

CASE REPORT



Incidental p16-positive oropharyngeal carcinoma found during tonsillectomy for palmoplantar pustulosis

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ABSTRACT

The tonsillar crypt is thought to be a hiding site for early cancer detected after tonsillectomy for primary lesion search in cancer of unknown primary site. In rare cases, a small lesion can be detected unexpectedly during surgical treatment for chronic tonsillitis and tonsillar focal diseases. We report the case of a 47-year-old woman undergoing tonsillectomy for palmoplantar pustulosis (PPP), resulting in the diagnosis of p16-positive oropharyngeal cancer (OPC) in the left tonsil. Postoperative radiation therapy was performed due to the presence of an adhesive lesion during surgery. Radiotherapeutic adverse effects were mild and improved 3 months after the radiotherapy. The symptoms of PPP completely resolved 3 months after the tonsillectomy and no recurrence has been observed so far. With an increase in the cases of HPV-related OPCs, routine pathological examination after tonsillectomy for benign-appearing tonsils in adults is necessary to detect incidental OPC regardless of its low cost-effectiveness.

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Introduction

In Japan, tonsillectomy is primarily indicated in patients with recurrent or chronic tonsillitis and tonsillar focal diseases like IgA nephropathy and palmoplantar pustulosis (PPP) [1,2]. There, routine histologic evaluations of tonsillectomy specimens are performed, whereas it is still controversial in other countries due to cost effectiveness [3]. Here, we describe a patient surgically treated for PPP, in which the tonsillectomy specimen was unexpectedly found to be a p16-positive squamous cell carcinoma. Considering an increasing number of HPV-related oropharyngeal cancers (OPCs) nowadays, routine histologic examination of benign-appearing tonsils should be recommended to detect an incidental neoplasm.

Case presentation

A 47-year-old woman suffering from refractory PPP was referred to our department for a tonsillectomy. No general symptoms except blisters on her palms and soles, and arthralgia accompanied by PPP were found. A pharyngeal fiberscope revealed a tonsillar

hypertrophy classified as Mackenzie's Class II, and slight asymmetry without inflammation (Figure 1). Plain CT scanning for systemic assessment also showed a slightly larger tonsil on the left and no cervical lymphadenopathy (Figure 1). Tonsillectomy was undertaken for the treatment of PPP about 4 months after the first consultation. During the surgery, each tonsil adhered to the neighboring muscles despite no history of chronic tonsillitis, requiring the resection of a part of muscle on the left side. There were no significant complications in the intra and post-operative period. In the pathological gross findings, the resected right tonsil seemed to be normal while the left tonsil appeared to have a tumor which was harder and more whitish in the cutting surface located in the upper region (Figure 2). On the histological examination, the right tonsil showed a severe invasion of lymphocytes and neutrophils into the epithelium of the crypt, indicating a chronic tonsillitis. On the other hand, an expansive invasion of atypical cells showing abnormal keratinization was observed in the left tonsil, indicating a moderately differentiated squamous cell carcinoma. The tumor was 15 × 17 mm in size, centered in the tonsillar crypts, extended to the surface, with p16 immunostaining 70%–80% positive in

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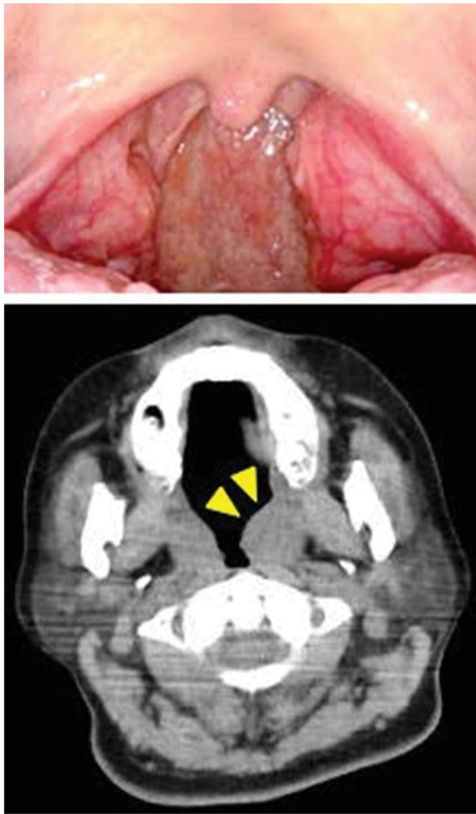


Figure 1. Oropharyngeal fiberscopy and plain computed tomography (CT). The tonsils showed moderate hypertrophy and slight asymmetry without any inflammation (upper panel). A plain CT scan also indicated slight asymmetry (arrow heads).

