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Association between Septal Deviation and Sinonasal Papilloma

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Sinonasal papilloma is a common benign epithelial tumor of the sinonasal tract and accounts for 0.5% to 4% of all nasal tumors. The etiology of sinonasal papilloma remains unclear, although human papilloma virus has been proposed as a major risk factor. Other etiological factors, such as anatomical variations of the nasal cavity, may be related to the pathogenesis of sinonasal papilloma, because deviated nasal septum is seen in patients with chronic rhinosinusitis. We, therefore, investigated the involvement of deviated nasal septum in the development of sinonasal papilloma. Preoperative computed tomography or magnetic resonance imaging findings of 83 patients with sinonasal papilloma were evaluated retrospectively. The side of papilloma and the direction of septal deviation showed a significant correlation. Septum deviated to the intact side in 51 of 83 patients (61.4%) and to the affected side in 18 of 83 patients (21.7%). Straight or S-shaped septum was observed in 14 of 83 patients (16.9%). Even after excluding 27 patients who underwent revision surgery and 15 patients in whom the papilloma touched the concave portion of the nasal septum, the concave side of septal deviation was associated with the development of sinonasal papilloma (p = 0.040). The high incidence of sinonasal papilloma in the concave side may reflect the consequences of the traumatic effects caused by wall shear stress of the high-velocity airflow and the increased chance of inhaling viruses and pollutants. The present study supports the causative role of human papilloma virus and toxic chemicals in the occurrence of sinonasal papilloma.

Keywords: airflow; chronic rhinosinusitis; human papilloma virus; inverted papilloma; septal deviation
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Introduction

Sinonasal papilloma is a common benign epithelial tumor of the sinonasal tract and accounts for 0.5% to 4% of all nasal tumors, but has been associated with possible malignant transformation (Hyams 1971; Lawson and Patel 2009). Sinonasal papillomas consist of well-differentiated columnar or ciliated respiratory epithelium with variable squamous differentiation. In general, papillomas are polypoid and occur unilaterally. Three different histological types of sinonasal papilloma have been classified by the World Health Organization: exophytic papilloma, inverted papilloma and columnar cell papilloma (Kraft et al. 2003). The etiology of sinonasal papilloma remains unclear but human papilloma virus (HPV) has been proposed as a major risk factor (Kashima et al. 1992; Beck et al. 1995). Other etiological factors may include smoking, exposure to pollutants and toxic chemicals, nasal allergy, sinusitis, nasal polyp, nonsinonasal malignancies and genital and dermal warts (Sham et al. 2010).

Septal deviation is an anatomical variation that may cause narrowing of the nasal cavity. Anatomical abnormalities have not been considered to be a significant factor in the pathogenesis of rhinosinusitis, but the septal deviation may be associated with increased prevalence of rhinosinusitis (Orlandi 2010). If the nasal cavity is wide open with good ventilation, more viruses and pollutants can enter the nostril. On the other hand, if the cavity has poor ventilation, drainage problems and rhinosinusitis may occur. Viruses, pollutants, rhinosinusitis and nasal polyps are thought be factors in the occurrence of papilloma. However, whether the occurrence of sinonasal papilloma is related to good or poor ventilation of the nasal cavity is unknown.

The present study analyzed the relationships between the occurrence of sinonasal papilloma and the direction of septal deviation.

Materials and Methods

This study retrospectively evaluated patients with sinonasal papilloma who underwent surgery at Tohoku University Hospital, Sendai, Japan, between July 2005 and August 2013, and at Tohoku

