GRAND ROUND PRESENTATION

RHINOLOGY
CASE PRESENTATION

• 41 year-old male presented to the clinic with complaint of nasal obstruction ....

More than 5 years duration
Mainly left sided
Progressive
Incomplete ➔ complete .. since one year
NoT improved with intranasal Steroids smoker

Associated with :
Frontal headache (left side)
Snoring
Mouth breathing
Post nasal dripping
Sneezing and itching ..
Epiphora from left eye
Other ENT Sx : -ve
PHYSICAL EXAMINATION

Vital signs
Complete ENT examination
Ears: normal intact TM bilaterally
RIGHT NASAL ENDOSCOPY
LEFT NASAL ENDOSCOPY
WHAT YOU WANT TO DO NEXT?
Sinuses 1mm
Sinuses 1mm
CT REPORT

- Soft tissue mass opacifying left maxillary antrum, ethmoid, frontal and nasal cavity.
- Bony remodeling without destruction
- Right sided concha bullosa

**Impression:**
left sided antrochoanal polyp
WHAT IS YOUR DDX?
WHAT YOU WILL DO?
ADMISSION DIAGNOSIS

Chronic Rhinosinusitis with left sided nasal polyp and right concha bullosa

?? Antrochoanal polyp ..
CT Guided FESS + RT Conchoplasty and bilateral turbenoplasty
OR
WHAT IS YOUR POST OP DX?
POST OP

S: no complaint
O: intact visual acuity
   EOM intact
   No eccymosis
   Bilateral nasal packs removed
   No bleeding
P: Pt D/c home
On: AUGMENTIN
   TYLENOL 3
   NASONEX
   NASAL IRRIGATION
HISTOPATHOLOGY REPORT

Inverted Papilloma
2\textsuperscript{nd} CASE PRESENTATION
• 19 y/o male, presented to the clinic complaining of nasal obstruction
• More on the right side.
• Continuous for the last 4 years
• Associated with post nasal discharge, yellowish in color
• Sneezing for the last 6 years
• No response to medical treatment
P/E

- **Nose**: mild DNS to the right side
polypoidal warty mass in the right nasal cavity
HIT in the right side
- **Ear**: NL
- **Throat**: NL

**CT Scan PNS**
Showed rt sided pan sinusitis
Deviated Nasal Septum to rt side
Left sided concha bullosa
PLAN

• Admission
• Pre operative diagnosis :
  Rt pan Sinusitis with antrochoanal polyp?? Rt warty papiloma + Left concha Bullosa
• Operation :
  Rt polypoidal mass removal from nasal cavity, middle meatus and ethmoid region
  Rt intranasal ethmoidectomy
  Rt middle and inferior antrostomy
  Bilateral partial inferior turbinectomy
HISTOPATHOLOGY

- Sino nasal inverted papilloma
FOLLOW UP

• After one year ...

• Still complaining of nasal obstruction, mainly on the right side
• Getting worse with AR exacerbation
• No response to nasal sprays

• O/E: Congested nasal mucosa bilaterally with purulent discharge + right nasal mass
• Extensive regrowth of inverted papilloma in the right side, involving right nasal cavity, extending to the right maxillary sinus and ethmoid region
PLAN

- Admission
- Pre operative diagnosis: right nasal inverted papilloma + left chronic maxillary sinusitis
- Operation:

  LEFT FESS + RIGHT LATERAL RHINOTOMY + RIGHT VERTICAL MAXILLECTOMY

1995
FOLLOW UP

• Symptoms free for the past 2 years.
• .. Then he started to have the same symptoms
• Right sided nasal obstruction and AR symptoms

• O/E: Polypoidal mass in both sides..
   Right side: mass was filling the nasal cavity extending to maxillary and ethmoid sinuses and MT.
   Left side: polypoidal mass involving middle meatus, IT, MT and left maxillary sinus
CT SCAN PNS

• Right maxillary antrum completely filled with polypoidal soft tissue density... filling also right nasal fossa
• Polypoidal soft tissue density has been also noticed in the left side.
• OMC blocked in both sides
• Admission
• Pre operative diagnosis: recurrent right sided inverted papilloma.
• Operation: Revision CT guided FESS
FOLLOW UP

