



Case Report

Inverted Papilloma-A Case Report and Literature Review

Ali Sadeghi^{1,2}, Joel Epstein^{3,4}, Ayushi Naik⁵, Firoozeh Samim^{6*}

¹Associate Clinical Professor, Dentistry, University of British Columbia, Vancouver, BC, Canada

²Department head, Oral and Maxillofacial Surgery, Lions Gate Hospital and Coastal, Canada

³Professor and Medical Director, Cancer Dentistry, Cedars-Sinai Health System, Los Angeles, CA, USA

⁴Medical Director, Dental Oncology, the City of Hope Comprehensive Cancer Center, Duarte, CA, USA

⁵M.Sc. Dental Science Candidate, McGill University, Faculty of Dental Medicine and Oral Health, Montreal, Quebec, Canada

⁶Assistant Professor, McGill University, Faculty of Dental Medicine and Oral Health, Montreal, Quebec, Canada

***Corresponding author:** Firoozeh Samim, Faculty of dental medicine and oral health science, McGill University, Montreal, Quebec, Canada

Citation: Sadeghi A, Epstein J, Naik A, Samim F (2023) Inverted Papilloma-A Case Report and Literature Review. Ann Case Report. 8: 1299. DOI:10.29011/2574-7754.101299

Received: 03 May 2023, **Accepted:** 08 May 2023, **Published:** 10 May 2023

Abstract

Sinonasal inverted papilloma is a benign tumour with a risk of recurrence and malignancy. The lesion rarely presents with oral/dental symptoms. We present a case of a 62-year-old man who presented with a one-and-a-half-year history of intermittent right facial pain. The presentation emphasizes the need for awareness of dental providers and highlights the steps to achieve diagnosis leading to successful treatment. The case was a very rare, inverted papilloma arising from the lateral wall of the nasal cavity with maxillary sinus involvement and extension toward the oral cavity. To date, only two additional cases of sinonasal-inverted papilloma have been reported with extension to the oral cavity, one of which was also a maxillary sinus lesion. In addition to the need for recognition, allowing diagnosis, the dysplastic epithelium lining of the lesion suggests malignant potential. The role of dental providers in detection and diagnosis and post-treatment follow-up is reviewed.

Keywords: Inverted Papilloma; Malignancy; Recurrence; HPV; Surveillance

Introduction

Schneiderian or sinonasal papillomas belong to a rare benign epithelial neoplasm frequently occurring in the sinonasal tract lined with Schneiderian epithelium, ectodermal derived respiratory mucosa [1]. Three histologically unique types of Schneiderian papillomas were identified as exophytic (everted, fungiform, or septal), inverted, and oncocytic (columnar, or cylindrical cell) papillomas. Exophytic papilloma originates from the nasal septum and inverted and oncocytic originate from the lateral nasal wall or maxillary sinus [2]. The frequencies are in descending order of the three histological types. Recurrence and malignant

transformation of an exophytic papilloma are unusual but is associated with inverted papilloma. Sinonasal papilloma was first reported by Ward in 1854 [3], and classified by Hyams based on the histological features [4]. Sinonasal papilloma is rare because its incidence is 0.75-1.5/100,000 annually responsible for 0.5-4% of primary nasal tumours; [5] and its total reported cases were found as 1956 cases from 1950 to 2012 in English literature [6]. As a benign tumour with a malignant tendency, inverted papillomas have a risk of malignancy as 5-15% [7], or as high as 27% [8], with squamous cell carcinoma as the common histopathologic type. Due to its aggressive nature and high recurrence rates, surgical management of inverted papilloma is the mainstay of treatment and historically has included several approaches including 1) non-endoscopic endonasal, 2) limited external (i.e. Caldwell-Luc), 3)

radical external (i.e. lateral rhinostomy or midfacial degloving with en-bloc resection and 4) endoscopic endonasal [5]. Inverted papilloma generates significant interest because of its risk of malignant progression and high recurrence rates. This tumour has received little attention in the dental literature.

