CASE REPORT

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Metastatic Adenoid Cystic Carcinoma: Case Report

Baş Boyun Metastatik Adenoid Kistik Karsinomu Olgu Sunumu

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We regret to inform you that Ahmet YOLCU MD, has passed away.

ABSTRACT

Among head and neck cancers, adenoid cystic carcinoma (ACC) has a separate place compared to other histological types. Our case report is about the follow-up of a patient with ACC originating from the left parotid gland, who applied to our clinic for about 10 years, after different treatments were applied in different centers.

Keywords: Adenoid cystic carcinoma, metastatic, radiation oncology, oncologic surgery, chemotherapy, radiotherapy

ÖZ

Baş boyun kanserleri içinde adenoid kistik karsinom (AKK) diğer histolojik tiplere göre ayrı bir yere sahiptir. Bizim olgu sunumumuz yaklaşık 10 yıldır farklı merkezlerde farklı tedaviler uygulanmış, ardından kliniğimize başvuran sol parotis bezinden kaynaklanan bir AKK hastasının takibi hakkındadır.

Anahtar Kelimeler: Adenoid kistik karsinom, metastatik, radyasyon onkolojisi, onkolojik cerrahi, kemoterapi, radyoterapi

INTRODUCTION

Approximately 4% of head and neck cancers originate from the salivary gland. Adenoid cystic carcinoma (ACC) is a rare malignancy of the glands, accounting for approximately 1% of head and neck cancers and 10% of salivary gland cancers[1]. It is more common in the submandibular gland, minor salivary glands and mucinous glands in the oral cavity and oropharynx, but less common in the parotid gland. It can also occur in glands in other tissues where mucinous glands are present, such as the tracheobronchial tree, esophagus, breast, lungs, prostate, cervix uteri, lacrimal, Bartholin's glands and skin[2]. Salivary gland malignancies are pathologically heterogeneous tumor groups. According to the World Health Organization 2017 classifications, 32 subgroups characterized by morphological and genetic features as well as specific clinical behaviors have been classified[3]. Among salivary gland cancers, ACC has a distinct place compared to other histologic types due to its different clinical course including perineural spread, progression rate and late systemic metastasis. In our case report, we present the treatment and follow-up of a patient with ACC arising from the left parotid gland, who was treated in different centers and then admitted to our clinic.

CASE REPORT

A 49-year-old female patient was admitted to our outpatient clinic in April 2014 after recurrent ACC operation in the left parotid lobe.

The patient underwent mass excision and superficial parotidectomy operation in February 2013 due to a mass in the inferior left auricle and total parotidectomy + left radical neck dissection in March 2014 due to recurrence. The adjuvant radiotherapy schedule of the patient was performed in our

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clinic between May and June 2014 with field-in-field (FIF) technique using 6 MV photon energy in 33 fractions of 2 Gy/day with a total dose of 66 Gy (Figure 1).

Carboplatin (AUC 5.5) and paclitaxel (175 mg/m^2) were administered six times as three-hour infusions every three weeks by the Medical Oncology clinic.

Metastasis was detected in the 3rd lumbar vertebra approximately 4 years later. The patient's palliative radiotherapy program was performed in June 2018 in our clinic using the FIF technique for the lumbar 1-4 vertebrae using 6 MV photon energy in 10 fractions of 3 Gy/day, with a total dose of 30 Gy. As a precaution for medication-related osteonecrosis of the jaw, the patient was started on bisphosphonate treatment after oral and dental health examination. The local treatments applied to the patient are schematized in Figure 1.

Approximately 3 months later, lung metastasis was detected, etoposide treatment was started at an external center and pulmonary metastasectomy was performed in October 2019. In the molecular examination of the tissue biopsy taken from the pulmonary metastatic lesion, *AKT1, ALK, BRAF, CTNNB1, DDR2, EGFR, HER2 (ERBB2), ERBB3, ERBB4, ESR1, FBXW7, FGFR1, FGFR2, FGFR3, FLT3, GNA11, GNAQ, HRAS, KIT, KRAS, MAP2K1, MAP2K2, MET, NOTCH1, NRAS, PDGFRA, PIK3CA, RAF1, SMAD4, STK11* genes were studied. ALK, BRAF, EGFR, ERBB2, FGFR1, FGFR2, FLT3, KIT, KRAS, MAP2K1, MET, PIK3CA copy number changes were also investigated. No clinically significant mutation was found according to the available medical literature.