- 36 Y/O
- Patient is having partial rt sided nasal obstruction 3 years after last surgery
- O/E : NOSE : Polypoidal mass filling right nasal cavity left sided HIT
PLAN

• ADMISSION
• Pre operative diagnosis: recurrent inverted papilloma
• Operation: revision FESS
FOLLOW UP

• 3 months later ....
• Pt presented to the clinic complaining of swelling in the right eye associated with pain and discharge
• No change in vision
• No epiphora

• O/E : Erythmaticus,tender swelling over the right medial canthus
  
  Nose: few polyps on right side
  large middle meatal antrostomy on the right side, absent MT in the rt side and IT in both sides
PLAN

• Admission
• Diagnosis: right recurrent IP complicated by chronic dacrocystitis
• Operation: ENDOSCOPIC CT GUIDED DACROCYSTORHINOSTOMY
FOLLOW UP

• One year later..
• Pt is still having recurrent attacks of dacrocystitis
• Referred to ophthalmology department
• admitted
• Underwent :
  **RIGHT EXTERNAL DCR+M.M.C+STENT**
FOLLOW UP

• Patient is complaining of nasal obstruction
• More in the right side
• Sneezing, rhinorrhea and itching.

• O/E: NOSE: right nasal cavity filled with mass, pinkish in color with yellowish discharge
PLAN

• Admission
• Diagnosis: recurrent right inverted papilloma
• Operation: revision FESS
FOLLOW UP

• 40 Y/O
• NASAL OBSTRUCTION
• More on the right side
• For the past 2 years

• O/E: NOSE: grade 1 polyps bilaterally more in the right side with yellowish secretion
CT PNS

ALBEDAWI, FAISEL, , MOHAMMED, HAMD
KA193888
01/01/95
Series 80256 Img: 17
Sinuses 1mm
PLAN ..

- BOOKED FOR SURGERY
- REVISION FESS
INVERTED PAPILOMA

LITRETURE REVIEW
INTRODUCTION

- IP is rare tumor; the incidence rate is 0.74:100,000 per year.
- accounts for approximately 70% of all sinonasal papillomas

- Two to five times more common in males
- 40–70-year age group
- Mainly unilateral
- Reported to be bilateral in 0–10% of cases
- Bilateral IP should always rise the suspicion of septal erosion and perforation from unilateral disease

papilloma means neoplasia with epithelial growth.

According to the World Health Organization, sinonasal papilloma is defined as a benign epithelial tumor composed of well-differentiated columnar or ciliated respiratory epithelium with variable squamous differentiation.

US National Cancer Institute's has defined inverted papilloma as a type of tumor in which surface epithelial cells grow downward into the underlying supportive tissue.
In 1600s, C. Victor Schneider demonstrated that nasal mucosa produces catarrh and not CSF and identified its origin from the ectoderm. The first report of this type of tumor in the nasal cavity was made by Ward in 1854.

Ringertz et al. in 1938 was the first to identify endophytic growth pattern of IPs with its characteristic tendency to invert into the underlying connective tissue stroma, which differs from other types of papillomas, and called it “inverting papilloma.”
The lining of the nasal cavity and paranasal sinuses is unique in that it is ectodermal in origin.

- Ciliated, pseudostratified columnar epithelium (Schneiderian membrane)
- thin submucosa containing seromucous glands.
1-fungiform (everted) papillomas (septal papilloma) (50%):  
- arise from the nasal septum  
- exophytic growth pattern

2-oncocytic Schneiderian papillomas:  
- arise from the lateral sinus wall or paranasal sinuses.  
- lined with a distinctive stratified lining of bright pink granular columnar cells with microcysts.  
- more often with typical inverted papilloma, rather than presenting in its pure form

3-inverted papillomas:  
- arise from the lateral nasal or sinus wall or paranasal sinuses.  
- Endophytic or mixed exophytic/endophytic growth pattern

