DIAGNOSIS AND MANAGEMENT OF ONCOCYTIC TYPE SINONASAL PAPILLOMAS: A CASE REPORT

Dolly Irfandy[1*], Bestari J Budiman[1], Zulda Musyarifah[2], Wahyu Tri Novriansyah[1]

[1] Department of Otorhinolaryngology Head and Neck Surgery,
[2] Department Anatomy and Pathology
Dr. M. Djamil Hospital/ Faculty of Medicine Universitas Andalas, Padang

ABSTRACT

Sinonasal papilloma is a rare benign epithelial tumor. Symptoms are non-specific, namely unilateral nasal congestion, may be accompanied by rhinorrhea and a feeling of fullness in the paranasal sinuses. These tumors have three subtypes; inverted, oncocytic, exophytic. The main treatment is surgery, with varying rates of recurrence. **Case Report:** A 51-year-old woman complained of left nasal congestion since 6 months. On nasoendoscopy examination, a lumpy mass was found that filled left nasal cavity, and CT-scan Paranasal sinuses showed an isodens mass in left maxillary sinus, nasal cavity and left ethmoid sinus. Patient was diagnosed with a tumor on left nasal cavity with suspected inverted papilloma. Endoscopic approach and medial maxillectomy were performed. Histopathological results showed a sinonasal papilloma of the oncocytic type (SNOP). Follow-up 10 weeks postoperatively showed no recurrence. **Clinical Question:** "Does the endoscopic surgical approach give satisfactory results in oncocytic type papilloma sinonasal ?" **Method:** Literature search was performed through Cochrane database, Pubmed, and Google Scholar with keywords *"oncocytic sinonasal papilloma endoscopic surgery*". **Result:** SNOP recurrence rate between the non endoscopic surgery and the endoscopic surgery was not significantly different **Conclusion:** Sinonasal papilloma oncocytic type has symptoms and signs similar to inverted papilloma. The main management of the oncocytic type of sinonasal papilloma is surgery, with the endoscopic approach being the most widely used approach. Periodic follow-up is required to assess for recurrence.

Keywords: sinonasal tumor, oncocytic papilloma, inverted papilloma,

INTRODUCTION

Sinonasal papillomas, also known as Schneiderian papillomas, are benign epithelial neoplasms that arise from the sinonasal (Schneiderian) mucosa, ectodermally
derived epithelium consisting of pseudostratified columnar respiratory epithelium, basal cells, and goblet cells that produce mixed mucus. Sinonasal papillomas, which are also known as Schneiderian papillomas, are non-cancerous epithelial growths that originate from the Schneiderian mucosa, a type of mucous membrane lining the sinonasal cavity. This mucosa is derived from the ectoderm and consists of pseudostratified columnar respiratory epithelium. Sinonasal papillomas tend to occur more frequently in older individuals, particularly those in their fifth decade of life, and there is a higher incidence among males. While the overall prognosis for sinonasal papillomas is usually favorable, these tumors often have a tendency to recur and can cause local tissue damage.

Furthermore, in a small percentage of cases, sinonasal papillomas can undergo a malignant transformation, leading to the development of synchronous or metachronous sinonasal carcinoma. It is important to note that there are three subtypes of sinonasal papilloma: sinonasal exophytic papilloma (SNEP), inverted papilloma (SNIP), and oncocytic papilloma (SNOP). Sinonasal papillomas, also referred to as Schneiderian papillomas, are benign epithelial neoplasms that arise from the Schneiderian mucosa, a type of mucous membrane found in the sinonasal cavity. This mucosa is derived from the ectoderm and is composed of pseudostratified columnar respiratory epithelium. It is worth mentioning that these papillomas are more commonly observed in older patients, typically in their fifth decade of life, and there is a higher prevalence among males. Although the overall prognosis for sinonasal papillomas is generally favorable, there is a notable tendency for these tumors to recur and cause localized damage. Moreover, in a small proportion of cases, sinonasal papillomas have the potential to undergo malignant transformations, leading to the development of synchronous or metachronous sinonasal carcinoma. It is crucial to understand that there are three distinct subtypes of sinonasal papilloma: sinonasal exophytic papilloma (SNEP), inverted papilloma (SNIP), and oncocytic papilloma (SNOP). Each subtype presents unique characteristics and clinical implications. [1,2]

