

Two Cases with Adenoid Cystic Carcinoma with Epidermal Growth Factor Receptor and c-KIT

Epidermal Büyüme Faktör Reseptörü ve c-KIT Pozitif Adenoid Kistik Karsinomlu İki Olgu

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ABSTRACT

Adenoid cystic carcinoma of the lung (ACCL) is a very rare tumor with a slow course. Primary treatment is surgery. However, recurrences are common. Although chemotherapy is an option in cases not suitable for surgery, response rates are quite low. Identifying the tumor-specific biology and individualized treatment play an important role in these patients. We detected epidermal growth factor receptor (EGFR) positivity and c-KIT positivity by molecular profiling performed in two of our patients diagnosed with ACCL. We evaluated the efficacy of erlotinib and imatinib treatments aimed at these targets. In our case with EGFR positivity due to ACCL and using erlotinib, a 16-month progression-free survival (PES) was found. In our erlotinib used/given case with EGFR positivity due to ACCL, a 16-month PFS was found. In our patient who used imatinib for c-KIT, PFS was observed to be 9 months. Longer survivals were achieved with both treatments compared to chemotherapies. Low survival rates have been found with chemotherapies in locally advanced and metastatic ACCL patients. Molecular profiling plays a very important role in this disease group for patients.

Keywords: Adenoid cystic carcinoma, c-KIT, epidermal growth factor receptor, erlotinib, imatinib.

ÖZ

Akciğerin adenoid kistik karsinomu yavaş seyirli, çok nadir görülen bir tümördür. Primer tedavisi cerrahidir. Ancak özellikle rekürrensler sık görülmektedir. Cerrahiye uygun olmayan durumlarda kemoterapi bir seçenek olsa da yanıt oranları oldukça düşüktür. Tümöre özgü biyolojiyi belirlemek ve bireyselleştirilmiş tedavi bu hastalarda önemli bir rol oynamaktadır. Akciğerin adenoid kistik karsinomu tanısı alan iki hastada yapılan moleküler profillemeye ile EGFR pozitifliği ve c-KIT pozitifliği saptandı. Bu hedeflere yönelik erlotinib ve imatinib tedavilerinin etkinliği değerlendirildi. Akciğerin adenoid kistik karsinomu nedeniyle EGFR pozitifliği saptanan ve erlotinib kullanan olguda 16 aylık progresyonsuz sağkalım saptandı. c-KIT nedeniyle imatinib kullanan hastada ise progresyonsuz sağkalım dokuz ay olarak gözlemlendi. Her iki

Cite this article as: Gürsoy P. Two Cases with Adenoid Cystic Carcinoma with Epidermal Growth Factor Receptor and c-KIT. Journal of Izmir Chest Hospital 2022;36(2):118–120.

Received (Geliş): March 07, 2022 **Accepted (Kabul):** June 16, 2022 **Online (Çevrimiçi):** August 02, 2022

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tedavi ile kemoterapilerle elde edilen sağkalımdan daha uzun sağkalımlar elde edildi. Lokal ileri ve metastatik akciğerin adenoid kistik karsinomu hastalarında kemoterapilerle düşük sağkalımlar saptandı. Bu hastalık grubunda moleküler profileme hastalar açısından çok önemli bir rol oynamaktadır.

Anahtar kelimeler: Adenoid kistik karsinom, c-KIT, EGFR, erlotinib, imatinib.

INTRODUCTION

Adenoid cystic carcinoma (ACC) often originates from the salivary glands of the head-and-neck. However, it is a malignant tumor that is rarely seen in the breast, skin, and lung.^[1] Adenoid cystic carcinoma of the lung (ACCL) accounts for 0.04–0.2% of all primary lung cancers.^[2] Although ACCL is a slow-growing, low-grade malignancy, it has a more frequent risk of recurrence and late hematogenous metastasis, unlike salivary glands.^[3]

Although the primary treatment for ACCL is surgical resection, in locally advanced or metastatic ACCL that is not suitable for resection, the standard treatment is chemotherapy. However, no matter which chemotherapeutic agent is used, response rates are low and response times are short.^[4] c-KIT, epidermal growth factor receptor (EGFR), fibroblast growth factor receptor 1 (FGFR 1), and erb-b2 receptor tyrosine kinase 2 (HER-2) overexpression have been identified in ACCs.^[5] There are case-based studies on these molecules. In this case report, we aimed to present our patients who were diagnosed with ACC and received imatinib and erlotinib because of c-KIT and EGFR positivity.

