Abstract

Introduction: Inverted papillomas are benign sinonasal lesions that arise primarily from the lateral nasal wall that are characterized by their tendency to recur and propensity to be associated with malignancy. The aim of this study is to analyse our experience in the treatment of these lesions, especially through the endoscopic approach.

Material and methods: We present 61 cases of sinonasal inverted papillomas that have been treated at our hospital since 1983. The patients were studied by age, gender, tumour presentation site, symptoms, radiological studies, surgical treatment, and evolution. The mean follow-up was 51 months (range, 6-228 months).

Results: Thirty-eight of the patients (62%) were males and 23, females (38%). The average age was 58 (range, 22-80). The most common symptom was unilateral nasal obstruction in 91% of the cases, followed by rhinorrhea in 46%. The most frequent location was the ethmoid region in 51% of cases, followed by the maxillary sinus in 28%, and the lateral nasal wall in 21% of the cases. Seventy-eight percent of cases had associated sinusitis and 43% polyposis. Tumours were classified with the Krouse staging system as follows: thirty-five percent stage I, 37% stage II, 18% stage III, and 8% stage IV. Thirty-seven percent of the patients showed bony erosion in the CT scan. Six of the 42 patients treated by endoscopic procedures presented recurrence (14%), compared with 6 of the 9 patients (67%) who were treated by open approaches. The average time to the recurrence was 41 months. Seventeen percent of the patients had malignant inverted papillomas, 9 of them diagnosed from the beginning as malignant neoplasm and 1 that became malignant during follow up.

Discussion and conclusions: The endoscopic approach is the method of choice for treatment of the majority of inverted papillomas. The close follow up of the patient for a long period of time is necessary for early detection of recurrence and to allow for surgical salvage.

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KEYWORDS
Sinonasal inverted papillomas;
Benign tumour of the nasal cavity;
Endoscopic surgery
Introduction

In 1991 the World Health Organization classified rhinosinusal papillomas into 3 histological types: everted or exophytic papillomas, cylindrical or oncocytic cell papillomas, and inverted or schneiderian type papillomas. Inverted papillomas are the most common within this group, representing about 70% of rhinosinusal papillomas and about 0.5% to 4% of all neoplasms of this area. They are characterised by being unilateral, having a tendency to relapse, being capable of becoming malignant and causing multicentric invasion.

Histologically, inverted papillomas have endophytic growth, with polypoid changes of the nasal mucosa. The nasal mucosa presents a metaplasia of respiratory epithelium to squamous epithelium, while maintaining the basal membrane intact.

Inverted papillomas primarily affect men between the fifth and sixth decade of life. The aetiology remains unknown, although the human papillomavirus has been involved, especially HPV types 6, 11, 16, and 18, as a possible causative agent of the neoplasm.

The aim of this study is to analyse our experience in treating sinonasal inverted papillomas, with particular emphasis on the results of endoscopic treatment.

Methods

We reviewed the inverted papillomas diagnosed and treated in our hospital from January 1983 to May 2009. Patients were studied according to the characteristics of age, gender, presentation site, primary symptoms, radiological characteristics, treatment, and outcome. Patients were staged according to the system described by Krouse. The average follow up of patients was 51 months (range, 6-228 months), with a median of 38 months. Results

During the study period, 61 inverted papillomas were treated in our hospital; 56 were primary cases diagnosed in our hospital and 5 were patients with recurrences who were treated at other centres (all with malignant inverted papillomas). There was a predominance of males, with 38 men out of the 61 patients (61%). The average patient age was 58 years (range, 22-80). Sixty-one percent of the patients had sinusitis and nasal polyps. The clinical presentation was dominated by nasal obstruction followed by epistaxis, nasal bleeding, and anosmia.

Discussion and conclusions: La CEN es el método de elección para el tratamiento de la mayor parte de los papilomas invertidos con resultados equiparables o, incluso, mejores que con las técnicas abiertas. El estrecho seguimiento de los pacientes por largos períodos de tiempo es necesario para detectar de forma precoz las recidivas y poder practicar cirugías de rescate.

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(2%), and the septum in 1 patient (2%). The sphenoid sinus (6 patients), frontal sinus (4 patients), and orbit (4 patients) were less frequent locations and associated with the previously mentioned ones.

