Beyond Abdominal, Extra-abdominal and Intra-abdominal Desmoid Tumors

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Disclosure slide

• Novartis speakers bureau for GIST
• Ad hoc consultant for Amgen, Ziopharm
• Clinical research funding from AB Science, Amgen, Janssen, SARC, Threshold, Ziopharm
Desmoid tumor / Aggressive fibromatosis

- Clonal fibroblastic proliferation
- No metastatic potential
- Share features with MSC
- 2-4 cases/million/yr
- Peak incidence 30-40 yrs of age
- Risk factors
  - APC mutation in germ-line
  - Pregnancy
  - Trauma
Desmoid tumor by location

- Abdominal wall
  - Most common in pregnancy
  - Women >> men
Desmoid tumor by location

- Extra-abdominal
  - Shoulder/limb girdle, chest wall, head/neck
  - Most common location in children
Desmoid tumor by location

- Intra-abdominal
  - Mesenteric & pelvic involvement
  - More common in Gardner’s syndrome
Desmoid tumor by patient group

- Genotype: APC / Beta-catenin mutation
- Pregnancy-associated
- Age group: childhood/adulthood
- Unifocal/Multifocal
Familial adenomatous polyposis and DT

- Gardner’s syndrome
  - Polyposis coli, desmoid, osteomas, epidermoid cyst, Gardner fibroma, hypertrophy of retinal pigmented epithelium, thyroid cancer

- 10-20% lifetime risk of desmoid

- Desmoid incidence 1000x greater in FAP than non-affected populations

- 5-10% of pts with desmoid have APC mutation

- APC mutation downstream of codon 1400
Genotype and phenotype factors as determinants of desmoid tumors in patients with familial adenomatous polyposis

- Mutation beyond codon 1444
- Family history of desmoid
- Female
- Osteomas

Cumulative lifetime risk of desmoid

Bertario L et al.  
*International Journal of Cancer*  
Volume 95, Issue 2, pages 102-107, 27 FEB 2001
DT in Gardner’s syndrome

- **Location**
  - 50% abdominal wall
  - 20-30% mesentery
  - 10-20% extra-abdominal

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**Mortality of Intra-Abdominal Desmoid Tumors in Patients With Familial Adenomatous Polyposis: A Single Center Review of 154 Patients.**

Quintini, Cristiano et al.

**A Nation-wide Study Comparing Sporadic and Familial Adenomatous Polyposis-related Desmoid-type Fibromatoses**

Nieuwenhuis, MH et al.

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Log rank $P = 0.0001$
DT and pregnancy

- Occur during pregnancy and within 6-36 months post-partum
- Median age 30 yrs
- Rectus abdominus most common location (>50%) followed by mesentery
- 10-15% of desmoids
- Infrequently associated with FAP
DT and pregnancy

- Often treated by resection
  - Recurrence <15%
- High rate (>50%) of growth during pregnancy
- 10-20% spontaneous regression
- Very low risk of mortality
- Subsequent pregnancy safe in majority
- Pregnancy not contraindicated in FAP-associated desmoid

Fiore M et al.
Ann Surg. 2013

Robinson WA et al.
Desmoid tumors in pregnant and postpartum women.
Cancers. 4:184-192. 2012

Church JM and McGannon E.
Prior pregnancy ameliorates the course of intra-abdominal desmoid tumors in patients with familial adenomatous polyposis.
DT and pregnancy – 4 institution study

<table>
<thead>
<tr>
<th>TABLE 4. Available Data for Counseling in Women Affected by Sporadic DF</th>
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</thead>
<tbody>
<tr>
<td>New diagnosis of DF during or shortly after pregnancy</td>
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<tr>
<td>Risk of relapse after complete resection</td>
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<tr>
<td>Risk of progression with watchful waiting</td>
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<tr>
<td>Spontaneous regression</td>
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<tr>
<td>Risk of failure after any first active treatment (initial or delayed until the time of progression)</td>
</tr>
<tr>
<td>Overall managed without resection</td>
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<tr>
<td>Pregnancy after previous diagnosis of DF</td>
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<tr>
<td>Risk of DF recurrence/progression</td>
</tr>
<tr>
<td>DF recurrence/progression safely managed with either active treatment or watchful waiting</td>
</tr>
<tr>
<td>Multiple lines of active treatments needed for progression</td>
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<tr>
<td>Spontaneous regression was described after progression as well</td>
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<tr>
<td>Obstetric risk</td>
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<tr>
<td>Obstetric complications related to DF in both mother and fetus</td>
</tr>
<tr>
<td>Intra-abdominal/pelvic DF should be anyway considered at higher risk (few data available)</td>
</tr>
<tr>
<td>Cesarean delivery to be considered in case of macroscopic DF in particular anatomic sites</td>
</tr>
<tr>
<td>Postpartum incisional hernia after previous abdominal wall full-thickness mesh repair is an issue</td>
</tr>
</tbody>
</table>

Fiore M et al.  
Ann Surg. 2013  
18-19 February 2014, Milan, Italy
Spontaneous Regression of Primary Abdominal Wall Desmoid Tumors: More Common than Previously Thought

Sylvie Bonvalot, MD, PhD¹, Nils Ternès, MS², Marco Fiore, MD³, Georgina Bitsakou, MD¹, Chiara Colombo, MD³, Charles Honoré, MD¹, Andrea Marrari, MD⁴, Axel Le Cesne, MD⁵, Federica Perrone, MD⁶, Ariane Dunant, MS², and Alessandro Gronchi, MD³

- 147 patients
- 97% female
- 25% associated with pregnancy
- 28% spontaneous regression
- 16% managed by observation or drug therapy required surgery
- Size >7 cm associated with change in management
DT in childhood

• Median age 11
• Equal sex distribution
• Location
  – Extremity 50%
  – Head/neck 30%
  – Chest wall/trunk 15%
  – Intra-abdominal 5%
• 5-yr EFS 35-45%
  – 77% R0
  – 30% R1
  – 35% observation

Honeyman, JN et al.
Desmoid fibromatosis in children and adolescents: a conservative approach to management.
Meazza, C et al.
Aggressive fibromatosis in children and adolescents: the Italian experience
Skapek, SX et al>
Vinblastine and methotrexate for desmoid fibromatosis in children: results of a Pediatric Oncology Group phase II trial.
Survival in childhood DT

Oudot, C et al.
Desmoid fibromatosis in pediatric patients: management based on retrospective analysis of 59 patients and a review of the literature.
DT recurrence risk

Crago, AM et al.
A prognostic nomogram for prediction of recurrence in desmoid fibromatosis
Multifocal DT

- 1\textsuperscript{st} reported by HM Barber in 1973
- Most often confined to same anatomic region
- May be synchronous or metachronous
- <5% of patients with desmoid
- No identified risk factors for multifocal versus unifocal disease
- No clear difference in management strategy
Summary

- DT have variable natural history
- Consider context in which DT arises
- Watch and wait strategy is gaining traction
- Spontaneous regression common in pregnancy and abdominal wall DT
- Consider presenting symptoms and long-term impact of intervention in management decisions