CASE REPORT

Case Report 1

A 64-year-old male patient presented with cough in 1999. The patient's history had no remarkable features. He had no history of smoking. The right upper lobectomy was planned for the patient, whose mass was detected in the right upper lobe of the right lung on computed tomography (CT). Operational pathology revealed adenoid cystic carcinoma. Radiotherapy and chemotherapy were not planned and the patient was followed up. In 2017, two newly developing nodules, the largest of which was 7 mm, were detected in the lower lobe and upper lobe of the left lung. The left lower lobe and left upper lobe wedge resection was performed. The pathology was adenoid cystic carcinoma. Since the surgical margins were tumor-free, the patient continued with follow-up. In 2018, when nodules reaching 8 mm were detected in the lower and middle lobes of the right lung, the patient was operated again.

During the follow-up, multiple nodules, the largest of which was 8 mm, were detected in both lungs in 2020. It was considered surgically inoperable. Although the patient suggested the option of chemotherapy, the patient did not accept the option of chemotherapy. Next-generation sequencing (NGS) was performed on the patient and exon 19 positivity was detected. In September 2020, erlotinib was started at a dose of 150 mg/day. No side effects were observed in the patient, except for Grade 1 skin toxicity. A stable response was obtained in the response evaluations of the patient. His response was still ongoing in his most recent examination, dated January 2022 (Fig. 1). No decrease was observed in the quality of life of the patient, who continued with a stable response at the 16th month of erlotinib treatment.

Case Report 2

A 43-year-old female patient presented with a left parapharyngeal mass in 2014. The patient's history features were unremarkable. She had no history of smoking. The right lung lobectomy+parapharyngeal mass excision was applied to the patient who had a nodule in the lung in the CT scan. Post-operative radiotherapy and cisplatin chemotherapy were applied to the patient who was found to have lung adenoid cystic carcinoma+parapharyngeal mass of ACC metastasis in the operative pathology. The patient was then followed up radiologically. In 2018, a mass covering 2/3 of her liver was detected on CT in the patient. The patient underwent right hepatectomy. The operative pathology was found to be compatible with adenoid cystic carcinoma metastasis. After the operation, the patient was followed up with 3 cycles of etoposide chemotherapy. In the 12th month of the follow-up, imatinib 400 mg/day treatment was started due to c-KIT CD 117 positivity due to the newly developed liver lesions and dimensional progression of lung lesions. In response evaluation, the patient's response was stable at 6 months, but progression was detected in CT scans at 9 months.

DISCUSSION

We report two of our patients who responded with targeted tyrosine kinase inhibitors in locally advanced or metastatic ACCL patients whose response rates were low with standard chemotherapy. These cases are important in terms of showing the necessity of requesting molecular tests, especially in patients with the same condition.

Lung adenoid cystic carcinoma is more common in patients with young age, male gender, and no smoking history.^[6,7] Lesions are mostly observed in the central.^[6] Although it is a slowly progressing disease, recurrences are frequently observed after surgical treatment. There is no standard treatment for metastatic disease. Response rates are very low with cisplatin-based regimens, paclitaxel, gemcitabine, vinorelbine, and pemetrexet treatments. In recent years, targeted agents with molecular tests detected in NGS have emerged as a treatment option. EGFR, anaplastic lymphoma kinase, platelet derived growth factor receptor alpha, and discoidin domain receptor tyrosine kinase 2 positivity were detected by profiling using NGS by Huo et al.^[9] Especially in tumors originating from the salivary gland, 90% of c-KIT expression is detected. Hotte et al.^[10] used imatinib in 16 patients with these tumors, although it was well tolerated, no efficacy was found in the treatment. In the case report of Demiray et al.,^[11] a 24-month response was obtained with imatinib treatment. Progression-free survival (PFS) was also found to be 9 months in our case.

