Practical Approach to Desmoid Tumours

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Objectives:

- To appreciate the evolving treatment of desmoid tumours – from surgical disease to multidisciplinary condition
- To describe a surgical approach to desmoid tumours based on their biologic aggressiveness
Classification of Soft Tissue Tumors

- Locally recurring ST neoplasm with little or no metastatic potential
- Sarcomas with metastatic potential of LESSER aggressiveness
- Aggressive Sarcomas
Locally Recurring Soft Tissue Neoplasms with Little or No Metastatic Potential

- Desmoid Tumour
- Atypical Lipomatous Tumour
  - Low grade liposarcoma
- Dermatofibrosarcoma protuberans
  - (DFSP)
Definition

• **Synonyms** – musculoaponeurotic fibromatosis, deep fibromatosis, aggressive fibromatosis, desmoid tumor, well-differentiated nonmetastasizing fibrosarcoma, grade I fibrosarcoma

• Locally aggressive, histologically benign neoplasms with unpredictable growth, invasion, and symptoms including pain, deformity, dysfunction, and possible death

• No metastatic potential; do not de-differentiate

Weiss and Goldblum Soft Tissue Tumors 2001
Schajowicz et al Cancer 1995;75:1208-14
Presentation

- Incidence 2-4/ million/ yr

- Present as a **mass** in general locations
  - Intra-abdominal/ Mesenteric (5-10%)
  - Abdominal wall (20%)
  - Extra-abdominal – limb, chest, breast, neck (65-70%)

- Young adults, peak incidence 30 years, 2/3:1/3 female: male gender distribution, majority are solitary (5% multicentric), majority are sporadic (95-98%)

Etiology

• Unclear
• Trauma, especially surgical trauma
• Hormonal – 2/3 female, may grow during pregnancy

• Genetic – Familial Adenomatous Polyposis
  • Aka Gardner’s syndrome
  • 1/5 patients with FAP will develop desmoid tumours
  • 1000 x greater than population
  • ≈2 years after surgery; median age 30; usually intra-abdominal

Evaluation

- **History**: lump or swelling
  - growth plateau, regression
  - location specific symptoms

- **Physical Examination**: size, superficial vs. deep
  - neurovascular evaluation, deficits

- **Investigations**: plain radiographs, U/s to confirm mass
  - CT or MRI to define location, margins, relation, heterogeneity

Guglielmi et al Radiol Med 2009;114:1292-1307
Biopsy Approach

• Image directed core biopsy
  • Multiple samples sufficient to make diagnosis in 90% of STS

• Incisional biopsy
  • Same principles as STS

• Excisional biopsy
  • Unusual since deep

• Review by expert soft tissue pathologist
  • Well-differentiated intertwining fibroblasts in bundles with abundant collagen matrix

Welker et al Cancer 2000;39:2677-86
Hoeber et al Ann Surg Oncol 2001;8:80-7
Surgical Principles

- Treatment should be tailored – consider multidisciplinary input up front
- **Ideal** – surgical resection with wide (1-2 cm) gross margin/ pathologically clear margins
- Many **caveats**
  - Surgical resection may not be possible/ feasible
  - Surgical resection may not be possible with negative margins without major disability
  - Role of microscopic margins not clear cut
Biology...?

When is a Neoplasm not a Neoplasm?
When it is a Desmoid

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The Enigma of Desmoid Tumors

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Optimizing Treatment of Desmoid Tumors


INDIVIDUALIZING MANAGEMENT OF AGGRESSIVE FIBROMATOSES

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Desmoid-Type Fibromatosis: A Front-Line Conservative Approach to Select Patients for Surgical Treatment

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Biology...?

- Well described variation in growth
  - 50% have period of stability
  - 30% cycles of progression / stability
  - 10% rapidly progress
  - 10% regress/ resolve

- Key study – 198 pts, 68 pts with recurrent desmoid tumours were followed
  - Median f/u 6 yrs; 60 stable, 6 regressed
  - Stability of lesion considered a ‘success’

Church JM Semin Colon Rectal Surg 1995;6:29-32
• MD Anderson – comparison of 189 pts from 1965-94 with 189 pts from 1995-2005

• Trends in 2nd compared to 1st time period
  • Increased multimodal therapy
  • Less reliance on surgery alone
  • Higher rates of macroscopic residual disease and equivalent positive margins
  • 5 yr local recurrence 20% vs. 30%
  • More patients had radiation alone (9) or systemic treatment alone (29) – all have remained alive with at least stable disease
  • A subset refused treatment

Milan Series - since 2003, all patients initially recommended a conservative approach (non-operative; no RT)

- 142 pts (74 primary, 68 recurrent)
  - 83 pts had wait and see approach (W&S)
  - 59 pts offered medical therapy (MT)

- 5 year PFS - 49.9% (W&S), 58.9% (MT)

- Multivariate analysis did not identify predictors of stability or regression

- Overall, 1/2 avoided any treatment; 2/3 of pts avoided surgery

Summary

- Paradigm shift – from a ‘cancer’ paradigm to a ‘chronic’ condition
- Stability may be a success
- Period of observation warranted

- Role of alternate agents and primary irradiation underappreciated
- Surgery still has a major role

Zippel, Temple J Surg Oncol 2007;95:190-1
Surgical Approach/ Principles

- Ideally treatment should be tailored - consider multidisciplinary input up front
- Ideal – surgical resection with wide (1-2 cm) gross margin/ pathologically clear margins
- Many caveats
  - Surgical resection may not be possible/ feasible
  - Surgical resection may not be possible with negative margins without major disability
  - Role of microscopic margins not clear cut
- Need to start somewhere…. 
Surgical Approach/ Principles