The most common symptoms were unilateral nasal respiratory failure, which was found in 91% of cases, rhinorrhea in 46%, headache in 29%, epistaxis in 28%, anosmia in 18%, eye symptoms (proptosis, epiphora), and nasal itching in 7%. The average time from the onset of symptoms to diagnosis was 22 months.

Imaging studies were performed in 49 patients (80%); computed tomography (CT) in 49 patients and magnetic resonance imaging (MRI) in 4 patients. The CT detected bone remodelling in 37% of cases. Observation of occupation of the paranasal sinuses by secretions in 79% of cases (Figure 2) could also be observed in the imaging studies.

Preoperative biopsy was carried out in 40% of the cases, being consistent with the final biopsy in 92% (2 patients had false negatives and there were no false positives). Rhinosinusal inflammatory polyposis was detected in 26 patients (43%). According to the Krouse classification, 21 patients (34%) were, at the time of diagnosis, in stage I, 21 (34%) in stage II, 10 (16%) in stage III, and 9 (15%) in stage IV. Of the 61 patients included in the study, 10 had malignant inverted papillomas (16%), in 8 of them the malignancy had evolved into squamous cell carcinoma and in 2 into transitional cell carcinoma. Nine of the cases were treated from the start as malignant inverted papillomas and were classified in Krouse stage IV, while 1 patient had multiple relapses (3) before malignancy and was classified as stage III.

Within the group of 51 non-malignant inverted papillomas, 42 were operated on through endoscopic nasal surgery (ENS), procedures that have been conducted consecutively since 1993. The stage distribution of these patients was of 18 patients in stage I, 17 patients in stage II, and 7 in stage III. Six patients
(14%) presented relapses. Relapses occurred on average after 57 months. Four patients with recurrence corresponded to Krouse stage III (Figure 3). All patients were rescued by ENS and 3 of them (50%) had no additional recurrences. Of the 3 remaining patients, 1 was lost during follow-up, 1 required an approach by an open technique, and 1 has a small recurrence which, due to advanced age and comorbidity, is regularly monitored in our outpatient service.

The remaining 9 patients underwent an open procedure (the oldest in the series). Five were operated on with a non-endoscopic endonasal approach, 2 by external ethmoidectomy, and 2 patients by a paralateronasal approach. Tumour relapse occurred in 6 of 9 cases (67%). The stage distribution of these patients was 3 patients in stage I, 3 patients in stage II, and 3 patients in stage III. The surgical technique which presented the most recurrences

Figure 3  Surgical treatment of patients with rhinosinusal inverted papillomas.

### Table  Stage, treatment, and outcome of patients with malignant inverted papilloma

<table>
<thead>
<tr>
<th>Case number</th>
<th>Stage (Krouse)</th>
<th>Surgical treatment</th>
<th>Radiotherapy</th>
<th>Time to relapse</th>
<th>Relapse</th>
<th>Rescue Treatment</th>
<th>Intervention</th>
<th>Evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>IV</td>
<td>ENS</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td>VST 42</td>
<td></td>
</tr>
<tr>
<td>2</td>
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<td>ENS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VST 6</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>IV</td>
<td>ENS</td>
<td>38 X</td>
<td>x</td>
<td></td>
<td>CEN</td>
<td>VST 59</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>IV</td>
<td>Craniofacial approach</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td>MPT 81</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>IV</td>
<td>Craniofacial approach</td>
<td>x</td>
<td>11 X</td>
<td>x</td>
<td>Subcraneofacial</td>
<td>DBOC 30</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>IV</td>
<td>Infratemporal maxillectomy</td>
<td>x</td>
<td></td>
<td>X</td>
<td></td>
<td>MPT 3</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>IV</td>
<td>Infratemporal maxillectomy</td>
<td>x</td>
<td>8 X</td>
<td>x</td>
<td>Orbitectomy + parotidectomy</td>
<td>MPT 13</td>
<td></td>
</tr>
<tr>
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<td>IV</td>
<td>Infratemporal maxillectomy</td>
<td>x</td>
<td>10 X</td>
<td>x</td>
<td>Orbitary exenteration + parascapular free flap</td>
<td>MPT 28</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>IV</td>
<td>Subcranial approach</td>
<td></td>
<td>5 X</td>
<td></td>
<td></td>
<td>MPT 36</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>III</td>
<td>Paralateronasal approach</td>
<td>x</td>
<td>7 X</td>
<td>x</td>
<td>Partial maxillectomy</td>
<td>VST 10</td>
<td></td>
</tr>
</tbody>
</table>

