BACKGROUND AND OBJECTIVES

Based on cell of origin, Lung cancers are broadly divided into small cell lung cancer 15% and non-small cell lung carcinoma 85%. Historically it was thought that both have distinct cell lineages. However, increasing incidence of coexistence, transformation of NSCLC to SCLC is supporting the hypothesis of common cells of origin.

CASE SERIES

CASE 1: 75 YOF with extensive smoking history, have poorly differentiated stage IV adenocarcinoma with no targettable genomic alteration. She attained complete resolution after 4 cycles of Carbo/Pemetrexed/Pembrolizumab and completed one year of maintenance pembrolizumab with no grade 3-4 toxicities. Three months after completion of therapy she presented with SOB and found to have upper lobe lung mass extending to mediastinum and on biopsy found to be small cell carcinoma and was started on cisplatin and irinotecan.

CASE 2: 60 YOM had a stage IIA moderately differentiated lung adenocarcinoma s/p lobectomy with path showed angiolymphatic invasion, 0/11 nodes negative and no adjuvant treatment given. After 4 months, patient becomes symptomatic with SOB and presents with RUL mass, biopsied and found positive for limited stage initially and later progressed to extensive stage SCLC. Currently on Chemo-immune therapy

CASE 3: 61 YOM with hx of metastatic NSCLC adenocarcinoma, PDL 1 >50%, completed 8 cycles of pembrolizumab. After few months, left hilar lymphadenopathy present which was found to be small cell carcinoma with Ki67% index 80%. Started on Cisplatin and etoposide but course complicated with worsening of peripheral vascular disease and decided to only pursue radiation therapy and hold off on chemotherapy

CASE 4: 57 YOF presented with synchronous metastatic lung adenocarcinoma, cholangiocarcinoma, neuroendocrine carcinoma of unknown origin, metastatic disease to the brain of unknown origin. NGS showed KRAS G12C, STK 11 mutations, MSI stable and TMB 8.No targetable mutations. Treated with 4 cycles of chemotherapy with carbo/Pem/Pembro and on Lanreotide for symptomatic small cell neuroendocrine, status post whole brain radiation with repeat PET/MRI showed mixed response, was maintained on Pembrolizumab

CONCLUSIONS

1) Histological transformation to SCLC is a potential mechanism of acquired resistance to Immune check point inhibitor in NSCLC
2) Repeat tissue biopsies should be considered at the time of progression.
3) Several hypotheses have been proposed to explain the transformation of NSCLC to SCLC.
4) Tumor transformation was observed in 5% to 14% of EGFR-mutated NSCLC.
5) Resistance to EGFR inhibitors was thought to be a potential etiology for transformation from EGFR-mutant adenocarcinoma to SCLC.
6) Another hypothesis is that the alveolar type II cells can give rise to both SCLC and EGFR-mutant adenocarcinoma. It is also thought that NSCLC and SCLC share common cells of origin.

REFERENCES