Response of malignant thymoma to erlotinib

A 43-year-old female developed diplopia and drop of her eyelids in November 2003. Myasthenia was diagnosed and the investigation revealed a large mass of 5.5 cm in the upper anterior mediastinum and deposits in lungs and pleura.
She underwent a radical surgical resection of the tumor in December 2003. Pathology showed a mixed population of epithelial cells and lymphocytes consistent with malignant mixed thymoma stage IV. Three cycles of chemotherapy with cisplatin 50 mg/m², doxorubicin 50 mg/m² and cyclophosphamide 500 mg/m² were administered. Myasthenic symptoms improved after surgery; mestinon and corticosteroids were coadministered.

She remained free of disease until November 2005 when myasthenia relapsed. A computed tomography (CT) scan of the chest confirmed recurrent disease and a second surgical intervention was carried out in February 2006. Extensive disease to the lung and pleura was removed. The patient refused chemotherapy.

In June 2006, a CT scan of the chest revealed a new relapse consisting of a paravertebral mass, left lung mass and subpleuritic nodules. At the same time, the patient’s clinical condition deteriorated with generalized myasthenic symptoms and she became bedridden (performance status = 3) despite treatment with mestinon and corticosteroids.

In October 2006, the patient was started on erlotinib 150 mg once daily. Within 10 days of initiation, the patient displayed significant improvement of her myasthenic symptoms and remained in excellent condition until October 2007. Serial CT scans confirmed an excellent response of the disease. Side-effects were limited to grade I diarrhea and grade II rash.

In October 2007, the patient presented in another hospital with dyspnea, fever and recurrence of her myasthenic symptoms. A CT scan revealed almost complete regression of the paravertebral mass and bilateral consolidation with airbronchogram consistent with bilateral lower lobe pneumonia. She gradually developed severe respiratory failure and was admitted in the intensive care unit, where she passed away few days later.

Paraffin-embedded biopsies from both resections (2003 and 2006) were tested for the expression of epidermal growth factor (EGFR) by immunohistochemistry (IHC) and found positive (score 3+). No mutations were observed for EGFR or Kras in either specimen and no gene amplification of EGFR was detected. EGFR is often overexpressed in thymic epithelial tumors and as such may prove to be a potential therapeutic target [1, 2].

In a small series of 20 cases of thymomas and thymic carcinomas, 17 of 20 tumors were positive for EGFR expression by IHC. Sequence alterations were detected in four cases, but none of these led to amino acid changes in the tyrosine kinase domain of EGFR, comparable to those in nonsmall lung cancer [2].

In a recent phase II study, gefitinib, an EGFR-tyrosine kinase inhibitor (TKI), was administered in 26 pretreated patients with advanced thymic malignancies showing modest activity [3]. Cetuximab, an anti-EGFR mAb, was given to a female with a recurrent thymoma with overexpression of EGFR. The patient responded and remains free of disease for 12+ months [4].

We treated our patient with erlotinib, which is another EGFR-TKI. To the best of our knowledge, this is the first case showing response to erlotinib in a patient with malignant thymoma.

C. Christodoulou, S. Murray, J. Dahabreh, K. Petraki, A. Nikolakopoulou, A. Mavri & D. Skarlos

1Oncology Department, Metropolitan Hospital, Athens, 2Alfa Institute of Biomedical Sciences, Athens, 3Athens Medical Center, Athens, Greece (*E-mail: c_christodoulou@yahoo.gr)

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