Case Presentation

A 62-year-old man presented with a one-and-a-half-year history of right facial pain, swelling and episodes of bloody discharge from the right nostril. The lesion was initially diagnosed as an endodontic lesion by patient's general dentist nearly a year earlier and endodontic treatment was initiated on the maxillary right first molar. After no improvement in symptoms was noted, patient was subsequently referred to an endodontist who correctly identified that patient's symptoms were non-odontogenic in origin and referred the patient to an oral and maxillofacial surgeon for further evaluation. The surgeon noted tenderness on palpation over the apices of the right maxillary molars with crepitus and ordered further imaging. A computed tomography (CT) scan of the maxilla and the paranasal sinuses in Figures 1 to 5 demonstrated a large lesion obliterating the right maxillary antrum with the destruction of the medial wall of the maxillary sinus, displacement of the middle turbinate and direct extension into the right nasal cavity. The absence of the cortical bone was noted in the apical region of the right maxillary first and second molars (tooth 1.6 and 1.7). Indications for biopsy included intermittent right facial pain, swelling and bloody discharge from the right nostril for more than a year, and evidence of bone loss due to the invasion to the right maxillary molars. An incisional biopsy demonstrated a 2 cm area of buccal cortical wall destruction. The lesion was extremely soft and friable, and a "cheesy" substance was expressed from the lesion on curettage. The Histopathology of the biopsy sample confirmed that the diagnosis of the lesion was an inverted squamous papilloma. The patient was subsequently referred to an otolaryngologist specializing in endoscopic sinus surgery for definitive treatment. Ear nose and throat physical examination including nasal endoscopy noted a unilateral polypoid expansile lesion involving the right nasal cavity. The patient underwent an image-guided endoscopic endonasal tumour resection with a wide endoscopic medial maxillectomy and complete anterior and posterior ethmoidectomies on the right side. After tumour debulking with an angled microdebrider, it was found that the lesion was involving the posterior-lateral and superior walls of the maxillary sinus mucosa diffusely, extending into the ethmoid cavity through the medial wall of the sinus. A sphenopalatine artery ligation was performed to achieve adequate tumour resection of the posterior wall of the maxillary sinus. Once the tumour attachments

were identified, all the mucosa compromised was eliminated and the underlying bone was drill polish with a diamond burr. The frontal and sphenoid sinuses were opened and examined to ensure no tumour involvement. The patient received ongoing surveillance as endoscopic debridement once every three months for the first year after surgery and every six months subsequently to exclude the recurrence of the sinonasal inverted papilloma. There was no evidence of tumour recurrence at the last follow-up visit 3 years after surgical resection.

Discussion

While rare, sinonasal inverted papilloma most often originates from the lateral wall of the nasal cavity; and only 5% of them have exclusive sinus involvement, in which the maxillary and ethmoid sinuses are most affected [9]. It often erodes adjacent bones and extends to the orbit or intracranial cavity [5,10]. The etiology of inverted papilloma remains unclear although an association with chronic inflammation, allergy, tobacco, occupational pollutants, and human papillomavirus (HPV) have been described (Table 1) [11-13]. It affects predominantly males with a mean age of 50 years [14].

Histological Types	Patient % (Case)	HPV Infection %
Normal mucosa	13.2% (315)	7.00%
Nasal polyp	5.1% (121)	4.10%
Exophytic papilloma	6.4.5% (153)	65.30%
Inverted papilloma	74.1% (1,767)	37.80%
Cylindrical cell papilloma	1.3% (30)	22.50%

Table 1: Sinonasal inverted papilloma: histological types and HPV prevalence [4].

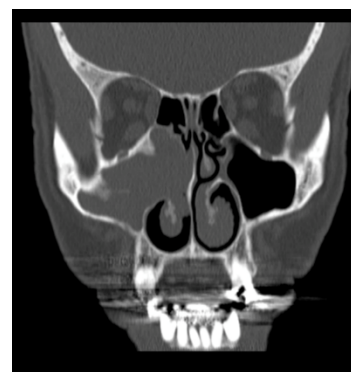


Figure 1: A computed tomography (CT) scan of the maxilla and the paranasal sinuses.

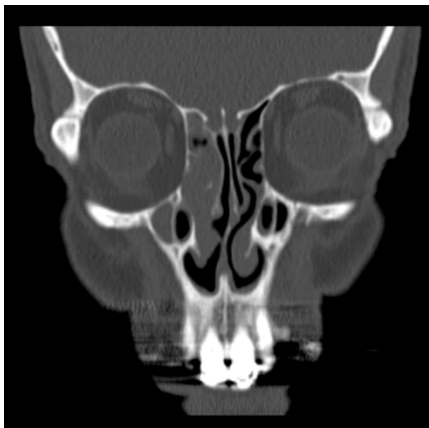


Figure 2: A computed tomography (CT) scan of the maxilla and the paranasal sinuses.



Figure 3: A computed tomography (CT) scan of the maxilla and the paranasal sinuses.