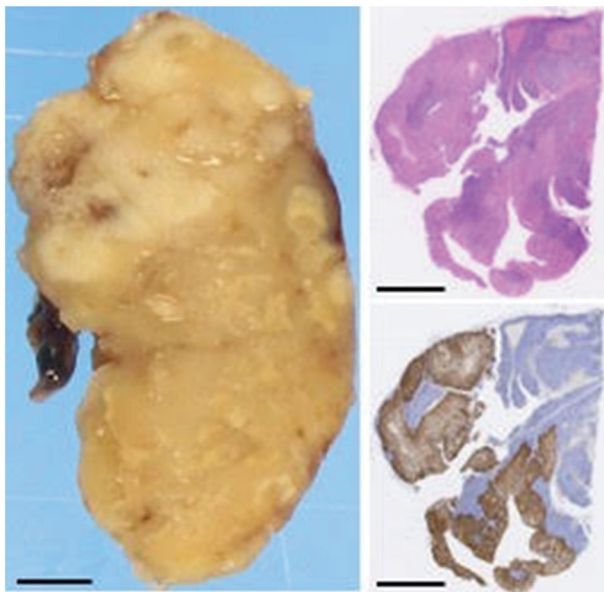


Figure 2. Pathological gross and microscopic findings of the left tonsil. The upper region of the tonsil had a harder and more whitish area. Histological examination revealed 70%–80% p16-immunoreactivity in the lesion. Bar: 5 mm.

the lesion (Figure 2). There was no lymph-vascular invasion and the pathological margin was negative.

With informed consent, we attempted to do several imaging modalities including positron emission tomography for the cancer staging and a gastrointestinal fiberscope to check for a secondary cancer. Consequently, this case was diagnosed with a p16-positive OPC, stage I based on T1N0M0 (UICC 8th edition). From the perspective of the intraoperative findings and young age, a postoperative radiotherapy, intensity-modulated radiation therapy (IMRT), was planned with a total radiation dose of 70 Gy and started 2 months after the surgery. Although the tumor in the left tonsillar sinus has been gradually growing until the beginning of the IMRT, it disappeared completely at the end (Figure 3). Radiotherapeutic complications such as mucositis, skin reaction and dysgeusia were mild, recovering 3 months after IMRT.

The blisters on her palms and soles, and sternoclavicular arthritis caused by PPP improved 3 months after the tonsillectomy. No recurrence was observed 10 months from the end of the IMRT.

Discussion

OPC is frequently detected in the process of seeking for the primary tumor involving the cervical lymph node [4]. Tonsillectomy for cancer of unknown primary origin reveals the primary cancer with a 44.7% probability [5]. On the other hand, pathological examinations of the tonsillectomy piece in benign disease in adults rarely reveal a neoplasm. Whether histological evaluation should be routinely performed is controversial. Starry reported an unsuspected tonsillar neoplasm first in 1939 and advocated a routine histological examination of tonsillectomy specimens [6]. Pathological examination has since been performed in cases presenting with various risk factors. The majority of authors recommend that the examination should be restricted to cases with the following unfavorable clinical features: notable tonsillar asymmetry, visible lesion, tonsillar firmness, cervical adenopathy, systemic symptoms, and history of malignancy, previous radiotherapy, or immunodeficiency [7]. In our case, however, the patient had no unfavorable clinical features and was unexpectedly diagnosed with SCC after tonsillectomy. According to a systematic literature review by Rokkjaer and Klug, only 11 patients (0.015%) among 72,322 patients extracted from 37 articles were found to have an unsuspected malignancy [8]. Here, we analyzed

