



Percentage of Malignancy in Sino Nasal Inverted Papilloma, our Experience

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Abstract

Introduction: Sino nasal inverted Papilloma (IP) is benign epithelial tumors, characterized by their capacity of bone destruction, tendency to relapse and malignancy potential. They represent 70% of the papilloma in the nasal cavity and 0.5% to 4% of neoplasms in the Para nasal sinuses. They appear at any age, with higher incidence in men (2:1); and most often affects a single nostril.

Objective: Evaluate our experience in the diagnosis and treatment of Sino nasal inverted Papilloma, as well as the salinization and relapse incidence of HPV-related IP.

Materials and methods: A retrospective study of Sino nasal Inverted Papilloma diagnosed in patients treated in the Otolaryngology service at the Hospital general de Agudos Dr. Ignacio Pirovano (CABA, Bs. as., Argentina), from 2015 to 2018.

Results: 15 surgeries interventions were performed in patients with a sinonasal IP diagnosed from June 2015 to September 2018. The patients were in an age range between 35 and 75 years, whom 7 were women and 8 men. The average age was 53 years. 100% of the patients (n=15) were treated with endoscopic endonasal resection, and in 27% of these cases (n = 4) were combined with Caldwell-Luc approach.

Conclusions: Sinus inverted Papilloma is a potentially aggressive benign tumor whose gold standard treatment is endoscopic approaches. In our experience the recurrence rate was 20%. In relation to the percentage of malignancy, which does not correlate with the bibliography since it arose in 40% of patients; only 27% of them were HPV-related.

Keywords: Papillomavirus invested sinus; Nasal endoscopic surgery; HPV

Introduction

Inverted papilloma (IP) is a benign tumor that affects the nasal cavity and Para nasal sinuses; it was first described by Ward in 1854. IP makes reference to its microscopic features, which denotes the cryptic invaginations within the underlying stoma, respecting the basement embrane. Histologically they are classified as inverted, fungiform, and oncotic [1].

IP has an incidence of 0.5 to 1.5 cases per 100,000 inhabitants, corresponding to 0.5% - 4% of Sino nasal tumors; its clinical

interest is based on the tendency of the tumor to be locally aggressive, with a high recurrence rate and tendency for salinization [2]. It is predominant in males between the fifth and sixth decades of life [2].

The IP is generally located in the lateral wall of the nasal cavity, or the middle meatus, and spreads to the Para nasal sinuses, orbital floor, and central nervous system [3]. Krause classified IP into 4 groups (Table 1), based on invasion and salinization [4].

T1	Tumor limited to nasal cavity
T2	Tumor limited to ethmoid sinus and middle and superior portion of maxillary sinus
T3	Tumor involves frontal sinus, sphenoid sinus or the lateral and inferior portion of maxillary sinus
T4	Tumor extends beyond the nasal cavity or sinuses, or salinization

Table 1: Krause classification.

Objective

The objective of this work is to evaluate our experience in the diagnosis and treatment of Sino nasal inverted Papilloma, as well as the salinization and relapse incidence in HPV-related IP.

