

Case Report

Malignant transformation of a large sinonasal squamous cell papilloma with bilateral nasopharyngeal, cervical lymph node metastasis

Hongmiao Ren, Xuan Wu, Kejun Zuo

Otorhinolaryngology Hospital, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou 510080, Guangdong, P. R. China

Received March 12, 2016; Accepted May 27, 2016; Epub August 15, 2016; Published August 30, 2016

Abstract: Sinonasal squamous papilloma is a benign epithelial tumor having variable squamous differentiation. It occurs in the nasal cavity and paranasal sinuses. Malignant transformation of sinonasal squamous papilloma is responsible for cancer-related deaths worldwide. We reported a 52-year old man diagnosed as malignant transformation of a large sinonasal squamous cell papilloma. Moreover, bilateral nasopharyngeal metastasis followed by parapharyngeal space and cervical lymph node metastasis are appeared. The pathology results of sinonasal and nasopharyngeal mass are both malignant transformation of inverted squamous cell papilloma. Considering the extension of the tumor and the fact that nasopharyngeal carcinoma is more sensitive to chemotherapy and radiation, we had strongly counseled the patient that operation should be evaluated after he received concurrent chemoradiation.

Keywords: Malignant transformation, sinonasal squamous papilloma, concurrent chemoradiation

Introduction

Sinonasal squamous papilloma is a benign epithelial tumor having variable squamous differentiation. It occurs in the nasal cavity and paranasal sinuses. Associated clinical characteristics include a tendency towards local destruction, recurrence and malignant transformation into squamous cell carcinoma [1]. The incidence of Sinonasal squamous papilloma has been reported as 0.5-4 percent among primary sinonasal tumors [2].

The exact aetiology of malignant transformation is not fully understood. However, human papillomavirus (HPV) which thought to be the leading cofactor in the pathogenesis of papilloma, plays a role in the procedure [3]. In 2005, D'Souza found that people with head and neck cancer were 15 times more likely to be infected with HPV than those without [4]. The researchers surmised that pre-malignant lesions in some HPV-positive sample may be the earliest stages of the cancer.

Malignant transformation of a sinonasal squamous cell papilloma is the most common histo-

logic subtype of tumor among patients. The reasons for advanced disease at presentation are not entirely clear but are thought to be due in part to delays in diagnosis. (1) The condition is most probably under-diagnosed, as it may coexist or develop alongside simple inflammatory polyps. It is possible to miss an squamous cell carcinoma coexisting with simple papilloma, if biopsy samples collect papilloma only. (2) It is also possible to miss an malignant transformation of a sinonasal squamous cell papilloma developing later in the course of an sinonasal papilloma, if examination of subsequent specimens was not performed. We report A 52-year old man diagnosed as malignant transformation of a large sinonasal squamous cell papilloma with bilateral nasopharyngeal, cervical lymph node metastasis.

Case report

In November, 2015, a 52-year old man was admitted to our hospital with a 8-year history of longstanding right nose blockage, 18-month history of eminence of the right nose and maxillofacial region. In 2013, he was diagnosed as "nasal polyps" and received a endoscopic sinus