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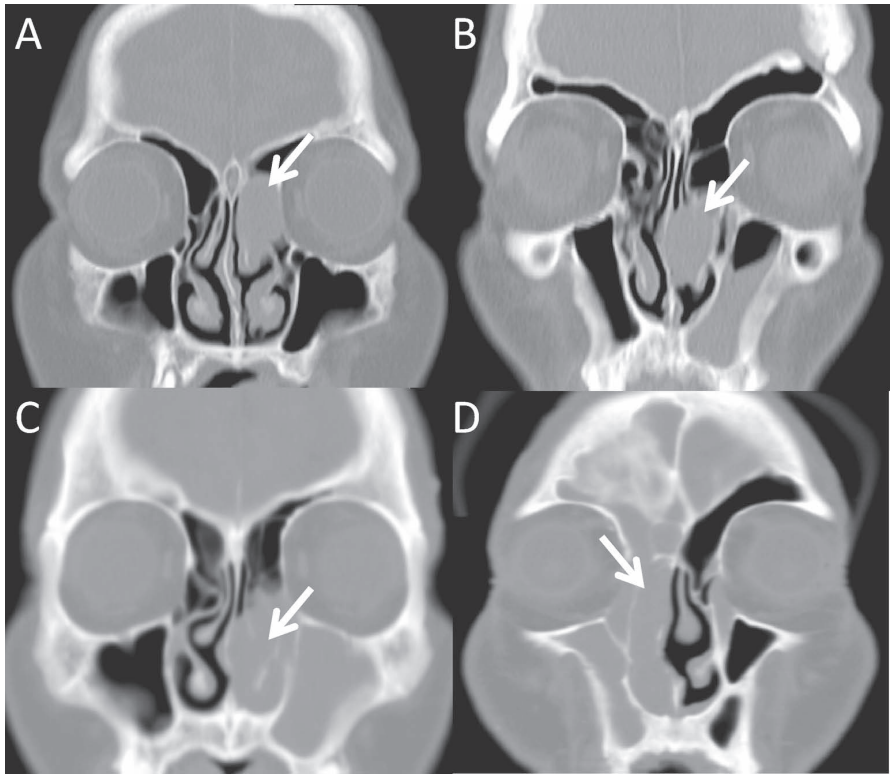

Fig. 1. Examples of tumor location and deviated septum. (A) Tumor localized in the left ethmoid. Nasal septum and the tumor are separated. An arrow indicates the tumor. (B) Small tumor (arrow) originating from the left middle turbinate touches the concave portion of the nasal septum. Because the tumor is small, the possibility of the septal bone remodeling is low, but the shape of the septum before tumor emergence cannot be assessed. (C) Moderate-sized tumor occupying the left common meatus (arrow). The septum is directed to the intact side. This type of septum is sometimes seen in the clinical setting. The septum might have been remodeled with the consistent pressure from the tumor. (D) Tumor (arrow) completely blocking the right nasal cavity. The septum is directed to the affected side. In this case, the direction of the nasal septum was the same before tumor emergence.

Kosai Hospital, Sendai, Japan, between March 2010 and August 2013. The inclusion criteria were pathologically confirmed sinonasal papilloma and either computed tomography (CT) or magnetic resonance (MR) imaging acquired prior to surgery. The exclusion criteria were papilloma in the bilateral nasal cavities and malignant transformation. Finally, 63 male and 20 female patients aged from 31 to 86 years (mean 61.1 years) were included. The images of these 83 patients were reviewed and the septal deviations were measured and classified.

Septal deviation was assessed with CT or MR imaging. If the tumor does not touch the nasal septum, the shape of the septum before the occurrence of the tumor is not changed after the development of the papilloma (Fig. 1A). If the tumor touches the most deviated part of the nasal septum, the original direction of the nasal septum is considered to be unknown (Fig. 1B and C). Even if the tumor touches the septum and is deviated to the affected side, the septum is considered to be consistent with original shape (Fig. 1D). The relationship between the occurrence of sinonasal papilloma and the direction of the nasal septum was calculated using a cumulative binomial distribution with the BINOMDIST function in MS Excel 2010 (Microsoft Corp., Redmond, WA). The study was approved by the institutional review boards of Tohoku University Graduate School of Medicine and Tohoku Kosai Hospital.

Results

The characteristics of the patients in this study are summarized in Table 1. Among the three histological types, inverted papilloma was the most prevalent tumor (n = 80/83, 96%). The relationship between septal deviation and the presence of tumor is summarized in Fig. 2. The tumor was located in the convex side in 18 of the 83 patients, and in the concave side in 51 patients ($p < 0.001$). In the primary patients who had no history of sinonasal surgery, the tumor was also most often located in the concave side ($p < 0.001$). Statistical analysis of the primary patients without the possibility of septal remodeling caused by the tumor showed that the tumor was located in the concave side with statistical significance ($n = 22/33$, $p = 0.040$).

Discussion

The present study investigated the possible association between the occurrence of sinonasal papilloma and the presence of septal deviation that causes narrowing of the nasal cavity, which decreases the possibility that viruses and pollutants can reach the nasal cavity, but disturbs the drainage pathway, which increases the possibility of rhino-

sinusitis and inflammation. The clinical characteristics of the patients in this study, mean age 61 years and male predominance (76%, Table 1), were similar to those in a previously reported series (Lawson and Patel 2009) of 200 patients, with mean age 57 years and male predominance (78%).