<table>
<thead>
<tr>
<th>Papilloma</th>
<th>Fungiform</th>
<th>Inverted</th>
<th>Oncocytic Schneiderian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Former name/synonyms</td>
<td>Septal</td>
<td>Ringertz</td>
<td>Cylindrical, columnar</td>
</tr>
<tr>
<td>Prevalence %</td>
<td>50</td>
<td>47</td>
<td>3–5</td>
</tr>
<tr>
<td>Origin</td>
<td>Nasal septum</td>
<td>Lateral nasal wall and paranasal sinuses</td>
<td>Lateral nasal wall and paranasal sinuses</td>
</tr>
<tr>
<td>Epithelium pattern of growth</td>
<td>Everted, exophytic</td>
<td>Infolded, endophytic</td>
<td></td>
</tr>
<tr>
<td>Microscopy</td>
<td>Thick squamous epithelium and, less frequently, respiratory epithelium arranged in papillary fronds</td>
<td>Thickened squamous epithelium admixed with mucocytes and intraepithelial mucous cysts</td>
<td>Multilayered epithelium with an eosinophilic cytoplasm among which intraepithelial mucin cysts</td>
</tr>
<tr>
<td>Age group</td>
<td>Younger</td>
<td>50–60</td>
<td>30–80</td>
</tr>
<tr>
<td>Malignancy</td>
<td>35% have invasive squamous cell carcinoma</td>
<td>Locally aggressive, extending into the sinuses, the orbit, nasopharynx [20], or meninges. Three to 24% (mean 13%) may have an invasive focus of squamous cell carcinoma</td>
<td>14% ~19% Malignant change potential</td>
</tr>
<tr>
<td></td>
<td>25% multifocal</td>
<td></td>
<td>Mixed with typical inverted papilloma</td>
</tr>
</tbody>
</table>
TABLE II.
Origin Sites of Inverted Papillomas (N = 939).

<table>
<thead>
<tr>
<th>Site</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial wall of MS</td>
<td>299 (31.8)</td>
</tr>
<tr>
<td>Nasal cavity</td>
<td>264 (28.1)</td>
</tr>
<tr>
<td>Anterior ethmoid sinus</td>
<td>224 (23.9)</td>
</tr>
<tr>
<td>Lateral wall of MS</td>
<td>109 (11.6)</td>
</tr>
<tr>
<td>Posterior wall of MS</td>
<td>97 (10.3)</td>
</tr>
<tr>
<td>Superior wall of MS</td>
<td>92 (9.8)</td>
</tr>
<tr>
<td>Anterior wall of MS</td>
<td>90 (9.6)</td>
</tr>
<tr>
<td>Inferior wall of MS</td>
<td>81 (8.6)</td>
</tr>
<tr>
<td>Posterior ethmoid sinus</td>
<td>75 (8.0)</td>
</tr>
<tr>
<td>Frontal sinus</td>
<td>28 (3.0)</td>
</tr>
<tr>
<td>Sphenoid sinus</td>
<td>25 (2.7)</td>
</tr>
<tr>
<td>Septum</td>
<td>21 (2.2)</td>
</tr>
</tbody>
</table>

Kim et al, inverted sinonasal papilloma
PATHOLOGY: NEOPLASTIC CHANGE

Features associated with recurrence or malignant transformation include:
• bone invasion
• high grade dysplasia
• increased mitotic activity
• epithelial hyperplasia,
• epithelial overgrowth of stroma.

Favorable histologic features include:
• presence of inflammatory polyps
• high eosinophil counts
The etiology of inverted papillomas is still unclear. There have been many causes suggested such as allergy, chronic sinusitis viral infections, and inflammation.

Although IPs have long been suspected of being of viral origin, the results of publications on the association of human papillomavirus (HPV) and Epstein–Barr virus (EBV) with IP have been variable.

Significant association has been identified between the presence of human papilloma virus DNA in inverted papilloma and recurrence after surgical excision.

HPV 16 and HPV 18 were found to be related to the malignant transformation of IP and to the pathogenesis of SCC originated in the nasal cavities and paranasal sinuses.