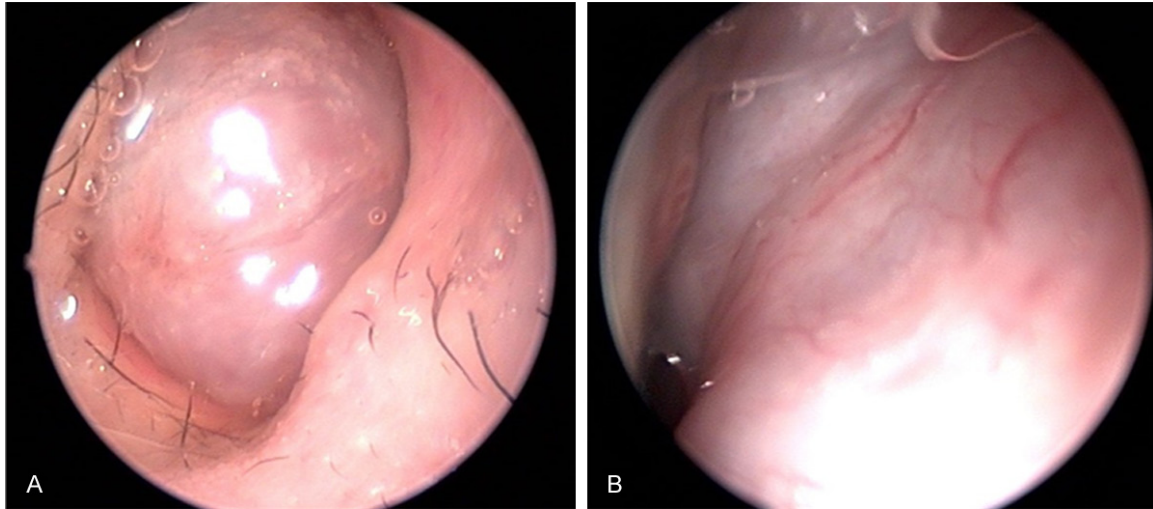


Figure 1. Fiberoptic nasal endoscopic examination. A. Mucosal inflammation and masses in the right nasal cavity. B. The left nasal cavity is stenosis owing to the nasal septum crushed by the mass.

surgery to relieve nasal blockage. However, nasal blockage reappeared 15 days later. He had presented to our institution in December, 2014. Although we carried out right nose biopsy but he declined to consultation for consideration of further immunohistochemistry. 4 months before his admission, he had had recurrent headache and a weak sense of vision.

The patient worked as a farmer in a mountain village, He smoked a pipe and had a remote history of cigarette use (40 pack-years, with no cigarette use for more than 1 month), He reported that he did not drink alcohol. His family history was negative for cancer. His physical examination remained unremarkable except for the bilateral cervical, supraclavicular lymphadenopathy, especially in the right. Fiberoptic nasal endoscopic examination revealed mucosal inflammation and masses in the right nasal cavity (**Figure 1A**), the left nasal cavity is stenosis owing to the nasal septum crushed by the mass (**Figure 1B**). Laboratory evaluation remained unremarkable. Computed tomography (CT) of the paranasal sinuses and cervical with the use of contrast material confirmed: (1) The presence of a large high signal mass measuring 57 mm by 75 mm by 49 mm filled in the right nose cavity and maxillary sinus, ethmoid sinus, sphenoid sinus and protruding to the right choanae. (2) The mass involved to the basal bones of anterior cranial fossa, middle cranial fossa, optic canal and Infraorbital. Moreover, the mass extend to nasopharynx and infratemporal fossa. (3) There is a cyst in the

posterior of nasal cavity. (4) It combined with metastasis to bilateral cervical, supraclavicular lymph node especially in bilateral parapharyngeal space (**Figure 2A-D**). Meanwhile, the result of a sinonasal magnetic resonance imaging (MRI) is similar to the aforementioned CT results. Ultrasonography of viscera, thyroid gland and cervical lymph nodes showed that there is no metastasis in viscera, thyroid gland, but metastasis to bilateral cervical, supraclavicular lymph node were detected. Bone scintigraphic imaging showed no metastasis except for the bones around the mass.

We suspected a sinonasal malignant tumor. Simultaneously, We noted the mass in nasopharynx. Then the question is appeared: whether pathology of the mass in nasopharynx is similar to the sinonasal mass or there is a second tumor, nasopharyngeal carcinoma, in the patient. If so, the therapeutic mode of nasopharyngeal carcinoma is totally different to sinonasal mass. In December 17, 2015, we observed hyperemia of the bulbar conjunctiva, swelling of palpebra frontalis in his right eye, as well as fever (temperature 38.5°C). He reported shivering, cold sweat and severe ophthalmalgia of the right eye. Laboratory evaluation showed high concentrations of C-reactive protein (41 mg/L), a white-cell count of 9,600 per cubic millimeter, (83.4% polymorphonuclear cells, 11.1% lymphocytes, 5.3% monocytes, and 1% eosinophils). Blood bacterial cultures reported that there is no bacterial grew in blood. Testing for HIV antibody was negative. We consider as the

