Prostate Specific Membrane Antigen (PSMA) in Urothelial Cell Carcinoma (UCC): A systematic review of the literature

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Introduction

Bladder UCC is the 9th most common oncological diagnosis, with high morbidity and mortality worldwide.

• Staging, re-staging and surveillance of UCC is challenging
• Improvements in standard of care (SOC) modalities have occurred through MRI & FDG-PET.
• Recently, pilot studies have begun investigating the role of PSMA PET in UCC after promising results in other non-prostatic malignancies.

Aim: To undertake a review on the available data, including the histopathological basis of PSMA expression in UCC, the role of PSMA based imaging, clinical implications, current limitations and future opportunities.

Methods

• Prospective registration on the PROSPERO database ID: CRD42020186744.
• Systematic review of Web of Science, Embase, Pubmed and Cochrane scientific databases in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines was performed.
• All articles, including case reports, case series, clinical trials and conference abstracts published from 1990 to 2020 were included for a comprehensive methodology.
• All relevant texts relating to immunohistochemical (IHC) analysis and PSMA based imaging in UCC were reviewed for relevant parameters, which were collated and analysed.

Results

Tumour Neovasculature

• Six IHC studies were identified, with total samples included = 301;
• PSMA expression ranged from 44%-100%, with 4 out of 6 studies showing an expression rate of >93%, mean expression was 83%.

RNA & Tumour Biology

• Cancer Cell Encyclopedia & Cancer Genome Atlas (TCGA) demonstrate PSMA mRNA expression in UCC.
• C-Bioportal & TCGA 2017 bladder cancer cohort analysis evidenced PSMA (through encoding FOLH1 gene) to be implicated in multiple gene mutations associated with UCC (depicted in figure 1) through PTEN/AKT carcinogenesis pathways.
• Selective PSMA expression in neovascularization of UCC. Potential role in malignant angiogenesis via its enzymatic activity and nitric oxide production.

Imaging UCC with PSMA: Clinical implications

• Nine texts of PSMA based imaging in UCC were identified (median age 66 years).
• Metastasis deposits were accurately identified in 86% of cases, organ specific lesions in 70% and nodal lesions in 44%.
• Clinical importance: Small metastatic lesion detection (ie below RECIST cut offs), Surveillance, useful alternative for patients with allergies & renal failure.

Conclusions

• The current IHC and molecular data evidences consistent PSMA expression in the neovascularisation of UCC
• Early PSMA imaging studies are promising. PSMA has a sound mechanistic basis to be a PET based target for metastasis detection & assessing response to anti-angiogenic therapies in UCC.
• Larger, well designed studies are required to better define role in primary tumour characterisation, exact link to UCC biology & overall utility.