Case Report

A case of ameloblastoma with extensive pulmonary metastasis survived for 14 years without treatment of the lung

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A R T I C L E   I N F O

Article history:
Received 17 April 2015
Received in revised form 29 June 2015
Accepted 3 September 2015
Available online 21 October 2015

Keywords:
Metastasizing ameloblastoma
Pulmonary metastasis
Clear cell
Mandible

A B S T R A C T

Although ameloblastoma is generally considered to be a benign tumor, local recurrences have often been noted. On the other hand, however, lung metastasis is quite rare. Here, we present a case of a patient who had ameloblastoma in the mandible with metastases in a lung and several recurrences. The patient was a 24-year-old man who was treated, but developed lung metastasis 1 year later. Once it had metastasized, recurrences occurred twice. Histologically, both the primary tumor and lung metastasizing tumor were benign. The patient died 27 years after the initial treatment and 14 years after detection of pulmonary metastasis. To our knowledge, this patient was the longest-survival case in Asia for such conditions.

1. Introduction

Ameloblastoma represents 11–13% of all odontogenic tumors [1], with 80–85% occurring in the mandible [2–5]. Ameloblastoma is generally considered to be a benign tumor of the odontogenic epithelium. However, recurrences have been noted for more than 10 years after the initial treatment [6]. Moreover, there is a type of ameloblastoma known as metastasizing ameloblastoma or ameloblastic carcinoma which metastasizes to the lung. The metastasizing ameloblastoma, however, is different from ameloblastic carcinoma. Metastasizing ameloblastoma causes distant metastasis despite it having the benign histological appearance. Ameloblastic carcinoma behaves more aggressively and demonstrates distinct cytologically malignant tumors [7]. However, lung metastasis is not common.

We present a case of metastasizing ameloblastoma of a patient with bilateral pulmonary metastases, who survived for 14 years after detection of metastasis without treatment for lung lesions.

2. Case report

In 1983, a 24-year-old man was referred to our hospital for a swelling of the right premolar region in his mandible. A panoramic radiograph showed a cystic radiolucency. Biopsy and histological examination revealed an ameloblastoma. The patient was admitted to our hospital and underwent a marginal resection of the right premolar region in the mandible under general anesthesia. There was no sign of invasion into the bone at the margin. The tumor was not attached to the surrounding bone and therefore easily removed. Then we finally performed curettage of the surrounding bone with a burr. The pathological findings included nests which had formed follicular variant and increased in the connective tissue; the nests consisted of stellate reticulum and spindle cells in the central region, and palisaded cuboidal or columnar cells in the peripheral region. In the nests, clear cells without atypia were occasionally seen (Fig. 1).

After the surgery, there was no event for more than 10 years. In January 1996, the patient had a medical check-up and an abnormality was detected in his chest radiograph (Fig. 2). We referred him to the department of internal medicine in our hospital to assess the lesion in his lung. A CT showed some small nodules in both lungs; other organs had no abnormality. As we suspected metastasis of the mandibular ameloblastoma, the patient underwent an open biopsy of the pulmonary tumor. The pathological findings of the biopsy included tumor cells forming small nests in the pulmonary alveoli tumor cells forming small nests in the pulmonary alveoli. The nests consisted of spindle cells in the central region and cuboidal cells in the peripheral region (Fig. 3).
Those were compatible with the specimen that we obtained from his mandible in 1983. The lung specimen showed no malignant feature. As we considered that chemotherapy was not effective in the lung, the patient was followed up periodically. The doctor in the internal medicine department prescribed him a traditional Chinese medicine but nothing else. In July 2003, the patient visited our hospital with a chief complaint of persistent gingival swelling of the right molar region in the mandible for several months. Examination revealed an elastic hard mass, and radiography showed a radiolucent image at the root apex and surrounding bone of the right molar (Fig. 4). Biopsy was performed and histological examination revealed recurrent ameloblastoma. Under general anesthesia, the operation which included extraction of the molar and marginal resection of the mandible was performed. No malignancy was found pathologically in the resected specimen. However, in the specimen, clear cells consisting of ovoid, clear cytoplasm and pyknotic nuclei were observed in the nests at various degrees (Figs. 5 and 6). From 2004 to 2006, the healing course was uneventful. Periodic CT and radiography of the lung at 3-month intervals demonstrated stability of the nodules. There was no sign of growing pulmonary foci. The condition of the oral wound was satisfactory. The patient received a new partial denture. And we checked his oral hygiene and took periodic radiographs of his mandible.

In 2007, although the oral wound showed no signs of recurrence, the lung nodules had increased in size and spread out. By December 2008, the size of each pulmonary tumor increased even more. By August 2009, gingival swelling of the right mandible was detected. It was an elastic hard mass and radiograph showed radiolucent image of the anterior tooth apex (Fig. 7). Pathologic examination of a biopsy sample of the molar gingiva and anterior tooth apex revealed a recurrence of ameloblastoma. The patient underwent a partial resection of the right molar region of the mandible, including extraction of the anterior incisors. In May 2010, his oral condition was stable, with no recurrence. However, the patient felt dyspnea and returned to our hospital. Examination of a chest radiograph by the physician in charge revealed bilateral pleural effusion, which was drained. In June 2010, the patient’s oral intake gradually worsened and his body weight decreased noticeably (Fig. 8). Thereafter, fluid drainage from his lungs was less efficacious. The pleural effusion gradually increased and compressed his heart, and the lung and heart function worsened. In July 2010, the patient died, 27 years after the initial treatment and 14 years after the diagnosis of pulmonary metastasis.