From a histological perspective, sinonasal inverted papillomas (SNIP) are distinguished by the presence of inwardly growing epithelial structures, whereas sinonasal oncocytic papillomas (SNOP) exhibit a combination of inverted and outwardly projecting epithelial components, often accompanied by numerous intraepithelial microcysts and eosinophilic cytoplasm. This histological variation contributes to the diverse characteristics observed in these papillomas.

The primary treatment modality for sinonasal papillomas is surgical intervention, which can be performed using either an endonasal endoscopic or external approach. The choice of surgical technique depends on the size and extent of the tumors, as well as their specific features. Regular post-operative follow-up is crucial to detect any local recurrences, enabling prompt treatment initiation. This is particularly

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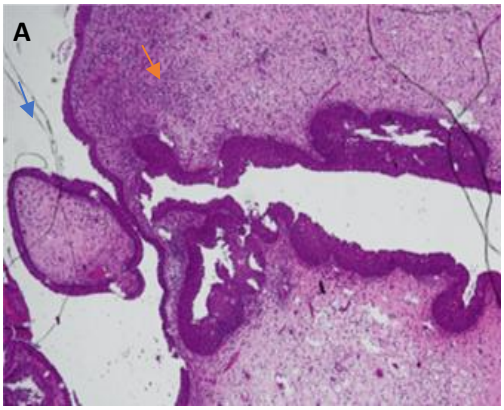

Figure 1. Photo of histopathological examination results A. Enlargement 40x; visible growth of endophytic (orange arrow) and exophytic (blue arrow) cells

important in cases where malignant transformations or associated malignancies are suspected.

It is worth emphasizing that an in-depth understanding of the histological features and clinical behavior of sinonasal papillomas is essential for optimal management. By employing surgical intervention and closely monitoring patients post-operatively, healthcare professionals can effectively address local recurrences and promptly identify any potential malignant transformations or concurrent malignancies. Regular follow-up visits serve as a vital component of comprehensive care for individuals affected by sinonasal papilloma

CASE REPORT

A 51-year-old woman, with a major complaint of nasal congestion for 6 months. Complaints are accompanied by thick rhinorrhea sometimes minor bleed, hiposmia, full sensation on left cheek in the last 3 months. On nasoendoscopy: left nasal cavity: mass with *raspberry* apperance between inferior turbinate and septum. Paranasal CT-scan revealed isodens density mass, slight inhomogen (HU 35-57) fills left maxillary sinus and left nasal cavity. An erosion in medial wall of maxillary sinus.

The patient was diagnosed with a sinonasal tumor

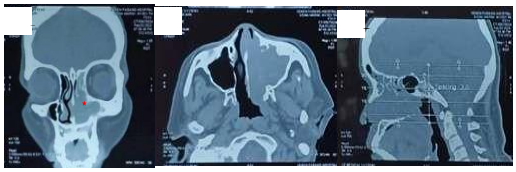

Figure 3. *CT scan* of the patient's paranasal sinuses. Interspersion appears

suspected *of inverted papillomas*, with differential diagnoses sinonasal polyps and sinonasal carcinoma. Tumor excision per endoscopic with medial maxilleectomy was planned. Laboratory examination and thorax X-ray was within normal limits (Hb:13.2 mg/dL) and 2 packs of PRC was prepared. Patient explained about surgical procedure and its complications, patient agrees and signs an *informed consent* sheet.