Patients with proof of HPV types 6 or 11 have a lower rate of recurrence than patients with HPV types 16 or 18.

Human Papilloma Virus and Epstein-Barr Virus in Sinonasal Inverted Papilloma

Kayhan Başak†, Şükran Kayıpmaz¹, Hammi İstem Köse¹ and Nimet Karadayı¹

Department of Pathology, Dr.Lütfi Kirdar Kartal Education and Research Hospital, İstanbul, Turkey

*Corresponding author: Kayhan Başak, Department of Pathology, Dr.Lütfi Kirdar Kartal Education and Research Hospital, Şems Denizer Cad, E-5 Karayolu, Cevizli Mevkii, 34890 Kartal, İstanbul, Turkey, Tel: +90 216 4413900/ 1054; Fax: +90 216 3520083; Email: drkayhanbasak@yahoo.com/ kayhan.basak@sbkeah.gov.tr

Received: August 13, 2014; Accepted: September 08, 2014; Published: September 10, 2014

Abstract

**Background:** Schneiderian papillomas are uncommon benign tumors of the sinonasal area. They tend to present local aggressiveness and recurrence, and some undergo malignant progression. This study aimed to search of human papillomavirus (HPV) and Epstein–Barr virus (EBV) in sinonasal inverted papilloma (IP) in order to elucidate possible role in its pathogenesis.

**Methods:** Forty-eight IPs were subjected to chromogenic in-situ hybridization (CISH) for HPV DNA (HPV-III family16), Real-time PCR for HPV, p16, anti-EBV and Ki67 immunohistochemical (IHC) studies.

**Results:** p16 was positive in 30 of 48 (62.5%), CISH for HPV was positive in 1 of 48 IPs (2.1%). All specimens were EBV negative. In total, 33.3% of IPs showed suprabasal Ki67 reactivity. HPV prevalence of our IP is high. EBV is not present in IP.

**Conclusion:** This evidence suggested that HPV infection but not EBV plays a role in pathogenesis of IP. Negative PCR results possibly depend on age of the paraffin blocks.

**Keywords:** Human papillomavirus; Epstein-Barr virus; p16; Inverted papilloma; PCR
• The theory concerning allergy as a causing factor is not supported, mainly because most patients have no allergic background and polyps.
• Allergic rhinitis is mainly bilateral, while inverted papilloma is almost always unilateral.
• Sinusitis is common in patients with IP, but it is rather a complication caused by the occlusion of the sinuses from the enlarging tumor.
Unilateral nasal obstruction is the most common presenting symptom.

- Other manifestations include
  nasal discharge
  epistaxis (10–20% of cases)
  anosmia
  headaches (especially frontal)
  epiphora
  proptosis
  diplopia.

Pain, is an uncommon initial complaint, occurring in only about 10% of all cases. When present, it should always arouse suspicion of secondary infection or even a malignant change.
### SIGNS AND SYMPTOMS OF INVASION

**Table 4:** Signs and symptoms of invading IP, classified by site of invasion.

<table>
<thead>
<tr>
<th>Intracranial Invasion</th>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior cranial fossa via the cribriform plate</td>
<td>Anosmia or symptoms related to displacement of the globe</td>
<td>Anosmia, proptosis</td>
</tr>
<tr>
<td>Orbital involvement</td>
<td>Proptosis, periorbital swelling, epiphora, diplopia, blurred vision, trigeminal paresthesias, trismus, retroorbital pain and visual loss, or complain of facial numbness</td>
<td>Impaired ocular mobility, anesthesia or hypesthesia of the infraorbital, sphenopalatine, or greater palatine nerves</td>
</tr>
<tr>
<td>Inferior extension into the oral cavity</td>
<td>Painful loose teeth, poorly fitting dentures, mass in the oral cavity, swelling of cheek, nose, or around the eye.</td>
<td>Oral cavity mass on the palate, upper Alveolus, or upper gingivobuccal sulcus or with malocclusion or loose teeth</td>
</tr>
</tbody>
</table>
On physical examination:

IPs present as pink, tan, or gray; nontranslucent; soft to moderately firm polypoid growths with a convoluted or wrinkled surface.
INVESTIGATIONS

- CT and MRI are both typically performed for evaluation of sinus tumors ..... IP included within this pathological group.