DBOC indicates patient death by other cause; ENS, endoscopic nasal surgery.
was the non-endoscopic endonasal approach, which failed in 4 of 5 cases. The 6 patients who presented relapses were surgically rescued: four by ENS and 2 by a paralateronasal approach. One of those in the group rescued by ENS suffered a further recurrence, which was treated by an open technique.

The treatment and outcome of patients with malignant inverted papilloma can be seen in Table. Five of the 10 patients (50%) with malignant inverted papillomas were operated at other centres and referred to our hospital to evaluate the surgical treatment of tumour relapses. The average time to recurrence in malignant cases was 17 months. Recurrences were discordant with the implantation site of the primary tumour in 10% of cases.

The average length of hospital stay was 5 days (range, 1-32 days). Ten patients presented complications, 5 within the group of patients treated by ENS: three formed synechiae and 2 mucoceles. The remaining 5 patients belonged to the group with malignant inverted papillomas, in which 1 formed a mucocele; 1 had a surgical wound infection; 1 a pneumocephalus that was treated surgically; 1 a partial necrosis of the temporal muscle flap; and 1 presented a cerebrospinal fluid fistula that was controlled conservatively. There were no deaths due to surgical complications.

**Discussion**

Inverted papillomas are rhinosinusal tumours that can be diagnosed at any age, although some authors consider them common of the fifth and sixth decades of life, and with male dominance in these lesions. The findings in our series are consistent with those data, as 61% of the patients in the series were male and the average age was 58.

The symptoms of our patients are consistent with those described by other authors, the most common being unilateral nasal respiratory failure that was found in 91% of cases, rhinorhoea in 46%, headache in 29%, epistaxis in 28%, and anosmia in 18%. The poor specificity of these symptoms makes it difficult to distinguish inverted papillomas from other injuries and delays diagnosis in many cases. This results in the fact that, in our series, the average time from onset of symptoms to diagnosis was 22 months. It should be noted that most of the signs and symptoms are usually unilateral (91%), which should alert for tumour pathology.

Examination usually detects unilateral masses with polypous appearance, more opaque and rugged than inflammatory polyps. However, in many cases (between 20% and 50%), inflammatory polyps (usually more visible by rhinoscopy) can coexist with papillomas (usually deeper into the nasal cavity). Between 4% and 9% of tumours are bilateral, but in our series, only 2 (3%) of the 61 patients had bilateral presentation.

The definitive diagnosis is determined by biopsy, although in some cases false negatives can appear because these lesions may coincide with benign polyps. In our series, 2 patients had false negative preoperative biopsies, which can be attributed to rhinosinusal polyposis, present in 43% of cases.

The locations of inverted papillomas are consistent with those published by other authors, highlighting in our series those originating in the lateral nasal wall (ethmoid and maxillary sinus), which were affected by papillomas in 75% of cases.

The performance of imaging studies is considered important in preoperative studies, in particular CT, through which it is possible to locate lesions, assess their extent and assess whether the frontal sinus, the orbit or anterior cranial fossa are affected.

The characteristic findings of CT are tumours from the lateral nasal wall with homogeneous density that are enhanced intensely and heterogeneously after injection of contrast medium. Bone remodelling is characteristic and can be found in 43% of cases, presenting itself as calcifications within the tumour and swelling of the paranasal sinuses, with erosion and sclerotic changes in some cases. In our series, bone remodelling was detected in 37% of cases and occupation of the paranasal sinuses in 79%. The occupation of the sinuses is usually secondary to blockage of the drainage ostium, with MRI being useful to differentiate the tumour from retained secretions in the paranasal sinuses.

In our department, CT is requested routinely for all patients with suspicion of inverted papilloma before surgery, so it is absent only in the older cases (before 1990). An additional MRI was performed in cases where there was suspicion of extension to extra-sinus locations.