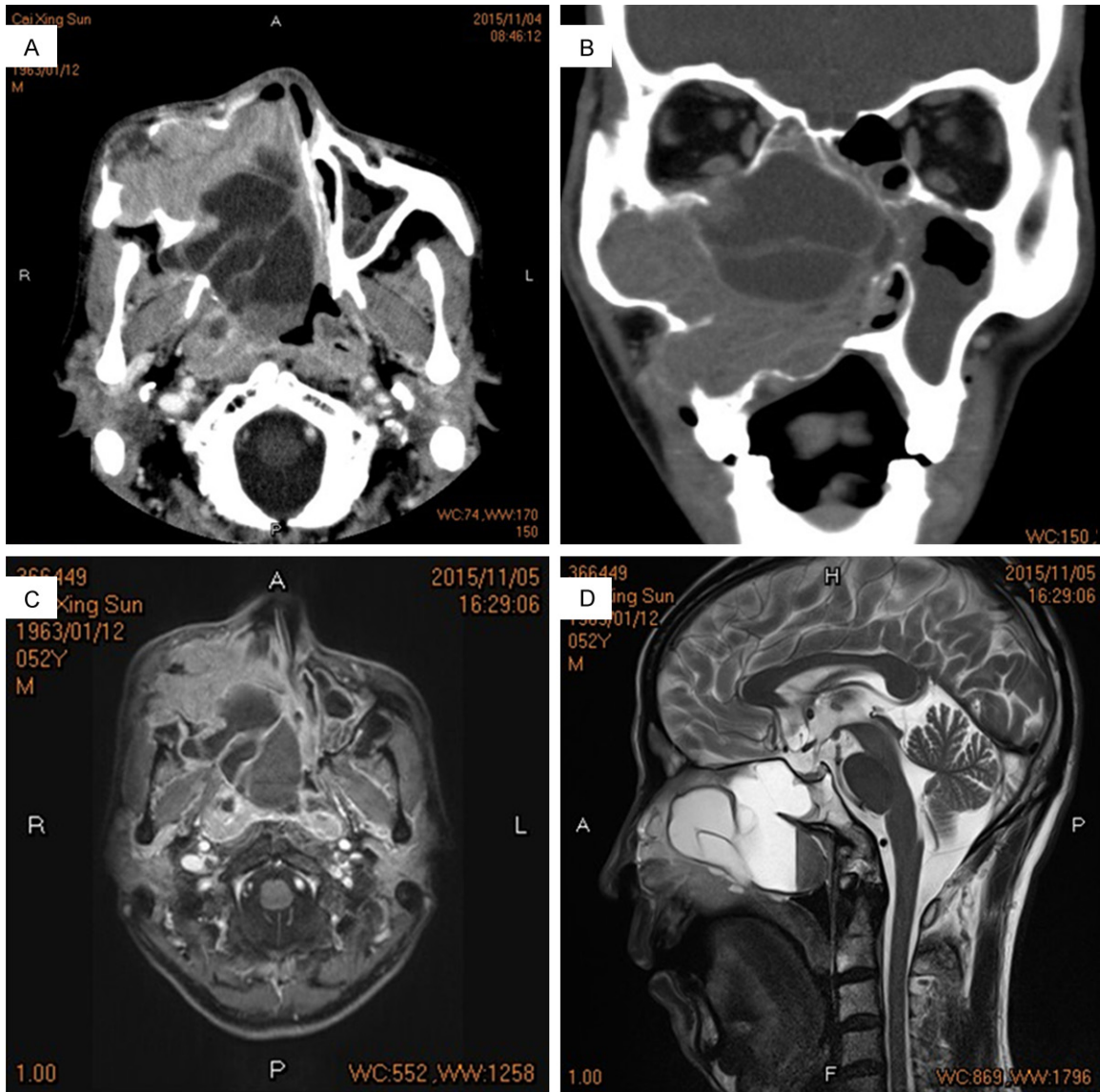


Figure 2. CT and MRI of the paranasal sinuses with the use of contrast material (A, B). The presence of a large high signal mass measuring 57 mm by 75 mm by 49 mm filled in the right nose cavity and maxillary sinus, ethmoid sinus, sphenoid sinus and protruding to the right choanae. The mass involved to the basal bones of anterior cranial fossa, middle cranial fossa, optic canal and Infraorbital. Moreover, the mass extend to nasopharynx and infratemporal fossa. There is a cyst in the posterior of nasal cavity (asterisk). it combined with metastasis to bilateral cervical, supraclavicular lymph node especially in bilateral parapharyngeal space (arrowhead). (C, D) MRI results which is similar to the aforementioned CT results.

infection of the mass. On admission, antibiotic was started. The symptoms were alleviated soon.