On March 10, 2022, a tumor excision surgery procedure was performed per endoscopy with a medial maxillectomy approach. Patient was in supine position under general anesthesia, aseptic and antiseptic procedures. Evaluation using endoscopy showed mass in left nasal cavity, up to the meatus media, and easily bleeds when manipulated. The mass carried out using forceps for histopathological examination. Next, using *a microdebrider*, the mass was picked. Medial wall of left maxilla appears to have been erosion, and inferior turbinate was depressed and distorted. Injury to branches of sphenopalatine artery occurs when reducing inferior turbinate. Bleeding was controlled using cautery, *bone wax*® and then mass in left maxillary sinus was cleaned up. Mass in ethmoid sinuses was cleaned, frontal recess was opened. There was an injury to left sphenopalatine artery when cleaning medial and posterior walls of maxilla. The bleeding was then controlled with gauze, cautery, and fibrillars®. Roll gauze was applied on maxillary sinus and on left nasal cavity. Bleeding during surgery about ±800cc.

Post operatively, 2 bags of PRC was administered, followed by IVFD+ analgetic, Ceftriaxone 2x1 gr, dexamethasone 2x5 mg, tranexamic acid 3x500 mg, Vitamin K 3x10 mg. Routine blood tests after transfusions were obtained with Hb 11 mg / dL. On third day, nasal gauze was removed,

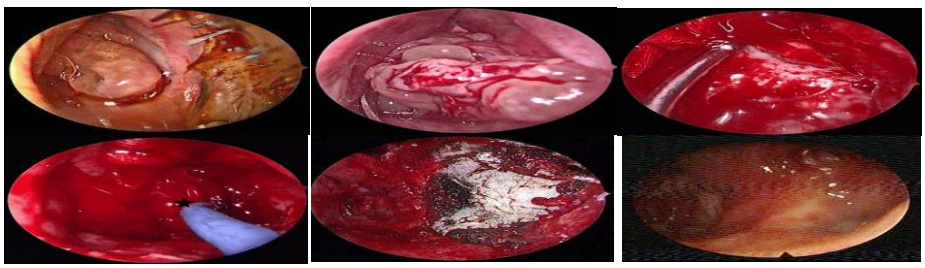

Figure 2. Nasal endoscopy. A and B. Mass in left nasal cavity, "*raspberry"* appeareance and easily bleeds. C. Intraoperative; superior lateral wall of

and patient was discharged and given oral antibiotics and analgetics. One week postoperatively, patient complained minimal nasal congestion and no bleeding. Nasoendoscopic exam revealed wide nasal cavity, blackish crusts, mucoid discharge, tumor mass is not visible. Patients continued the prescribe antibiotic. Histoplatology result was a sprawling epithelium were partially coated with respiratory epithelium, cytoplasm was partially eosinophilic granular (oncocytic), which grew partially endophytic into stroma forming an epithelial islet and partly exophytics formed papillary structures with fibrovascular stalks. Lymphocyte cell, PMN leukocytes and mucin-filled cavities in epithelium appear. Connective tissue stroma beneath it partially densely encapsulated a group of lymphocyte cells, plasma cells, histiocytes, PMN leukocytes and seromusinous glands, in other parts appeared to be parts of cells that infiltrated bone trabeculae, Conclusion: sinonasal papilloma, oncocytic type (with part that infiltrates the bone). In addition, PCR detection examination for *human papilloma virus* serotype 6,11,16,18 was not found.

On the week 6th and 10th postoperative, patient showed no complaints. On nasal endoscopic examination, no mass was found, minimal crusts, minimal discharge, open meatus media, open frontal recessus (Figure 2F). Patients were recommended to nasal irrigate with normal saline routinely at least twice a day. Patients are recommended to control next 6 months.

CLINICAL QUESTION

"Does the endoscopic surgical approach give satisfactory results in oncocytic type papilloma sinonasal?"

