Sarcomatoid Urothelial Carcinoma: Contemporary Analysis of 99 Cases with Emphasis in Patients with pT1 Tumors who underwent Early Cystectomy

Vamsi Parimi[1], MD.,MPH., Kara Lombardo[2], BS., Woonyoung Choi[2,4], PhD., Trinity Bivalacqua[2,4], M.D, Ph.D., Max Kates[2,4], MD., Noah Hahn[2,3,4], MD., David McConkey[2,3,4], PhD., Andres Matoso[1,4], MD.

[1]Department of Pathology, [2]Department of Urology, [3]Department of Oncology, [4]Greenberg Bladder Cancer Institute. Johns Hopkins University School of Medicine

BACKGROUND

- Sarcomatoid urothelial carcinoma (SUC) is a histologic variant of Urothelial carcinoma (UCa).
- Guidelines recommend consideration for early radical cystectomy (RC) in patients with SUC and pT1 tumors.
- We studied clinico-pathologic parameters associated with prognosis including 5 patients with pT1 tumors who underwent early RC.

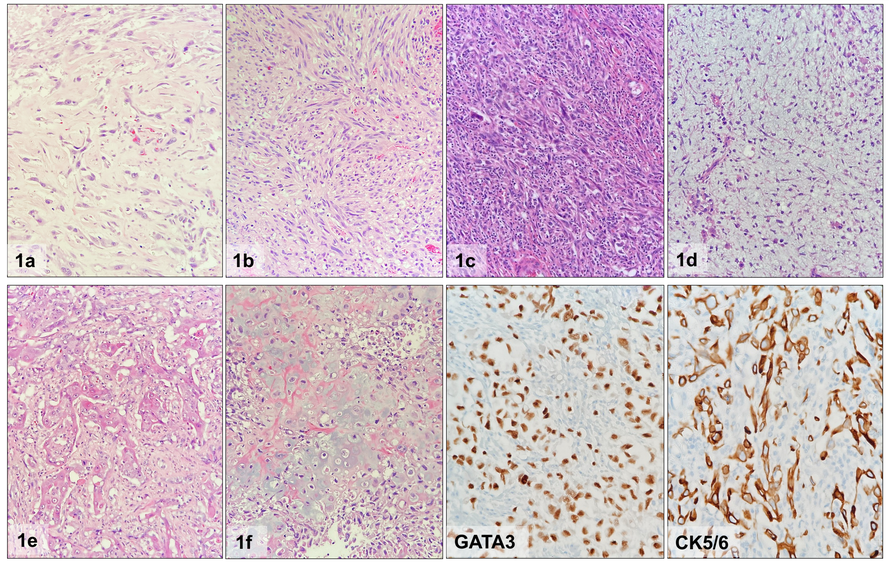
METHOD

- A retrospective review identified 99 patients who were diagnosed as SUC between 1993 and 2019. Clinical records for all patients were reviewed, with emphasis on type of therapy administered and overall survival. H&E were reviewed to annotate tumor size, size of sarcomatous component and percent of sarcoma.
- Log-Rank test, Cox regression and Spearman correlation tests were used to assess clinico-pathologic outcomes.

RESULTS

- Demographics: The median patient age at diagnosis was 70 yrs. Patients were White (83%), Black (14%), Asian (3%). Similar to UCa, SUC was 3-4 times more common in males.
- Urothelial Bx/TURB: In 30% of cases, initial biopsy/TURB did not identify SUC component.
- Surgical procedures: Twelve patients (Mean±SD =70±13 yrs, Range= 48-82 yrs) did not undergo cystectomy. The remaining 81 underwent the following resection procedures: RC (13), partial cystectomy (4), cystoprostatectomy (59), and pelvic exenteration (5).
- Non-invasive carcinoma: 55% of cases had a urothelial precursor lesion (76% CIS, 35% HGTCC, 4% LGTCC).
- Epithelial components: 27% are pure SUC with spindle cell morphology, and 73% were mixed with UCa or with other variants of urothelial carcinoma. **Fig.1** Among which 30% of SUC cases were associated with other variants [64%, squamous cell carcinoma; 32%, glandular/signet cell features; 14%, micropapillary; 10%, small cell carcinoma; 7%, anaplastic; and 7% large cell carcinoma]. **Fig.2**
- Sarcomatous components: 88% are non-specific malignant spindle cell phenotype and 12% of cases showed specific subtypes of sarcomatous heterologous components (HE); chondroid, osteoid, myxoid and rhabdoid differentiation. Heterologous elements (HE) had significant worse overall survival (p=0.045). **Fig.3**

