Innovative Approaches to Prolong Survival: Case Studies

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Where discoveries are delivered.™
34 year-old healthy pregnant female at 8 weeks presents with abdominal pain.

- Symptoms started 6 months earlier with abdominal fullness.
- Ultrasound (A): 13.9-cm complex right adnexal mass
- MRI (B): Complex mass thought to arise from the right ovary
Differential Diagnosis

- Differential diagnosis:
  - Dermoid cyst
  - Hemorrhagic ovarian cyst
  - Leiomyoma

- Her serum CA125 tumor marker level was mildly elevated at 81 U/mL (normal, 0–34)
Specialist Referral

• After consultation with a perinatologist, she was referred to gynecologic oncology.
Operation Recommended

- At 16 weeks' gestational age, she underwent an exploratory laparotomy.
Intra-operative Findings

• Normal bilateral adnexa
• Gravid uterus
• 14 x 10-cm solid mass arising from the mid-jejunum
• No additional disease
• Mss was resected *en bloc* with the jejunum, followed by a primary anastomosis
Pathological Diagnosis

- Gastrointestinal Stromal Tumor (GIST)
  - IHC positive
    - KIT
    - DOG-1
  - Size
    - 14.0 x 10.0 x 7.0 cm
  - Mitotic rate
    - 3 per 5 mm²
## High Risk of Recurrence

### Modified NIH Criteria (Joensuu)

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Tumor size (cm)</th>
<th>Mitotic index (per 50 HPFs)</th>
<th>Primary tumor site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low risk</td>
<td>&lt;2.0</td>
<td>≤5</td>
<td>Any</td>
</tr>
<tr>
<td>Low risk</td>
<td>2.1-5.0</td>
<td>≤5</td>
<td>Any</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>2.1-5.0</td>
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<td>Gastric</td>
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<tr>
<td></td>
<td>&lt;5.0</td>
<td>6-10</td>
<td>Any</td>
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<tr>
<td></td>
<td>5.1-10.0</td>
<td>≤5</td>
<td>Gastric</td>
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<tr>
<td>High risk</td>
<td>Any</td>
<td>Any</td>
<td>Tumor rupture</td>
</tr>
<tr>
<td></td>
<td>&gt;10 cm</td>
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<td>2.1-5.0</td>
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<td>5.1-10.0</td>
<td>≤5</td>
<td>Nongastric</td>
</tr>
</tbody>
</table>

High Risk of Recurrence

MSKCC/Gold Nomogram

Adjuvant Imatinib?

Phase III randomized Scandinavian Sarcoma Group (SSG) XVIII/AIO trial

A fusion involving the N-terminus of BRAF was identified. This fused exons 9-18 of BRAF, including the kinase domain, to exons 2-9 of PRKAR1B.

Loss of the Ras-binding domain (RBD) of BRAF
Gain of a dimerization region present within PRKAR1B.
Imatinib Targets Upstream

Pantaleo et al., Cancer Medicine. 2015.
Shi et al., J Transl Medicine. 2016.
Considerations

- 12 reported cases of GIST diagnosed in pregnancy (including this one)
  - More than half of these cases were thought to be adnexal or uterine masses prior to surgery, based on imaging and clinical presentation
- Teratogenic risks of imatinib during pregnancy, including an increased incidence of congenital anomalies when given in the first trimester, but a relatively low risk to the fetus in the second and third trimesters.
Plan

- Elected for surveillance
- At 40 weeks 1 day, she presented for labor and delivered a healthy baby boy, weighing 3,634 g, via normal spontaneous vaginal delivery
- At 3.5 years postoperatively, she remains without evidence of disease
A Novel PRKAR1B-BRAF Fusion in Gastrointestinal Stromal Tumor Guides Adjuvant Treatment Decision-Making During Pregnancy

Lindsey M. Charo, MD; Adam M. Burgoyne, MD, PhD; Paul T. Fanta, MD; Hitendra Patel, MBBS; Juliann Chmielecki, PhD; Jason K. Sicklick, MD; and Michael T. McHale, MD

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- GIST can be a diagnostic dilemma in pregnancy
- Demonstrates the importance of tumor sequencing
- First reported *BRAF* fusion in GIST
- Highlights personalized approach to precision oncology that helped avoid unnecessary toxicity to the patient and fetus