Desmoid Tumors:
The Nonmalignant Malignancy

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Disclosures

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- Past President, Connective Tissue Oncology Society
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- President-Elect, ABJS
- Co-Chair NCCN ST Sarcoma Cmte
- The University of Utah is MTF Institution

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Desmoid Tumor – What Is It?

• Benign soft tissue tumor
  – Derived from mesenchymal (connective) tissue
  – Driven most commonly by a genetic aberration involving the beta-catenin or APC gene

• No metastatic potential

• Can be locally aggressive, painful, and potentially morbid
  – Locally “malignant”
  – Can malign one’s life
Tumors Derived from Fibrous Tissue

- Fibromas
- Fibromatosis – dupytren / lederhosen
- Nodular Fasciitis
- *Desmoid Tumors*
- Dermatofibrosarcoma Protuberans
- Fibrosarcoma
Desmoid Tumor – Classification

Tumor = mass
(in this case from a neoplasm)

Benign
(does not metastasize)

Indolent

Active

Aggressive

Malignant
(cancer)

Low Grade

Intermediate

High Grade

Pre-Cancerous

Desmoid Tumors
Desmoid Tumors – What Do They Do?

Concise, accurate description of behavior is difficult to make, due to their:

• Low incidence
• Variable anatomic locations
• Wide spectrum of locally aggressive behavior
Desmoid Tumor
Two Clinical Entities

1. Sporadic
   85% of desmoid cases
   More commonly occur in the extremities
   Beta-Catenin gene mutation

2. Familial Adenomatous Polyposis (FAP)
   15% of desmoid cases
   FAP desmoids are usually in the abdomen
   APC gene mutation
   People with FAP have 1000x higher incidence of desmoid than the general population
Desmoid Tumor – Presentation

Highly variable because of the highly variable nature of the tumor itself:

– Size
– Location
– Rate of growth and/or infiltration
Desmoid Tumor – Presentation

- A Bump
- Growth may be slow or rapid
- Pain may occur, from local nerve compression or rapid growth causing swelling
- Depending on location of tumor, neighboring anatomic structures may become compressed
  - Neck ➔ airway or vascular obstruction ➔ shortness of breath or lightheadedness
  - Extremity ➔ nerve compression ➔ numbness, tingling, weakness
  - Abdominal ➔ nausea, bowel obstruction
Desmoid Tumor – The Numbers

• New Cases diagnosed/year in the US: 900

• Age
  – Range: any
  – Most common: 30-50 years

• Gender
  – 2:1 female: male
  – Hormone sensitivity?
    • Higher prevalence in females
    • Growth often changes with pregnancy, menopause and oral contraceptive
Desmoid Tumor – Anatomic Locations

• Extra-Abdominal – Usually Sporadic Cases
  – 50% Limbs
  – 43% Trunk
  – 7% Head and Neck
  – 10% have multi-focal presentation

• Intra-abdominal – Usually associated with FAP
  – Patients with an intra-abdominal desmoid should be screened with colonoscopy

Merchant et al, Cancer 1999
Desmoid Tumor – Evaluation

• History and Physical
• Imaging
• Biopsy
• Team Approach

Goal:
Establish the diagnosis and develop a comprehensive plan of care
Desmoid Tumor – Evaluation

• History and Physical
  – History of the mass
    • First appearance
    • Rate of growth
  – Local symptoms
  – Systemic symptoms
  – Physical nature of the mass: mobile, firm …

• Imaging
• Biopsy
• Team Approach
Desmoid Tumor – Evaluation

• History and Physical
• Imaging
  – Ultrasound
  – Radiographs
  – MRI
  – CT
• Biopsy
• Team Approach
Examples
MRI of a 26 year old female with a desmoid tumor in the gluteal musculature
Examples

MRI of a 40 year old female with a superficial desmoid tumor of the flank
Examples
MRI of a 27 year old female with desmoid tumor of the left leg

Radiograph  Ultrasound  MRI
Examples
MRI of a 46 year old female with desmoid tumor of the right arm
Desmoid Tumor – Evaluation

- History and Physical
- Imaging
- Biopsy
  - Image-guided
  - Open
- Team Approach
Desmoid Tumor – Evaluation

- History and Physical
- Imaging
- Biopsy

- Team Approach
  - Orthopedic and General Oncologic Surgeons
  - Medical Oncologist
  - Radiation Oncologist
  - Musculoskeletal Radiologist
  - Pathologist
Desmoid Tumor
What Should We Do?

