Transdifferentiation of prostate adenocarcinoma to carcinosarcoma

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Background

In prostate cancer, it is recognized that adenocarcinoma can transdifferentiate into neuroendocrine prostate cancer (NEPC) owing to lineage plasticity; however, transdifferentiation into other histological types is rare. We encountered a case of a patient who initially underwent surgery for adenocarcinoma, which later recurred as prostate carcinosarcoma following androgen deprivation therapy. We performed comprehensive genomic and transcriptomic analyses to characterize this rare tumor.

Methods

Immunohistochemical staining for adenocarcinoma-, NEPC-, and sarcoma-associated markers (α-SMA, calponin) was performed to characterize both the primary and recurrent tumors. Genomic profiling of the recurrent tumor was conducted using the FoundationOne CDx assay. RNA sequencing was performed, and the data were compared with samples from patients with NEPC and castration-resistant adenocarcinoma (CRPC-adeno).

Results

Hematoxylin and eosin staining of the recurrent tumor revealed predominantly spindle-shaped cells. Immunostaining demonstrated only a few AR-positive cells, loss of PSA and ERG expression, and strong positivity for α-SMA and calponin, consistent with prostate carcinosarcoma. Staining for p53 and Rb indicated wild-type status in the primary tumor, but both were lost in the recurrent tumor. NEPC markers were negative in both the primary and recurrent tumors. Genomic analysis identified a *TMPRSS2-ERG* gene fusion, *TP53* mutation, *RB1* loss, and *PTEN* loss. Transcriptomic analysis showed that the tumor clustered distinctly from both CRPC-adeno and NEPC. ssGSEA demonstrated enrichment of EMT-related and immune-related pathways.

Conclusions

To our knowledge, this is the first report to comprehensively evaluate the clonal origin of

prostate carcinosarcoma and characterize it through integrated genomic and transcriptomic analyses.

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