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CASE REPORT

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Complete clinical response to chemoradiation in adenoid cystic carcinoma of the base of tongue: Case report of a rare tumor in a rare location

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Key Clinical Message

Adenoid cystic carcinoma (ACC) is an uncommon malignancy of head and neck. Although the cornerstone of treatment is surgery, concurrent chemoradiotherapy (CRT) might be used as an effective treatment for unresectable tumors. Herein we report a case of massive ACC of base of tongue with durable complete response to definitive CRT.

Abstract

Adenoid cystic carcinoma (ACC) is a rare tumor accounting for 1% of all head and neck cancers. The best treatment option is complete surgical resection with or without adjuvant radiotherapy. When surgical resection is not feasible, definitive radiotherapy with or without concurrent chemotherapy can be considered. Herein we report a non-smoker 72-year-old woman presented with throat discomfort and sensation of a lump. Evaluation revealed an unresectable adenoid cystic carcinoma of the base of tongue in whom complete clinical response was achieved after definitive concurrent chemoradiation. Although the cornerstone of treatment is complete surgical resection, this case report indicates that concurrent chemoradiotherapy might result in complete clinical response and could be used as a definitive treatment in selected ACC tumors.

KEYWORDS

adenoid cystic carcinoma, clinical response, radiotherapy, tongue cancer

1 | INTRODUCTION

Adenoid cystic carcinoma (ACC) is a rare tumor accounting for about 1% of all head and neck cancers.[1] The most common sites of ACC are major and minor salivary glands, but it can also occur in other secretory gland sites such as trachea, oropharynx, nasopharynx, breast, lacrimal gland, external ear, skin, and lower female genital tract. It typically presents in the 5th decade of life with a slight predilection towards females.[2,3] The clinical course of ACC is generally indolent. It has a tendency to spread along the cranial nerves but infrequently involves

lymph nodes. Regardless of the primary tumor site, the best treatment option is complete surgical resection with or without adjuvant radiotherapy.[4,5] Most studies indicate a survival benefit for adjuvant radiotherapy especially in locally advanced cases.[6–8] However, it is noteworthy to mention that two studies utilizing national population-based data have shown that postoperative radiotherapy does not significantly impact survival outcomes.[3–9] In cases where resection is not feasible, definitive radiotherapy can be considered. Additionally, the response of this tumor to chemotherapy is limited, and the primary role of chemotherapy is restricted to palliation in cases of recurrence or metastasis.[10] Limited experience exists with the combined use of chemotherapy and radiation as the primary treatment for ACC. In this report, we introduced a rare case of base of the tongue ACC which had a complete clinical response to definitive chemo-radiation.

2 | CASE HISTORY/EXAMINATION

A 72-year-old, non-smoker woman, was consulted for throat discomfort and sensation of a lump. The Patient's symptoms started 1 year ago but intensified over the last 2 months. She also mentioned intermittent mild dysphagia and a weight loss of approximately 5 kg in the past 2–3 months. There was no complaint of tingling, numbness, or any symptoms suggesting neural invasion. In the clinical examination, no facial asymmetry was noted. In spite of the strong gag reflex, limiting the intraoral examination, a bulky non-ulcerated mass at the base of the tongue could be observed. No cervical lymphadenopathy was palpable. The patient was not cachectic and had a good performance status.

3 | METHODS (DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS, AND TREATMENT)

Neck MRI revealed a large lesion measuring 60 × 58 × 35 mm located in the base of the tongue causing relative narrowing. The mentioned mass involved central part of the tongue and sublingual space and showed low T1 and high T2/STIR signal in MRI (Figure 1). No lymphadenopathy was reported. Laryngeal video stroboscopic examination reported a large cystic mass on the right side of the base of the tongue and several small cystic masses on the left side of the base of the tongue that extended to the anterior region of the epiglottis. Functional analysis was normal only lateral compression of the larynx during phonation was observed. Biopsy was taken from the base of the tongue and findings were consistent with adenoid cystic carcinoma (Figure 2). Thoracic CT scan was conducted to rule out lung metastasis. Subsequently, the patient was referred to a head and neck surgeon, but the mass proved to be unresectable due to its wide extension. The multi-disciplinary team decided to candidate the patient for definitive concurrent chemoradiotherapy.