- CT and MRI are the techniques of choice for pretreatment staging in inverted papilloma.

- Several radiologic patterns could be seen, therefore it is difficult to categorize any as specific for inverted papilloma.

CT OF IP

- Bone remodelling is characteristic and can be found in 43% of cases presenting as calcifications within the tumour and swelling of the paranasal sinuses, with erosion and sclerotic changes in some cases.

Ojiri et al. discussed the following MRI features as potentially distinctive of sinonasal inverted papilloma on MR imaging.

- **First**, IPs have a heterogeneous appearance on MRI.
  - **T1** - isointense to muscle
  - **T2** - generally hyperintense to muscle alternating hypointense lines
  - **T1 C+ (Gd)** - heterogeneous enhancement alternating hypointense lines

- A **convoluted cerebriform pattern on T2 and enhanced T1-weighted MRIs for inverting papilloma may be potentially distinctive in 80% of cases**
  - Inflammatory polyps and inspissated material in the sinuses secondary to obstruction by the papilloma are hyperintense on T2-weighted images

---

Convoluted cerbriform pattern This represents alternating lines of high and low signal intensity, the appearance of which has been likened to cerebral cortical gyrations.
### STAGING

**Table 5: Krause staging system (2000) for inverted papilloma [324].**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Location and spread</th>
<th>Malignant changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumor totally confined to the nasal cavity, without extension into the sinuses. (The tumor can be localized to one wall or region of the nasal cavity or can be bulky and extensive within the nasal cavity but must not extend into the sinuses or into extranasal compartment)</td>
<td>There must be no concurrent malignancy</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor involving the ostiomeatal complex, and ethmoid sinuses, or the medial portion of the maxillary sinus, with or without involvement of the nasal cavity.</td>
<td>There must be no concurrent malignancy</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor involving the lateral, inferior, superior, anterior, or posterior walls of the maxillary sinus, the sphenoid sinus, or the frontal sinus with or without involvement of the medial portion of the maxillary sinus, the ethmoid sinuses, or the nasal cavity</td>
<td>There must be no concurrent malignancy</td>
</tr>
<tr>
<td>T4</td>
<td>All tumors with any extranasal/extrasinus extension to involve adjacent, contiguous structures such as the orbit, the intracranial compartment, or the pterygomaxillary space</td>
<td>All tumors associated with malignancy</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Limited to the nasal cavity.</td>
</tr>
<tr>
<td>T2</td>
<td>Limited to ethmoid sinus and/or medial and superior portions of maxillary sinus.</td>
</tr>
<tr>
<td>T3</td>
<td>Involving lateral, inferior, anterior, or posterior walls of maxillary sinus, sphenoid sinus, or frontal sinus.</td>
</tr>
<tr>
<td>(T3-A)</td>
<td>Without extension to frontal sinus or supraorbital recess.</td>
</tr>
<tr>
<td>(T3-B)</td>
<td>Involving frontal sinus or supraorbital recess.</td>
</tr>
<tr>
<td>T4</td>
<td>Extending outside sinonasal cavities (orbital or intracranial extension) or associated with malignancy.</td>
</tr>
</tbody>
</table>
## STAGING

**Table 2:** Cannady’s et al. staging system about prognosis (as operationally defined by RR) for IP managed by advanced endoscopic techniques.

<table>
<thead>
<tr>
<th>Group</th>
<th>Location and spread</th>
<th>Recurrence rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>IP confined to the nasal cavity, ethmoid sinus, and medial maxillary sinus</td>
<td>3.0%</td>
</tr>
<tr>
<td>Group B</td>
<td>IP with lateral maxillary sinus, sphenoid sinus, or frontal sinus involvement</td>
<td>19.8%</td>
</tr>
<tr>
<td>Group C</td>
<td>IP with extrasinus extension.</td>
<td>35.3%</td>
</tr>
</tbody>
</table>

• The rare occurrence of IP has limited the development and testing of treatment strategies.

