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**Title**

Case Report: Novel Uterine Tumor Resembling Ovarian Sex Cord Tumors-Like Lesion

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The data associated with this publication are not available for this reason: NA



# Case Report: ESR1-CITED2 Fusion in a Uterine Tumor Resembling Ovarian Sex Cord Tumor (UTROSCT)

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## BACKGROUND

- **UTROSCTs are rare** (<0.5% of all uterine malignancies and 10-15% mesenchymal uterine malignancies) and **mostly benign** uterine tumors
- **Gross:** circumscribed (non-infiltrative) myometrial mass
- **H&E:** low grade epithelioid morphology
- **Unusual immunohistochemistry:** positive for epithelial, sex cord-stromal, and smooth muscle markers, CD10, Estrogen Receptors (ER) and Progesterone Receptors (PR)
- **Translocations:**
  - Typically *NCOA1-ESR1* translocations, but can include *NCOA2*, *NCOA3*, *CTNNB1*, *NR4A3*, and *SS18*.
  - More aggressive tumors harbor *GREB1* translocation [3]

## CASE PRESENTATION: PRIMARY TUMOR

- A 21-year-old G0P0 female presented to the ER for acute, severe left abdominal pain, severe anemia, dysmenorrhea, and unintentional 15 lb weight loss over a few months.
  - **Family history:** Uterine cancer on paternal side
  - **Physical exam:** LQ tenderness to palpation, no guarding/rebound
  - **Imaging:** CT showed heterogeneously enlarged uterus with a 16.5 cm complex uterine mass, most consistent with a uterine fibroid.
  - **Tumor Markers:** Normal Human Epididymis Prot 4 (HE4), Inhibin B, Alpha-fetoprotein (AFP), hCG tumor marker, and CA125
- Patient underwent abdominal myomectomy, total abdominal hysterectomy and bilateral salpingectomy.
  - **Gross Pathology:** 18.6 cm pink-tan to yellow-tan cerebriform mass with an irregular border + surrounding myometrium (Figure 1A-B)
  - **Histology:** *myoinvasive* cellular spindle cell neoplasm with multiple architectural growth patterns including fascicular, corded, nested, and solid, and intercellular and peritumoral stroma ranging from fibroblastic to myxoid and hyalinized (Figure 1C-G)
  - **Cytology:** *Low to moderate grade nuclear atypia* with relatively scant eosinophilic to focally microvesicular cytoplasm. Low-grade cells had elongated nuclei with mildly hyperchromatic uniform chromatin, scattered pinpoint basophilic nucleoli, scattered nuclear grooves (Figure 1H). Moderate grade cells had ovoid nuclei, vesicular chromatin, prominent basophilic to eosinophilic nucleoli (Figure 1I)
  - **Mitotic activity:** very low (<1 mitotic figure/50 high power fields)
  - **Immunohistochemistry:**
    - Positive for AE1/AE3, ER, PR, WT1, vimentin, CD99, CD56/NCAM (Figure 2A-E, G, H)
    - Negative for inhibin (sex cord-stromal) and desmin (muscle) (Figure 2F)
  - **Sequencing:** **NOVEL ESR1-CITED2 fusion** (Figure 3)

## RECURRENCES

- **R1:** 15 months after surgery, patient re-presented with abdominal pain.
  - **Imaging:** MRI showed multiple R ovary and pelvic masses up to 10 cm. CT scan showed new 1.9 cm nodule in periumbilical hernia
- Surgery revealed a 13.6 cm tumor in pelvis and smaller masses in ovary, small bowel, hernia sac, and omentum
  - **Histology:** Hemorrhagic and almost entirely corded
  - **Immunohistochemistry:** Almost identical to the primary tumor except more proliferative (Ki67 5% vs <0.1% in primary tumor) (Figure 2I)
- **Treatment:** Based on the ESR1 translocation and activation of estrogen response pathways by gene expression analysis, patient was treated with the estrogen antagonist/modulator letrozole
- **R2:** CT scan performed 3 months later revealed new masses
- **Chemotherapy regimen:** carboplatin, paclitaxel, and bevacizumab
- Patient is currently alive 27 months after initial surgery (Jan 2024)

