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Treatment associated changes in the inflammatory microenvironment composition of brain metastases

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Background

Radio- and immunotherapy were postulated to have synergistic efficacy in brain metastasis (BM) treatment due to the immune modulating properties of radiation. Therefore, we aimed to investigate changes in the inflammatory microenvironment after local radiation treatments in BM specimens.

Methods

Formalin fixed and paraffin embedded BM samples from treatment naïve patients (group 1) and from patients treated whole brain radiotherapy (WBRT) (group 2) or stereotactic radiosurgery (SRS) (group 3) or combined WBRT and SRS (group 4) or prophylactic cranial irradiation (group 5) before BM resection were identified from the Vienna Brain Metastasis Registry. T cell subsets (CD3+, CD8+, CD45RO+, FOXP3+ and LAG3) as well as expression of PD-L1 were investigated.

Results

Specimens from 81 patients (55 lung cancer, 15 breast cancer, 4 renal cell cancer, 1 melanoma, 1 colorectal cancer & 5 other tumor types) were available for analysis. Group 1 presented with statistically significantly higher CD3+ (median: 492.6 cells/mm2), CD8+ (median: 116.3 cells/mm2) and LAG3+ (median: 17.6 cells/mm2) TIL densities than group 2 (CD3+ median:55.5 cells/mm2; LAG3+ median: 4.6 cells/mm2), group 3 (CD3+ median: 67.7 cells/mm2; CD8+ median: 40.6 cells/mm2) and group 4 (CD3+ median: 38.28 cells/mm2; p-value <0.05; Kruskal Wallis test). No significant changes of the inflammatory microenvironment in group 5 compared to the other groups, and in PD-L1 expressions between the groups were observed (p-value >0.05; Kruskal Wallis test). Of 24/81 (29.6%) patients matched samples of initial resected BM and recurrent BM were available. All investigated T cell subsets were numerically lower in recurrent BM from patients treated with radiation therapy between resections than in recurrent BM from patients without radiation treatment between BM resections (p > 0.05; Mann-Whitney U-test).

Conclusions

Our data indicate an immunosuppressive effect of radiotherapy on BM, as evidenced by decreased T cell infiltration in radiated versus non-radiated BM specimens. Future clinical studies should focus on the optimal timely sequencing of immune modulating therapies and radiotherapy.

Legal entity responsible for the study

The authors.

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Disclosure

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