3. Discussion

According to the 2005 World Health Organization classification of odontogenic carcinomas among malignant tumors derived from odontogenic tissues, ameloblastomas are divided into metastasizing ameloblastoma, ameloblastic carcinoma-primary type, and ameloblastic carcinoma-secondary type (intraosseous, peripheral) [8]. Metastasizing ameloblastoma is defined as ameloblastoma that metastasizes despite benign histological appearance. Ameloblastic
carcinoma is defined as a rare primary odontogenic malignancy with histological features of ameloblastoma and cytological atypia. Ameloblastoma has several histologic types: follicular, plexiform, acanthomatous, granular cell, desmoplastic, stellate, and basal cell. The commonest one is the follicular type; however, with regard to metastatic ameloblastoma, the plexiform type is predominant [9–11]. Even so, the cytological and histological patterns reported do not differ significantly between the metastatic lesion and the primary tumor [9–13]. Considering that it could be difficult to predict metastasis from histological patterns, careful periodic observation is crucial for detection of metastasis.

Previous literature reported the duration between the time of the initial diagnosis and the detection of primary metastasis as well as survival after metastasis. According to Ueda’s review [14], the median survival period after treatment of primary tumor ranged from 11 to 14 years, with average survival after detection of metastasis 3 years and 96 days, and median survival after development of symptoms of metastatic disease ranged from 3 months to 5 years [2,3,9,11,12,14,15].

Van Dam et al. [16] reviewed literature published from around the world between 1923 and 2009 and identified 101 reports of suspected metastasizing ameloblastoma, including 27 cases which were classified as metastasizing ameloblastoma based on convincing photomicrographic documentation of “well-differentiated” ameloblastomas in the metastatic site and similar innocent/typical histology (presumed or documented) of the primary maxillary or mandibular tumor. The average duration between the time of diagnosis of the primary tumor and diagnosis of metastasis was 18 years (range: 3–45 years). The average survival time after diagnosis of metastases in 12 of these patients was approximately 3 years. The remaining patients (13 of 25, 2 patients unknown) were still alive at the time when their reports were made and had survived for 10 years on average since the diagnosis of metastasis. Three patients lived for more than 20 years after diagnosis of metastasis [17–19]. Dissanayake et al. [20] reviewed 66 cases of metastasizing (malignant) ameloblastoma in the previous reports made between 1923 and 2009. They reported that the time between the primary tumor and the first metastasis ranged from 2 months to 42 years, with the median of 14 years and the mean of 14.33 years; the survival after development of metastasis ranged from 0 to 37 years with the mean of 6.7 years and 5-year survival of 44%. To our knowledge, Hasim et al. [19] reported the longest survival period. The patient was treated at the age of 54, and had recurrence several times. At the age of 57 years, she had a lung metastasis. After 37 years since metastasis, she was still alive (in 2007).

In addition to the metastasizing ameloblastoma cases reported between 2010 and 2014 [21–30], we included 10 more cases to review.

A total of 38 cases including our case were analyzed with regard to survival after diagnosis of metastasis. As a result, the longest survival was 37 years, and the second one was 25 years [31]. However, in the case of the second-longest survival, it was reported that the patient was Caucasian and received an operation in the pulmonary metastasizing site [31]. To our knowledge, as for the report of pulmonary metastasis without treatment of the lung, our case led to the second-longest survival among all reported cases and to the longest one for Asians.

Some authors reported that treating the primary tumor with curettage was associated with high local recurrence rate and gave the poorest result, whereas resection with margins of unaffected tissue gave the best result [9,12,14]. Previous case reports clearly indicate that inadequate or inappropriate treatment of the primary lesion plays a significant role in the recurrence of ameloblastoma, and that multiple recurrences place patients at increased risk for metastatic disease. In the case we presented, the region of the tumor invasion was limited only in the alveolar bone and its covered soft tissue. We thus concluded that marginal resection was appropriate, and regional resection of the mandible would be overtreatment.
Some authors reported chemotherapy to be effective [5,36]. However, others report that chemotherapy has only a palliative effect, and induces only a partial response. Ramadas et al. [5] used a combination of cisplatin, adriamycin and cyclophosphamide with good symptomatic response. Elisson et al. [36] reported a partial tumor response with a combination of vinblastine sulfate, bleomycin and cisplatin leading to a 50% reduction in tumor size; however, metastasis eventually recurred. Chemotherapy seems to be useful for inoperative lesions, giving relief for the pain rather than the primary treatment for the metastasis site.

Radiation therapy gives uncertain results and has a high recurrence rate; however, some authors have advocated its use in specific situations [3,4,9,36]. Miyamoto et al. [37] used radiation to good effect. However, Laughlin [9] considered radiotherapy to be no more effective than chemotherapy for inoperable metastatic lesions. The most common treatment method for pulmonary metastasis is a surgical wedge resection or lobectomy. Although an earlier biopsy had indicated that the pulmonary lesion was not malignant, unfortunately, when we noticed the pulmonary metastasis in this patient, the lesion was already spreading in both lungs, and was inoperable. However, even a benign metastasizing tumor is a foreign body in the lung that can gradually reduce respiratory function. To prevent metastasis, close observation and medical follow-up are indispensable after the initial treatment.

**Funding**

None.

**Conflict of interest**

None.

**Ethical approval**

Not required.

**References**


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