CASE REPORT

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Early Recurrence Adenoid Cystic Carcinoma of Paranasal Sinus: A Case Report

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ABSTRACT

Introduction: Adenoid cystic carcinoma (ACC) of the head and neck is a rare salivary gland tumor. It grows and spreads in silence until causing a symptom. Surgery is still the main treatment of choice although complete resection is hard to achieve most of the time.

Case Presentation: This report presents an adult female with ACC of the left hard palate and left maxillary sinus, this patient also had slight lymph nodes enlargement. She underwent sub-total maxillectomy followed by locoregional radiotherapy. The tumor spreads out to vertebral bones within one year and keeps on progressing despite bone radiation. It recurred locally and appeared in the neck lymph node 2 months after bone metastasis. Lung metastasis happened 3 months later and soon she passed away. Mortality happened in less than two years after initial treatment.

Conclusions: High tumor grade, advanced T stage, lymph node involvement, perineural invasion, and paranasal sinus location clearly define poor prognostic factors. In this case, adjuvant radiotherapy for poor prognostic factors ACC doesn't give any benefit in locoregional control or overall survival.

INTRODUCTION

Adenoid cystic carcinoma (ACC) is a tumor that originates from the salivary gland. Commonly known as a slow-growing tumor and is treated with less caution. Accounting for only 1% of all head and neck cancers, ACC is an uncommon tumor of the head and neck. The most common sites of occurrence are salivary glands, palate, and paranasal sinuses [1].

ACC is a persistent growing tumor that can invade important structures and perineural invasion is common. Surgical resection is still the primary treatment for ACC, even though complete resection is sometimes difficult to achieve. Positive margins and the infiltrative nature of ACC make way for radiotherapy. Some studies found radiotherapy useful to improve local control but not overall survival. Other literature has shown that adjuvant radiotherapy did not reduce local recurrence [2].

Late diagnosis generally happens because the tumor grows and spreads before causing any symptoms, this is characterized by the unpredictable and insidious nature of this disease. Metastatic ACC is the leading cause of mortality, and the most common site is the lungs [2].

This case report is intended to better understand the prognostic factors of ACC from the literature. It also tries to confirm whether adjuvant radiotherapy is beneficial for disease outcomes in this kind of case. By getting knowledge and experience from this case we could propose a better treatment option for similar patients in the future.

CASE PRESENTATION

A thirty-one-year-old woman came with a blocked left nose, nosebleed, pain in her left face, and palpable mass in her upper oral cavity. A computed tomography (CT) scan revealed a solid lesion with no clear border, size 3.6 by 3.2 cm, filling left nasal cavity, left maxillary sinus, left anterior space of nasopharynx, and infiltrated left hard palate. Jugular lymph nodes are slightly enlarged (0.3–0.5 cm) on both sides. Thorax x-ray, bone scan, and abdominal ultrasound showed no metastasis. This condition is staged as T3N2M0 according to the

American Joint Committee on Cancer (AJCC) staging system 8th edition 2017.

She underwent left sub-total maxillectomy surgery, removing the lower part of the maxilla, some of the left nasal concha, the hard palate, and some teeth. No neck node dissection. Continued with locoregional radiation. The tumor bed and surrounding area (red) suspected for micro infiltration received 70 Gy (high-risk area), regional pharyngeal nodes, and neck nodes received 60 Gy (intermediate-risk area) (**Figure 1**). Histopathology examination reported that the tumor already infiltrates bony structures but no lymph vascular space invasion. The surgical margin status is free of tumor. Perineural invasion was found. Cellular morphology consists mostly of solid patterns.

Eight months after radiation we evaluated the patient. The follow up suspended for 6 months because of the COVID-19 outbreak and government limitations on public movement. There was no residual local mass and no enlargement in peri jugular lymph nodes from paranasal magnetic resonance imaging (MRI) (**Figure 2**). However, the patient complained of lower back pain. From the bone scan, we found metastasis with corpus compression in 4th lumbar vertebrae.

Evaluation and follow-up were halted for another 4 months for COVID-19 reasons. That lesion keeps deteriorating, it causes pathologic fracture with instability signs. Spinal stabilization surgery was done with palliative intent. Nevertheless, we also found multiple metastatic lesions in the vertebral body and pelvic bones. Radiotherapy was given to those areas to reduce pain.

Two months after stabilization surgery, paranasal MRI showed a local and regional recurrence (**Figure 3**). There was a 2.6 cm mass in the posterior wall left maxillary sinus and a 0.7 cm mass in the left submandibular lymph node. Tumor biopsy describes solid hyperplastic cells with some cribriform pattern.

