AB035. P-03. Explore the mutational landscape and immune profile of EBV-associated lymphoepithelioma-like cholangiocarcinoma

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Background: Lymphoepithelioma-like cholangiocarcinoma (LELCC) is a rare variant of intrahepatic cholangiocarcinoma, which is highly associated with Epstein-Barr virus (EBV) infection and abundant lymphoplasmacytic cells infiltration. However, the genetic background of LELCC and the immune profiling of their microenvironment remain largely un-elucidated.

Methods: Retrospectively collected formalin-fixed, paraffin-embedded (FFPE) tissue of 5 EBER-positive LELCCs and 7 non-LELCCs were included. PDL1 expression was examined by anti-PD-L1 immunohistochemical (IHC) 22C3 PharmDx (Agilent Technologies, Santa Clara, CA, USA). Peripheral blood mononuclear cells (PBMCs) from two LELCC patients were served as background of germline mutations. Gene expression profiling was determined by next generation sequencing (ACTOnco®+ Comprehensive Cancer Panel, ACT Genomics Co., LTD) on DNA samples. The nCounter® PanCancer Immune Profiling Panel (NanoString Technologies, Inc., Seattle, WA, USA) was used for Immune profiling on RNA samples.

Results: All EBV-related LELCCs were positive for PD-L1 staining, with combined positive score of 25 to 80, mainly in peritumoral immune cells. After adjusting for frequency of germline mutation from PBMC, only mutations with allele frequency less than or around 10% were considered as somatic mutations. Overall, LELCCs with 10 nonsynonymous somatic mutations were detected in 4 LELCCs with 0 to 5 mutations per sample. Identified mutations included BARD1 (allele frequency: 8.1%), EPHA5 (5.8%), MUC16 (7.6%), TNFAIP3 (5.8%), CD19 (5.6%), PTEN (8.8%), TET1 (7.2%), RECQL4 (6.4%), CD79B (10.1%), and KDM5A (10.2%), with all 20% of incidence. Each mutation is independent between four cases. Of the immune profiling, EBV-related LELCCs display significantly higher signature of cytotoxic cells, CD45 cells, T cells, Th1 cells, CD8 T cells, NK cells, and B cells than those of non-LELCC. Of the one LELCC patient who had anti-PD-1 treatment after gemcitabine/cisplatin therapy failure got a durable partial response to the anti-PD-1 immunotherapy.

Conclusions: LELCC is highly correlated with PDL1 expression in tumor and immune cells. Based on results of NanoString immune panel, EBV-related LELCC is characterized by a T cell-inflamed tumor microenvironment.

Keywords: Mutation; immune profile; Epstein-Barr virus (EBV); EBV-related cholangiocarcinoma

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