

Diagnosis and treatment of nasal and paranasal inverted papillomas – epidemiology and own experience

Joanna Nowosielska-Crygiel, Piotr Pietkiewicz, Kalina Owczarek, Jurek Olszewski, Jarosław Miłośki

Department of Otolaryngology, Oncological laryngology, Audiology, and Phoniatics, II Chair of Otolaryngology, Medical University, Lodz, Poland
Head: prof. Olszewski, MD, PhD

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ABSTRACT:

Introduction. The aim of this study was to analyse the occurrence of inverted papillomas of the nose and paranasal sinuses in patients that underwent endoscopic sinus surgery in our department.

Material and methods. Between 2006 and 2016, 3,574 patients underwent surgery due to paranasal sinus diseases. Patients were qualified for surgery based on medical history, computed tomography, and laboratory tests. Data were gathered from medical files, and they included age, sex, and histopathological diagnosis.

Results. Among 3,574 patients that underwent surgery due to chronic inflammatory changes, on histopathology, inverted papillomas were diagnosed in 80 patients, including 31 women (38.75%) and 49 men (61.25%). Most patients were aged 60-70 years (women, 12.5%; men, 15%) or 50-60 years (women, 5%; men, 21.25%). Between 2006 and 2016, the number of surgeries ranged from 264 (7.38%) in 2013 to 355 (9.93%) in 2016, and the number of inverted papillomas ranged from 4 in 2007 and 2015 (1.23%) to 12 in 2014 (3.87%). Over the last 4 years of the study period, the incidence of inverted papillomas increased.

Conclusions. Among 3,574 patients operated on due to chronic inflammatory changes, on histopathology, inverted papillomas were diagnosed in 80 cases (2.23%); thus, all patients qualified for endoscopic surgery due to inflammatory or hypertrophic changes should undergo rhino-fiberoscopy. Recurrence of inverted papillomas was observed in 17.50%, typically in patients with nasal polyps that co-occurred with inverted papillomas. We regard rhino-fiberoscopy as the most valuable method for detecting tumour recurrence in patients after surgery for inverted papillomas.

KEYWORDS:

inverted papilloma; endoscopic surgery; paranasal sinuses

Inverted papilloma is a benign tumour that originates from mucous membrane epithelium of the nose and paranasal sinuses. Inverted papillomas are found mostly in the maxillary sinus, the ethmoid sinus, and the lateral nasal wall. Inverted papillomas develop from remnants of the Schneiderian membrane, present during the embryogenesis, at the border between the nose and the paranasal sinuses. Inverted papillomas have characteristic histological features such as multiple digit-like ingrowths of the tumour tissue into the stroma; hence, the name *inverted* papilloma. These histological features and an aggressive growth of inverted papillomas make complete resection difficult, which often leads to recurrence.

In patients with inverted papillomas, tumour recurrence after surgical resection is a common problem.

Inverted papillomas comprise 0.5%-4% of primary nasal tumours [1,2], with a prevalence among men of 1.5 per 100,000. Among people aged 40-60 years, men are 3 times more likely than women to have inverted papillomas.

Inverted papillomas have a high recurrence rate (20%-47%) and are locally malignant [3,4]. In patients with inverted papillomas, non-radical tumour resections are associated with an increased risk of recurrence. The Krouse classification [5], which takes into account tumour malignancy, is used most commonly for classifying inverted papillomas in research studies (Tab. I) [6, 7].

The aetiology of inverted papillomas is not clear, but certain factors increase the risk of inverted papillomas, such as HPV infections, allergy, chronic sinusitis, cigarette smoking, occu-

pational exposure to chemical solvents, and genetic factors [8,9,10]. In particular, the HPV types 6, 11, 16, and 18 are associated with the aetiology of inverted papillomas, and the HPV genetic material is found in one-fourth of patients with inverted papillomas.

