

## **EGFR-mutant lung adenocarcinoma that transformed to small cell lung cancer - case report**

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**Background:** Transformation of EGFR (epidermal growth factor receptor) -mutant non–small cell lung cancer (NSCLC) to small cell lung cancer (SCLC) is one of the mechanisms of resistance to the tyrosine kinase inhibitors (TKI) treatment, seen approximately in 3% to 10% cases. Such transformed SCLC often retains the original EGFR mutation (EGFRM).

**Case:** A 67-year-old woman, non-smoker, presented with symptoms of headache, nausea and mild cough. Scans revealed central lung cancer with mediastinal lymphadenopathy, small fluidothorax, and numerous brain metastases. At time of diagnosis pancreas was atrophic, with cysts, without signs of metastases. Bronchoscopy and transbronchial biopsy from left lower lobe bronchus (LLB) confirmed TTF1+ pulmonary adenocarcinoma (AC). Genetic analysis revealed EGFRM of deletion type on exon 19. After whole brain radiotherapy, TKI afatinib was introduced, with response. After 7 month progression in mediastinum and pancreas was observed. Liquid biopsy detected deletion on exon 19 and T790M mutation. Osimertinib was not available, so 4 cycles carboplatin plus pemetrexed were administered, with no response. Rebiopsy from LLB confirmed AC, genetics from biopsy revealed deletion on exon 19. Then osimertinib was introduced, response was achieved. After 12 months progression in lung and pancreas was detected, 4 cycles of docetaxel were used, with next progression. The biopsy from LLB found SCLC. Treatment with carboplatin and etoposide was not effective. The next biopsy from LLB found two populations of cells: SCLC and AC. Biopsy from pancreatic lesion revealed metastasis of SCLC. PCR confirmed EGFRM deletion on exon 19 in sample from SCLC from lung. The next treatment with topotecan was not effective. Erlotinib was started in September 2021. Patient survives 36 months from diagnosis of EGFRM+ NSCLC, 7 months from detection of SCLC.

**Conclusion:** The possibility of transformation EGFR-mutant NSCLC to SCLC after TKI treatment should be taken into account. In the presented case this transformation was confirmed in the lung biopsies after 26 months of treatment with TKI and chemotherapy. We also confirmed pancreatic SCLC metastasis. PCR detected the EGFRM in lung SCLC, identical with that of primary lung AC.

**Conflict of Interests:** no conflict of interest