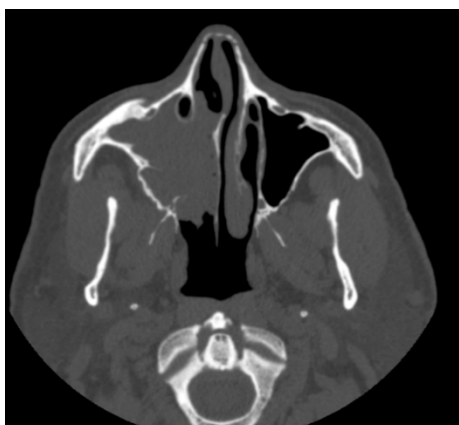


Figure 4: A computed tomography (CT) scan of the maxilla and the paranasal sinuses.

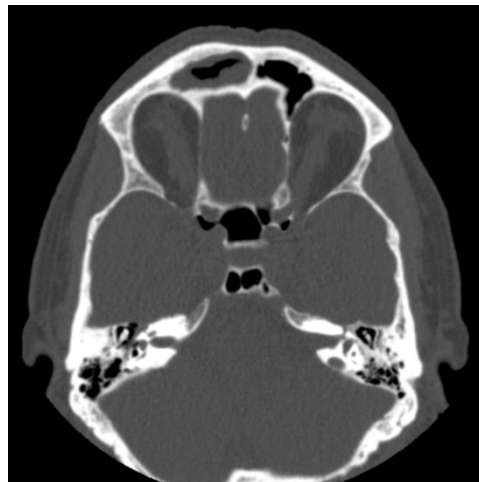


Figure 5: A computed tomography (CT) scan of the maxilla and the paranasal sinuses.

Our case was a very rare, inverted papilloma because it was from the lateral wall of the nasal cavity with maxillary sinus involvement, and a risk of extending toward the oral cavity resulting in dental symptoms. To the best of our knowledge, only two additional cases of sinonasal inverted papilloma were reported with extension toward the oral cavity [12,15]. One of them was also a maxillary sinus lesion involved the oral cavity possibly due to the buccolingual communication resulting from dental extraction in the region [15]. In our case, the CT scan of the maxillary sinus and the histological analysis of the biopsy sample defined the diagnosis as an inverted squamous papilloma. The dysplastic areas in the epithelium lining the lesion and the confirmation of the presence of squamous cells corroborate its malignant potential. As reported in the literature, inverted papillomas have a high risk of evolving into a verrucous or squamous cell carcinoma; and the risk of the latter is much higher. According to Tsou et al., the risk of squamous cell carcinoma in inverted papilloma can be as high as 10% as it onset in 10 cases out of a total of 60 [16]. The WHO related the malignant potential of inverted papilloma to be associated with keratinization of lesions since its lining epithelium is keratin free in most cases. One of the chances of keratinization can result from tissue communication with the oral cavity through dental extraction, for example [1]. Inverted papillomas are reported as associated with non-sinonasal head-and-neck carcinoma. A retrospective regional cohort compared 197 sinonasal papilloma patients to 1583 nasal polyp patients in their head and neck carcinoma rates [17]. It found that the papilloma patients had a 12.8% higher rate of non-sinonasal head-and-neck squamous cell carcinoma (HNSCC) compared to the polyp patients, and 12.3%

for male patients only. It was estimated that tobacco smoking might be a causative link in the developed non-sinonasal head-and-neck carcinoma. Another study showed that the histology of low-grade squamous cell carcinoma of the nose might mimic and coexist with inverted papilloma. (2) Recent studies addressed the use of histological parameters to predict the clinical course of the lesion with new molecular markers applied to the diagnosis. Early identification and effective management are keys to decrease the morbidity and improve patient survival. Due to the risk of recurrence and malignancy, a conservative intranasal piecemeal excision is replaced with an aggressively wide excision using endoscopic surgery, which has the lowest recurrent rates. Analyzing 2,297 cases of sinonasal papilloma, a study found that the recurrent rates were 34.2% post limited resections such as nasal polypectomy and Caldwell-Luc approaches; 17.0% post lateral rhinotomy with medial maxillectomy; and only 12.8% post-endoscopic surgery [5]. It is recommended that sinonasal papilloma patients should undergo thorough surgery to remove all involved mucosal tissues, most probably using the endoscopic and endonasal route to make complete resection possible. Stereotactic anatomical localization (SAL), also known as image-guided surgery, is recommended by the American Academy of Otolaryngology-Head and Neck Surgery for endoscopic sinus surgery in more complex procedures, such as sinonasal neoplasms [18]. Since the inverted papilloma in our patient extended into the ethmoid sinuses and the lateral wall of the nose posterior, it fit the requirements of SAL. In our case, the surgical outcomes using SAL was the satisfactory removal of the whole mass of the complex lesion. The additional benefits from SAL are that it reduces the risk of perioperative complications and increases the surgical accuracy, as confirmed in a meta-analysis with 2,381 studies [17]. Systematic reviews and meta-analyses of the literature suggest that HPV is present in approximately 24% to 38% of cases, with HPV 6, 11, 16, and 18 representing the most prevalent types. Marked surface keratinization and moderate to severe dysplasia are worrisome histopathologic findings that warrant careful microscopic examination to rule out malignancy. Nonetheless, there are no histopathologic features that are reliably predictive of malignant transformation in inverted papillomas [19]. A few studies suggest that increased immunohistochemical expression of p53 and p21 (cell cycle-related proteins), decreased immunohistochemical expression of CD44 (a cell adhesion molecule), and the presence of HPV 16 or 18 may be associated with an increased risk for malignant transformation. Notably, immunohistochemical expression of p16 in inverted papillomas does not appear to be a reliable surrogate marker for high-risk HPV infection [5]. It is important to conduct the postoperative surveillance for tumour in inverted papilloma patients due to its high risks of recurrence and malignancy, even though no consensus guidelines available currently. It is suggested to perform tumour surveillance based on the guidelines for HNSCC surveillance [20].