In a study conducted for ACCL, EGFR positivity was found in one of 11 patients.^[12] In series of Macarenco et al.,^[13] EGFR positivity was not detected in any of the 12 patients. Although the positivity rate is low, there are cases in the literature using erlotinib and gefitinib on a case-by-case basis. Fujita et al.^[14] provided a 7-month PFS in a patient who used gefitinib. In a case report with erlotinib, 8-month PFS was observed.^[15]

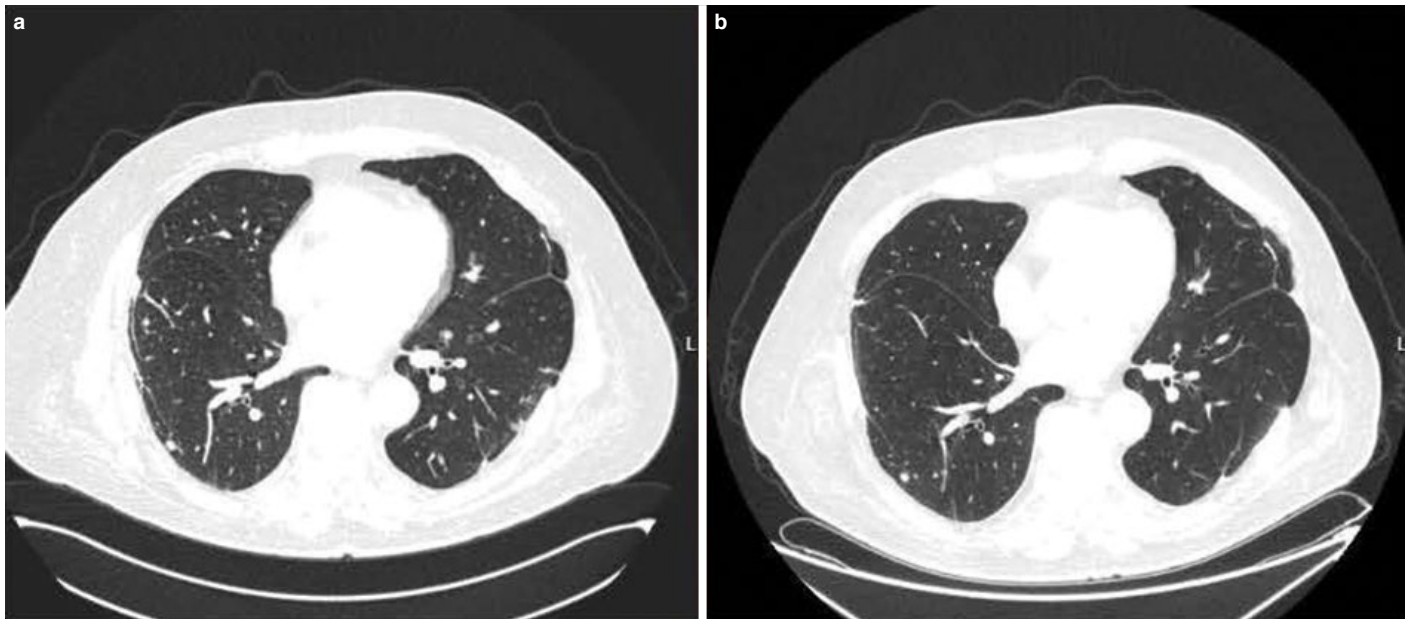


Figure 1: (a) Pre-treatment radiological image. (b) Post-treatment radiological image.

In our first case, the patient using erlotinib due to EGFR positivity continued the treatment with a stable response at the 16th month, while in our second case, a 9-month survival was achieved in the patient using imatinib due to c-KIT positivity. Although targeted therapies are not used as standard in ACCL, clinicians should be aware of the potential use of these therapies. Studies with a large number of patients are needed to determine the tumor-specific biology and for individualized treatment.

Disclosures

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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