Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology

journal homepage: www.elsevier.com/locate/jomsmp

Case Report

A case of the pleomorphic adenoma of minor salivary gland that resulted in maxillary metastasis 20 years after primary tumor resection

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ARTICLE INFO

Article history:
Received 31 May 2016
Received in revised form 5 August 2016
Accepted 1 September 2016
Available online xxx

Keywords:
Metastasizing pleomorphic adenoma (MPA)
Benign tumor
Minor salivary gland

ABSTRACT

Metastasizing pleomorphic adenoma (MPA) is a rare neoplasm of the salivary glands, and the metastatic foci are histologically identical to the benign tumor. The minor salivary glands are rarely the origin of MPA. We describe the case of a 63-year-old woman with maxillary MPA occurring 20 years after primary resection for PA that originated in the minor salivary gland of the hard palate. The metastatic site was bilateral maxillary bone, and we performed tumor resection in combination with Le Fort I osteotomy. The metastatic deposits resembled benign PA of the primary lesion with no histological evidence of malignancy.

In addition to this case, we undertook a review of the literature about all identified MPA cases that the minor salivary gland origin reported in the English language up to 2015. The most frequent primary site was the palate (66.7%), and the most frequent metastatic site was the cervical lymph nodes (33.3%). The mean interval from primary tumor to metastasis was 8.9 years and all cases were treated with surgical resection for MPA, except for one. PA should be followed up with consideration of metastasis over the long term.

1. Introduction

Pleomorphic adenoma (PA) is the most common benign tumor in the salivary glands [1]. This tumor commonly occurs in the parotid gland, and is also found in minor salivary glands, particularly on the palate. Microscopy shows a characteristic combination of epithelial, myoepithelial and stromal components and the tumor is known as benign mixed tumor [2]. Thus, PA is a benign tumor, but it is considered to have metastatic potential and rarely may metastasize without demonstrating any morphological features of malignancy [3,4,1].

This disease was introduced as metastasizing PA (MPA) in 1942 [5], and was classified in 2005 according to the World Health Organization classification of tumors of the head and neck, and Armed Forces Institute of Pathology classification of tumors of the salivary glands [6]. To date, the most frequent site of the primary tumor for MPA is the major salivary glands [7–10]. However, there are few reports of MPA originating in the minor salivary glands [11].

In the present study, we report a case of MPA occurring in the hard palate, with multiple maxillary metastases 20 years later, and review the literature of MPA originating in the minor salivary glands.

2. Case report

A 63-year-old woman presented with occlusal pain of the left maxillary molar in December 2010. In 1990, the patient had been diagnosed with PA of the left hard palate by incisional biopsy and underwent surgical treatment (Fig. 1A). The size of the primary PA of the left hard palate was approximately 20 mm × 23 mm × 15 mm, and we took a margin of circumference 3 mm and resected every membrane. Histopathological examination of the specimen revealed the presence of a benign PA without

☆ AsianAOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

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http://dx.doi.org/10.1016/j.ajoms.2016.08.009

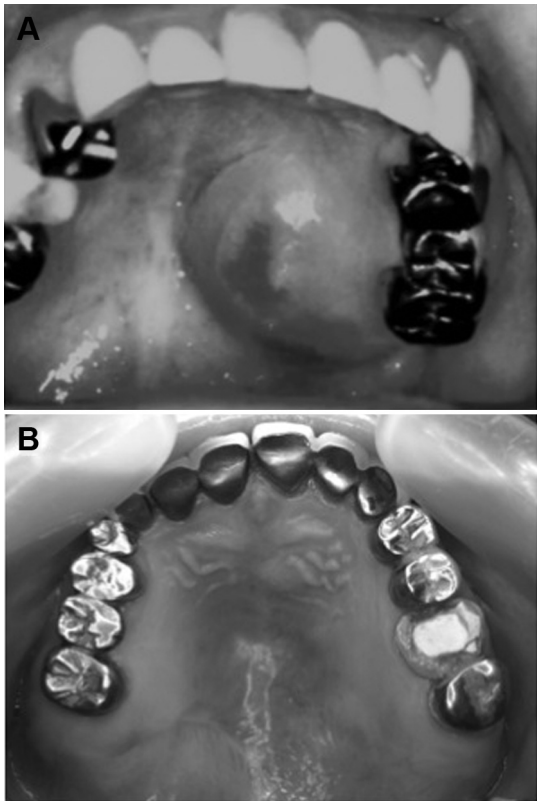

Fig. 1. (A) A hemispherical mass was present in the left side of hard palate at initial diagnosis. (B) The clinical examination at the time of 20 year after the initial resection.

evidence of any extracapsular growth. After the operation, she was lost to follow-up, but returned 20 years later because of right-sided occlusion pain and the discomfort in left maxilla.

