

Case Report

# Squamous cell carcinoma arising in a sinonasal inverted papilloma

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## ABSTRACT

Sinonasal inverted papilloma (SNIP) has the capability to recur and undergo pre-malignant/malignant transformation. The estimated incidence of carcinoma associated with sinonasal papilloma varies widely, ranging from 5% to 15% across published literature. It may occur as coexistence of carcinoma and papilloma in the same lesion (synchronous), or a small focus of carcinoma developing within an inverted papilloma, and lastly, a carcinoma appears at the site of excision of a benign papilloma (metachronous). Possible factors like human papillomavirus infection (HPV), smoking, occupational exposure, and genetic abnormalities, including epidermal growth factor receptor (EGFR) mutations, have been implicated in the malignant transformation of sinonasal papillomas. We report malignant transformation in an inverted papilloma of maxilla in a 31-year-old female.

**Key words:** Inverted papilloma, Malignant transformation, Sinonasal papilloma, Squamous cell carcinoma

## INTRODUCTION

Papillomas arise from Schneiderian mucosa and are benign tumors. Sinonasal papillomas have three subtypes: exophytic, oncocyctic, and inverted.<sup>1</sup> The inverted papilloma is the most prevalent kind of Schneiderian papilloma. Although the tumors have a benign character, sinonasal inverted papilloma (SNIP) has great potential for local recurrence and malignant transition into dysplasia/carcinoma in situ or squamous cell carcinomas. The cause of inverted Schneiderian papilloma is unclear, although potential causes include chronic inflammation, allergies, occupational toxins, and infection with the human papillomavirus.<sup>2</sup>

We hereby report a 31-year-old lady with a squamous cell carcinoma arising from an inverted Schneiderian papilloma, leading to destruction of the maxillary sinus.

## CASE REPORT

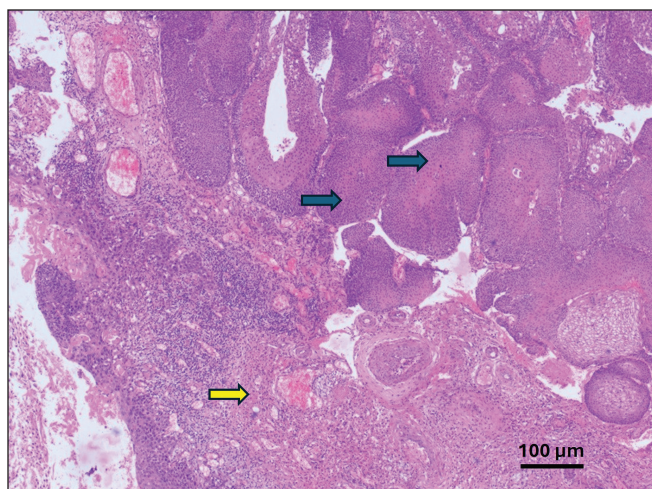
A 31-year-old female presented to the surgical clinic with a rapidly growing mass in the right maxillary region. The patient had undergone right modified endoscopic Denker's approach for medial maxillectomy under general anesthesia, and a large, grey-white friable mass was excised from the

sinus. Contrast-enhanced magnetic resonance imaging (CE-MRI) of the paranasal sinuses revealed a large lobulated mass lesion in the right sinonasal region, with an uneven pattern of contrast enhancement, epicentered in the right nasal cavity in the region of the right middle turbinate with extension into right paranasal sinuses, and intra-orbital as well as intracranial extensions. The presumptive diagnosis was a neoplastic papilloma/ inverted papilloma. Gross examination of the resected specimen showed multiple grey white friable soft tissue bits, measuring 7 × 5.5 × 1 cm. Histopathological examination showed features typical of inverted Schneiderian papilloma, i.e., multilayered and thickened nonkeratinizing squamous epithelial islands and sheets growing inward into the underlying edematous and myxoid stroma [Figure 1]. There was increased mitosis, dyskeratosis, and areas with dysplasia in the present case, with foci of breach of basement membrane and invasion into stroma [Figure 2]. Thus, the ultimate diagnosis rendered was squamous cell carcinoma originating in inverted papilloma. Immunohistochemistry for p16, a surrogate marker of human papilloma virus, showed both cytoplasmic and nuclear positivity [Figure 2 inset]. The patient received 6 cycles of chemotherapy, and there is no evidence of recurrence on follow-up of 1 year.

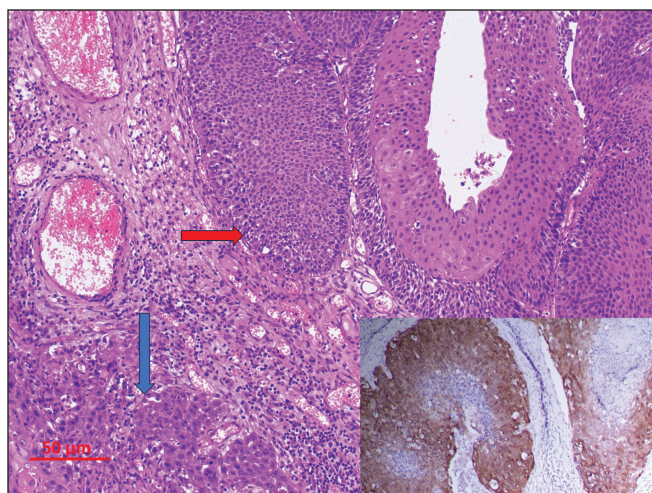
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**Figure 1:** Photomicrograph showed typical features of inverted Schneiderian papilloma (green arrow) with islands of multilayered nonkeratinizing squamous epithelium growing inwards into the underlying edematous and myxoid stroma (yellow arrow) (Hematoxylin & eosin, 40x).