Regular endoscopic examination and contrast-enhanced magnetic resonance imaging (MRI) are the best detections for tumour recurrence. Prompt identification of recurrence of inverted papilloma from other benign and malignant tumours are important. Based on the literature, a majority of the recurrence occurs within the first two years post-surgery; Additionally, a longer term than two years post-surgery and potentially lifelong follow-up are recommended for sinonasal papilloma patients, particularly those diagnosed with higher stages [5,21]. For example, papillomas with high-risk factors, such as HPV+, high T stage, and recurrent tumours, should be surveilled and evaluated more frequently than those without. For inverted papilloma surveillance and detection, positron emission tomography/computed tomography (PET/CT) images can be used to identify between inverted papilloma, nasal polyp, and squamous cell carcinoma, due to the fluorodeoxyglucose (FDG) uptake nature. The mean maximum standardized uptake (SUVmax) values were found as 2.9 in nasal polyps; 7.8 in inverted papilloma; and 17.8 in squamous cell carcinoma respectively in a study of 27 patients [22]. In this case, an SUVmax of 6 or higher can be used to rule out the presence of a nasal polyp. Another study of twelve of suspicious cases, an SUVmax of 1-8.1 can be used to diagnose inverted papilloma, in which the correct diagnostic rate was 71.4% (5/7); and all of the five papilloma cases had SUVmax higher than 3 [23]. The five cases with absence of FDG uptake were diagnosed as the absence of inverted papilloma. It can also be used to detect recurrence of inverted papilloma effectively [24]. Dentists must be aware of the potentially overlapping symptoms between oral dental and sinus disease, and that sinus conditions can refer pain, and present as oral and dental pain. Questioning the patient about sinus related symptoms such as midface stuffiness, change in symptoms with change in head position (e.g., standing, laying down, head forward, etc.), postnasal drip, and epistaxis can be helpful. These symptoms may assist in differential diagnosis. Symptoms of pain and pressure can of course, be associated with sinus or dental disease. Therefore, symptoms associated with sinus involvement, and findings of potential extension of sinus disease should be thoroughly assessed. The antral disease can result in orofacial symptoms, changes on dental imaging, and on clinical examination require awareness of the dentist so that detection leading to diagnosis and treatment can occur expeditiously. Furthermore, due to overlapping symptoms, these conditions can present to the dentist, and in known cases of prior sinus disease require that the dental provider is aware of the overlap and have a heightened awareness to promote detection and differential diagnosis. The case presented has multiple unique features that relate to sinus pathosis and dental findings.

Declarations

Funding: There is no source of funding for this project to declare.

Conflict of Interest: There is no conflict of interest to declare for this study.