Inverted papillomas without dysplasia or with low-grade dysplasia are most commonly associated with HPV types 6 and 11. Moreover, HPV types 6 and 11 increase the recurrence risk of inverted papillomas. HPV type 16 and 18 infections, found in 10%-15% of patients with inverted papillomas, increase the risk of malignant transformation into squamous cell carcinoma.

This study aimed to assess the frequency of inverted papillomas in the nose and paranasal sinuses among patients that underwent sinus endoscopic surgery in our department.

MATERIALS AND METHODS

Between 2006 and 2016, in our department, 3,574 patients underwent endoscopic sinus surgery due to diseases of the paranasal sinuses. Patients were qualified for surgery based on medical history, physical examination, 3-plane computed tomography of the paranasal sinuses, and laboratory results. The following data were gathered from patients' medical records: age, sex, and histopathological results of samples excised during surgery. Only data of patients with inverted papillomas diagnosed on histopathology were analysed.

RESULTS

Among 3,574 patients that underwent endoscopic sinus surgery due to chronic inflammatory disease, 80 patients had inverted papillomas on histopathology (31 women, 38.75%; 49 men, 61.25%; age range, 20-75 years; mean age, 51.5 years). Most patients were aged 60-70 years (10 women, 12.5%; 12 men, 15%), 50-60 years (4 women, 5%; 17 men, 21.25%) (Tab. II), or over 70 years (9 women, 11.25%; 9 men, 11.25%) (Tab. II). Less frequently, patients were aged 30-40 years (6 men, 7.5%) or 20-30 years (2 women, 2.5%; 1 man, 1.25%),

Tab. II. Age groups and sex of patients with inverted papillomas

SEX	20-30 YEARS		30-40 YEARS		40-50 YEARS		50-60 YEARS		60-70 YEARS		OVER 70 YEARS		TOTAL	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Women	2	2,50	-	-	6	7,50	4	5,00	10	12,50	9	11,25	31	38,75
Men	1	1,25	6	7,50	4	5,00	17	21,25	12	15,00	9	11,25	49	61,25
Total	3	3,75	6	7,50	10	12,50	21	26,25	22	27,50	18	22,50	80	100,00

Tab I. The Krouse classification, taking into account tumour malignancy, of inverted papillomas [5]

THE KROUSE CLASSIFICATION OF INVERTED PAPILLOMAS	
T1	Tumour totally confined to the nasal cavity, without extension
T2	into the sinuses. There must be no concurrent malignancy.
T3	Tumour involving the ostiomeatal complex, and ethmoid sinuses, and/or the medial portion of the maxillary sinus, with or without involvement of the nasal cavity. There must be no concurrent malignancy
T4	Tumour involving the lateral, inferior, superior, anterior, or posterior walls of the maxillary sinus, the sphenoid sinus, and/or the frontal sinus, with or without involvement of the medial portion of the maxillary sinus, the ethmoid sinuses, or the nasal cavity. There must be no concurrent malignancy
All tumours with any extranasal/extrasinus extension to involve adjacent, contiguous structures such as the orbit, the intracranial compartment, or the pterygomaxillary space. All tumors associated with malignancy	

Table III presents the number of surgeries performed between 2006 and 2016. The greatest number of surgeries was performed in 2016 (355, 9.93%), and the lowest number of surgeries was performed in 2013 (264, 7.38%). Over the period of 2006 -2016, the number of inverted papillomas ranged from 4 in 2007 and 2015 (1.23%) to 12 in 2014 (3.87%). Among 3,574 patients that underwent endoscopic sinus surgery, 2.23% had inverted papillomas.

In the studied patients, inverted papillomas were localized most commonly in the middle nasal concha and the ethmoid sinus (28, 35%), the middle nasal concha and the maxillary sinus (21, 26.25%), and the middle nasal concha, the ethmoid sinus, and the maxillary sinus (18, 22.50%; Tab. IV). Inverted papillomas were found least commonly in the middle nasal concha, the ethmoid sinus, and the sphenoid sinus (3, 3.75%).

The rare malignant form of the inverted papilloma was not found in the studied patients. In 77 patients (96.5%), inverted papillomas were unilateral, and the remaining 3 inverted papillomas (3.75%) were bilateral.