Anatomical variations are associated with rhinosinusitis to some extent. Concha bullosa (pneumatized cavity within the middle turbinate) and septal deviation are more common in patients with rhinosinusitis (Calhoun et al. 1991). Septal deviation is the well-known anatomic factor associated with recurrent sinusitis. Many studies on the effect of septal deviation on sinusitis have been reported with conflicting results. Quantitative and qualitative analysis of previously published studies found that increasing angles of septal deviation were associated with increasing prevalence of rhinosinusitis, and septal deviation of $\geq 10°$ was significantly associated with rhinosinusitis ($p = 0.0004$, χ^2 analysis), but the clinical effect was modest with an odds ratio of 1.47 (Orlandi 2010). Patients with septal deviation tend to have bilateral rhinosinusitis (Elahi et al. 1997). In general, sinusitis may arise on either side of the septal deviation. In the convex side, a lateral shift of the middle turbinate narrows the middle meatus and sinus ostium. On the other hand, concha bullosa tends to occur in the concave side, so the sinus ostium is also narrowed (Suzuki et al. 1999). Interestingly, rhinosinusitis was more common in the concave side than in the convex side in patients with cleft palate (Suzuki et al. 1999). The etiology of sinonasal papilloma is unknown and seems different from that of rhinosinusitis, which is mainly caused by drainage problems. Recent studies have demonstrated the effect of septal deviation on airflow using computational fluid dynamics (Chen et al. 2009; Orlandi 2010). The concave side shows increased velocities and turbulence in the middle meatal area. The traumatic effects of the wall shear stress caused by the high velocity of airflow in the concave side might result in the high incidence of sinonasal papilloma. Septal deviation may also lead to increased particle deposition and resulting inflammation in the region of the ostiomeatal complex on the concave side (Schroeter et al. 2006; Tian et al. 2007; Orlandi 2010). Consequently, pollutants contaminate the concave side and may lead to sinonasal papilloma.

In our study, septal deviation was present in 69 of the 83 patients (83.1%). The septum deviated toward the sides with papilloma in 18 of 83 patients (21.7%) and toward the

Table 1. Patients' characteristics in this study.

Total no. patients	83
Characteristics	
Sex	
Male, *n* (%)	63 (76)
Female, *n* (%)	20 (24)
Age, mean yr (range)	61 (31-86)
Pathology, *n*	
Inverted	80
Exophytic	2
Columnar	1
Side of papilloma	
Right, *n* (%)	32 (39)
Left, *n* (%)	51 (61)
Nasal septum	
Deviated to right, *n* (%)	45 (54)
Deviated to left, *n* (%)	24 (29)
S-shaped, *n* (%)	10 (12)
Straight, *n* (%)	4 (5)

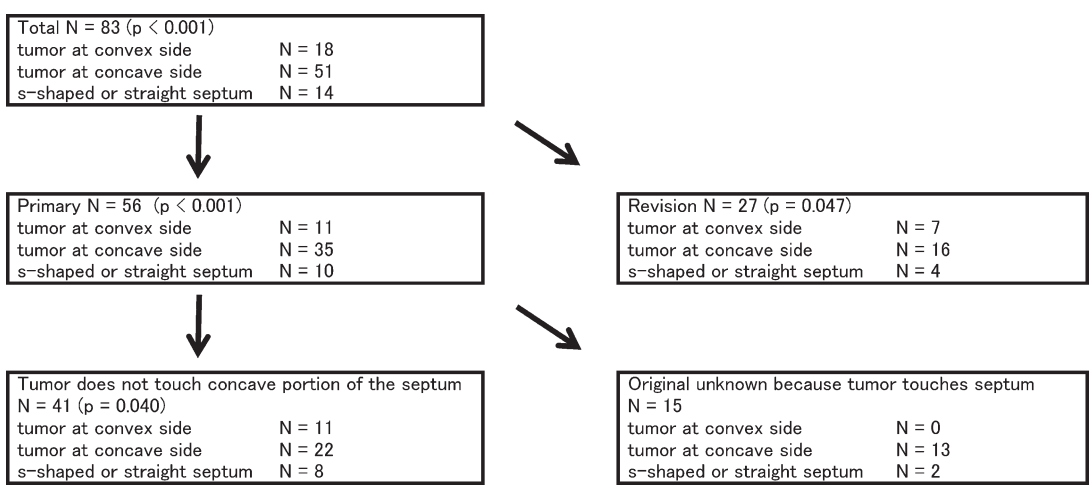

Fig. 2. Relationship between nasal septum and sinonasal papilloma. Top box: All patients. Papilloma is more common in the concave side than in the convex side ($p < 0.001$). Middle left box: Primary patients. Papilloma is more common in the concave side than in the convex side ($p < 0.001$). Middle right box: Twenty-seven patients who underwent revision surgery. Bottom left box: Forty-one patients with preserved original shape of the nasal septum. Papilloma is more common in the concave side than in the convex side ($p = 0.040$). Bottom right box: Fifteen patients with tumor touching the nasal septum, so the direction of the nasal septum might have been changed by consistent pressure.