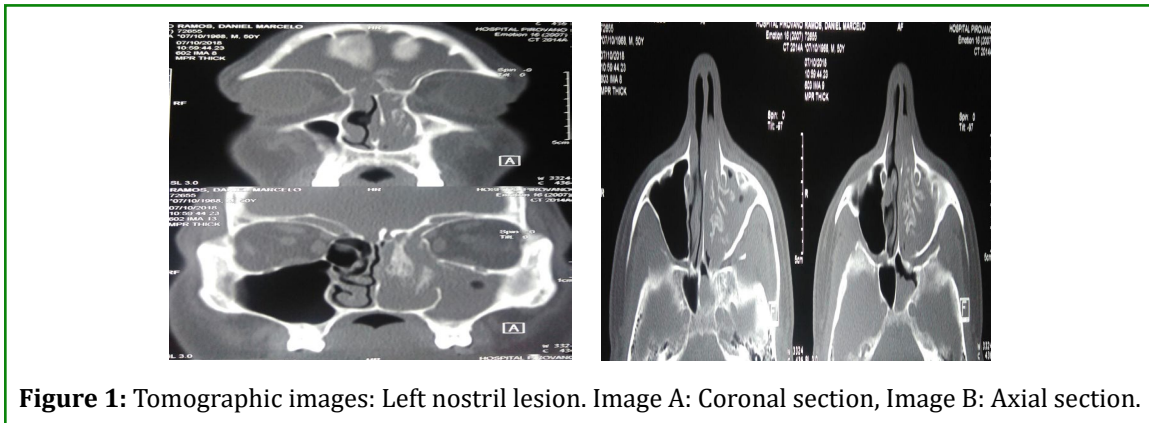


Figure 1: Tomographic images: Left nostril lesion. Image A: Coronal section, Image B: Axial section.

All patients were intervened under general anesthesia, and underwent nasal endoscopic surgery. None of the patients included had a previous biopsy. Four were treated with the combined open Caldwell-Luc approach, since it was not possible to perform a total resection of the lesion by endoscopy. All the biopsies were analyzed by the Anatomic Pathology Department. All of them underwent immunohistochemical techniques to detect p16 for HPV.

Results

We studied 15 patients with diagnosis of IP of which 46.6% (n = 7) were female and 53.3% (n = 8) male. The age range was 35 to 75 years (average age 53 years).

The nasal ventilator insufficiency was the most frequent clinical manifestation in all patients. Rhinorrhea was present in 73.3 % (n = 11) and epistaxis occurred in 20 % (n = 3) of the patients studied.

The location of the lesion in the patients was determined by endoscopic evaluation and tomographic image

Material and Methods

We retrospectively collected data from medical records of 15 patients diagnosed with Sino nasal IP during the period from June 2015 to September 2018. Inclusion criteria in this study were histologically proven PI and a minimum follow-up period of 12 months. Patients were sorted according to age, sex, symptoms, site of injury, surgical procedures, the stage according to Krause's Classification, and the malignization and recurrence rate. To evaluate patients according to Krause's Classification we took into consideration imaging studies and intraoperative findings.

Endoscopic nasal surgery was done on 15 patients within 36 to 73 years with IP diagnosis. Computed Tomography (CT), nasofibrolaryngoscopy (Figure 1), and rhinoscopy with a rigid endoscope were performed in all patients.

(Figure 2). The 93.3 % (n = 14) of our patients presented an unilateral vegetating polypoid lesion, whereas 6.6 % was bilateral (n = 1). The right and left nostril proportion was 46.6% (n = 7) respectively.

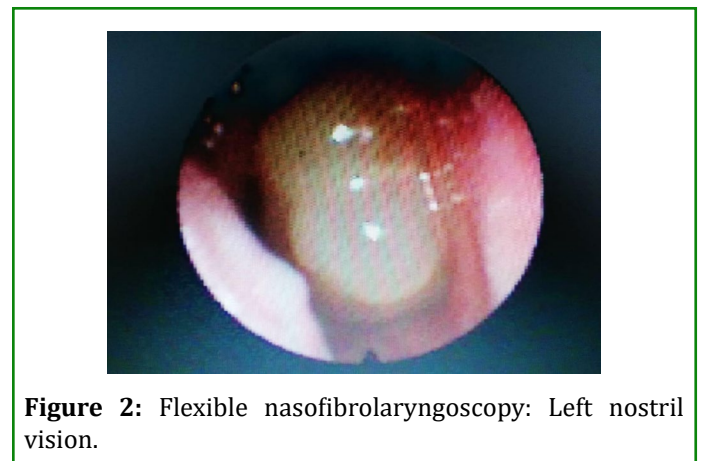
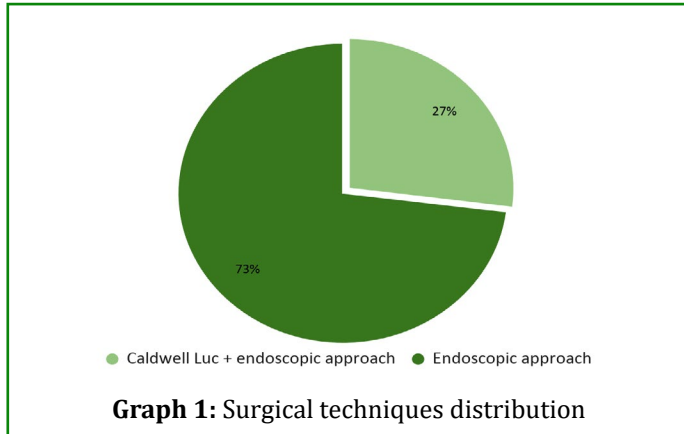


