374O Mismatch repair deficiency (MMRd) in glioma patients (PTS): Frequency and correlation with clinical, histological and molecular characteristics

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Background: Immune-checkpoint inhibitors (ICI) represent a new interesting approach in oncology. The presence of DNA MMRd would seem to be a predictor of ICI efficacy. We analyzed MMRd frequency in glioma PTS and its correlation with clinical, histological and molecular characteristics.

Methods: From July 2017 to May 2018, we prospectively analyzed histologically confirmed glioma PTS for the presence of MMRd by immunohistochemistry (IHC): MSH2, MSH6, PMS2, MLH1. Clinical, histological and molecular characteristics (MGMT methylation and IDH mutational status, PD-L1 expression) were recorded. Chi-square test was used for analyzing their correlations with MMRd.

Results: 167 PTS were enrolled: 78% glioblastoma (GBM), 14% anaplastic astrocytoma (AA), 1% ependymoma, 2% anaplastic oligodendroglioma (OD) and 5% LGG. The analyses were assessed on tissue samples of first (82% of the cases) and second surgery (18%). All PTS performing a second surgery received radiotherapy and temozolomide as first-line therapy. 134 PTS were analyzed for IDH status: 99 were IDH wt; 117 for MGMT status: 68 were methylated. 27 PTS (16%) showed MMRd by IHC (MSH2 in 48%, MSH6 in 55.6%, PMS2 in 18.5% and MLH1 in 14.8%): 33% of AA, 14% of GBM, 33% of OD and 0% of LGG ($p = 0.2$). MMRd was found in 13% and 32% on first and second surgery samples ($p = 0.03$). PD-L1 expression analysis was performed in 60 cases: no expression was showed in 58% of cases, $\geq$ 1% and $<$50% in 38%, $>$ 50% in 10%. MMRd was not correlated with PD-L1 expression ($p = 0.3$). MMRd was found in 10% and 29% of IDHwt and IDHmut gliomas ($p = 0.008$); MMRd was showed in 10% and 21% of PTS with unmet and metMGMT ($p = 0.1$). Among MMRd tumors, 7 were also investigated by molecular analysis (PCR) of mononucleotide markers: in only 1 PT (14%) was confirmed MMRd in agreement with IHC analysis ($p = 0.1.$).

Conclusions: We showed a small group of glioma PTS have MMRd by IHC, expecially at second surgery. Correlation was observed between IHC MMRd and IDH mutational status. No association was demonstrated between IHC MMRd and histology, MGMT status, PD-L1 expression or molecular analysis of MMRd. A prospective study analyzing ICI efficacy in MMRd PTS should be warranted.

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