To the Editor: A 32-year-old Chinese woman, complained diplopia, exophthalmos, and upper-right orbital pain and was admitted into the hospital in July 2009. Computerized tomography (CT) scan showed an upper-right orbital mass, measured 25 mm × 14 mm [Figure 1a]. Extensive surgical resection of the tumor was done on January 14, 2010. The histology confirmed the tumor was lacrimal gland adenoid cystic carcinoma (LGACC) [Figure 1b]; tumor cells infiltrated into the orbital soft tissue but were free of the orbital bone. Three-dimensional conformal external beam irradiation on the upper-right orbital area was implemented at 2 weeks after surgery with the total dose of 66GY/33F. The patient was scheduled to follow-up periodically after irradiation.

In December 2016, the patient complained left chest pain and short of breath on exertion. Chest CT scan was conducted, which revealed multiple nodules in the left lung and left pleura. These tumors were measured 5–15 mm in diameters; most of them were located in the outer 1/3 of left lung or located in the left pleura [Figure 1c]. There was a small amount of pleural effusion in the left. Laboratory examinations including the C-reactive protein, hepatic function, renal function, carcinoembryonic antigen, neuron-specific enolase, and cancer antigen 19-9 were in normal range. Core needle biopsy of the left pleura was made; the diagnosis of metastatic ACC from lacrimal gland was confirmed by pathologists [Figure 1d]. Next-generation sequencing was performed on the biopsied tissue, gene mutations were found on Cyclin D2 (CCND2) at c.721-110A>C, epidermal growth factor receptor (EGFR) at c.1298+722C>A and notch homolog 1 (NOTCH1) at c.4571C>T; and mutation frequencies were 7.1%, 4.3%, and 0.5%, respectively.

Erlotinib (Tarceva, Roche, Switzerland), an EGFR tyrosine kinase inhibitor (TKI), was used with a dose of 150 mg orally every day from January 13, 2017. CT scan of the chest was performed after 1 month of erlotinib treatment, and every 2 months thereafter. It showed the metastatic tumors of left lung and pleura were shrunk at 1-month treatment and continued response to 14-month treatment on the last follow-up on March 9, 2018 [Figure 1e and 1f]. LGACC is a rare and slow-growing tumor, tends perineural invasion, and spreads to adjacent tissues, such as the bone and cranial nerves. [1] Local recurrence frequently happens several years after surgical excision. Hematogenous metastases to the lungs are most commonly being found at late stage, but rarely spreading to local lymph node.[2] Histologically, the tumor consisted of cribriform, tubular, and solid formations of atypical epithelial cells with dark compact angular nuclei and frequent mitotic figures.[3] The cribriform pattern is the most common and has the best prognosis, whereas the solid type is less frequent and has a poorer prognosis.[4]

Recent molecular insights regarding lacrimal gland carcinomas highlight potential opportunities for targeted therapy for the unresectable or metastatic disease. By conducted whole exome sequencing in patients with LGACC, Sant et al.[5] found that functional plausible mutations were located within the NOTCH1 gene including deletions and insertions that could result in frameshifting and potential functional activation. The mutations in NOTCH genes were located in heterodimerization domain, notch intracellular domain, and epidermal growth factor (EGF)-like repeats;[6] this finding suggested the possibility of targeted therapy aimed at the EGFR pathway. This patient harbored EGFR and NOTCH1 mutations, which might be the predictor factor of EGFR-TKIs therapies.

In conclusions, EGFR-TKI is effective in the management of metastatic LGACC and its toxicities are tolerable. The EGFR pathway might play an important role in tumor proliferation and metastasis; more patients of LGACC are needed to enroll in the study in the future.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Address for correspondence: Dr. You-Xin Ji,
Department of Oncology, The Affiliated Qingdao Central Hospital of Qingdao University, 127 Si Liu South Road, Qingdao, Shandong 266042, China
E-Mail: mdjji001@gmail.com
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Figure 1: Representative image of the patient who was diagnosed as lacrimal gland adenoid cystic carcinoma. (a) CT scan showed an orbital mass on the upper-right side (white arrow). (b) Tumor consisted of glandular or adenoid structure with basophilic secretion, with areas of cribriform, tubular, trabecular, solid, and basaloid structures (Hematoxylin and Eosin [H&E], ×200). (c) CT scan showed multi metastatic lesions in left lung and pleura (black arrow). (d) Tumor with cribriform structures invaded the pleural tissue (H&E, ×200). (e) Metastatic lesions shrunk after 1-month of erlotinib therapy (black arrow). (f) Tumor maintained response at 14-month (black arrow). CT: Computerized tomography.