**Figure 2:** Photomicrograph showed inverted papilloma (red arrow) with foci of dyskeratosis and significant epithelial dysplasia with areas of invasion into underlying stroma suggestive of invasive squamous cell carcinoma (blue arrow) (Hematoxylin & eosin, 200x). Inset shows p16 immunohistochemistry with both cytoplasmic and nuclear positivity.

## DISCUSSION

The inverted Schneiderian papilloma is a benign epithelial neoplasm of sinonasal tract, most frequently occurring in 5<sup>th</sup>-6<sup>th</sup> decades and has great chance to recur and undergo malignant transformation in around 10% of the patients. Clinically, patients present with clinical symptoms like nasal obstruction, epistaxis, rhinorrhea, and facial pain or pressure.<sup>3,4</sup> In our study, the patient presented with nasal obstruction due to sinonasal mass with intracranial extension on the right side.

SNIP has the propensity to recur and undergo pre-malignant/malignant transformation, encompassing atypia, dysplasia, carcinoma *in situ*, and squamous cell carcinoma. Squamous cell carcinoma is the most frequent type of carcinoma associated with sinonasal papilloma; however, other rare types like verrucous carcinoma, mucoepidermoid carcinoma, small cell carcinoma, and undifferentiated carcinoma have also been documented. The definitive cause of SNIP is not clearly known. Moreover, no reliable predictive/biological markers for the development of recurrence or malignancy have been documented. Potential risk factors, including human papillomavirus infection (HPV), smoking, occupational exposure, and genetic abnormalities, including epidermal growth factor receptor (EGFR) mutations, have been implicated in the malignant transformation of sinonasal papillomas.<sup>2</sup> The present case also revealed evidence of HPV infection in the form of p16 positivity. The relationship between inverted papilloma and malignancy can be observed in three forms. Firstly, the coexistence of carcinoma and papilloma in the same lesion is referred to as synchronous tumors. Secondly, a small focus of carcinoma is seen to develop within an inverted papilloma similar to our case. Lastly, a carcinoma appears at the site of excision of a benign papilloma, also called a metachronous lesion. Clinically, the first two categories are more commonly seen.<sup>5-7</sup>

The estimated incidence of carcinoma associated with sinonasal papilloma varies widely, ranging from 5% to 15% across published literature.<sup>1-10</sup> Lund *et al.*<sup>4</sup> (2010) reviewed many published papers comprising 3181 patients, reported a 10.4% prevalence of malignancies associated with inverted papilloma (both synchronous and metachronous), with most frequent being squamous cell carcinomas being the most frequent. Mirza *et al.*<sup>8</sup> (2007) reviewed 2000 inverted papillomas and reported the occurrence of synchronous and metachronous carcinomas in 7.1% and 3.6% cases, respectively. Ruggeri *et al.*<sup>6</sup> (2022) detected malignancy in 7/63 patients (11%) with papilloma: five synchronous lesions and two with metachronous lesions. Re *et al.*<sup>10</sup> (2017) performed a meta-analysis to provide a better understanding of the incidence of sinonasal malignancies arising from papilloma by analyzing 29 studies including a total of 3177 patients and observed the overall rate of occurrence of malignancy in a sinonasal papilloma to be 9% (95% CI = 7-11).

Surgery is the treatment of choice for patients with SNIP. In cases with malignant transformation, the primary treatment modality is surgery, often followed by a multidisciplinary approach including radiation and chemotherapy, especially for advanced-stage or recurrent cases. Several reviews and studies have helped in improving our understanding of the prognosis of patients with malignant SNIP. In a meta-analysis by Lee *et al.*<sup>7</sup> (2021) they observed that patients

with carcinomas arising in inverted papilloma had half the risk of mortality compared to those with squamous cell carcinomas unrelated to inverted papilloma. Birkenbeuel *et al.*<sup>9</sup> (2022) conducted a systematic review of 663 patients with squamous cell carcinoma associated with inverted papilloma; 73.7% were T3/T4 (TNM classification), while 155 (23.8%) developed recurrence within 24.3 months (mean time interval).

## CONCLUSION

This case re-emphasizes the need for extensive sampling in cases of sinonasal papilloma to avoid missing out on a focus of malignant transformation in a sinonasal papilloma.

**Authors' contributions:** VC, MP: Idea and design; HG, MJ, AS: Data acquisition; JS, VC: Analysis; MP, JS: Interpretation of findings; SK: Preparation of manuscript; MP, JS: Critical revision.

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