P: Patient with oncocytic sinonasal papilloma, **I**: Tumor resection per endoscopic surgery, **C**: Tumor resection per endoscopic surgery vs open approach, **O** : complete tumor resection and less complication

REVIEW METHOD

Literature search was performed through Cochrane database, Pubmed, and Google Scholar with keywords *"oncocytic sinonasal papilloma endoscopic surgery*". The search was using inclusion criteria: 1) histopatologically confirmed for oncocytic sinonasal papilloma, 2) tumor resection per endoscopic or open approach, 3) systematic review/meta-analysis of RCTs, cohort, case control studies, case report or serial case report.

RESULT

We found 14 papers that suit with the keyword and one study highlighting the outcome of SNOP management. A case series of SNOP by Lilja[5] did not demonstrate a statistically significant difference in the recurrence rate between non endoscopic surgery group and endoscopic surgery group.

DISCUSSION

In a case study, a female patient who was 51 years old presented with a suspected sinonasal tumor, specifically an inverted papilloma. The patient underwent a tumor excision procedure utilizing endoscopy, and subsequent histopathological examination confirmed the diagnosis of sinonasal papilloma of the oncocytic type. It is generally observed that sinonasal inverted papillomas (SNIP) and oncocytic papillomas (SNOP) tend to manifest more frequently in individuals within their fifth or sixth decade of life. On the other hand, sinonasal exophytic papillomas (SNEP) typically occur in slightly younger patients, ranging from the third to the fifth decade. However, it is important to note that these three types of papillomas can potentially develop at any age. In terms of gender distribution, there is a higher incidence of SNIP and SNEP among males, with a male-to-female ratio of approximately 2-3:1 for SNIP and a significant male predominance of 10:1 for SNEP. In contrast, SNOP does not display a specific preference for either males or females. These gender disparities suggest a potential underlying biological or hormonal influence on the development of these different subtypes of sinonasal papillomas. This case highlights the importance of considering the age and gender of patients when evaluating and diagnosing sinonasal papillomas. By recognizing these demographic patterns, healthcare professionals can enhance their understanding of the disease and tailor treatment approaches accordingly. Further research is warranted to explore the underlying factors contributing to the age and gender disparities observed in the occurrence of SNIP, SNEP, and SNOP.[4,6]

Clinical symptoms of SNOP are not specific and are similar to other sinonasal subtypes of papillomas. Almost all patients with SNOP come with complaints of unilateral nasal congestion and the presence of soft tissue masses is found. Other symptoms include rhinorrhea, intermittent epistaxis, pain or a feeling of fullness in the face and headaches. [7]

Pathogenesis of sinonasal papilloma remains unclear.[2] Similar to SNOP, the pathogenesis of SNIP is also still a conflict today. Based on the main study and meta-analysis of recent years shows SNIP is related to HPV, but the rate of positive findings varies between 17% and 38%, even from 0% to 70% in SNIP. Based on the WHO report, positive frequency of HPV in SNIP is around 38.5%.[1]

In this case, HPV examinations of 6,11,16, and 18 were found to be negative. HPV examination is not a routine examination in SNOP cases. Studies have found SNOP is not associated with HPV infection, but is related to the KRAS mutation.[6] Meanwhile, in SNIP and SNEP, HPV examination is needed to assess the risk of malignant transformation. [1,5] HPV is more commonly found in SNIPs with severe or carcinoma-related degrees of dysplasia (55%) compared to SNIPs without or with mild dysplasia (22%). HPV serotypes 6 and 11 are more commonly found in benign SNIPs, and serotypes 16 and 18 (associated with a high oncogenic risk) in SNIP with severe dysplasia or associated carcinoma. Thus, HPV is very likely to be involved in the pathogenesis of SNIP, but the current data still do not provide certainty regarding its exact role.[4,8]

Sinonasal papilloma of the oncocytic type are the rarest type of papilloma, about 6%. The rate of malignant transformation is 4% to 17%, and squamous cells carcinoma is the most frequent histological picture.[1,6]