Radiotherapy was performed with a 3D conformal technique to a total dose of 70 Gy in 35 fractions. High-risk clinical target volume (HR-CTV) included gross tumor volume (GTV) + 1 cm margin while considering anatomic barriers. A 3 mm margin was added for PTV. Elective nodal

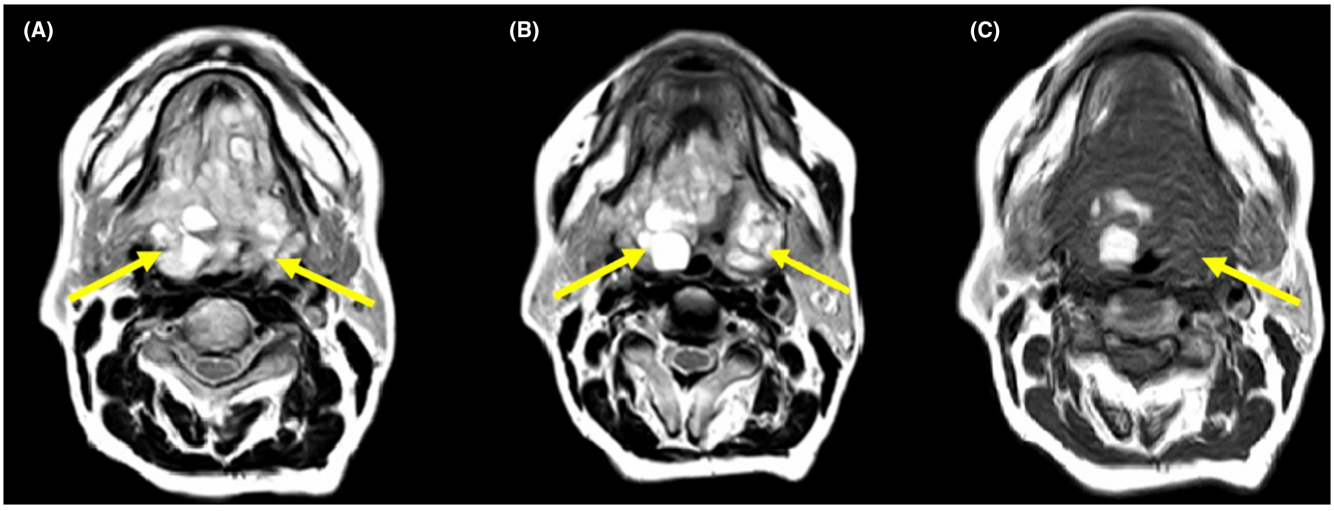

FIGURE 1 Axial images of pre-treatment head and neck MRI. (A and B) T1-weighted sequence with gadolinium contrast showing a large and multilobulated lesion in the base of the tongue involving central part of the tongue and sublingual space (yellow arrow). (C) T2-weighted sequence showing large and loculated mass (yellow arrow).

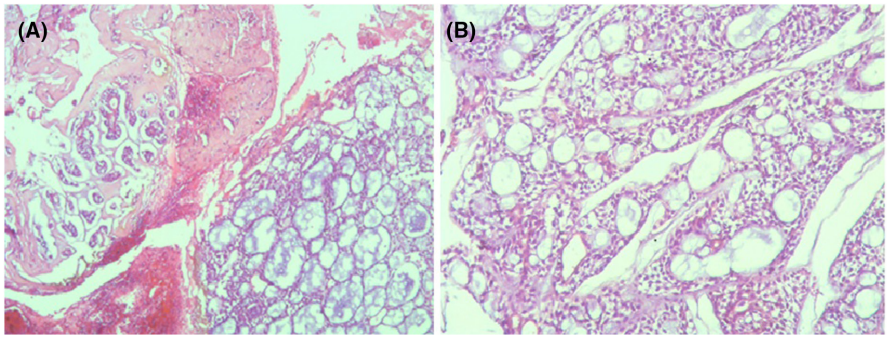

FIGURE 2 (A) Cribriform growth pattern showing several distinct pseudocysts surrounded by basaloid cells with basophilic centrally located nuclei (hematoxylin–eosin, original magnification 200×). (B) High-power view showing the eosinophilic basement membrane-like material in pseudocysts. Multiple true glands lined by cuboidal epithelium are obvious in the center (hematoxylin–eosin, original magnification 400×).