- Consider resection alone when feasible
  (i.e. easy)

46 y.o. female
4 month hx of painless mass
2.5x1.5cm
Local Recurrence/Surgery Alone

- Review 22 series, 381 pts - 1983-99
  61% overall local control rate - 72% m-; 42% m+
  45% overall local control rate

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<thead>
<tr>
<th>Series</th>
<th>Patients (#)</th>
<th>Local Control (5 yr) (%)</th>
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<tr>
<td>MD Anderson</td>
<td>122</td>
<td>66</td>
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<tr>
<td>Milan</td>
<td>198</td>
<td>73</td>
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<td>MSKCC</td>
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• Outcomes influenced by location, proximity to vital organs, and association with FAP

• Significance of positive margins – review of 23 studies
  • Most older studies suggest higher LR with microscopically positive margins; Larger more recent publications have challenged this assumption
  • Local recurrence itself doesn’t predict uncontrolled tumor growth

• Options may include re-resection, adjuvant radiation or close follow-up

• If a desmoid has ‘stopped’ growing, margin status becomes less critical, especially if function / QoL may compromised

Prognostic Features

- Prior recurrence predicts worse outcome
- Age (\(\leq 30\) yrs worse than \(>30\))
- Surgery alone worse than combined therapy
- Size \(>5\text{cm} >8\text{cm}\)
- Difficult sites – intra-abdominal vs. extra-abdominal or abdominal wall
  - Calf, foot, supraclavicular fossa, popliteal fossa, buttock

Nuyttens et al Cancer 2000;88:1517-23
Catton et al Radiother Oncol 1995;34:17-22
Surgical Approach/Principles

- Consider alternate modalities if not feasible or too disabling

16 y.o. female
2 year hx of slowly growing mass
15x5x3cm; on sciatic nerve
Surgical Approach/Principles

- Consider alternate modalities if not feasible or too disabling

18 y.o. male
U/s screen for polycystic kidneys
Large pelvic mass
11.7x11x9.4cm
Surgical Approach/Principles

- Consider alternate modalities if not feasible or too disabling

52 y.o. female
Presented with anemia and abdominal mass
Root of mesentery encasing sma/smv
Alternate therapies include:

- Anti-inflammatories, tamoxifen, irradiation as primary treatment, cytotoxic chemotherapy....
Alternate Therapy

- **Tamoxifen/ anti-inflammatories**
  - 20-30% overall response rate but stable in 40-50%
  - Sulindac – 10-30% - often in combination

- **Cytotoxic chemotherapy**
  - 68 patients – median age 32; 2/3 female; 53% had an intrabdominal tumor; 1/3 had Gardner’s; range of surgeries (1-5)
  - 50% had tumors >10 cm; 5 were multifocal
  - Median of 2 lines of chemotherapy (1-7)
  - Best responses with anthracycline agents (35-60%)
  - Vinblastine/ MTX – 30-40%; Imatinib 5-16%
  - Overall – 21% partial response and 15% progressed
  - Progression-free survival – 12 months
  - Median survival – 13 years (FAP); 90% 10-20 year sporadic
Surgical Adjuncts?

- Insertion of spacer to facilitate irradiation
- Bypass surgery, control of perforation

Surgical Approach/Principles

• Is there an operation? Is it possible to get ‘good’ margins?

60 y.o. female with progressive, painful mass
7x6.8x2.3 cm involving 6-8th ribs
Surgical Approach/Principles

- Is there an operation? YES
- Is it possible to get ‘good’ margins? Difficult
- Patient had preoperative chemoradiation, wide resection including chest wall, reconstruction with alloderm, latissimus flap

Surgical Approach/Principles

• Is there an operation? Is it possible to get ‘good’ margins?

43 y.o. female with
initially asymptomatic
RLQ mass
7.7x5.1x5.8 cm mass in
mesentery
Right hydroureter; intimate
with iliac vessels
Surgical Approach/ Principles

- Is there an operation? Yes
- Is it possible to get ‘good’ margins? Unlikely
- Patient had preoperative irradiation (50 Gy) with use of spacer
- Surgery included Rt colectomy, Rt nephrectomy, Iliac vessel resection/ replacement
Surgery as part of Multimodal Treatment

- Review 22 series, 381 pts - 1983-99
- Surgery alone - 61% local control (72m-; 41m+)
- Surgery + radiation - 75% (94m-; 75m+)
- Primary radiation - 78%

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Comments – differing definitions of local control for primary surgery and primary irradiation; in general patients receiving adjuvant radiation were worse

Preoperative Radiation
- less commonly used – 7 pt series

Ballo et al J Clin Oncol 1999;17:158-167
Surgery as part of Multimodal Treatment

- Cancer Centre Review - 52 patients - 1990-2008
- 52 patients (40 female, 12 male) - 45 month f/u
- Overall - 39 had surgery; 13 non-operative

- Tamoxifen/ NSAID (all after 2001) -
  - 16 pts - 6 stable, 1 PR, 1 CR, 6 progressed - 50% success

- 9 surgery alone - 78% (7/9) control

- Preoperative Chemoradiation and Surgery
  - 30 patients - 90% local control rate

• Trial of observation should be standard to determine the underlying growth pattern/biology

• Hormonal therapy and anti-inflammatories may be considered early with stabilization considered a success
• Beyond this, surgery is a key component of the **multidisciplinary care** of desmoid tumours

• Surgery alone when feasible (...easy, although rare)

• Avoid surgery or use surgery in a supportive fashion (i.e. facilitate RT) when not feasible or will result in major disability or disfigurement

• As a component of multimodal treatment (reserve most aggressive treatment for more aggressive biology)