Preoperative biopsies are important to rule out malignant inverted papilloma or malignant neoplasm; nevertheless, preoperative biopsy was performed in only 26 of our 61 patients, so it was possible to carry out 40% of diagnoses preoperatively. Surgery was indicated in the rest of cases, based on the findings of examination and imaging studies that suggested the diagnosis of inverted papillomas.

The treatment of choice is complete surgical resection of the lesion. Traditionally, open methods were considered, such as ethmoidectomy and medial maxillectomy, among others, with the disadvantage of the aesthetic consequences and greater morbidity that open procedures involve. There are several publications that support the use of the ENS as a method of choice for resection of inverted papillomas. In our series, we have divided the treatments into those that were malignant inverted papillomas and those that were not. The better results obtained by the ENS are probably due to the better exposure achieved with this technique, allowing experienced surgeons a more accurate resection of inverted papillomas.

Within the group of non-malignant inverted papillomas, external or open approaches were used in the older patients in the series (9 of 51 patients). It should be noted that, although there are reports of successful surgical results, we had a recurrence rate of 67%. The technique with most recurrences was non-endoscopic endonasal resection, which had recurrences in 4 of 5 cases.

ENS was the technique used in the remaining 42 cases, all of them consecutively since 1993, with the exception of some of the malignant cases. Six patients (14%) presented relapses, 4 patients with relapses corresponding to Krouse stage III; this recurrence rate is in agreement with that described by other authors.
Inverted sinonasal papillomas. Review of 61 cases

One limitation of ENS is the technical difficulty involved in accessing lesions in the frontal sinus and anterior and inferior wall of the maxillary sinus, thus making it necessary to use an endoscopic (or open) approach via Caldwell-Luc in 15% to 30% of cases. Of the patients who were operated by ENS and had relapses, 3 presented a compromised frontal sinus and 1 a compromised anterior wall of the maxilla. In this series of patients, we used the combined ENS and endoscopic approach via Caldwell-Luc in 6 patients, obtaining good results in all.

Because relapse can occur even several years after the primary tumours, we recommend long-term monitoring of these patients. Note that the average time from intervention to recurrence in our series was 41 months; there was a patient who presented a recurrence 10 years after surgery. Recurrences during the first year should be considered as residual tumours due to incomplete resections.

In the group of malignant inverted papillomas, 7 patients presented recurrences in the first 12 months after surgery, which could be explained by the aggressive behaviour of these tumours. In contrast, in the group of non-malignant inverted papillomas, only 1 of the lesions was reproduced in the first year after treatment and it was considered as tumour persistence.

Strict monitoring of these patients allows early detection of relapses to consider rescue surgery rescue treatment. In our series, rescue surgery was performed in 85% of patients, except for 4 patients with malignant papillomas with extensive local recurrence that prevented total resection of the lesion and one patient whose monitoring was lost after multiple relapses.

Endoscopic surgery has also proved useful for resection of recurrences caused by open approaches. In our series, it was used for rescue surgery in 7 patients, and was effective in 4 cases.

We note that recurrences were discordant with the area in which the primary tumours appeared in 10% of cases, which could be explained by the possible multicentricity that has been described in inverted papillomas.

The malignancy (towards SCC) of inverted papillomas occurs between 5% and 15% of cases. In this series, 10 patients (16%) had malignant inverted papillomas. One of them had multiple relapses (3) before becoming malignant, 6 were sent to our hospital for treatment, and 3 were diagnosed from the start at our centre as malignant inverted papillomas. The aggressive behaviour of malignant inverted papillomas is reflected in the relapse rate of 80% that we obtained, which was the direct cause of death in 50% of patients.

In conclusion, inverted papillomas are benign neoplasms of the nasal passages and paranasal sinuses that are characterised by an ability to recur and a potential for transformation to malignancy. ENS is the surgical method of choice in all inverted papillomas in Krouse stages I and II and in stages III and IV when the surgeon’s experience and the lesion size ensure complete tumour resection. Close patient monitoring is needed to detect and treat tumour recurrence at an early stage. The poor prognosis of patients with malignant inverted papillomas necessitates the development of new therapeutic strategies for treating these patients.

Conflict of interests

The authors declare no conflict of interests.

References