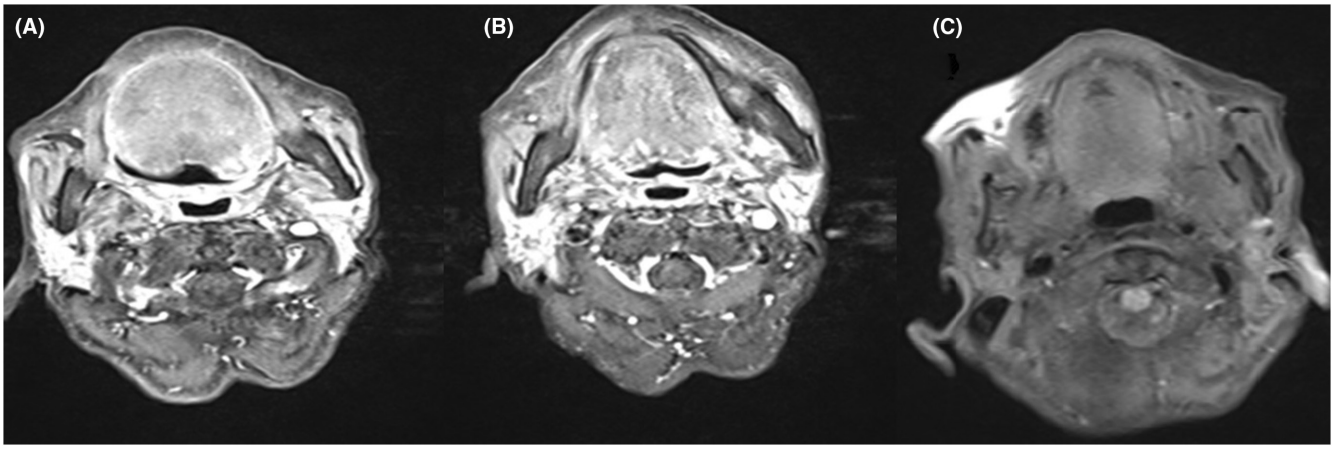

FIGURE 3 Post-treatment MRI (19 months after completion of chemoradiotherapy) showing dramatic response to treatment. (A and B) T1-weighted sequence with gadolinium contrast. (C) T2-weighted sequence showing complete clinical response.

irradiation was done to a total dose of 46 Gy. Despite the historically limited response of adenoid cystic carcinoma (ACC) to chemotherapy, a weekly regimen of cisplatin at 35 mg/m2 was initiated concurrently with radiotherapy as a radiosensitizer.

4 | CONCLUSION AND RESULTS (OUTCOME AND FOLLOW-UP)

At the end of the treatment, patients' signs and symptoms were improved. A subsequent MRI conducted 1 month later revealed a significant decrease in tumor volume. Additionally, a Video Laryngeal Stroboscopy which was performed 8 weeks after completion of treatment also confirmed a remarkable reduction in tumor volume, indicating a favorable response to the treatment. The patient was followed up with an MRI every 3 months. In the latest MRI, performed 19 months after the completion of treatment, a sustained and complete clinical response was still evident (Figure 3). further, follow-up will be necessary to rule out any potential late recurrence.

5 | DISCUSSION

Adenoid cystic carcinoma (ACC) typically poses a considerable challenge in diagnosis and treatment due to the uncommon nature of the lesion. While most salivary gland tumors are found in the major salivary glands, a small fraction (approximately 10%–20%) develop within the minor salivary glands located predominantly in the oral cavity.[11] ACC is the most frequent malignancy of minor and sublingual salivary glands.[12,13] The palate is the most common site for ACC of minor salivary glands, and only 8.8% occurs in the base of the tongue and 2.9% in the anterior two-thirds of the tongue.[14] These tumors often present with painless swelling. Tumors gradually progress and due to the ambiguity of symptoms, are usually diagnosed in advanced stage.

Histologically, ACC is divided into three histological subtypes based on the growth pattern: cribriform, tubular, and solid. These subtypes may occur either separately or together within the same tumor. The solid subtype is the most aggressive, while the tubular pattern (well differentiated) has been established to have the best prognosis.

