Low Mitotic Count May Affect the Prognosis of Uterine Leiomyosarcoma: A Report of Two Cases

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Introduction

- uLMS represents 1-2% of uterine malignancies
- Characterized by aggressive behavior and poor prognosis (5-year survival: 10-15% in metastatic disease)
- Diagnosis requires two of three Stanford Criteria:
  - Diffuse moderate-to-severe nuclear atypia
  - Coagulative necrosis
  - High mitotic rate (≥10 mitoses/10 HPF)
- Three pathological subtypes: spindled/conventional, myxoid (poorest prognosis: 11.1% five-year survival), and epithelioid
- No grading system considers mitotic index variation
- Low mitotic uLMS subset potentially misunderstood
- Treatment protocols don't account for mitotic rate
- Our cases demonstrate two low-mitotic rate uLMS patients (<10 mitoses/10 HPF)
  - Indolent disease course with long survival
  - Excellent response to hormonal therapy
  - Findings suggest mitotic rate may be critical for prognosis and treatment planning

Methods

This is a retrospective case review of two patients with uLMS with low mitotic index.

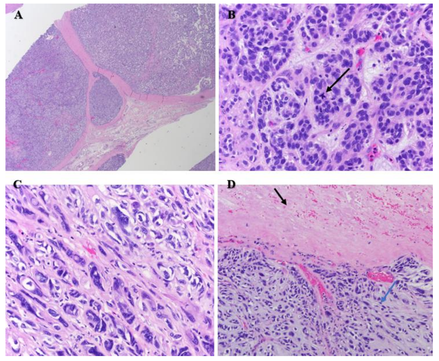

Figure 1

Case 1

- 43-year-old female diagnosed with uLMS after supracervical hysterectomy
- Pathology findings: Tumor cell necrosis, Cytologic atypia 6 mitoses per 10 HPF, Estrogen receptor (ER) positive
- Multiple recurrences requiring chemotherapy and debulking
- Recent debulking pathology showed 7 mitoses per 10 HPF
- Hormone therapy response: Disease stable on letrozole: 11 months, disease stable on tamoxifen: 26 months, currently on exemestane

Case 2

- 75-year-old female underwent a total abdominal hysterectomy and bilateral sapingo-oophorectomy
- Initially classified as a smooth muscle tumor of uncertain malignant potential, revised to leiomyosarcoma following biopsy of a pulmonary metastasis, confirming stage IVB disease.
- Pathology findings: tumor cell necrosis, cytologic atypia, and 2 mitoses per 10 HPF.
- The tumor was ER positive and she was initiated on letrozole and stable for 11 months.

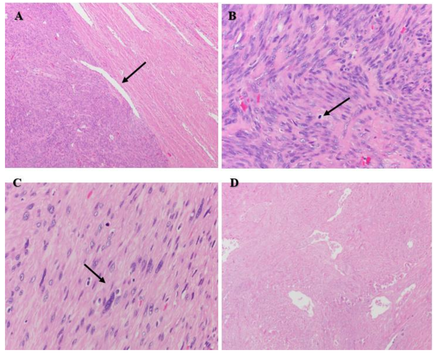

Figure 2

Figure 1. Case #1 A. Malignant mesenchymal neoplasm composed of multiple nodules of atypical spindled cells within a fibrous tissue background. B. The neoplasm is composed of nests of pleomorphic spindled to round cells with dark chromatin and occasional atypical mitotic figures (arrow). The mitotic index is measured at 7/10 high power fields. C. Area of extreme nuclear atypia. D. Areas of myxoid stromal changes (blue arrow) and large foci of tumor cell necrosis (black arrow).

Figure 2: Case #2 A. Well circumscribed neoplasm composed of intersecting fascicles of spindle cells and scattered, thin walled “staghorn” vessels (arrow). B. Marked cytologic atypia characterized by large pleomorphic nuclei with course to smudged dark chromatin. The maximum mitotic index is measured at 2/10 high power fields (arrow). No atypical mitotic figures are seen. C. The tumor cellularity is variable. Occasional bizarre (symplastic) multinucleated cells are seen (arrow). D. Focal areas of tumor-cell (geographic) necrosis are identified.

Conclusions

- Case studies demonstrate indolent progression in low mitotic index uLMS
  - Case 1: 18-year survival with hormone therapy response
  - Case 2: 11 months disease stability on letrozole
  - Both exceeded typical sarcoma survival metrics
- Evidence suggests biological diversity within uLMS classification
  - MSKCC nomogram predicted favorable outcomes (69%/75% 5-year survival)
  - Outperforms traditional staging systems
- Clinical implications:
  - Low mitotic uLMS may warrant less aggressive treatment approaches
  - Hormone therapy could be preferable to chemotherapy
  - Need for personalized treatment strategies based on mitotic index

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