

# Isolated inverted papilloma of the sphenoid sinus associated with HPV type 16

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## Abstract

The inverted papilloma (IP) arising in the sphenoid sinus is rare. Currently, human papilloma viruses are accepted as tumor-inducing and promoting agents involved in benign and malignant tumors of mucosal tissues in the upper aerodigestive tract. A 29-year-old man visited our institution with three years history of right side of nasal obstruction. An endoscopic sphenoidotomy was performed and histological analysis was consistent with an IP without cellular atypia. In the present report, we describe for the first time a case of IP involving the sphenoid sinus that presented with HPV type 16 genome verified by PCR.

## INTRODUCTION

Sinonasal papillomas include three histopathological types as defined by the WHO: exophytic papilloma; columnar cell papilloma; and inverted papilloma (IP).<sup>(1)</sup> IP is a rare type of tumor that constitutes only 0.5-4% of all nasal tumors.<sup>(2,3)</sup> IP originated mainly from the lateral nasal wall and middle meatus.<sup>(1)</sup> The sphenoid sinus as a site of origin for IP is extremely rare. IP is known to be locally destructive, erode bone through pressure necrosis, and to invade other structures including the orbit and skull base.<sup>(4)</sup> Early diagnosis and treatment of sphenoid IP is critical considering the potentially erosive nature of this lesion.<sup>(5)</sup> Recent evidence proposes that human papilloma viruses (HPVs) may play a role in the pathogenesis of IP, a benign but locally aggressive neoplasm with a high recurrence rate and an association with squamous cell carcinoma (SCC).<sup>(6)</sup> In the present report, we describe for the first time a case of IP involving the sphenoid sinus that presented with HPV type 16 genome verified by PCR.

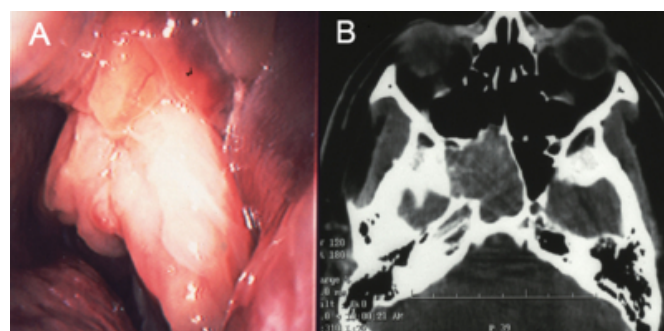
## CASE REPORT

A 29-year-old man presented with three years history of right side of nasal obstruction. The patient reported that six months prior to admission following an upper respiratory infection the obstruction became firm. He did not have nasal discharge, epistaxis, double vision, and eyesight disorder but did have a slight headache. In previous illness, he did not have nasal allergy or nasal chronic inflammation. Anterior rhinoscopy and endoscopy revealed that a yellowish and edematous mass existed in the right common nasal meatus.

The surface of the mass was papillary form. (Figure 1A) The foundation of the mass originated from the right sphenoid sinus. The left nasal cavity was normal. A computed tomography (CT) scan of the sinuses revealed a well defined, heterogeneously, slight hyperintense soft tissue mass within the sphenoid sinus, not associated with calcification and bony destruction. (Figure 1B) The tentative diagnosis was an inflammatory polyp or mucocele and the patient was scheduled for an endoscopic sphenoidotomy under general anesthesia.

## Figure 1

Figure 1: (A) Pre-operative endoscopic view of a polypoid-like mass. (B) Axial computed tomography (CT) scan through the level of the mid sphenoid sinus.



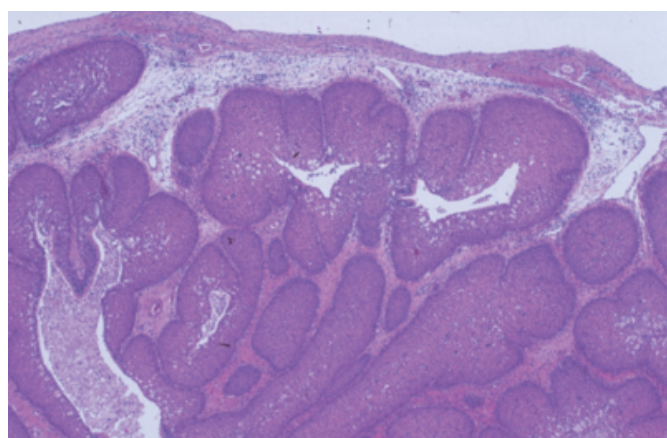
By endoscopic sinus surgery, anterior and posterior ethmoidectomies were performed on the right side, followed by a sphenoid sinusotomy. The anterior sphenoid sinus wall was removed to reveal a firm, greyish mass that filled the whole sphenoid sinus, the mass was meticulously removed piece meal with the use of a microdebrider system. A curved

upward punch was used to gently remove the mass from the lateral areas of the sphenoid sinus, which is particularly dangerous due to their proximity to the optic nerve and the internal carotid artery.