The patient's condition was getting worse every month. Bone metastatic spreading to almost all of the vertebral body even though palliative bone irradiation was given. Patient conditions declined rapidly when lung metastasis was found 3 months later. The patient was hospitalized and passed away 2 weeks after confirmed lung metastasis

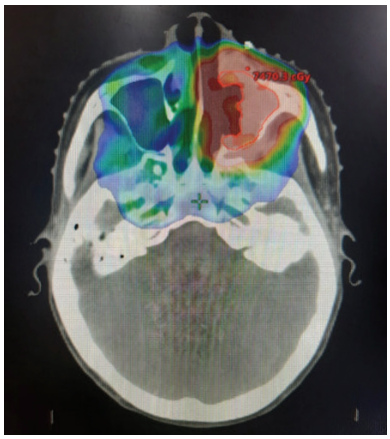

Figure 1. Tumor bed and radiation volume after surgery. High-dose volume (red), intermediate-dose volume (blue).

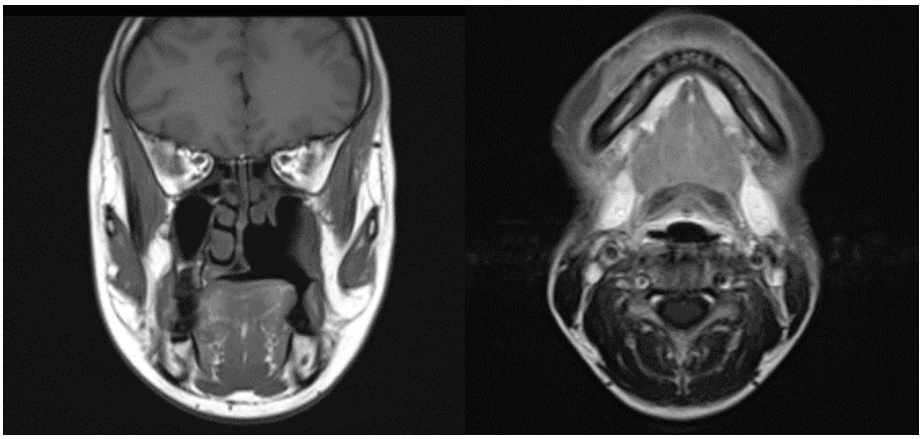

Figure 2. MRI Evaluation after radiation. No residual local mass and no enlargement in peri jugular lymph nodes. T1 weighted image of maxillary sinus (left), T2 weighted image of cervical lymph nodes (right).

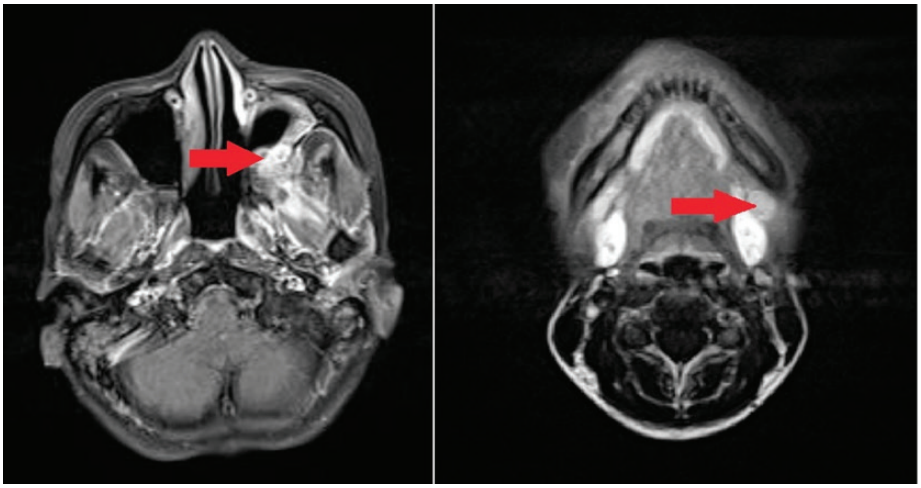

Figure 3. Recurrent mass in the posterior wall left maxillary sinus T2 weighted image (left). Left submandibular lymph node recurrent T1 weighted image (right).

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DISCUSSION

In general, ACC has slow growth and long clinical course. It also has numerous local recurrences and late distant metastasis. Five years of overall survival (OS) is diverse between 64–92 %. After 15 years, overall survival drops about 24.5–37% and keeps dropping until 30 years [1,2,3]. Local recurrence is also varied, about 12–40% [2]. ACC indeed has certain distant failures; it happens independently out of local treatment. Disease-free survival (DFS) is about 53–63.2% at five years and 23% at ten years [4,5]. But in this case, ACC behaves more aggressively, resembling a high-grade tumor. Bone metastases happen within a year, lung metastasis, and local recurrence less than 2 years, despite locoregional adjuvant therapy [1].

