52 cases were FIGO stages I-II (42 U, 10 TO) and 73 stages III-IV (48 U, 25 TO). HMGA2 expression was seen in most U (81%) and TO (91%) CS (Fig 1). Table 1 shows significantly increased H-scores in paired CA vs SA, specifically CA of TO vs U tumors (Fig 2), as well as het+ vs het- tumors and ER- vs ER+ CA.

HMGA2 Expression in Gynecologic Carcinosarcoma Provides Evidence for Epithelial Stem-Like Cell Origin and is Differentially Expressed Based on Primary Tumor Site

Mckinzie Johnson MD[1], Marisa R. Moroney MD[2], Benjamin Bitler PhD[2], Miriam D. Post MD[1]

Departments of [1]Pathology and [2]Obstetrics & Gynecology, University of Colorado Anschutz Medical Campus, Aurora, CO *(No disclosures for any authors)*

Background

High Mobility Group AT-Hook 2 (HMGA2), a protein upregulated in many malignancies, is enriched in stem cells and regulates cell differentiation, including epithelial-mesenchymal transformation. Carcinosarcoma (CS) is an aggressive biphasic tumor containing malignant epithelial and mesenchymal components. Its origins are poorly understood, and it is not known whether differences exist between CS from the uterus versus tubo-ovarian complex.

Design

Uterine (U) and tubo-ovarian (TO) CS resected at a tertiary care center from 2008-2024 were identified and data abstracted, including patient age, primary site, presence of heterologous elements (het), ER and p53 status, and FIGO stage. HMGA2 (D1A7) immunohistochemical (IHC) staining was performed. The carcinoma (CA) and sarcoma (SA) components were scored for intensity (0, 1+, 2+, 3+) and percent positivity (0-100%), then multiplied to give an H-score. Paired t-tests compared CA and SA components. One-way ANOVA compared H-score with tumor site, het, ER and p53 status, and stage; p-values <0.05 were analyzed with a pairwise Uncorrected Fisher's LSD test. A p<0.05 was considered significant.

Results

125 CS were included (age 37-89, 90 U, 35 TO). Het+ cases included 40 U (44%) and 19 TO (54%), most commonly with skeletal muscle (n=29) and cartilage (n=26). Of 88 cases, 54 (61%) were ER+ and 34 (39%) ER-. Aberrant p53 expression was seen in 20 (100%) TO CS and 48 (83%) U CS, while 10 (17%) U CS showed wild-type staining. 52 cases were FIGO stages I-II (42 U, 10 TO) and 73 stages III-IV (48 U, 25 TO). HMGA2 expression was seen in most U (81%) and TO (91%) CS (Fig 1). Table 1 shows significantly increased H-scores in paired CA vs SA, specifically CA of TO vs U tumors (Fig 2), as well as het+ vs het- tumors and ER- vs ER+ CA.

Results

Table 1. H-score comparisons among CS tumors based on tumor site, het, ER and p53 status, and stage. A p<0.05 is considered significant.

	H-score (n)	p-value
Carcinoma component	76.3 (110)	0.013
Sarcoma component	57.5 (110)	
Tubo-Ovarian CS	109.9 (30)	0.004
Uterine CS	65.4 (78)	
Het+	89.6 (54)	0.014
Het-	51.0 (39)	
P53-aberrant	70.3 (52)	0.023
P53 wild type	13.6 (10)	
ER-negative	76.5 (21)	0.016
ER-positive	28.3 (30)	
Stage I	22.9 (20)	0.004
Stage III/IV	76.4 (43)	

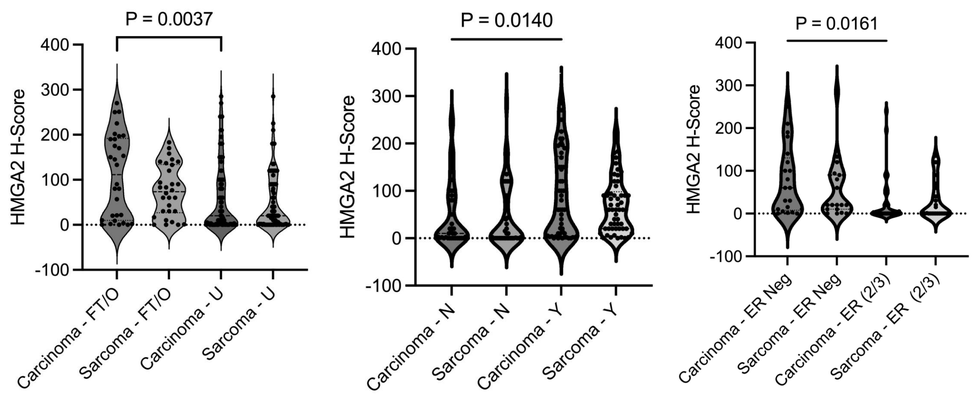

Figure 2. HMGA2 expression is elevated in carcinoma component (CA) of TO CS compared to U CS, in all CS with heterologous differentiation (N – none, Y – yes), and in CA from ER-negative tumors.

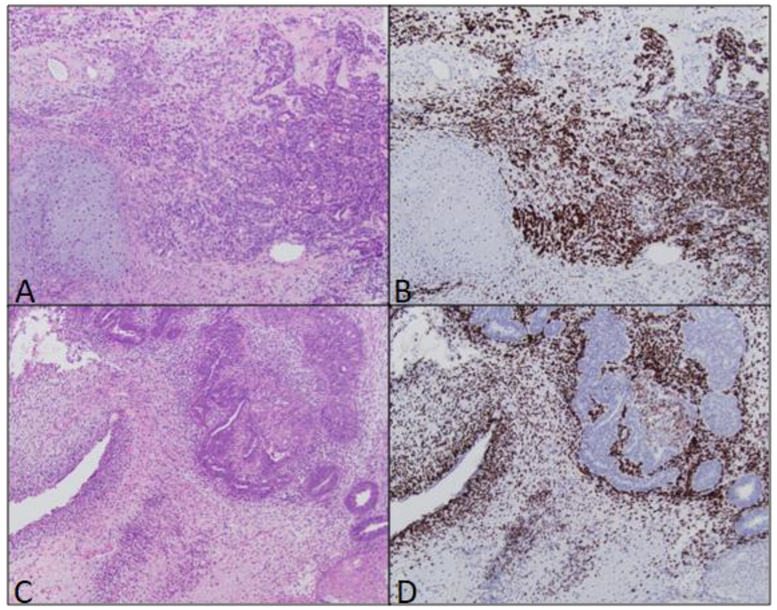

Figure 1. Tubo-ovarian CS (A- H&E, B- HMGA2, 100x) with increased staining of CA compared to SA. Uterine CS (C- H&E, D- HMGA2, 100x) with dominant SA staining in a case with low-grade carcinoma.

Conclusions

- HMGA2 is expressed in most U and TO CS, particularly in CA from tumors with aggressive features.
- Expression is higher in CA compared to matched SA, suggesting that as tumors differentiate from CA to SA, expression is reduced, supporting origination from an epithelial stem-like cell.
- The differential expression between U and TO CS suggests these tumors may have distinct differentiation pathways.
- Limitations include sample size and exclusively IHC analysis, and future investigation of the genesis of gynecologic CS is warranted.