Goblet Cell Tumors of the Appendix: Clinical & Molecular Features

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Background

- Goblet Cell tumors (GCTs) of the appendix are a rare, distinct, and under studied malignancy
- Since 2019 the preferred World Health Organization (WHO) terminology is Goblet Cell Adenocarcinoma (GCA), but previously many terms have been used to describe these tumors including Goblet Cell Carcinoid and Adenocarcinoma ex goblet cell carcinoid as these tumors have a histological appearance that blends neuroendocrine and adenocarcinoma features
- Historically goblet cell tumors have been considered one of the more aggressive subtypes of appendiceal cancer, but limited data exists and is mostly in the form of case reports
- Here we present the retrospective analysis of a large single institution cohort.

Patients and Methods

- The internal database of the University of Texas MD Anderson Cancer Center (MDACC) was queried to identify all patients diagnosed with goblet cell appendiceal tumor
- Patients were classified to two different histopathological groups, GCA (n=220) and GCA with signet ring adenocarcinoma (SRA) (n=146)
- Clinical, histopathological, and molecular data were extracted from the database in semi-automated fashion
- Survival analysis were performed using Kaplan Meier methodology

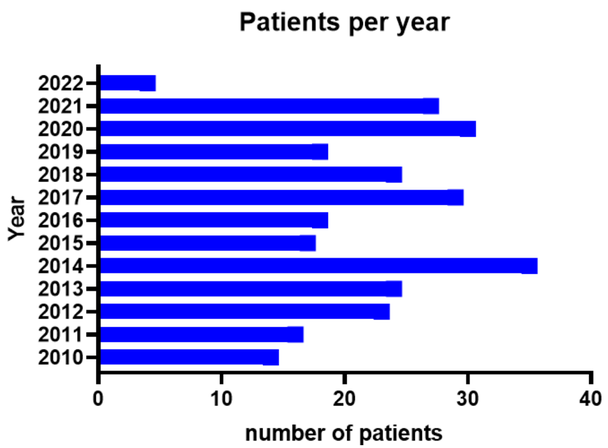

Fig 1. MDACC Goblet Cell Adenocarcinoma patients distribution by year

Results

- 366 patients with GCTs were identified from 1986 to 2022
- 132 (36%) patients were seen during the last five years, with an average of 26 patients per year
- Median follow up time was 54 months, while median age at diagnosis was 57 years
- Tumor grade data was available for 294 patients. 95% of the patients had high grade tumors (moderately, moderately to poorly and poorly-differentiated) (n= 278), and 5% had low grade tumors (well and well to moderately-differentiated (n=16)
- The median overall survival was 85 months, and significantly different between the two groups, 118 months for the GCA group and 57 months for the GCA with SRA (HR, 1.7; 95% CI, 1.2 to 2.4; p = 0.003)

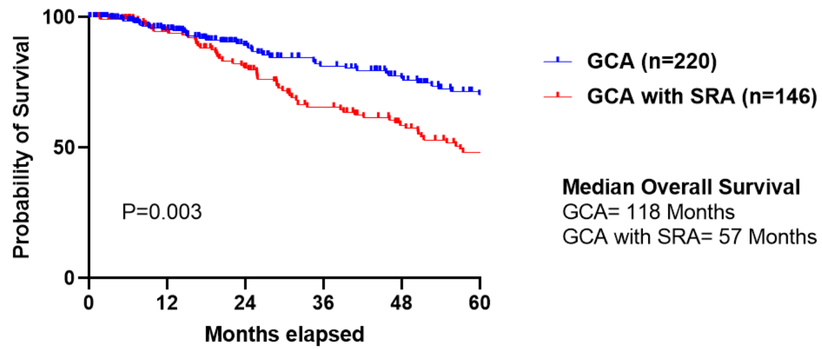

Fig 2. KM plots for patients with GCA vs GCA with SRA

- Lymph node (LN) status was known for 168 patients, rate of LN involvement was 53% (n=89) and significantly different between the two groups with 41% (n=39) for GCA and 68% (n=50) for GCA with SRA (p= <0.0006)
- The median overall survival was significantly different between the LN positive and negative patients, 84.5 months for the LN positive group and 50.6 months for the LN negative group (HR, 2; 95% CI, 1.2 to 3.2; p = 0.004)

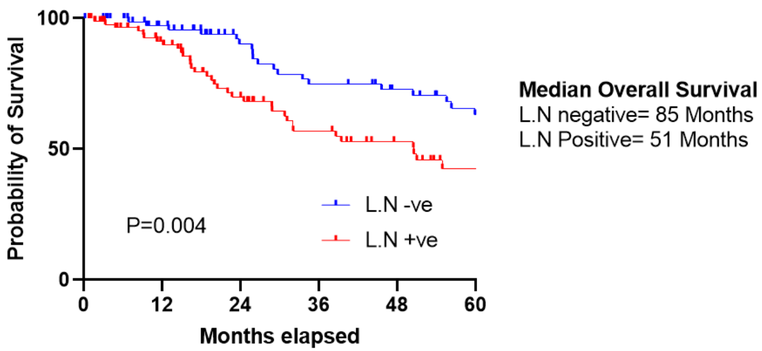

Fig 3. KM plots for patients with LN positive and LN negative status

- The internal database of MDACC was queried for LN status of Mucinous adenocarcinoma (MA) (n=242) and SRA (n=104) for comparison purposes, rate of LN positivity was 13% in MA and 76% in SRA
- By multivariate analysis, both LN status and SRA component were independent predictors of overall survival
- 107 patients had gene mutation analysis tested, TP53, SMAD4, GNAS and KRAS were the most commonly mutated with 13%, 9%, 4%, and 3% respectively

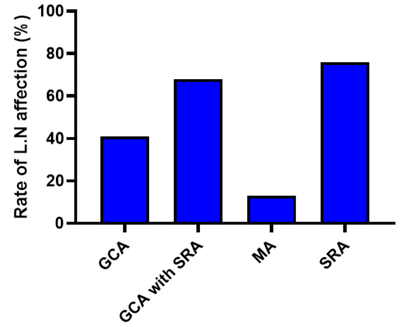

Fig 4. Rate of LN affection in different histopathological subtypes of Appendiceal Adenocarcinoma among MDACC patients

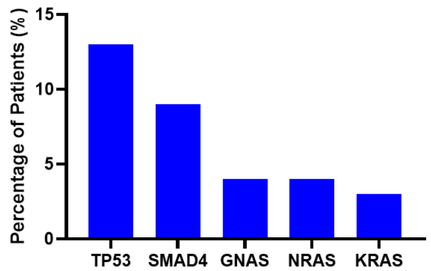

Fig 5. Most commonly mutated genes in the patients and rate of each one

Conclusions

- This study highlights the heterogenicity of GCTs of the appendix and the importance of the histopathological classification in this distinct entity. GCT are much more likely to spread to LN and have a distinct somatic mutation profile relative to MA

Acknowledgement

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