Histologically, the lesions show an ingrowing pattern of thickened, pseudostratified schneiderian epithelium which inverts into the stoma. The patient was diagnosed with an IP that is not associated with SCC. (Figure 2)

### Figure 2

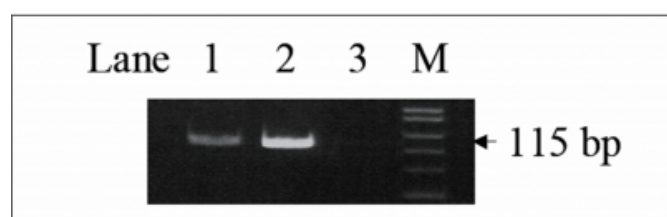
Figure 2: Histology of inverted papilloma. Exophytic papilloma composed of papillary folds covered by stratified squamous epithelium. This is not associated with squamous cell carcinoma (SCC). (Hematoxylin and eosin stain.)



In this case we tested for the prevalence of HPV types 16 and 18 using polymerase chain reaction (PCR)-based methods. DNA extractions from the fresh material and PCR conditions have been described previously.<sup>(7)</sup> Two pairs of primers specific for HPV types 16 and 18 were used. We detected the target band of HPV type 16. (Figure 3)

### Figure 3

Figure 3: Electrophoresis of HPV type 16. The amplification products for HPV type 16 are visualized at approximately 115bp. Band in lane 1 represents positive reactivity for HPV type 16 in this case, whereas lanes 2 and 3 correspond to control patients known to be HPV type 16-positive (lane 2: tonsillar carcinoma) and -negative (lane 3: nasal inflammatory polyp). The DNA size marker is located on the lane 4.



The patient did well and his symptoms were completely

relieved post-operatively. He continues to do well three years later.

## DISCUSSION

Over the last 10 to 20 years, IP has been the subject of much fascination and controversy.<sup>(2)</sup> The IP most commonly (over 90%) arises from the lateral nasal wall with frequent extension into the maxillary, anterior, and posterior ethmoid sinuses.<sup>(3)</sup> Involvement of the sphenoid sinus, frontal sinus and nasal septum is less common. A review of the literature available showed 17 documented patients of isolated IP of the sphenoid sinus.<sup>(8,9,10,11,12,13,14,15)</sup> There were 14 males and three females with an average age of 47.3 years old (range, 37-60 years). Common complaints at initial visit were persistent headache, nasal obstruction and congestion. Thirteen of the 17 patients (76.5%) were treated by endoscopic sinus surgery. In two (16.7%, 2/12) patients, SCC or focal atypia were associated with IP. The recurrence rate was 12.5% (2/16) with a mean follow-up of 31.3 months (range, 5-96 months).

Recently, endoscopic approach to resection of the IP has been advocated.<sup>(16)</sup> This approach avoids many of the potential complications of Caldwell-Luc approach and the lateral rhinotomy/medial maxillectomy and has advantages of shorter hospitalization, improved cosmetic deformity, less blood loss, direct visualization of the precise extent of the tumor.<sup>(17)</sup> In Raveh's review of 19 related publications, several surgical approaches were used; intranasal excision or a Caldwell-Luc approach in 485 patients with a 61% recurrence rate, and an endoscopic procedure in 52 patients with a 17% recurrence rate.<sup>(16)</sup> For many years surgical access to the sphenoid sinus was problematic, however, the development of the rigid nasal endoscope improved the treatment of sphenoid sinus disease, and made the approach to the sphenoid sinus safer.<sup>(14,16)</sup>

Lawson W. et al. reported that malignant transformation is found in the IP in 8.9% of cases. The association between IP and SCC has two common characteristics. The first is being that the carcinoma and the papilloma coexist in the same lesion. The second is a small focus of carcinoma within an IP.<sup>(13)</sup> Currently, HPVs are accepted as tumor-inducing and promoting agents involved in benign and malignant tumors of mucosal tissues in the upper aerodigestive tract.<sup>(18)</sup> High-risk HPV types 16, 18, 31, 33 and 45 are frequently associated with invasive carcinoma of the oral cavity, oropharynx, larynx, and nasal cavity.<sup>(7)</sup> HPV plays a significant role in the pathogenesis of IP and/or carcinoma.

The benign IP contained HPV types 6 or 11, whereas the lesions exhibiting dysplasia or carcinoma were more likely to demonstrate high-risk HPV types 16 or 18.<sup>([618])</sup> The prevalence of HPV types 16/18 DNA in IP was found to be 31.0%(9/29). In cases of IP that were HPV types 16/18-positive, 77.8%(7/9) presented with severe dysplasia or SCC.<sup>([9])</sup> The subtypes of infecting HPV may be important in predicting the prognosis of the IP.<sup>([119])</sup>

We detected HPV type 16 DNA in the IP arising in the sphenoid sinus. Histologic analysis was consistent with the IP without cellular atypia and SCC. The existence of HPV type 16 DNA suggests that the patient is at high risk for recurrence and malignant transformation of the IP. This patient should have extensive follow-up due to the strong association between an HPV type 16 finding and malignant transformation.

## CONCLUSION

We reported a case of IP arising in the sphenoid sinus. In this study, we detected HPV type 16 in this specimen by using PCR. Histologically, this IP was diagnosed without malignancy. Despite the satisfactory early results, recurrence should always be kept in mind and follow-up should continue.

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