Endoscopic sinus surgery was performed for sinonasal and nasopharynx biopsy for further treatment and an expedited evaluation, which he agreed to pursue. The pathology results of sinonasal and nasopharyngeal mass are both malignant transformation of inverted squa-

mous cell papilloma (Figure 3A, 3B). Considering the extend of the tumor as well as the advice of department of Oncology and radiotherapy, we had strongly counseled the patient that operation should be evaluated after he received concurrent chemoradiation. If not, it could result in further progression and severe complications. However, the patients and his daughter declined consultation for consideration of concurrent chemoradiation, because

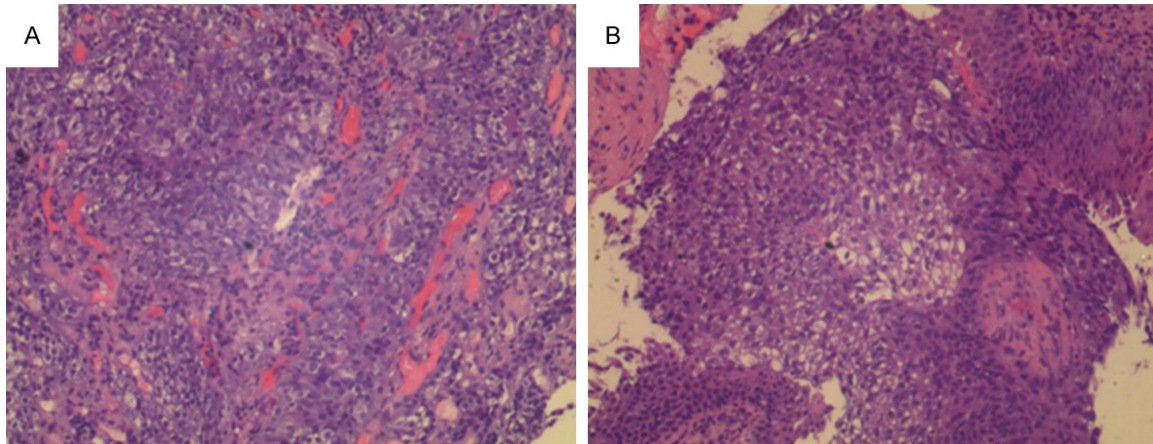


Figure 3. The pathology results of sinonasal and nasopharyngeal mass (A, B). The pathology results of sinonasal and nasopharyngeal mass are both malignant transformation of inverted squamous cell papilloma.

they were reluctant to confront the adverse effects along with concurrent chemoradiation. Ultimately, however, as long as a patient is competent to make decisions, he has the right to chose his destiny.

Discussion

Sinonasal squamous papilloma is a benign lesion. Malignant transformation of Sinonasal squamous papilloma is responsible for cancer-related deaths worldwide. The present case reported a 52-year old man diagnosed as malignant transformation of a large sinonasal squamous cell papilloma. Moreover, bilateral nasopharyngeal metastasis followed by parapharyngeal space and cervical lymph node metastasis are appeared.

The aetiological role of infection with high risk human HPVs in head and neck carcinomas is well established [4]. HPVs are double-strand viruses which infect epithelia of the mucosae. The virus's DNA integrates into the DNA of healthy cells in head and neck, the cells acts as a manufactory to produce two harmful proteins, E6 and E7 [5, 6]. E6 and E7 bind to and down regulate p53 and pRb expression which acts as important tumour-suppressor proteins. As a result, excessive cell growth without pRb manipulation combined with DNA damaged cell replication without p53 activates DNA repair or initiates cell death induced the occurrence malignant transformation process [3].