The CT scan of the paranasal sinuses in this case showed a unilateral isodense mass, with the origin of the lesion originating from the sinistra maxillary sinuses and the presence of a picture of osteitis on the latero-superior wall of the maxillary sinuses, and not accompanied by bone digestion. Based on literature, on a large mass, it can be found bone resorption and digestion like squamous cell carcinoma. Intralesional calcification representing bone fragments can be observed in 40% of cases. Presence of hyperostotic focal lesions, often conical, has been reported to correlate with the point of origin of the lesion with *a positive predictive value* (PPV) of 89–95%. However, CT scans have a drawback, namely that they cannot distinguish between lesions and surrounding

inflammation or fluid retention phenomena, which can lead to *over-estimating* of lesion size and inadequate pre-operative planning. [3,4]

Based on CT scan, some features can distinguish SNOP and SNIP, which include: (1) the location of origin of the SNOP usually comes from the maxillary sinus, while the SNIP comes from the lateral wall of the nasal cadvum. (2) The presence of osteitis / hyperostosis is more commonly seen in SNIP (94.1%) than SNOP (11.8%). [3]

Based on a pre-operative CT scan of this case the tumor extends from the maxillary sinuses, nasal cyrillic cavitum, etmoid sinuses, and frontal sinuses, so that the tumor stage is Krouse T3. The first *staging* system for sinonasal papillomas used was for *inverted papillomas*, which is based on the staging of Krouse et al al.[9] *Krouse staging* is made on basis of expansion from tumor into nasal cavity or affected sinuses, and is most commonly used.[10] Subsequently, as a modification from Krouse system, Oikawa divided the Krouse T3 stage into T3A and T3B.[11] Meanwhile, Cannady combined Krouse 1 and Krouse 2 into group A.[12] Han further strengthened the *staging* system that divided the maxillary sinus involvement as group 2, and the frontal sinus involvement as group 3.[13] Subsequently, Meng et al in 2019 proposed a *staging* system based on original place of lesion.[14]

Nakayama compared Krouse, Oikawa, Cannady, Han and Meng staging systems to predict recurrence of SNIP cases. Neither Krouse, Oikawa and Cannady staging systems showed any meaningful difference in recurrence rates between stages. The study advocated use of Han *staging* systems for preoperative and intraoperative staging, as it has a more accurate association with recurrence rate.[10] Although SNOP has similar clinical behavior to SNIP, *a staging* system for specifically predicting SNOP is still not available.[5,15]

In this case, removal of the tumor is carried out endoscopically with approach of medial maxillectomy. This technique was chosen because of lesion centered on left maxillary sinus and availability of instruments that facilitate visualization with various angles. Endoscopic approach has become the standard nowadays. However, an external or combination approach is still indicated at certain tumor locations that are difficult to reach with endoscopy such as lateral regions of frontal, anterior and lateral sinuses of maxillary sinuses. [16,17] In most cases with lesions in lateral-inferior or anterior to wall of maxillary sinuses, surgical approach can be by endoscopic/ and or Caldwell-luc, although some authors choose m*edial maxillectomy* approach in all cases with lesions in maxillary sinuses.[4,18] If lesions in frontal sinuses, most commonly used approach is DRAFT III, but it can be combined with an external approach through supraorbital or bicoronal to ensure lesion, especially in frontal lateral, can be completely lifted. External approach via paralatero-nasal is used in case of extra sinus expansion and carcinoma-related. [4]

In this case there is bleeding during surgery due to injuries of the sphenopalatine artery and its branches on the inferior turbinate. Based on the literature, bleeding complications due to vascular injury in endoscopic sinus surgery are about 0.2-0.8%.[19] Endoscopic sinus surgery in tumor cases has a higher risk of intra-operative and post-operative hemorrhage, with an *Odds Ratio of* 3.11.[20] Bleeding can be treated with a cautery and fibrillar®. The use of hemostatic agents of fibrillar® induces formation of a gel-like mass after saturated with blood, resulting in formation of stable blood clots.