References

1. Vorasubin N, Vira D, Suh JD, Bhuta S, Wang MB (2013) Schneiderian papillomas: comparative review of exophytic, oncocytic, and inverted types. *Am J Rhinol Allergy.* 27: 287-292.
2. Sandison A (2009) Common head and neck cases in our consultation referrals: diagnostic dilemmas in inverted papilloma. *Head Neck Pathol.* 3: 260-262.
3. Ward N (1854) A mirror of the practice of medicine and surgery in the hospitals of London: London Hospital. *Lancet.* 2: 480-482.
4. Hyams VJ (1971) Papillomas of the nasal cavity and paranasal sinuses. A clinicopathological study of 315 cases. *Ann Otol Rhinol Laryngol.* 80: 192-206.
5. Mirza S, Bradley PJ, Acharya A, Stacey M, Jones NS (2007) Sinonasal inverted papillomas: recurrence, and synchronous and metachronous malignancy. *J Laryngol Otol.* 121: 857-864.
6. Syrjänen K, Syrjänen S (2013) Detection of human papillomavirus in sinonasal papillomas: systematic review and meta-analysis. *Laryngoscope.* 123: 181-192.
7. Ungari C, Riccardi E, Reale G, Agrillo A, Rinna C, et al (2015) Management and treatment of sinonasal inverted papilloma. *Ann Stomatol (Roma).* 6: 87-90.
8. Nudell J, Chiosea S, Thompson LD (2014) Carcinoma ex-Schneiderian papilloma (malignant transformation): a clinicopathologic and immunophenotypic study of 20 cases combined with a comprehensive review of the literature. *Head Neck Pathol.* 8: 269-286.
9. Zangirolami AC, Oliveira FV, Tepedino MS (2015) Ortner's Syndrome: Secondary Laryngeal Paralysis Caused by a Great Thoracic Aorta Aneurysm. *Int Arch Otorhinolaryngol.* 19: 180-182.
10. Carlson ML, Sweeney AD, Modest MC, Van Gompel JJ, Haynes DS, et al (2015) Inverting papilloma of the temporal bone: Report of four new cases and systematic review of the literature. *Laryngoscope.* 125: 2576-2583.
11. Roh HJ, Procop GW, Batra PS, Citardi MJ, Lanza DC (2004) Inflammation and the pathogenesis of inverted papilloma. *Am J Rhinol.* 18: 65-74.
12. Govindaraj S, Wang H (2014) Does human papilloma virus play a role in sinonasal inverted papilloma? *Curr Opin Otolaryngol Head Neck Surg.* 22: 47-51.
13. Eggers G, Mühling J, Hassfeld S (2007) Inverted papilloma of paranasal sinuses. *J Craniomaxillofac Surg.* 35: 21-29.
14. Garcia AS, Bravo-Calderón DM, Ferreira MP, Oliveira DT (2014) Squamous cell carcinoma arising from inverted schneiderian papilloma: a case report with oral involvement. *Case Rep Otolaryngol.* 2014: 478092.
15. Piva MR, Santos Tde S, Martins Filho PR, Kumar PN, Souza LM, et al (2011) Inverted papilloma (Schneiderian papilloma) with involvement of the oral cavity: report of an unusual case. *An Bras Dermatol.* 86: 779-783.
16. Tsou YA, Huang HJ, Wang TC, Tai CJ, Chen CM, et al (2014) Evaluation of correlation of cell cycle proteins and Ki-67 interaction in paranasal sinus inverted papilloma prognosis and squamous cell carcinoma transformation. *Biomed Res Int.* 2014: 634945.
17. Dictor M, Johnson A (2000) Association of inverted sinonasal papilloma with non-sinonasal head-and-neck carcinoma. *Int J Cancer.* 85: 811-814.
18. Vreugdenburg TD, Lambert RS, Atukorale YN, Cameron AL (2016) Stereotactic anatomical localization in complex sinus surgery: A systematic review and meta-analysis. *Laryngoscope.* 126: 51-59.
19. Lawson W, Schlecht NF, Brandwein-Gensler M (2008) The role of the human papillomavirus in the pathogenesis of Schneiderian inverted papillomas: an analytic overview of the evidence. *Head Neck Pathol.* 2: 49-59.
20. Suh JD, Chiu AG (2014) What are the surveillance recommendations following resection of sinonasal inverted papilloma? *Laryngoscope.* 124: 1981-1982.
21. Busquets JM, Hwang PH (2006) Endoscopic resection of sinonasal inverted papilloma: a meta-analysis. *Otolaryngol Head Neck Surg.* 134: 476-482.
22. Yılmaz İ, Reyhan M, Canpolat T, Yilmazer C, Erkan AN, et al (2015) Positron emission tomography evaluation of sinonasal inverted papilloma and related conditions: a prospective clinical study. *Kulak Burun Bogaz Ihtis Derg.* 25: 9-15.
23. Allegra E, Cristofaro MG, Cascini LG, Lombardo N, Tamburrini O, et al (2012) 18FDG uptake in sinonasal inverted papilloma detected by positron emission tomography/computed tomography. *ScientificWorldJournal.* 2012: 943412.
24. Allegra E, Lombardo N, Cascini G, La Boria A, Garozzo A, et al (2010) Possible role of 18FDG PET/CT for the surveillance of sinonasal inverted papilloma. *Clinical Otolaryngology.* 35: 249-251.