Figure 2: Flexible nasofibrolaryngoscopy: Left nostril vision.

In relation to the Krause's Classification, none of the patients classified as a stage 1 tumor. Only one patient (6.6%) was

classified as a stage 2 IP. Seven patients (46.6%) presented the disease in stage 3. The same percentage, 46.6% (n = 7) were at stage 4 at the time of the study. Within stage 4, 27% (n = 4) positive for p16, and therefore linked to HPV infection.



All patients underwent endonasal endoscopic resection, of which 27 % (n = 4) underwent combined Caldwell-Luc and endoscopic approach (Graph 1).

Histopathological results of the biopsies in all patients revealed inverted schneiderian papilloma (n = 15). Salinization, described by anatomy pathology as “inverted papilloma with squamous foci”, occurred in 40 % (n = 6). All of the malignant IP belong to stage 4 of Krause Classification and were sent to the Oncology division for joint follow-up and radiotherapy.

Recurrent disease was diagnosed in 20% (n = 3) of the patients with IP. Of these, 66.6% (n = 2), underwent combined Caldwell-Luc approaches. The mean time of recurrence was 8.3 months (Table 2). The mean range for postoperative follow-up was 12 to 36 months.

Patient	Age	Symptoms	Location	Histopathology	Recurrence	HPV	Krause's Classification	Time recurrence
M	48	Right nasal ventilatory insufficiency + epistaxis	Right lamina papyracea	Schneiderian papilloma	Yes	No	T4	10 months
M	63	Left nasal ventilatory insufficiency + rhinorrhea	Left nostril	Schneiderian papilloma inverted	-	No	T3	-
F	63	Right nasal ventilatory insufficiency + epistaxis	Right nostril and sinus maxillary	Schneiderian papilloma of exophytic type with marked active chronic inflammatory process	Yes	No	T3	9 months
F	65	Right nasal ventilatory insufficiency	Right nostril and sinus maxillary	Inverted papilloma with squamous focus	-	Yes	T4	-
F	45	Left nasal ventilatory insufficiency + rhinorrhea	Left nostril	Schneiderian papilloma with focal inverted pattern	-	No	T3	-
F	36	Right nasal ventilatory insufficiency + rhinorrhea	Right nostril	Schneiderian papilloma with minimal sectors of inverted pattern and focus of dysplasia (low-grade)	-	No	T2	-

