Background Prostate cancer (PC) is the leading cause of cancer incidence among men in the US.\(^1\) For patients living with advanced PC, bone metastasis (mets) is a debilitating, yet common occurrence. As a result, bone mets are an acute source of pain, morbidity, and can contribute to patient mortality. To optimize immunotherapeutic strategies that target bone metastases, it is crucial to characterize their TIME.

Methods Bone metastases tissue samples (n=13) were procured from 9 patients having castration resistant PC. For decalcification, we used EDTA to optimize bone tissue preservation and optimal proteomic analysis. Adjacent FFPE bone mets sections were immune-stained using 3 validated multiplex immunofluorescence panels and opal technology. We investigated the expression of HLA-DR on tumor cells. Furthermore we looked at densities of lymphocytes (T helpers, CD8+ T-cells and regulatory T-cells), tumor associated macrophages (M1 and M2), and myeloid-derived suppressor cells (M-MDSCs and PMN-MDSCs) infiltrating the bone mets. We utilized bone marrow tissue as a positive control.

Results HLA-DR was found downregulated in all PC bone mets samples. The average CK+/HLA-DR+ ratio was approximately 16. HLA-DR downregulation is associated with T-cell immune escape. Additionally, CD4+ and CD8+ T-cell densities were relatively low in these samples (9 and 132 cells, respectively). Tumor associated macrophages were the most abundant immune cells found in these samples. M2-like macrophages (440) outnumbered M1-like macrophages (287), contributing to immunosuppression. M2/CD8+ ratio was 5.5. Furthermore, PMN-MDSC and M-MDSC densities were 38 and 9, respectively.

Conclusions Our data confirm previous findings about the immune suppressed phenotypes within the TIME in prostate cancer bone mets.\(^2\) The down regulation of HLA-DR in tumor cells point to using NK cells as a future immunotherapy target. HLA-class I is still to be investigated in these samples. While tumor associated macrophages were the most abundant immune cells found within these samples, among the subtypes, M2-like macrophages were most prevalent. This suggests that rational and accurate design of therapeutics which relieve immunosuppression through M2 macrophage depletion, or M1 macrophage repolarization, may help combat PC bone mets.

REFERENCES

Ethics Approval This study obtained ethics approval by Thomas Jefferson University IRB. Patients provided informed consent prior to participating in this study.

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