RESULTS



- Tumor characteristics: Average size of total tumor and SUC component was 6cm and 4.5cm respectively. Total tumor size, SUC size and maximum depth of invasion had no significant association with OS (p>0.05). The mean SUC tumor size at RC among patients receiving no chemotherapy (Chemo) vs Chemo was 4.6 and 2.8 cm respectively. Posterior wall SUC was associated with poor survival (p=0.06) **Fig.4**
- Immunophenotypic classification: GATA3 (luminal) and CK5/6 (basal) showed luminal (13), basal (21), mixed (21) and double negative (10) staining. GATA3-CK5/6- SUC cases had better survival compared to other groups (p>0.05) **Fig.5**
- TNM Staging: The distribution by pT stage (pretreatment) was 6%, 31%, 41% and 17% (T1, T2, T3 and T4). T-stage had significant association with OS (p=0.02) **Fig.6.** T1T2N0M0 had significant high OS (p=0.007) compared to T1-T4 ≥N1 M1 **Fig.7.** Primary tumor LVI and ≥N1 stage are significantly associated with worse survival (p<0.05), Pearson correlation=strong (p<0.05). M0 and M1 had similar OS.
- Survival outcomes: Clinical long-term follow up data was available in 51 patients. The median OS was 14 months. Only 10% survived beyond 5yrs. The >5 yr estimated probability of survival was 59%. The median OS among patients receiving chemotherapy (both NAC+ADJ) vs no chemotherapy was not significantly different from each other (p= 0.43) [n=83].

pT1 Subset: All five male patients (mean age 68 years) had RC (N0/M0). One patient had LGTCC, 1 had CIS and 3 with no noninvasive component. None received chemotherapy. One progressed to N0M1; 3 had no recurrent disease; 1 was lost to follow-up. 4/5 patients were alive (mean OS= 49 months); 1 with >2 urothelial variants and SUC, 1 with heterologous elements (osteosarcoma)

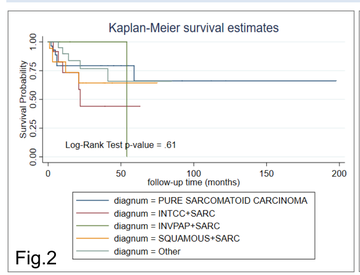


Fig.2

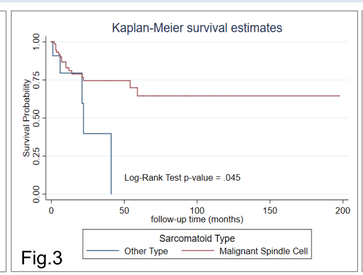


Fig.3

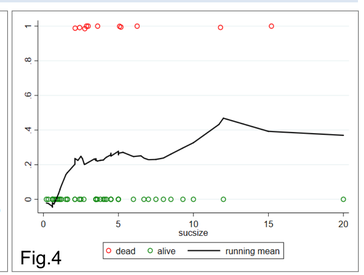


Fig.4

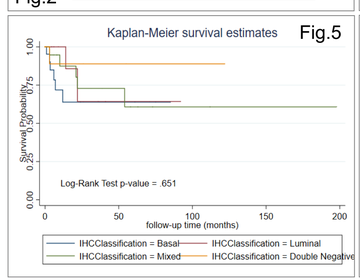


Fig.5

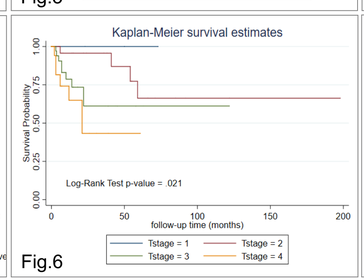


Fig.6

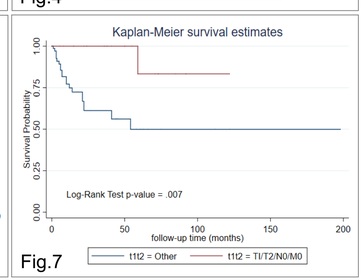


Fig.7

CONCLUSIONS

- Depth of invasion, size of total tumor and the proportion of the SUC component did not correlate with poor survival.
- Pure SUC (sarcomatoid carcinoma) and mixed SUC with other epithelial invasive carcinoma (carcinosarcoma) had similar survival.
- Posterior bladder wall SUC are associated with poor OS
- SUC patients with heterologous elements had significantly poor overall survival.
- IHC classification did not show any significant association to OS
- T1T2N0M0 had significant high OS
- The presence of LVI and nodal disease (≥N1) was significantly associated with poor survival.
- The median OS was 14 months. 71% SUC patients survive at 2 year time point. Among all the death events, 86% occurred before 2 year time point. Only 10% survived beyond 5yrs.
- Despite the small number of patients with pT1 tumors, they seem to have better survival after RC suggesting that early radical cystectomy in this patient group could be beneficial.