intact side in 51 of 83 patients (61.4%). These analyses include the patients with remodeling of the nasal septum because of consistent pressure exerted by the tumor, resulting in the septum directed to the intact side. To examine the relationship between the original direction of the nasal septum and the occurrence of sinonasal papilloma, 27 patients who underwent revision surgery were excluded from the statistical analysis, because large papilloma might have displaced the nasal septum before the previous surgery. Fifteen of the 56 primary patients were also excluded, in whom the tumor had touched the nasal septum and so could have deformed the septum resulting in a change in direction (Fig. 1B and C).

HPV is a species-specific DNA virus with 8,000 base pairs in a double-stranded circular DNA genome. HPV types 6 and 11 are the most prevalent types found in sinonasal papilloma (Kashima et al. 1992). HPV types 6 and 11 are associated with exophytic condylomata and low-grade dysplasia of the uterine cervix. On the other hand, HPV types 16 and 18 are found in squamous cell carcinoma of the oropharynx and sinonasal tract (Syrjänen 2005). Review of 1,041 sinonasal papillomas analyzed for HPV DNA found that 347 (33.3%) patients were positive (Syrjänen 2005). HPV types 6 and 11 are the viral types most frequently associated with benign squamous cell lesions of the oral, pharyngeal, laryngeal or sinonasal mucosa (papilloma), whereas HPV types 16 and 18 are found in premalignant lesions and squamous cell carcinomas. Unlike the oral cavity and genital organs where HPV is transmitted through direct contact, the mechanism of HPV transfection in the nasal cavity is not known. Since sinonasal papilloma occurs at various sites in the nasal cavity and most are physically untouchable from externally, direct contact infection is not likely. One possible explanation is that HPV from outside the nostril is adsorbed on the anterior nares and spread through the nasal cavity on the nasal mucosa.

This study focused on the anatomical structures, using the contralateral side as the negative control. Therefore, other risk factors, such as allergic rhinitis, smoking and occupation, which may predispose to sinonasal papilloma, were ignored. Chronic sinusitis is reported to occur in either side and inflammation is considered to be one of the causes of the sinonasal papilloma (Orlandi et al. 2002; Orlandi 2010). However, this study showed a different tendency. As the tumor grows and displaces the nasal septum, remodeling occurs and the septum moves toward the intact side. To exclude this effect, if the tumor touched the most deviated part of the nasal septum, the original direction of the nasal septum was considered to be unknown and was excluded from the statistical analysis.

Inflammation is a possible cause of sinonasal papilloma. Unilateral inverted papilloma is associated with contralateral inflammation, and the degree of contralateral inflammation is greater than that seen in the other sinonasal tumors (Orlandi et al. 2002). Inverted papilloma typically occurs within the ethmoid sinuses or near the ostium of the maxillary sinus. This is the area of the nasal cavity most often involved in chronic inflammation. Nasal polyps are commonly found in this area.

To examine the relationship between preclinical direction of nasal septum and the side of sinonasal papilloma, we excluded the patients, in whom the tumor contacted the concave portion of the nasal septum (Fig. 1B and C), from the statistical analysis (Fig. 2 bottom right, $N = 15$). Therefore, the number of tumors in the concave side was reduced. Despite this exclusion, the tumor tended to arise in the concave side with statistical significance ($p = 0.040$).

In conclusion, the present study found that sinonasal papilloma tends to occur in the concave side of septal deviation. We speculate that the increased chance of inhaling viruses, pollutants and toxic chemicals, and microtrauma as a result of high velocity of airflow is associated with the occurrence of sinonasal papilloma in the concave side. Rhinosinusitis and nasal polyps are less likely to cause sinonasal papilloma since these diseases occur on either side of the deviated septum. We suggest that HPV, pollutants and toxic chemicals rather than rhinosinusitis and nasal polyp are the more important factors in the pathogenesis of sinonasal papilloma.

Conflict of Interest

The authors declare no conflict of interest.

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