There are some factors that are worth reviewing again. Traditionally, after diagnosis and staging, the standard of care for ACC is radical surgery ensuring a negative pathological margin. There is no treatment after complete surgical resection with a clear margin. Unless sub-total resection or positive margin, radiotherapy is added to gross residual tumor, tumor bed, and high-risk area suspected for microscopic infiltration [1].

ACC has a strong tendency to infiltrate adjacent structures, especially neurons. This makes free margins while preserving organ function hard to achieve. Adjuvant radiotherapy could improve locoregional control and disease-free survival, although it's not proven to improve overall survival [5]. Local recurrence is generally low, especially if radiotherapy is added after surgery. But in this case, local recurrence and death occurred in less than 2 years.

Heavy ion radiotherapy has been used as a treatment for local recurrence of ACC. It shows acceptable toxicity and promising short-term local control (19 months), suitable for palliative intent [6]. However, reports at follow-up showed that even though high-dose re-irradiation was given, recurrence mostly happens within high high-dose irradiated field [6].

Some studies describe adjuvant radiotherapy as not having any positive effect [3]. This contradicts other studies, but similar to this case, the tumor recurs in less than 2 years, reflecting the ineffectiveness of radiotherapy. A study also describes that radiation field and dose do not affect outcome [7]. An old study from Memorial Sloan-Kettering Cancer Center provided data on radiotherapy as a definitive treatment for ACC. Radiotherapy was done in unresectable patients. From 49 patients, tumor reduction was seen in 47 patients and 93.5 % of them relapsed locally within 18 months to 5 years [8].

This patient experienced vertebral metastasis 1 year after initial treatment. A study by Jang et al. [2] describes that vertebral metastasis is associated with poor survival. Regarding recurrences, salvage (repetitive) surgery either locally or distant metastasectomy proves to increase disease-specific survival [9]. In this patient, it was impossible to remove the metastatic sites in vertebral bodies. Surgery for local recurrence also seems unworthy since the patient's declining condition and spreading of disease.

For systemic therapies in general, there is still no evidence of improving overall survival [10]. Chemotherapy and targeted therapy may improve treatment efficacy in locally advanced and metastatic ACC [11]. It can be used as adjuvant or concurrent with radiotherapy as locoregional control or as palliative treatment. Literature and research regarding systemic or targeted therapy are rare and the results varied. In this case, the patient does not get any chemo or targeted therapy.

The morphology of ACC is categorized into 3 patterns: cribriform, tubular, and solid. The grading system is classified into 3 grades, which are arranged by morphological pattern: grade I consists of tubular and cribriform pattern without solid components, grade II formed predominantly cribriform purely or at least 30% of solid components, and grade III with mostly solid component [12]. Solid form and higher tumor grade relate to poor prognosis [7,9]. In this case, tumor morphology is mostly solid or classified as high-grade. This perfectly matches unsatisfactory clinical results. The biopsy of recurrent local tumor also shows the same. There was a very rare case of dedifferentiation where tumor morphology could change from low to high grade at recurrence, which is very malignant [12,13].

Margin status, perineural invasion, tumor grade, stage, and lymph node metastasis are the most common prognostic factors for local control [3,12]. Stages 3 and 4, especially with paranasal sinus or sub-maxillary gland primaries predict worse prognosis [7]. Sinus paranasal tumor and perineural invasion are more likely presented with higher stage [7]. According to Spiro et al. [14], from 175 ACC patients treated mainly by surgery, the clinical stage at diagnosis predicts survival was more reliable than tumor grade alone.

In this case, the presence of perineural invasion, high-grade morphology, T3 tumor stage, N2 lymph node metastasis, and paranasal sinus origin related to poor outcome. Free margin status is the only favorable prognostic factor in this patient, but it may be inaccurate.

CONCLUSIONS

The course of head and neck ACC after standard treatment could be predicted by most of the existing prognostic factors. Recurrence happens independently out of local treatment. It means distant metastasis will happen for sure despite good local treatment. Vertebral metastasis might predict lower survival. Radiotherapy should be useful as locoregional control in good prognosis patients, either adjuvant or definitive. Also,

effective in reducing tumor size and relieving symptoms in palliative cases. Radiotherapy will not increase overall survival in any scenario. Radiotherapy might be ineffective for poor prognostic patients, but excluding radiotherapy from standard treatment needs further study with a bigger sample and better classification in determining which prognostic factors have radio-resistant properties. Salvage surgery might be an option in recurrence cases.

DECLARATIONS

Competing of Interest

The authors declare no competing interest in this study.

Acknowledgment

Not applicable

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