2.1. Local findings and treatment

On physical examination, her facial configuration was asymmetrical and presented with diffuse swelling, with tenderness of a lesion of the lower right nostril and nasolabial fold. The maxillary alveolar mucosa showed bulging of the tender area that was covered with normal mucosa and presented with partial parchment crepitation. The hard palate did not show signs of tumor recurrence (Fig. 1B). Computed tomography (CT) showed two masses in the right maxilla near the front tooth and the left maxillary bone (Fig. 2A). The mass extended from the maxillary antrum to the outside of the processus pterygoideus on the left side, and the nasal cavity became stenotic as a result of internal extension of the masses on both sides. In coronal T1 weighted-spectral attenuated inversion recovery (T1W-SPAIR) scanning, magnetic resonance imaging (MRI) also showed two hyperintense, well-defined soft tissue masses in the left maxillary sinus and in the right premaxillary region (Fig. 2B). After intravenous administration of gadolinium, the masses were markedly enhanced because of rich vascularity.

18F-fluorodeoxyglucose (FDG) positron emission tomography (PET)–CT also revealed an abnormal accumulation in the area of the left maxillary sinus and right premaxillary region. Each maximum standardized uptake value (SUV_{max}) was 4.9 in the area of the left maxillary sinus and 5.4 in the right premaxillary region (Fig. 2C). No other organs that FDG accumulated abnormally were found in systemic.

Histopathological diagnosis of MPA was obtained through biopsy of the mass in the right premaxillary region including alveolar bone, and the other masses of the left maxillary bone were considered to be the same lesion. Tumor excision via maxillary half side resection on a modification of Le Fort I osteotomy was performed under general anesthesia in January 2011 (Fig. 3A and B). After carrying out down-fracture of the left maxillary bone with a tumor (Fig. 3C and D), the tumor (a) was resected from the upper surface. The other tumor (b) in the maxillary posterior region was resected after isolation from the mucous membrane of maxillary sinus. Furthermore, a tumor presenting in the left concha nasalis inferior (c) was resected with nasal mucosa. The alveolar tumor of the right maxilla (d) was resected after isolating it from the nasal cavity, and then we performed apicoectomy. Finally, we replaced the maxillary bone and fixed it in a mini-plate and wire splint (Fig. 3E and F).

2.2. Histopathological findings

Microscopically, pathology revealed that the primary tumor of palate was composed of mixed tubular and ductal structures with dense eosinophilic luminal exudates and cells forming short trabeculae and aggregates. The ducts were lined with an inner layer of cuboidal cells and an outer layer of myoepithelial cells (Fig. 4A). Based on these histopathological findings, the resection specimen had a diagnosis of PA. These findings closely resembled the features of the MPA that occurred 20 years later (Fig. 4B), and also malignant transformation in the intraosseous lesion was not confirmed. Therefore, the histopathological features were compatible with a diagnosis of benign MPA.

The tissues were also examined by immunohistochemical analysis (Fig. 4C–F). Both pathological specimen of the primary palatal lesion and the metastatic lesions of maxillary bone were shown as positive for pleomorphic adenoma gene (PLAG) 1 antibody (Fig. 4C and D). Also, Ki-67 labeling index was 0.63% in primary lesion (Fig. 4E) and 3% in the metastatic lesions (Fig. 4F).

3. Discussion

Metastatic disease is the clearest sign of malignancy in a tumor. MPA is a rare tumor that develops from its origin in the minor salivary glands. It is a histologically benign tumor that develops distant metastasis, and is distinguished from carcinoma in PA and true malignant mixed tumor. Including this study, nine cases of MPA of minor salivary gland origin have been reported since 1988 [12–19] (Table 1). Among these cases, there were three male and six female patients. The age range at initial presentation was 13–73 years (mean, 34.9 years; median, 35 years). The primary site was soft palate in four cases (44.4%), hard palate in two (22.2%), nasal septum in two (22.2%), and tongue in one (11.1%). To confirm the diagnosis, four cases (44.4%) underwent fine needle aspiration or incisional biopsy. The metastatic sites were cervical including submandibular lymph nodes in four cases, lung in three, maxillary bone in two, and vertebrae and paranasal sinuses in one case each. These sites were either involved alone or in combination with other anatomical sites. The interval between detection of the primary tumor and metastasis ranged from 0 to 20 years (mean, 8.9 years; median, 7 years). All cases of MPA were treated by surgical resection, including cervical neck dissection, except for one case in which treatment was rejected. Furthermore, one case received radiotherapy (74 Gy) in addition to surgical excision [16]. After treatment for MPA, five patients were alive without disease, one had died, and three had unknown prognosis.

Please cite this article in press as: Taketomi T, et al. A case of the pleomorphic adenoma of minor salivary gland that resulted in maxillary metastasis 20 years after primary tumor resection. J Oral Maxillofac Surg Med Pathol (2016), http://dx.doi.org/10.1016/j.ajoms.2016.08.009