Telomere lengths differ significantly between small cell neuroendocrine carcinoma and adenocarcinoma of the prostate

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Background: Small cell neuroendocrine carcinoma (SCC) of the prostate is an aggressive subtype with frequent TP53 mutation and RB1 inactivation. However, the molecular phenotype remains an area of active investigation. Here, we compared telomere lengths in prostatic SCC and usual-type prostatic adenocarcinoma (AdCa).

Methods: We studied 32 cases of prostatic SCC (including 11 cases with concurrent AdCa) and 347 cases of usual-type AdCa on tissue microarrays (TMA). Telomere lengths in tumor cells were qualitatively compared to that in adjacent benign cells using a telomere-specific fluorescence in situ hybridization (FISH) assay. ERG, PTEN and TP53 status were assessed in a proportion of cases using genetically validated immunohistochemistry protocols. Clinical-pathologic and molecular characteristics of cases with normal or long telomeres were compared to those with short telomeres using the chi-square test.

Results: A significantly higher proportion of prostatic SCC cases (50%, 16/32) displayed normal/long telomere lengths compared to AdCa cases (11%, 39/347; p<0.0001). In 82% (9/11) of cases with concurrent SCC and AdCa, the components were concordant for telomere length status. Among AdCa cases, the proportion of cases with normal/long telomeres significantly increased with increasing tumor Grade Group (p=0.01) and pathologic stage (p=0.02). Cases with normal/long telomeres were more likely to be ERG positive (p=0.04) and to have a TP53 missense mutation (p=0.01) compared to cases with short telomeres. Although, among a small cohort of 54 surgically-treated very high grade (Gleason 9 and 10) AdCa cases, there were no significant associations between cancer cell telomere length category and biochemical recurrence- or metastasis-free survival.

Conclusions: Normal or long telomere lengths are significantly more common in prostatic SCC compared to AdCa and are similar between concurrent SCC and AdCa tumors supporting a common origin. Among AdCa cases, longer telomere lengths are significantly associated with high risk pathologic and molecular features, although in a small high grade AdCa cohort, there were not significant associations with oncologic outcomes.

Conflicts of Interest: None.

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