• Watch

• Medication

• Surgery

• Radiation
Desmoid Tumor – Treatment

Watch

- Watching ≠ Doing nothing
- Spontaneous Regression vs Disease stabilization vs Progression
- Spontaneous regression occurs in up to 50% of cases
- If regression occurs, average time to regression is 32 months
- Conversion to active treatment occurs in up to 50% of cases; as long as surveillance is adequate, no “bridges are burnt.”

Kasper et al, European Journal of Cancer, 21015
Park et al, Journal of Surgical Research, 2016
Desmoid Tumor – Treatment

• Will a Desmoid Progress?
  – Studies are contradictory
  – No single factor or genetic aberration has been identified to clearly predict behavior

• Potential Predictors of Progression
  – Female gender
  – Younger age at presentation (under 30-35)
  – Larger tumor size (>5-10 cm)
  – Anatomic location (extremity desmoids, particularly in hands / feet)
Many Medicine Options:

- NSAIDs
- Anti-estrogens & aromatase inhibitors
- Chemotherapy
- Targeted therapy
- Combination Therapy
Definitive and comparative response rates between medications are not available due to the small number of patients studied, variable application of medications and wide range of tumor characteristics studied.
## Desmoid Tumor – Treatment

**Medicine**

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drug</th>
<th>Regression</th>
<th>Stable Disease</th>
<th>Discontinuation Rate</th>
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<tbody>
<tr>
<td>NSAID</td>
<td>Sulindac</td>
<td>48%</td>
<td>20%</td>
<td>nr</td>
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<tr>
<td>Hormonal Therapy</td>
<td>Tamoxifen</td>
<td>58%</td>
<td>nr</td>
<td>nr</td>
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<td>Targeted Therapy</td>
<td>Imatinib</td>
<td>60-80%</td>
<td></td>
<td>15%</td>
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<tr>
<td>Chemotherapy / Chelating / Pegylation</td>
<td>Pegylated Doxorubicin</td>
<td>33%</td>
<td>67%</td>
<td>0%</td>
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</table>


Not apple-to-apple comparisons
Desmoid Tumor – Treatment

• Once considered the cornerstone of treatment, surgery is now reserved for a limited subset of tumors.

• Reports on the rate of relapse following surgical resection vary
  – Influenced by tumor characteristics and ability to excise the entirety of the tumor.

Melis et al, JCO, 2008
Recurrence rate after surgery based on extent of residual demonstrable disease

<table>
<thead>
<tr>
<th>Study</th>
<th>“Clean” Surgical Margins</th>
<th>Microscopic (+) Margins</th>
<th>Macroscopic (+) Margins</th>
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<tbody>
<tr>
<td>Spear et al</td>
<td>23%</td>
<td>44%</td>
<td>50%</td>
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<tr>
<td>Posner et al</td>
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<td>55%</td>
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<td>Merchant et al</td>
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<td>22%</td>
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<tr>
<td>Gronchi et al</td>
<td>23%</td>
<td>26%</td>
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Desmoid Tumor – Treatment

- Radiation can be used alone or as an adjunct to surgery
- Isolated radiation can control disease progression in 78% of cases
- Radiation following surgery has produced contradictory results
- Doses of 50-60 Gy are required
  - Can have unwanted side effects / risks, particularly in young patients with decades of life remaining

MRI guided Ultrasound Ablation

• MRI is used to determine the depth / width of the tumor, allowing ultrasound to be focused on the tumor, sparing neighboring tissues.

• Ultrasound increases micromotion within the tissue, resulting in a focused increase in energy – which manifests as heat

• Heating of the desmoid to 50-80 degrees C may cause tissue death

• Early reports (18 total patients) have demonstrated the ability of this ablation to reduce both total tumor volume and viable tumor volume

• In the report by Ghanouni, Tumor Volume decreased 39 -100%, but follow up was limited (5-39 months) due novelty of the technique
Diagnosis
Evaluation by a Multi-disciplinary team

Watchful Waiting
Repeat Exam
Repeat Imaging

Medication
NSAIDs
Hormones
Targeted Rx
Chemotherapy

Surgery
Symptomatic and/or resectable disease

Radiation
Alone for unresectable disease or Adjuvant to surgery

Ablation
Emerging technique for appropriate cases

Desmoid Tumor
A Multi-Disciplinary Approach
Additional References

Review Articles and General Clinical Guidelines


Desmoid Tumor and Familial Adenomatous Polyposis


Studies Investigating Desmoid Response to Medicine


Radiation


Ultrasound Ablation of Desmoid Tumors

• Bucknor MD, Rieke V. MRgFUS for desmoid tumors within the thigh: early clinical experiences. J Ther Ultrasound. 2017 Feb 3;5:4


Biology of Desmoid Tumors


Thanks for your Attention!