The trans-nasal endoscopic medial maxillectomy [7] can be performed according to the staging system for papilloma presented by Krouse

[8] (Tumours with extranasal, extrasinus extension and associated with malignancy are classified as stage IV). However, the patient not only suffered from malignant transformation of a large sinonasal squamous cell papilloma and cervical lymph node metastasis, but also appeared bilateral nasopharyngeal metastasis followed by parapharyngeal space. It means that it is impossible to excise the whole carcinoma by local excision. In addition, early evidence suggests that nasopharyngeal carcinoma is more sensitive to chemotherapy and radiation. When People suffering from nasopharyngeal/oropharyngeal cancers treated with chemotherapy and radiation, they seemed to have better survival rates than patients received surgical excision [9, 10]. Therefore, considering the extend of the tumor as well as the advice of department of Oncology and radiotherapy, we had strongly counseled the patient that operation should be evaluated after he received concurrent chemoradiation.

Based on the aforementioned phenomenon, what should we do to avoid or reduce the incidence of malignant transformation. Firstly, serial biopsies of recurrent papilloma may reduce the risk of missing a developing squamous carcinoma. Secondly, Long-term follow up of inverted papilloma patient is necessary for the development of recurrent inverted papilloma.

Acknowledgements

The research was supported by Natural Science Foundation of Guangdong Province, 2016-A030310148.

Disclosure of conflict of interest

None.

Authors' contribution

All authors have contributed to, read and approved the final manuscript for submission.

Address correspondence to: Hongmiao Ren and Kejun Zuo, Otorhinolaryngology Hospital, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou 510080, Guangdong, P. R. China. E-mail: renhongmiao123@163.com (HMR); 1329483486@qq.com (KJZ)

References

- [1] Anari S and Carrie S. Sinonasal inverted papilloma: narrative review. *J Laryngol Otol* 2010; 124: 705-715.
- [2] Lane AP and Bolger WE. Endoscopic management of inverted papilloma. *Curr Opin Otolaryngol Head Neck Surg* 2006; 14: 14-18.
- [3] Scudellari M. HPV: Sex, cancer and a virus. *Nature* 2013; 503: 330-332.
- [4] D'Souza G, Kreimer AR, Viscidi R, Pawlita M, Fakhry C, Koch WM, Westra WH and Gillison ML. Case-control study of human papillomavirus and oropharyngeal cancer. *N Engl J Med* 2007; 356: 1944-1956.
- [5] Honegger A, Leitz J, Bulkescher J, Hoppe-Seyler K and Hoppe-Seyler F. Silencing of human papillomavirus (HPV) E6/E7 oncogene expression affects both the contents and the amounts of extracellular microvesicles released from HPV-positive cancer cells. *Int J Cancer* 2013; 133: 1631-1642.
- [6] Bartkowiak T, Singh S, Yang G, Galvan G, Haria D, Ai M, Allison JP, Sastry KJ and Curran MA. Unique potential of 4-1BB agonist antibody to promote durable regression of HPV+ tumors when combined with an E6/E7 peptide vaccine. *Proc Natl Acad Sci U S A* 2015; 112: E5290-5299.
- [7] Erbek SS, Koycu A and Buyuklu F. Endoscopic modified medial maxillectomy for treatment of inverted papilloma originating from the maxillary sinus. *J Craniofac Surg* 2015; 26: e244-246.
- [8] Krouse JH. Development of a staging system for inverted papilloma. *Laryngoscope* 2000; 110: 965-968.
- [9] Ang KK, Harris J, Wheeler R, Weber R, Rosenthal DI, Nguyen-Tan PF, Westra WH, Chung CH, Jordan RC, Lu C, Kim H, Axelrod R, Silverman CC, Redmond KP and Gillison ML. Human papillomavirus and survival of patients with oropharyngeal cancer. *N Engl J Med* 2010; 363: 24-35.
- [10] Richards L. Human papillomavirus-a powerful predictor of survival in patients with oropharyngeal cancer. *Nat Rev Clin Oncol* 2010; 7: 481.