F	38	Right nasal ventilatory insufficiency + rhinorrhea	Right nostril	Inverted papilloma with squamous focus	Yes	Yes	T4	6 months
M	50	Left nasal ventilatory insufficiency + rhinorrhea	Left nostril	Inverted papilloma with squamous focus	-	No	T4	-
M	37	Bilateral nasal ventilatory insufficiency	Bilateral nostril	Inverted papilloma with squamous focus with signs of viral induction	-	Yes	T4	-
M	58	Right nasal ventilatory insufficiency + rhinorrhea	Right nostril	Sinonasal inverted papilloma	-	No	T3	-
F	50	Left nasal ventilatory insufficiency + rhinorrhea	Left nostril	Schneiderian papilloma inverted	-	No	T3	-
M	61	Left nasal ventilatory insufficiency + rhinorrhea	Left nostril	Inverted papilloma with squamous focus	-	No	T4	-
M	47	Right nasal ventilatory insufficiency + rhinorrhea	Right nostril and sinus maxillary	Schneiderian papilloma inverted	-	No	T3	-
F	73	Left nasal ventilatory insufficiency + rhinorrhea	Left nostril	Schneiderian papilloma inverted and exophytic type	-	No	T3	-
M	59	Bilateral nasal ventilatory insufficiency + epistaxis	Left nostril	Inverted papilloma with squamous focus	-	Yes	T4	-

Table 2: Demographic distribution.

-F (female), M (male)

Discussion

The IP is a benign tumor of epithelial origin, which originates in the nasal cavity and from there invades the Para nasal sinuses. Of the total of the rhinosinusal neoplasms, which constitute 3% of head and neck tumors, IP represents 0.5% to 4% [1].

Histologically is characterized by the entophytic growth and invasion of the epithelial cells within the underlying connective tissue, which gives the tumor the inverted morphological feature. It derives from the ectoderm, from the

Schneiderian membrane, which originates the three types of papilloma: inverted, exophytic (fungiform) and cylindrical or oncotoc cells [3].

Its etiology is uncertain but several etiopathogenesis have been described, including certain types of human papillomavirus (HPV) 16 and 18, allergy, chronic rhinosinusitis, environmental agents, tobacco exposure, hepatocyte growth factor and the overexpression of its receptor (c-Met), as well as several enzymes, such as metalloproteinase [1-8].

These rhinosinusal neoplasms can be diagnosed at any age, although some authors consider them typical between the fifth and sixth decades of life, with a male predominance [2-6]. The findings in our series coincided with the bibliography, since the 53.3% were men and the mean age was 53 years.

The symptoms of our patients are in agreement with those described by other authors [7], being the most common unilateral nasal ventilator insufficiency, which was found in 100% of the cases, rhinorrhea in 73%, and epistaxis in 20%.

Similarly, the locations of IP are compatible with the literature [8], highlighting in our series those originating in the lateral nasal wall (ethmoid and maxillary sinus) which represented the 78% of the cases.

The treatment of IP is the complete surgical resection [4]. The endoscopic approach is currently the gold standard in the treatment for the vast majority of authors, allowing complete resection of the tumor, with fewer complications and less postoperative morbidity compared to open approaches [4-9]. However, in cases related to malignancy and recurrence, an external approach is recommended due to greater exposure and control of the lesion margins [9]. In our study, 13.3% (n = 2) of the recurrences were found within the group treated with Caldwell-Luc approach.

Postoperative follow-up should be long-term, due to its aggressive behavior and significant risk of recurrence and salinization [10]. It should be noted that the mean time from surgery to recurrence in our series is 8.3 months. Recurrences during the first year should be considered as residual tumors due to incomplete resections [2-10].

The salinization of the IP to squamous cell carcinoma is between 5% and 15% according to the bibliography [11]. However, in our experience the salinization rate was 40%. We believed that the main risk factor in our patients for the elevated salinization rate is related with the late consultation and therefore late diagnosis, which increases the probability of a locally advanced stage [11].

Conclusions

IP is a potentially aggressive benign tumor whose gold standard treatment is the endoscopic approach. The complete resection of the lesion and a long-term follow-up as fundamental pillars for the success of the treatment. In recent years, many studies have confirmed the validity and efficacy of endoscopic approaches in the treatment of complex Sino nasal pathology, preventing the morbidity of external approaches. In our experience, the recurrence rate was 20%. In relation to the percentage of malignancy, which arose to 40% of patients, but only 27% of them related to

HPV.

Conflict of Interest Declaration

The authors of this article declare that they have no conflict of interest.

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