• The majority of published data consists of retrospective reports from single institutions, which have selection and treatment bias.
Inverted papilloma is a surgically manageable condition. The aim of the surgery is eradication of the complete disease in the first attempt itself. Remnants will cause recurrence of the lesion.

The available surgical techniques are as follows:

1. limited conservative surgery,
2. lateral rhinotomy,
3. transfacial with midface degloving,
4. craniofacial resection
5. endoscopic approaches.
TAILORED APPROACH

- All T1 & T2 lesions can be managed by conventional endoscopic sinus surgery.
- Endoscope can be used to perform anterior ethmoidectomy, middle meatal antrostomy and posterior ethmoidectomy. Middle turbinate can also be partially resected to improve access.

- T3 and T4 lesions need a combination of external and endoscopic approaches.
- The medial wall of maxilla will have to be removed to get access to the mass (medial maxillectomy).
LATERAL RHINOTOMY AND MEDIAL MAXILLECTOMY

- Provides excellent surgical access, but requires a significant external incision.

- The technique of lateral rhinotomy and en bloc excision of the lateral nasal wall, followed by meticulous removal of all mucosa in the ipsilateral paranasal sinuses, has been the standard therapy.
INDICATION OF RADIATION THERAPY

Patients unwilling or unable to undergo surgery
Poor surgical candidates
Intolerable morbidity of the radical surgery
Advanced and biologically aggressive SPs
Associated malignancy
Incompletely resected IP
Unresectable lesions
Early recurrence
There is wide range in the frequency of reported carcinoma in patients with IP, ranging between 1–50%

Carcinoma may occur with IP (synchronous carcinoma) or at a later time (metachronous carcinoma).

- Why carcinomas in inverted papillomas arise meta—or synchronous is also still unknown.
- The majority of cases in the literature are synchronous carcinomas.

- Sinonasal carcinomas arise in about 10 - 17% of patients with inverted papillomas.
- The average transformation rate of metachronous carcinomas was reported about 2–7 percent with a mean time of 52 months (range: six to 180 months)
• Bilateral inverted papilloma
• predominance of mature squamous epithelium
• the presence of all three epithelial types (metaplastic squamous, mature squamous, and cylindrical)
• severe hyperkeratosis
• mitotic index greater than or equal to 2 per high-power field (HPF),
• absence of inflammatory polyps among the papillomas,
• abundance of plasma cells,
• absence of neutrophils,
• presence of bone invasion

Skull Base Inverted Papilloma: Comprehensive Review, ISRN 2012

• presence of inflammatory polyp
• absence of hyperkeratosis, predominantly mucinous Tumors
• mitotic index less than 1 per HPF, a ratio of neoplastic epithelium/connective tissue stroma greater than or equal to 6,
• presence of inflammatory polyps among the papillomas
• Recurrence rate is often related to the selected surgical treatment.
• Recurrence is almost always at the origin site due to incomplete removal of the primary lesion.
• In a simple tumor removal using a polypectomy snare instrument, there is a 67-78% relapse.
• while with a lateral rhinotomy and midfacial degloving, relapse is between 0% to 14%.
• Waitz and Wigand report 17% relapse with endoscopic removal.

References:
• In a Korean multicenter study, the overall recurrence rate of IPs was 15.7%.
• There was no significant difference in recurrence rates according to clinical stage or surgical approach.
• Patients with IPs involving the Medial wall of maxillary sinus or Frontal sinus showed a significantly higher tendency for recurrence.
POST TREATMENT FOLLOW UP

- The recommended follow-up period is not clearly defined in the literature; it varies from at least two years to a lifelong follow up.
- The intensity of follow up is greatest in the first two to three years, which is the period of greatest risk for disease recurrence.
- **Lifelong follow up is recommended for possible late recurrences and metachronous multifocal disease.**
- It is suggested to do annual follow up radiological examinations, preferably with the aid of computed tomography.