Progression was detected and paclitaxel was added to the treatment. After the completion of the chemotherapy program, the patient was followed up and etoposide was started again upon the progression of lung nodules. When the treatment response was evaluated as stable disease, treatment was continued with oral endoxan.

The patient complained of low back pain radiating to the right leg and underwent an operation for laminectomy and stabilization by the department of neurosurgery in February 2022.

The patient is being followed up as Eastern Cooperative Oncology Group 1 at 120 months after the first operation with pulmonary metastasis at the last follow-up (Figure 2).

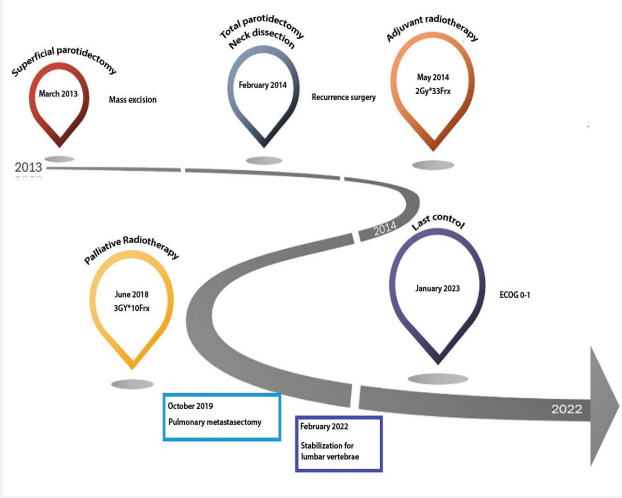

Figure 2. Local treatments during the course of the disease
ECOG: Eastern Cooperative Oncology Group

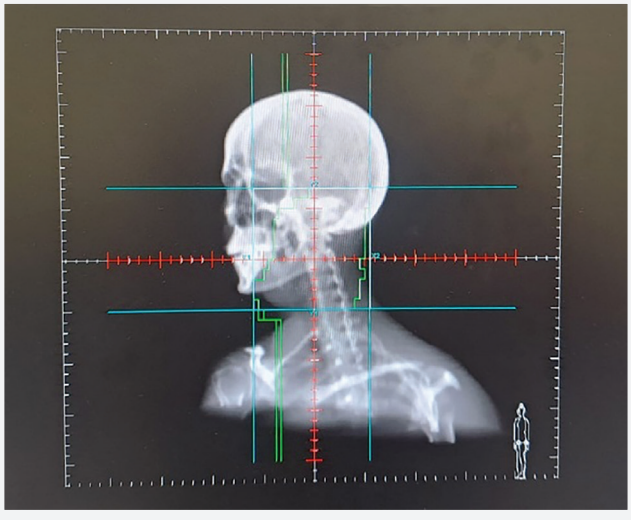

Figure 1. Digital reconstructed radiogram from adjuvant radiotherapy plan

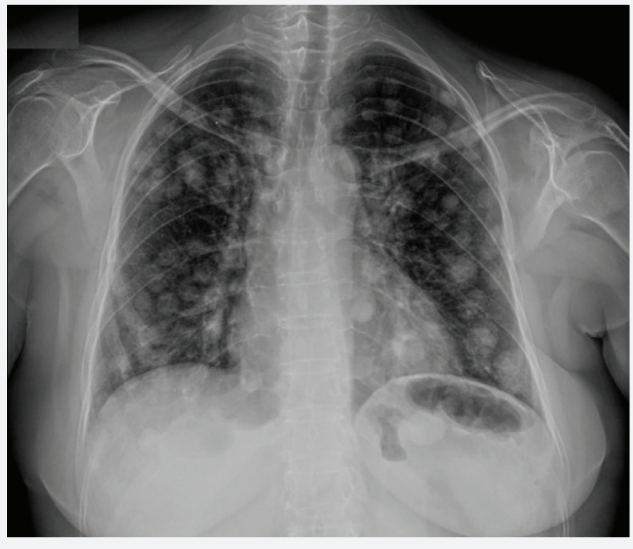

Figure 3. Posterior-anterior chest radiograph

DISCUSSION

A palpable mass is the most common finding on physical examination for superficial parotid gland tumors. Ultrasound examination with color Doppler imaging is an economical and reliable method widely used to detect and evaluate parotid gland masses. The disadvantage of ultrasonographic examination is its low sensitivity in differentiating malignant from benign masses[4].