The tumor has been graded according to histopathologic morphology criteria as follows: tubular or cribriform (grade I), less than 30% solid (grade II), or more than 30% solid pattern (grade III).[15,16] ACC is characterized by slow evolution but it is locally aggressive and has a high tendency for neural invasion. Regional metastases are rare, but late distant metastases occur more frequently. However long-term survival is expected.[14,17] Due to the rarity of this pathology, prognostic factors cannot be precisely determined, but it seems that advanced stage, solid component, peri or intra neural invasion, involvement of neck lymph nodes, and positive surgical margin might be associated with a poor prognosis.[18] Especially perineural invasion (PNI) is considered a poor prognostic factor as it is sometimes believed to be the fourth pathway of metastasis after hematogenous spread, lymphatic spread, and direct invasion of the adjacent organs by the tumor.[19]

Considering the slow growth and indolent course of ACC, it is assumed that these tumors are relatively radio resistant. Therefore, Surgery was developed as the mainstay of treatment for almost all head and neck ACC patients. Surgery is usually followed by adjuvant radiotherapy especially in case of close or positive surgical margins, residual disease, advanced stage, and PNI to yield favorable locoregional tumor control and improve survival.[4] However, in most cases, for the resection of tumors, extensive surgeries are needed, leading to significant morbidity in swallowing, speech, and quality of life for the patients. Alsubaie et al.[19] reported a literature review on nasopharyngeal ACC, in which the majority of patients were treated with definitive radiotherapy with or without chemotherapy to avoid the morbidity of surgery. Another case report by Rai et al. was related to a 78-year-old man with ACC of the base of his tongue who declined any surgical intervention. Instead, the patient underwent definitive concurrent chemoradiation, resulting in a significant reduction in signs and symptoms.[20] In another report by Wu and Xu[21] a 49-year-old woman with unresectable ACC of trachea was treated successfully with radiotherapy alone and had no recurrence after 5 years. In our case report, the patient was deemed suitable for definitive chemoradiation, considering the extension of the lesion at the base of tongue and potential surgical morbidities. Although definitive radiotherapy with/without concurrent chemotherapy has not been extensively studied as a primary treatment, but it represents an alternative option for patients with locally advanced or unresectable disease. This approach may offer sustained locoregional tumor control, as demonstrated in studies by Samant et al. and Mendenhal et al.[22,23]

As previously mentioned, the risk of nodal occult metastases in ACC is low, occurring in only 6%–10% of the cases. One possible explanation for this rarity is that the two primary sites for ACC, the parotid gland and the palate/maxilla, have a low tendency to metastasize to the lymph nodes. A retrospective study conducted by Kim et al.[24] involving 616 patients with ACC in the head and neck area, revealed that lesions located at the base of the tongue, mobile tongue, and floor of the mouth had the highest rates of cervical lymph node metastasis (19.2%, 17.6%, and 15.3%, respectively). A report by Salgado et al.[25] recommended electively treating lymph nodes especially when the primary tumor is located in sites with rich lymphatic capillaries, such as the base of tongue and nasopharynx, so we electively treated bilateral cervical lymphatic levels, up to total dose of 46 Gy.

It is crucial to emphasize the importance of long-term follow-up for patients with ACC due to the potential for late tumor recurrence. Annual lung CT scan might be considered to rule out pulmonary metastasis as the most common site of distant recurrence.

6 | CONCLUSION

ACC is a malignant tumor that is rarely seen in the base of tongue. It has slow growth and is usually diagnosed in advanced stage. currently, the preferred approach for these tumors is surgical resection with or without adjuvant radiotherapy. Definitive radiotherapy/chemo-radiotherapy has not been explored as a primary treatment. However, in this report, we treated the patient with concurrent chemoradiation which resulted in durable complete clinical response until the last follow-up 19 months after treatment. Although further follow up will be necessary to rule out any potential late recurrence, by reporting this case, we aimed to emphasize the ability of chemoradiotherapy as a definite treatment modality in eradicating ACC tumors which leads to preventing surgery and its associated morbidity.

AUTHOR CONTRIBUTIONS

Reyhaneh Bayani: Conceptualization; data curation; project administration; writing – original draft. **Elyas Hasanzadeh:** Data curation. **Etrat Javadirad:** Data curation; investigation. **Ali Reza Azarpeikan:** Writing – review and editing. **Mohammad Babaei:** Data curation; supervision; writing – review and editing. **Nima Mousavi Darzikolaee:** Supervision; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors whose names are listed above declare that there is no conflict of interest regarding the publication of this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONSENT

A written informed consent was obtained from the patient for the publication of this report and accompanying images.

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