Post-surgery, tumour recurrence on fiberoscopy or endoscopy was noted in 14 patients (17.5%). Those patients underwent

repeated endoscopic sinus surgery, and the recurrence of inverted papillomas was confirmed in all of them.

Recurrence of inverted papillomas in the studied patients occurred 3-9 months after initial surgery. Tumour recurrence was observed in 3 patients (3.75%) after 3 months, in 4 patients (5.%) after 8 months, and in 5 patients (6.25%) after 9 months.

DISCUSSION

Symptoms and signs of inverted papillomas are not specific and usually resemble the symptoms of chronic inflammatory diseases of the nose and paranasal sinuses. Diagnosing inverted papillomas is particularly challenging in patients after surgery due to chronic, polypous diseases of the nose and paranasal sinuses. The presence of inverted papillomas is typically first suspected on computed tomography of the paranasal sinuses because this examination is currently ordered commonly, not only by laryngologists, in patients with chronic diseases of the paranasal sinuses. However, computed tomography of the paranasal sinuses cannot reveal features that would be specific to inverted papillomas. Moreover, many authors have reported that tumour size in patients with inverted papillomas is often overestimated on computed tomography compared to the actual size found on surgery [11,12,13]. Magnetic resonance imaging seems to be a better method than computed tomography for estimating tumour size in patients with inverted papillomas, particularly with respect to tumours that penetrate outside the nose or paranasal sinuses. Final diagnosis of an inverted papilloma is always made based on a histopathological examination.

In our study, among 3,574 patients that underwent endoscopic sinus surgery due to chronic inflammatory diseases, on histopathology, inverted papillomas were found in 80 patients (2.23%; 31 women, 38.75%; 49 men, 61.25%); these patients were typically aged 60-70 years (12.5% women, 15% men) or 50-60 years (5% women, 21.25% men).

Over the period of 2006 -2016, the number of endoscopic sinus surgeries performed each year varied, from 264 (7.38%) in 2013 to 355 (9.93%) in 2016; also, the number of inverted papillomas ranged from 4 in 2007 and 2015 (1.23%) to 12 in 2014 (3.87%). The number of inverted papillomas increased over the last 4 years of the study period.

Among Polish authors, Starska et al. [14] noted 16 patients with inverted papillomas over 4 years, and Osuch-Wójcikiewicz et al. [15] noted 18 patients over 11 years.

Tab. III. Number of sinus endoscopic surgeries in patients with inverted papillomas between 2006 and 2016

ROK	NUMBER OF SINUS ENDOSCOPIC SURGERIES		NUMBER OF INVERTED PAPILOMAS		NUMBER OF SURGERIES / NUMBER OF INVERTED PAPILOMAS	
	N	%	N	%	N	%
2006	292	8,17	5	6,25	292/5	1,71
2007	323	9,03	4	5,00	323/4	1,23
2008	329	9,20	7	8,75	329/7	2,12
2009	330	9,25	8	10,00	330/8	2,42
2010	345	9,65	9	11,25	345/9	2,60
2011	330	9,25	7	8,75	330/7	2,12
2012	346	9,68	9	11,25	346/9	2,60
2013	264	7,38	6	7,50	264/6	2,27
2014	310	8,67	12	15,00	310/12	3,87
2015	350	9,79	4	5,00	350/4	1,14
2016	355	9,93	9	11,25	355/9	2,53
Łącznie	3574	100,00	80	100,00	3574/80	2,23

Tab. IV. Locations of inverted papillomas

Location of inverted papillomas	n	%
Middle nasal concha, ethmoid sinus, the sphenoid sinus	3	3,75
Lower nasal concha and maxillary sinus	10	12,50
Middle nasal concha, ethmoid sinus, and maxillary sinus	18	22,50
Middle nasal concha and maxillary sinus	21	26,25
Middle nasal concha and ethmoid sinus	28	35,00
Total	80	100,00

Among non-Polish authors, Pasquini et al. [16] diagnosed 89 patients with inverted papillomas over 20 years, and Akkari et al. [17] diagnosed 110 patients over 21 years.

