



Gene Mutation Status of Pulmonary Sarcomatoid Carcinoma of the Lung: An Advanced Review

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Editorial

Pulmonary Sarcomatoid Carcinoma (PSC) account for less than 0.4% of all tumors of lung. They are a heterogeneous group of non-small-cell lung carcinomas containing a sarcoma or sarcoma-like (spindle and/or giant cell) component. Generally, they were considered to have a very poor prognosis and resistance to conventional platinum-based chemotherapy [1]. For now, the development of targeted therapy drugs for Non-Small Cell Lung Cancer (NSCLC) has garnered an increased attention and remarkable successes. But the molecular features and presence of targetable genetic abnormalities in PSC are largely unknown. Therefore, we performed high-throughput sequencing on 7 PSC cases in our study, a total of 136 putative somatic variants and one gene fusion were identified, of which 16 variants were considered as hot spot mutation, including EGFR, EML4-ALK, MET, BRAF, PIK3CA, TP53. The high-throughput sequencing results imply that TP53 mutations were more often appeared in PSC, and EML4-ALK fusion event and EGFR exons mutation were also existed in these rare tumors [2]. In another study, V. Fallet performed high-throughput sequencing on 114 surgical biopsies from 81 PSC patients, they identified 67 distinct somatic alterations, the most frequent mutations were KRAS(27.2%), EGFR(22.2%), TP53(22.2%), STK11(7.4%), NOTCH1(4.9%), NRAS (4.9%), and PI3KCA (4.9%). More than 39.5% patients have co-existed mutations [3]. Xuwen Liu et al. [4] also reported in their publication, MET mutations leading to exon 14 skipping were identified in 8(22%) of 36 patient cases through whole-exome sequencing, and a patient with advanced chemotherapy refractory PSC carrying a MET exon 14 skipping mutation revealed dramatic sensitive to crizotinib. In Italy, some scientists discovered 39 PSCs (80%) showed at least one mutation. Survival probability decreased in patients with mutated PSC compared with those without mutations ($p=0.02$). In particular, mutations in KRAS, alone or in combination with TP53 mutations were associated with decreased survival probability and with the occurrence of local metastases at recurrence. They announced their findings of PSC were similar to that of smokers' lung adenocarcinoma with data in The Cancer Genome Atlas [5]. A study belongs to Mayo Clinic performed by Simone BSP Terra et al. [6] tested for approximately 2800 mutations in 50 oncogenes and tumor-suppressor genes of 33 PSCs, showed 24 of all cases (72%) had at least one genetic abnormality: 19 cases (58%) had TP53 mutations; 10 cases (30%) had KRAS mutations; AKT1, JAK3, BRAF, NRAS, and PIK3CA mutations were observed in 1 case each (3%). 6 of the 19 cases (32%) with a mutation in TP53 had simultaneous mutations in KRAS (18%). The cases with alterations in JAK3, BRAF, and NRAS also had mutations in TP53. But no EGFR mutations were observed. ALK rearrangement was observed in a single case of sarcomatoid carcinoma (3%), which has currently available targeted therapy. Four tumors had mutations in genes with experimental molecular based therapy, including BRAF, NRAS, PIK3CA, and AKT1. The result was similar to our findings. According to these findings above, testing for targetable mutations should be considered for patients with pulmonary sarcomatoid carcinoma, as a subset may benefit from currently approved drugs or clinical trials of novel therapeutic options available for other types of lung cancer.

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