Glioblastoma (GBM) is characterized by a high recurrence rate probably due to “immune-deserted” tumor microenvironment (TME) consisting of tumor-associated macrophages (TAMs) and tumor infiltrating lymphocytes (TILs). We aimed to investigate the prognostic role of tumor tissue markers correlating with overall survival (OS) and progression-free survival (PFS).

RESULTS

Results from 31 patients (23 males and 8 female) were observed. Median age was 58 years (range: 37-77 years). All analyzed tissues were negative for PD1L and only two were positive for CD20. We observed (Tab. 1) that CD68+ macrophage and CD66b+ neutrophils expressed in Vascular/perivascular area (CD68-V and CD66b-V) showed a statistically significant prognostic role for OS (p-value: 0.027 and 0.029 respectively) and a lower risk of death was observed for patients with CD68+ or CD66b+ equal to 2-4 respect to patients with 0-1. CD68-V showed a prognostic role for PFS (p-value: 0.032), while CD66b-V expressions did not (Fig 1). The expression levels of CD3, CD4, CD8, CD45 and CD163 were not associated with OS and PFS. Multivariable model that consider these immune markers concurrently, confirm their role for OS.

MATERIALS AND METHODS

We retrospectively analyzed TME on 31 archival formalin-fixed paraffin embedded (FFPE) tissue specimens by immunohistochemistry (IHC): CD3, CD4, CD8, CD20, CD45, CD68, CD163, CD66b and PDL-1. Expression values were classified according to density score from 0 to 4 (0=no expression; 1=1-25%; 2=26-50%; 3=51-75%; 4=from 75%-100%) in two areas: Vascular/perivascular (V) and diffuse in tumor parenchyma (D). Percentage of infiltrating immune system cell was calculated by the rate of absolute number of positive stained cells/total number of cells multiplied by 100. OS was calculated as the time from diagnosis to death or last follow up, while PFS was calculated as the time from diagnosis to the last documented date of disease or death. Patients without progression of disease were censored at the last follow up date. Estimated HRs with 95% CI were calculated using univariate Cox proportional hazard models. Multivariable models were carried out to assess if these immunomarkers could be considered independent prognostic factors for OS or PFS.

CONCLUSIONS

Despite having a smaller cohort of tissues, we showed a different expression of immune markers. In particular, CD68-V was associated with a significant positive impact on both OS and PFS. This relation could be partially explained because TAM do not raise only from peripheral blood, but also from resident microglia. Moreover, we observed high density of CD66b+ cells in V related to OS probably for growth factors overproduced by tumor cells with their recruitment from blood. Further studies are needed in large series to explore the prognostic role of selected TME immune molecules to develop therapeutic strategies that aim to hit different components of GBM.

REFERENCES


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