Success rate on operation depends on complete exposure to the tumor, which allows for complete resection. This is since most of relapses within 2 years after surgery, usually occur at site of primary lesion. Ideally, release of tumor implantation point is carried out up to subperiosteal, followed by erosion underlying bone to minimize re-implantation of tumor cells. Monoblock resection is very difficult to do via endoscopy. Tumor tissue delivered to pathologist should be adequate, when necessary as much as possible, to assess presence of location of malignant transformation of tumor lesion.[4,21]

There has been no consensus for radiotherapy in sinonasal papillomas.[4] In case of SNOP, effectiveness of radiotherapy has not been widely reported. Kang reported success of radiotherapy at a dose of 64 gray in 1 postoperative recurrent SNOP case. This implies the potential of radiotherapy as an adjuvant modality in SNOPs.[21]

Sinonasal papillomas tend to recurrent. In SNIP, most cases of sinonasal papilloma, recurrency rate varies, ranging from 8.5% to 44% in *follow-up* up to 5 years.[4] SNOP recurrence rate reported around 6%.[3] However, another study by Wang found a recurrence rate of about 13%, and Lilja's study found the SNOP recurrence rate reached 39% in a 77-month *follow-up* period.[5,15] Rate of malignancy of SNOP is reported to be around 4-17%. Squamous cell carcinoma is most frequent, followed by, undifferentiated carcinoma or small cell carcinoma. While malignancy rate of SNIP is 5-15%, and SNEP is close to 0%.[6]

It is strongly advised to maintain regular follow-up and monitoring of patients diagnosed with sinonasal papillomas to ensure optimal management and early detection of any potential complications. The recommended follow-up frequency typically involves evaluations at specific intervals throughout the post-operative period. During the initial year following the surgical excision of sinonasal papillomas, it is recommended to schedule follow-up appointments every 3 to 4 months. This frequent monitoring allows healthcare professionals to closely assess the healing process, identify any signs of recurrence, and promptly intervene if necessary. As the patient progresses into the second year after the surgical intervention, the follow-up frequency may be adjusted to occur every 4 to 6 months. This slightly extended interval still facilitates close observation of the patient's condition, providing an opportunity to detect any subtle changes or early indications of recurrence. Subsequently, in the following years, it is generally advised to continue monitoring the patient's sinonasal health on a semi-annual basis, with follow-up appointments scheduled every 6 to 12 months. Although the frequency is reduced, this periodic assessment allows for ongoing surveillance of the surgical site and overall well-being, enabling the timely identification of any potential relapse or complications that may arise over time. It is important to note that the suggested follow-up intervals may vary depending on the individual patient's specific circumstances and the healthcare provider's clinical judgment. The primary objective of these regular follow-up visits is to ensure the long-term success of the surgical intervention, monitor for any potential recurrence, and promptly address any emerging issues to optimize patient outcomes. Some authors suggest a lifelong

follow up.[21] Some of factors that cause recurrence include: smoking, incomplete resection, tumor location such as in the frontal sinuses (Odds Ratio =2.53), tumor stage, surgical techniques, and malignancy rates. Recurrence that occurs in 2 years may come from same lesion site.[21] Meanwhile, slow recurrence is associated with HPV virus infection factor.[21] Postoperative complication rate can reach 18.5%. Minor complications include epiphora, epistaxis, and periorbital edema. While major complications include rhino-liquor fistulas, frontal mucosa, and lacrimal duct stenosis. [21]

CONCLUSION

Sinonasal papillomas of the oncocytic type have similar symptoms and signs to *inverted papillomas*. Histopathological examination is used to determine the subtype of sinonasal papillomas and determine the degree of malignancy. HPV examination is necessary in addition to assess the risk of malignancy in the sinonasal papilloma. The main management of synnosal papillomas of the oncocytic type is surgery, with the endoscopic approach being the most widely used approach due to lesser complication rate. Complete resection will reduce the risk of recurrence and periodic *follow-up* is required.

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