It is commonly accepted that patients with inverted papillomas should be treated surgically [18,19,20].

However, it is not always clear what surgery type, open or endoscopic, should be performed. In patients with inverted papillomas, surgery type can be chosen based on tumour size, location, involvement of surrounding tissues, or surgeon experience. In recent years, the anatomical area that can be resected during endoscopic surgery of the paranasal sinuses has increased due to technical advancements and a growing experience of surgeons, who operate more and more patients. Tumour recurrence has been the main outcome on which open

and endoscopic surgery have been compared in patients with inverted papillomas [21,22,23]. Many authors underscore that surgery success is significantly related to tumour stage, which is the basis for choosing an appropriate surgery type. Currently, based on extensive research, open and endoscopic surgery for inverted papillomas seem to have an equal efficacy. However, due to other advantages of endoscopic sinus surgery, it is the treatment of choice for patients with inverted papillomas, also in the case of tumour recurrence [24,25,26].

In this study, 96.25% of patients had unilateral inverted papillomas, and the remaining 3.75% had bilateral inverted papillomas. Post-surgery, tumour recurrence on fiberoscopy or endoscopy was noted in 14 patients (17.5%). These patients underwent repeated endoscopic sinus surgery, and the recurrence of inverted papillomas was confirmed in all of them.

At the earliest, tumour recurrence was observed after 3 months, in 3 patients (3.75%), and at the latest, after 8 months in 4 patients (5%), and after 9 months in 5 patients (6.25%). Recurrence of inverted papillomas (17.5% in our study), particularly early recurrence, is due to incomplete recurrence or polypous changes that co-occur with inverted papillomas.

In patients with inverted papillomas, surgery success depends on choosing an optimal surgery scope, which should guarantee a tumour-free margin and the least possible destruction of the nose and paranasal sinuses. Thus, when deciding on the surgery scope based on computed tomography images of the paranasal sinuses, the most likely attachment site of the inverted papilloma should be determined, particularly in patients operated on due to tumour recurrence. In our patients, inverted papillomas were typically removed with the neighbouring bone wall of the suspected attachment site.

Large surgical excisions, associated particularly with open surgery, does not seem justified in patients with small inverted papillomas, especially because these tumours are benign. Thus, endoscopic sinus surgery is the treatment of choice for patients with inverted papillomas. However, surgeons are less experienced with regard to endoscopic surgery compared to open surgery, which can lead to less precise tumour excisions and consequently to tumour recurrence; indeed, incomplete resection is a major cause of recurrence.

Although an adequate care is given to patients with inverted papillomas both during diagnosis and surgery, tumour recurrence is relatively common (5%-30% of cases), which is a characteristic feature of inverted papillomas.

During the first year after surgery for inverted papillomas, we recommend that patients undergo endoscopic assessments every month and computed tomography of the paranasal sinuses every 3 months.

CONCLUSIONS

Among 3,574 patients that underwent endoscopic sinus surgery due to inflammatory diseases of the paranasal sinuses, 80 had inverted papillomas (2.23%). Thus, all patients qualified for endoscopic surgery due to inflammatory or hypertrophic diseases should undergo fiberoscopy.

Recurrence was found in 17.5% of patients operated on for inverted papillomas, typically in patients with polypous changes in the nose or paranasal sinuses that co-occurred with inverted papillomas. The most valuable method for detecting tumour recurrence in patients with inverted papillomas is fiberoscopy.

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Corresponding author: Prof. dr hab. med. Jurek Olszewski; Department of Otolaryngology, Oncological laryngology, Audiology, and Phoniatics, II Chair of Otolaryngology, Medical University, Lodz, Poland; ul. Żeromskiego 113, 90-549 Łódź; Tel. +48 42 639 35 80; Fax +48 42 639 35 80; e-mail: jurek.olszewski@umed.lodz.pl

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