Due to the rarity of the disease, it is difficult to prospectively examine head and neck ACC patients, but the French study (French National Network on Rare Head and Neck Cancers)[5], which started with 95 patients in 2012, was recently updated with 470 cases[6]. The female/male ratio in the study was reported to be approximately 3/2, in line with previous literature[7]. Minor salivary glands are more frequently involved than major salivary glands, similar to the sex ratio. In head and neck cancers, adjuvant radiotherapy is recommended in the presence of invasive margins and perineural invasion in low-grade T1 tumors, whereas it is recommended for ACC regardless of these after complete surgery. For ACC of the head and neck region, adjuvant radiotherapy at doses of 60 Gy and above after surgery is recommended as standard treatment[7].

In our case, systemic metastasis developed after local adjuvant radiotherapy after recurrence, although there was no recurrence at the primary tumor site. It is important to perform timely local adjuvant therapies by risk assessment of the patients. The symptomatic success of palliative radiotherapy to the metastasis sites has been of limited benefit despite persistent progression of the disease.

Metastatic ACC is a slowly progressive disease with limited response to treatment. Platinum-based standard chemotherapy regimens should be considered in metastatic patients who have no chance of local treatment due to differentiation of tumor cells. The combination of cisplatin, doxorubicin and cyclophosphamide is recommended for ACC, and the addition of 5-fluorouracil is not frequently preferred due to its side effects, although it affects treatment responses. Paclitaxel-carboplatin and cisplatin-vinorelbine regimens are often preferred[8,9]. Current studies have shifted to targeted therapies. Although the platelet-derived growth factor receptor and the tyrosine kinase receptor c-kit proto-oncogene, which is structurally similar to the colony stimulatory factor receptor, have been detected at a high rate in ACC, treatments with imitanib targeting the receptor have not yielded satisfactory responses (Table 1)[8,9].

Lenvatinib is a next-generation multi-kinase inhibitor against FGFR1-3, VEGFR2, cKIT, RET, and PDGFR alpha and beta and has been reported to have more promising results[11]. Following studies reporting median progression-free survival between 9.1 and 17.5 months, the combination of pembrolizumab in particular has found a place in current treatment guidelines[12].

Table 1. Current systemic agents and combinations in ACC[10]

Chemotherapy	Cisplatin
	Cyclophosphamide + doxorubicin + cisplatin
	Cisplatin + gemcitabine
	Paclitaxel
	Vinorelbine
	Vinorelbine + cisplatin
Targeted therapies	Imatinib
	Imatinib + cisplatin
	Dasatinib
	Cetuximab
	Gefitinib
	Lapatinib
	Dovtinib
	Sunitinib
	Regorafenib
	Nintedanib
	Lenvatinib
	Axitinib
	Sorafenib
Immunotherapy	Pembrolizumab
	Pembrolizumab + vorinostat
	Pembrolizumab + radiotherapy

ACC: Adenoid cystic carcinoma

CONCLUSION

Metastatic ACC patients have longer survival than patients with different histopathologic head and neck cancers in the metastatic stage. Planning studies with follow-up periods of more than 5-10 years seems to be more appropriate for slowly progressive and progressive disease. In addition to palliative treatments during the long treatment period, the appropriateness of the developments in the current literature to the patient should be checked periodically. Clinical studies and additional case reports in the literature on this subject should be taken into consideration in the treatment of patients in follow-up.

Ethics

Informed Consent: Consent form was filled out by all participants.

Authorship Contributions

Surgical and Medical Practices: A.Y., Concept: Y.B., Design: Ö.Ç., Data Collection or Processing: L.Ş., Analysis or Interpretation: A.Y., Literature Search: Ö.Ç., Writing: A.Y., L.Ş.

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