NTRK fusion gene as a primary resistant mechanism of EGFR-mutated lung adenocarcinoma: a case report

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Introduction: In patients with EGFR activated mutation, EGFR-TKI response rate is as good as 70-80%. However, 20-30% of the patients show primary resistance, Various mechanisms have been suggested to explain the resistance. We present a case in which a rare neutrotrophic receptor tyrosine kinase (NTRK) fusion was the primary resistance mechanism of EGFR mutated adenocarcinoma. Recently, NTRK gene fusion has emerged as a target for cancer therapy. **Case report:** A 57-year-old male visited the emergency room (ER), complaining of Rt. Facial palsy. Under impression of cerebral infarction, brain MRI was performed. Two masses suspected of metastatic lesion was found in Lt. frontal area. A five-centimeter lung mass in the left upper lobe on chest CT was found during diagnostic work-up performed to find the primary cancer origin. The patient was referred to the department of pulmonology. The patient was a non-smoker, and metastatic lesions were observed on Lt. axillary lymph nodes, liver, sacrum and iliac bone. On the histopathologic examination, adenocarcinoma with EGFR exon 19 deletion mutation was confirmed. ALK and ROS immunohistochemistry (IHC) were negative. Treatment with Gefitinib (IRESSA®) was initiated. On the 49th day of the treatment, the patient presented at the ER with persisting left chest pain. IRESSA treatment was stopped and restaging work-up was performed. On PET-CT examination, there was an increase of the primary lung lesion, and Lt. 3rd-4th rib and pubic bone metastasis were newly identified. Re-biopsy of the lung lesion was performed, and next generation sequencing of the tissue revealed NTRK3 fusion. The patient was treated with pemetrexed and cisplatin chemotherapy. After 5 cycles of chemotherapy, the patient showed partial response (PR). In case the patient shows any sign of progressive disease, we plan to try Larotrectinib, an NTRK inhibitor. **Conclusion:** NTRK fusion gene is rare mutation.It was found as a primary resistance mechanism in TKI treatment of EGFR-mutated adenocarcinoma. NTRK inhibitor(Vitrakvi®) under clinical trial can be another treatment option for this patient.