarlı tomografi (BT) skorları, uygulanan cerrahi yöntemler, malign transformasyon ve rekürrens açısından değerlendirildi.

**Bulgular:** Hastaların 65'i (%81.25) erkek, 15'i (%18.75) kadındı. Ortalama yaş  $53 \pm 12$  iken en genç hasta 20 en yaşlı hasta 79 yaşındaydı. En sık görülen şikayet tek taraflı burun tıkanıklığı (%96.2) idi. İkinci sırada başağrısı (%41) izlendi. İNP'nin görüldüğü en sık primer bölge lateral nazal duvar (%52.5) iken sırasıyla orta meatus (%32.5) ve ethmoid sinüs (%6.25) de izlendi. Olgularımızın 11 (%13.7) kadarında BT'de kemik erozyonu izlendi. Endoskopik sinüs cerrahisi (ESC) ile başladığımız 74 (%92.5) olgumuzun 23'üne (%28.8) tümör eksizyonunu tamamlamak için lateral rinosomi ile açık teknik uygulandı. Rekürrens nedeniyle dokuz (%11.3) olgumuza revizyon cerrahi uygulandı. Olguların dördünde (%5) nonkeratinize skuamöz hücreli karsinom izlendi.

**Sonuç:** İnverted nazal papillomalar endoskopinin rutin nazal muayeneye girmesiyle hem tanınmalarını hem de tedavilerini daha erken hale getirmiştir. Önceleri uyguladığımız klasik açık cerrahi müdahaleler yerini fonksiyonel ESC'ye bırakmıştır. Özellikle bu tür tümörlerin yüksek oranda rekürrensi ve maligniteye transformasyon göstermesi sebebiyle olguların yakın takibinin çok önemli olduğunu düşünüyoruz.

**Anahtar Sözcükler:** Benign tümör; burun tıkanıklığı; endoskopik sinüs cerrahisi; inverted nazal papillom; paranazal sinüs.