## CLINICAL IMAGES

Figure 1: Primary Uterine Tumor, 18.6 cm - Gross and Micro Histology

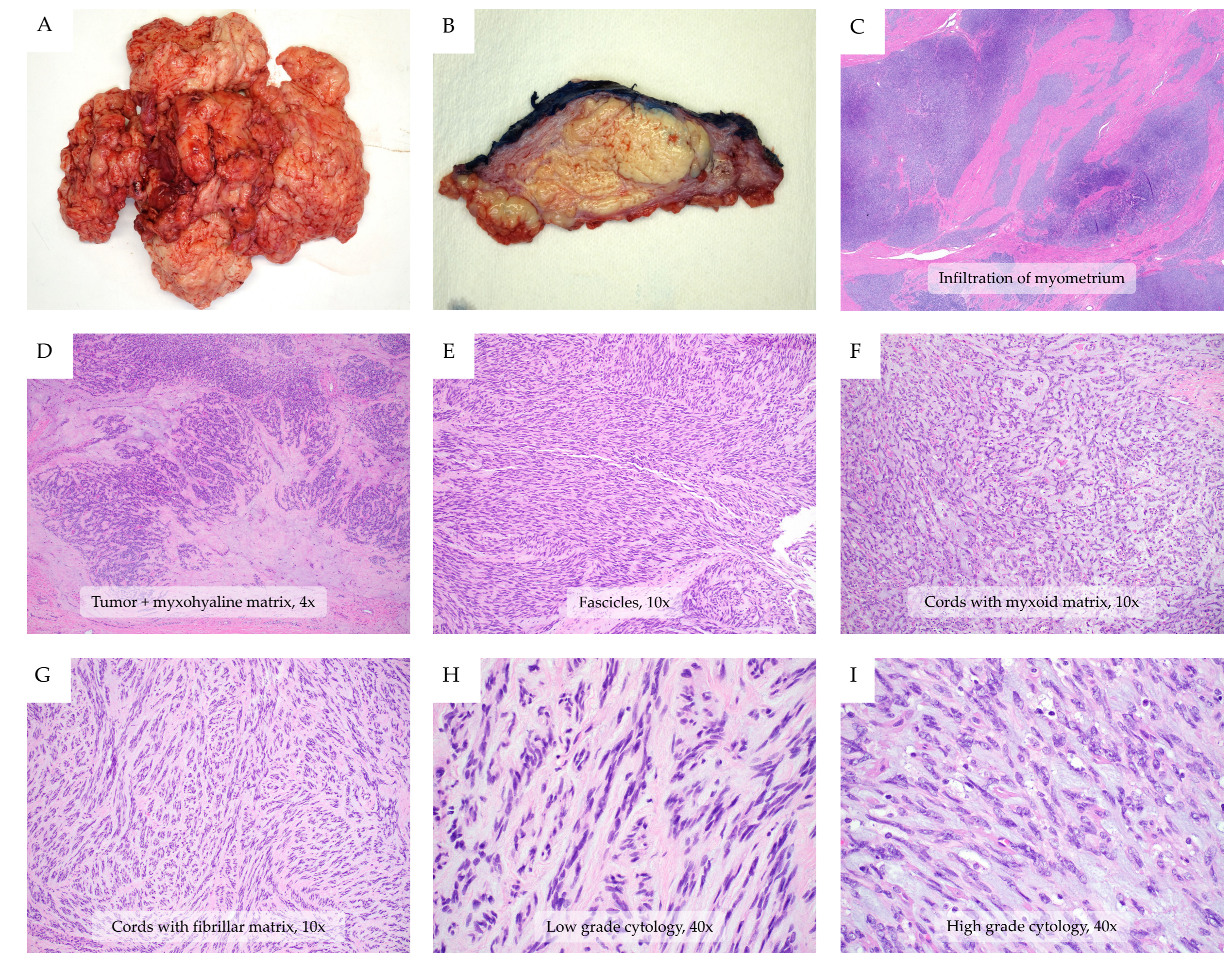


Figure 2: Immunohistochemistry

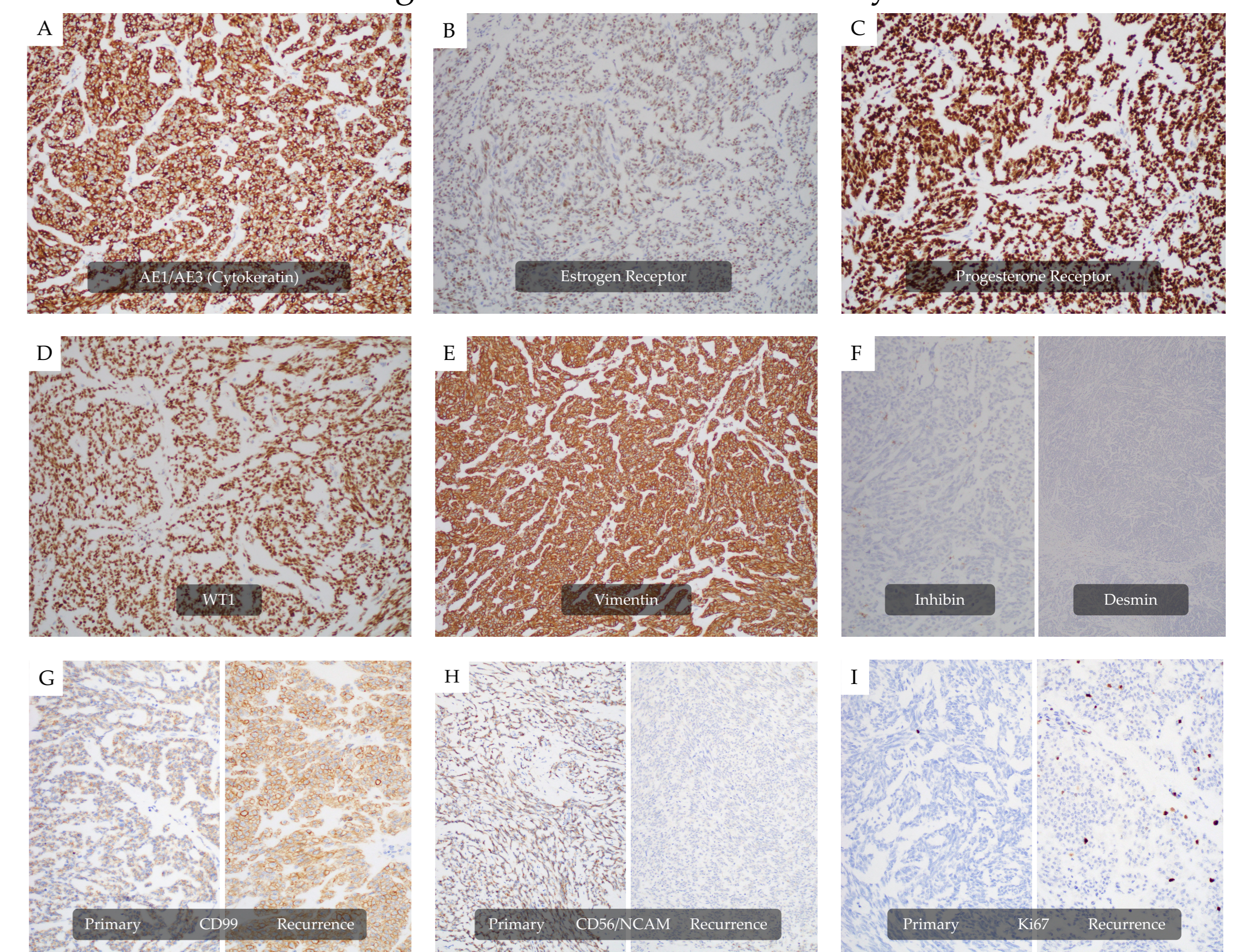
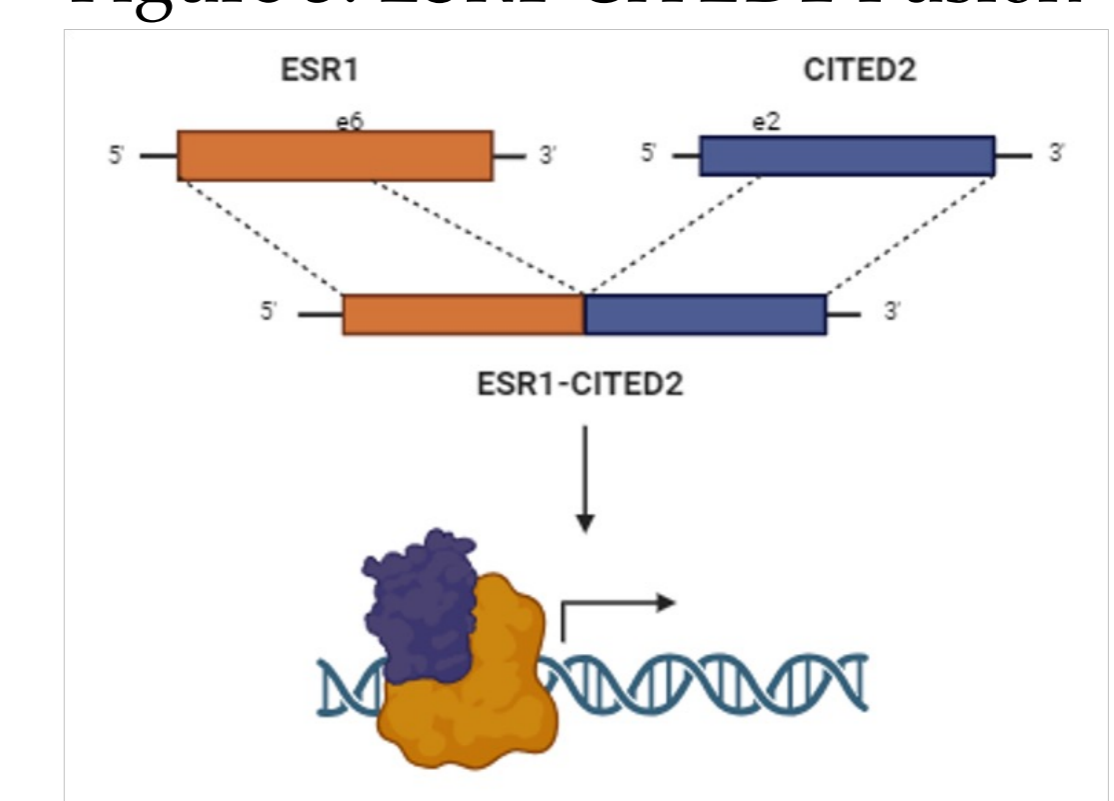


Figure 3: ESR1-CITED2 Fusion



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## CONCLUSION

- We present an infiltrative and metastatic UTROSCT with a novel *ESR1-CITED2* translocation
- *ESR1*: Estrogen Receptor 1, estrogen-activated nuclear receptor / transcription factor
- *CITED2*: p300/CBP binding protein, only rarely altered in cancer [4]
- While preparing this report, two new cases of *ESR1-CITED2* translocations reported in UTROSCT Jan 2024 [5]

**Malignant Uterine Tumor Resembling Ovarian Sex Cord Tumor (UTROSCT) variant found with extremely rare and novel ESR1-CITED2 fusion protein.**

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## References

