Detection of *NCOA2/3* Gene Fusions in Uterine Tumors Resembling Ovarian Sex Cord Tumors (UTROSCT)

Andre Pinto¹, Ricardo R. Lastra², Lauren L. Ritterhouse³, Jeremy Segal², Thomas Krausz², Jennifer A. Bennett²

¹ University of Miami, Miami, FL, USA; ² University of Chicago, Chicago, IL, USA, ³ Massachusetts General Hospital, Boston, MA, USA

Background

Uterine tumors resembling ovarian sex cord tumors (UTROSCT) are rare mesenchymal neoplasms of uncertain histogenesis that are challenging to diagnose due to their morphological and immunohistochemical overlap with more conventional entities. While DNA sequencing has failed to identify recurring mutations in these tumors, RNA sequencing recently detected *NCOA2/3* fusions in two small series.

Methods

We retrospectively evaluated the clinicopathological and immunohistochemical features of two UTROSCTs, and performed RNA sequencing to detect gene fusions.

Results

The patients were 52 and 57 years old, tumors measured 5 and 12 cm, and were confined to the myometrium. Both showed multiple histologic patterns including diffuse, cord-like and trabecular, with rhabdoid cells focally present. One UTROSCT had significant cytologic atypia and brisk mitotic activity. Variable immunohistochemical expression for sex cord and epithelial markers was noted. RNA sequencing detected an *ESR1-NCOA3* fusion in one tumor, whereas the other had a *GREB1-NCOA2* rearrangement. The former patient is alive and well 5 months after diagnosis, while the latter recurred two years later, and is currently alive with disease (54 months after original diagnosis). These findings are summarized in the table below.

CASE 1: UTROSCT with *ESR1-NCOA3* fusion:

1A: gross image, 1B: H&E, 40x magnification, 1C: H&E, 200x magnification, 1D: Inhibin IHC, 200 x magnification

CASE 2: UTROSCT with *GREB1-NCOA2* fusion:

2A: H&E, 100 x magnification, 2B: H&E, 400x magnification, 2C: H&E, 200x magnification, 2D: Calretinin IHC, 200 x magnification

Case	Age	Clinical Presentation	Type of Surgery	Gross	Size (cm)	Growth Pattern	Nuclear Atypia	Mitoses /10HPF	Necrosis	LVI	IHC	Molecular	Adjuvant Therapy	Recurrence	Follow-Up
1	57	PMB	TAH, BSO	Lobulated, yellow-tan, partially whorled, firm	5.0	Sheets, cords, trabeculae	1+	3	No	No	CAM 5.2, SMA, ER, PR, WT-1, Inhibin, Calretinin	<i>ESR1-NCOA3</i>	None	No	NED 10 months
2	52	Pelvic pain	TAH, BSO	Yellow-tan, fleshy, focally hemorrhagic	12.0	Sheets, trabeculae, pseudoglandular	2+	9	No	No	Keratin, Desmin, ER, PR, WT-1, Inhibin, Calretinin	<i>GREB1-NCOA2</i>	Chemoradiation, Letrozol	Yes	AWD 54 months

PMB: post-menopausal bleeding, TAH: total abdominal hysterectomy, BSO: bilateral salpingo-oophorectomy, LVI: lymphovascular invasion, IHC: immunohistochemistry, NED: no evidence of disease, AWD: alive with disease

Conclusion

The detection of *NCOA2/3* fusions in two additional UTROSCTs further supports this rearrangement as a characteristic finding in these rare tumors. Additional studies are warranted to determine its sensitivity and specificity in UTROSCTs compared to other gynecologic neoplasms.