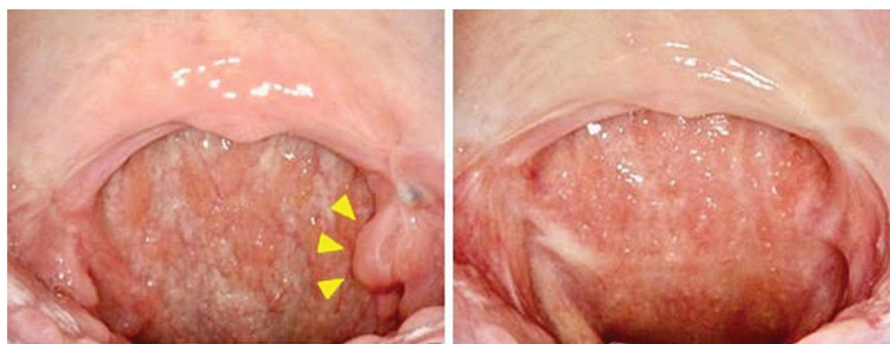


Figure 3. Oropharyngeal fiberscopy pre and post radiotherapy. The tumor indicated by arrow heads grew gradually in the left tonsillar sinus by the beginning of IMRT. As shown in the right panel, it disappeared completely at the end of IMRT.

patients undergoing tonsillectomy for benign diseases to understand the frequency of an incidental OPC at our hospital and their demographics from Jun. 2008 to Apr. 2020, who were over 18 years of age without unfavorable clinical features. A total of 290 patients were found with characteristics summarized in Table 1. The incidence of unsuspected malignancy was 0.34%, which was higher than previous reports, probably due to the smaller specimen sample [8,9]. It is worth noting that our analysis focused exclusively on adults without the above clinical features. The characteristics in this malignant case were a married woman, over 40 years of age, body mass index ≥ 25 , heavy smoker, little alcohol consumption and no history of tonsillar inflammation. In addition to the common pharyngeal cancerous risk factors such as smoking and alcohol consumption, more attention should be paid to married cases, which may be considered new unfavorable clinical feature. This can be explained by the fact that HPV-related OPC, which occurs in relatively young population less exposed to tobacco and alcohol, has increased while the overall incidence of head and neck cancers caused by smoking and drinking has decreased [10–13]. Furthermore, OPC is occasionally found as a small lesion. Since the patient characteristics for OPC have changed as mentioned above, it is vital for otolaryngologists to carefully inspect and palpate the tonsils both pre-and post-tonsillectomy and then routinely submit the specimen for examination to avoid missing a small lesion, even in adult cases thought to be benign.

The necessity of postoperative IMRT might be controversial since the pathological margin was negative. Considering adhesive lesions during tonsillectomy, the surgical margin was inadequate. Furthermore, the patient being 47 years of age was another reason for recommending postoperative IMRT. Moreover, since p16-positive tumors are likely to cause cervical lymph

Table 1. Patient characteristics.

Characteristics	Total (N = 290)	
	N	%
Age		
<40	227	78.3
≥ 40	63	21.7
Gender		
Male	144	49.7
Female	146	50.3
BMI		
<25	192	66.2
≥ 25	98	33.8
Smoking status		
Never	180	62.1
Smoker	110	37.9
Alcohol consumption		
Never or occasional	106	36.6
Drinker	184	63.4
Inflammation		
No	82	28.3
Yes	199	68.6
Abscess history	9	3.1
Tonsillar hypertrophy		
None	29	10
I	116	40
II	109	37.6
III	36	12.4
Reason for surgery		
IgA nephropathy* (including 4 purpura nephritis)	83	28.6
Palmoplantar pustulosis* (including 1 SAPHO syn.)	10	3.4
Psoriasis Vulgaris*	1	0.3
Nephrotic syn.*	7	2.4
Arthritis*	1	0.3
Chronic tonsillitis	167	57.6
Sleep apnea syn.	18	6.2
Hypertrophy	3	1

*Tonsillar focal diseases.

node metastasis, radiotherapy should be done in the affected upper cervical region as well.

Conclusion

To avoid delay in the diagnosis of unexpected cancer, the presence of a tumor should be considered in the preoperative examinations and during tonsillectomy even in the cases thought to be benign. It is

recommended that routine histological examination should be performed after tonsillectomy in patients with unfavorable clinical features.

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Informed consent statement

The written informed consent was obtained on June 23, 2020.

Disclosure statement

The authors declare that they have no conflicts of interest.

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