

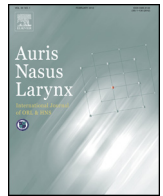


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Clinical features of nasal and sinonasal inverted papilloma associated with malignancy

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ABSTRACT

Objective: Nasal and sinonasal inverted papilloma (IP) are rare benign tumors and have the potential to exhibit malignancy in approximately 10% of cases. This study aimed to analyze the clinical features of IP associated with malignancy. Furthermore, we reviewed our therapeutic strategy and the clinical course of malignant IP.

Methods: Overall, 70 patients with IP at our institution were retrospectively analyzed from April 2006 to December 2015; of these, six (9%) had associated malignancy. Data was collected on sex, age, presenting symptoms (nasal bleeding, rhinorrhea, facial or cheek pain, and nasal obstruction), bone destruction, and extent of disease on CT and MRI. Categorical data of patients with and without malignancy were compared using the chi-square test. A p value of <0.05 was considered statistically significant. Our therapeutic strategy for IP with malignancy, particularly the surgical procedure, i.e., the external incision or the endoscopic nasal approach, varied based on when the carcinoma was detected. In addition, we considered postoperative radiation therapy depending on histological examination.

Results: Nasal bleeding ($p < 0.001$), pain ($p = 0.040$), bone destruction ($p < 0.001$), and extent of disease ($p = 0.026$) on CT and MRI findings were significantly associated with malignancy. Carcinoma was diagnosed preoperatively in two (33%) and postoperatively in four patients (67%). We operated five patients (one case was not treated because of end-stage pancreatic cancer). Two patients underwent endoscopic sinus surgery (ESS) alone, two ESS plus *Denker's method*, and one ESS plus anterior craniotomy. Three patients underwent surgery only, and two patients received postoperative radiotherapy. The median follow-up period was 69.3 months. One patient died of the disease and the remaining patients are alive without recurrence.

Conclusion: For IP patients exhibiting these clinical findings preoperatively, we should suspect complication with malignancy and plan a treatment. Even if postoperative histology does not confirm malignancy, we should ensure careful observation because of metachronous malignant transformation or the possibility to overlook small malignant lesions. Our result suggests that our strategy for malignant IP could be a reasonable option.

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1. Introduction

Nasal and sinonasal inverted papilloma (IP) is an uncommon benign tumor, which is complicated by malignancy in approximately 10% of cases [1,2]. Several reports have stated that malignant transformation of IP may be caused by human papillomavirus (HPV) infection, especially HPV type 18; however, the exact mechanism of carcinogenesis in IP is presently unclear [3,4]. Some studies have linked histological, morphological, and genetics features to malignant alterations, such as, increased neoplastic epithelium/stroma ratio, hyperkeratosis, elevated levels of epidermal growth factor receptor and transforming growth factor- α [5,6]. However, this information has been obtained from postoperative histological examination. If we could predict the presence of malignancy from the preoperative clinical findings rather than postoperative information, it could be even more useful in determining the therapeutic strategy. To our knowledge, there are few reports in the literature regarding predictive preoperative findings. Hence, this study aimed to analyze the preoperative clinical features of IP associated with malignancy. Furthermore, there is no consensus regarding a treatment strategy for IP with malignancy. We reported the clinical course of patients with malignant IP at our institution and reviewed the literature on this matter.

2. Materials and methods

We retrospectively reviewed the medical records of 70 patients with IP at our institution from April 2006 to December 2015. Data was collected on age, sex, presenting symptoms (nasal bleeding, rhinorrhea, facial or cheek pain, and nasal obstruction), bone destruction on CT with 5-mm slices, and extent of disease on CT and MRI. Based on common IP sites [2,7], we classified tumor extent into three groups to reflect the tumor volume and progression: (1) Tumor totally confined to the nasal cavity without extension into the sinus or involving only one sinus. (2) Tumor involving more than one sinus. (3) Tumors with any extranasal or extrasinus extension involving adjacent, contiguous structures, such as the intracranial

compartment. Our therapeutic strategy for IP with malignancy varied based on when the carcinoma was detected, i.e., whether the carcinoma was detected during preoperative biopsy or postoperative definitive histology. For all resectable lesions detected during preoperative biopsy, we uniformly performed open en bloc resection, not an endoscopic operation alone, whereas for all unresectable lesions, we performed chemoradiotherapy. For lesions detected during postoperative definitive histology, we did not perform additional resection but considered postoperative radiotherapy if the tumor base contained malignant tissue or the surgical margin being close or positive. On the other hand, if there was no evidence of malignancy in preoperative biopsy, even for the case suspected malignancy from image or clinical findings, we operated the endoscopic endonasal approach, but examine intraoperative frozen section from different location. If malignant findings is intraoperatively detected, changing the surgical approach or multidisciplinary treatment for malignant disease should be considered. Categorical data of patients with and without malignancy were compared using the chi-square test. A p value of <0.05 was considered statistically significant. This study was approved by the Ethics Committee of Kurashiki Central Hospital (Okayama, Japan).

3. Results

In our study, 6 out of 70 cases (9%) were complicated with malignancy and 64 cases (91%) were not. Nasal obstruction in 49 patients (70%) is the most common presenting symptom. Other manifestation include pain in 7 (10%), nasal bleeding in 7 (10%) and rhinorrhea in 6 (8%). Nine patients had bone destruction at the following part: turbinate ($n = 5$), maxillary bone ($n = 5$), orbital plate ($n = 1$), nasal septum ($n = 1$), and anterior skull base ($n = 1$). Table 1 shows the IP patients' characteristic between with malignancy and nonmalignancy. Nasal bleeding ($p < 0.001$), pain ($p = 0.040$), bone destruction ($p < 0.001$), and extent of disease ($p = 0.026$) were significantly associated with malignancy. Although five patients were treated for the malignancy, one was not because of advanced

Table 1

Background characteristic of IP patients between with malignancy ($n = 6$) and nonmalignancy ($n = 64$).

Characteristics	No. of patients		p value
	Malignancy	Nonmalignancy	
Sex			
Male/female	5/1	45/19	0.50
Age			
\leq / $>$ median = 63	3/3	34/30	0.88
Presenting symptom (yes/no)			
Nasal bleeding	3/3	4/60	<0.001
Rhinorrhea	1/5	5/59	0.45
Facial or cheek pain	2/4	5/59	0.04
Nasal obstruction	3/3	46/18	0.26
Bone destruction			
Presence/absence	4/2	5/59	<0.001
Extent of disease			
Group 1/2/3	1/1/4	15/39/10	0.02

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