Desmoid Fibromatosis Tumors: The Role of Surgery

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Visible / Palpable
Visible / Palpable
Invisible
Analysis of treatment situation

- Most often patients start at their general practitioner
- Growing lump is excised, then desmoid is detected
- Large (sarcoma-like) tumors or those located in the rectus abdominis muscle show up at centers more often
- After receiving the diagnosis > internet
Analysis of treatment situation in Germany

- 237 patients (160 females, 76 males, ratio 2.11)
- Median age: 37.4 years
- Delay until first doctor consultation: 77 days
- Remember trauma at desmoid site: 56%
- Primary diagnosis desmoid suspected: 24%
- Histologically correct diagnosis after 1st operation: 88%
Analysis of treatment situation in Germany

- Primary therapy: 157 patients
- Surgery 82%
- 1.7 operations/patient
- R0 resection rate: 29.5%
- R1 resections: 48%
- R2 resections: 13.5%
- Recurrence rate: 63%
- Radiation therapy: 42%
Sometimes: Does operation make sense?
Analysis of treatment situation

- 2.4 to 4.3 new cases per $10^6$ inhabitants/year
- Star shape tumors, devoid of a capsule, invade surrounding structures
- Wide range of local failure rates $>>$ great variability of accrual, treatments and follow-up
- Impact of surgical margins after excision remains unclear
- Biology of the different desmoid types not well characterized
- Discrepancies between the results of the impact of the quality of surgery
Rectus abdomins: resectable
Standard chest wall replacements

Goretex membrane
Vicryl - mesh
Marlex-mesh (Prolene)
(Lyodura)
Omentum + Meshgraft
Chestwall & abdominal wall wall reconstruction

Principles

- Function > aesthetics
- Wound closure mandatory
- Avoid fluid accumulation
- Wound infection detrimental if allografts implanted
Disease-free survival according to the quality of surgery

Bonvalot et al. EJSO 2008
Neck region: not R0 resectable
Radiation therapy postoperatively mandatory!
<table>
<thead>
<tr>
<th>Authors</th>
<th>Institution/Town</th>
<th>Period</th>
<th>N patients</th>
<th>Local recurrences</th>
<th>Progressions</th>
<th>Impact margins</th>
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</thead>
<tbody>
<tr>
<td>Philipps</td>
<td>Royal Marsden</td>
<td>86-03</td>
<td>109</td>
<td>20% 3 years</td>
<td>P+R</td>
<td>No</td>
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<tr>
<td>Posner</td>
<td>MSKCC</td>
<td>65-84</td>
<td>138</td>
<td>20% 2 years</td>
<td>P+R</td>
<td>Yes</td>
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<tr>
<td>Merchant</td>
<td>MSKCC</td>
<td>82-97</td>
<td>189</td>
<td>20% 2 years</td>
<td>P+R</td>
<td>No</td>
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<tr>
<td>Sorensen</td>
<td>Arhus</td>
<td>70-98</td>
<td>72</td>
<td>27% 5 years</td>
<td>P</td>
<td>Yes</td>
</tr>
<tr>
<td>Pignatti</td>
<td>Bologne</td>
<td>70-96</td>
<td>83</td>
<td>44% 2 years</td>
<td>P+R</td>
<td>Yes</td>
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<tr>
<td>Spear</td>
<td>Harvard</td>
<td>71-92</td>
<td>107</td>
<td>S RT S+RT</td>
<td>P</td>
<td>Yes</td>
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<tr>
<td>Goy</td>
<td>UCLA</td>
<td>65-92</td>
<td>61</td>
<td>R0 R1 S+RT</td>
<td>P</td>
<td>Yes</td>
</tr>
<tr>
<td>Gronchi</td>
<td>Milan</td>
<td>65-00</td>
<td>203</td>
<td>Primary: 25% 10 years</td>
<td>P+R</td>
<td>No</td>
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<tr>
<td>Lev</td>
<td>MDA</td>
<td>95-05</td>
<td>189</td>
<td>20% 5 years</td>
<td>P+R</td>
<td>Yes</td>
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<tr>
<td>Bonvalot</td>
<td>IGR</td>
<td>88-03</td>
<td>112</td>
<td>R0 35% 3 years</td>
<td>P</td>
<td>Yes</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No surgery/no RT 30% 3 years</td>
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</tbody>
</table>
**Surgery versus radiation therapy for patients with aggressive fibromatosis or desmoid tumors: Review of 22 articles**

<table>
<thead>
<tr>
<th>Year</th>
<th>Surgery alone</th>
<th>Surgery + RT</th>
<th>RT</th>
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<tr>
<td>1983</td>
<td></td>
<td></td>
<td></td>
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<td>1998</td>
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<table>
<thead>
<tr>
<th>Margins</th>
<th>-</th>
<th>+</th>
<th>overall</th>
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<tbody>
<tr>
<td>Surgery alone</td>
<td>72%</td>
<td>41%</td>
<td>61%</td>
</tr>
<tr>
<td>Surgery + RT</td>
<td>94%</td>
<td>75%</td>
<td>75%</td>
</tr>
<tr>
<td>RT</td>
<td>75%</td>
<td>78%</td>
<td></td>
</tr>
</tbody>
</table>

- RT or S + RT results in significantly better local control than S
- Even after dividing the groups into cases with +/-margins and primary and recurrent T: the best local control is achieved with RT or S + RT

LOCAL CONTROL
Fibromatosis meta-analysis

Free margins
Surgery
S + RT
RT

Positive margins

Unknown margins
Surgery
S + RT
RT
R0 surgery hardly feasible without major morbidity
Does it really need therapy?

Recurrent fibromatosis after surgery
No change 5 years later
If progressive: isolated limb perfusion

Primary fibromatosis (surgical biopsy)
No change 6 years later
A possible role for isolated limb perfusion with tumor necrosis factor-alpha and melphalan

<table>
<thead>
<tr>
<th></th>
<th>N patients</th>
<th>RR</th>
<th>CR</th>
<th>PR</th>
<th>Local progression</th>
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</thead>
<tbody>
<tr>
<td>Lev- chelouche</td>
<td>6</td>
<td>83%</td>
<td>33%</td>
<td>50%</td>
<td>2</td>
</tr>
<tr>
<td>(Surgery 1999C)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(Follow up 45</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>months)</td>
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<tr>
<td>Grunhagen</td>
<td>12</td>
<td>75%</td>
<td>17%</td>
<td>58%</td>
<td>?</td>
</tr>
<tr>
<td>(EJSO 2005)</td>
<td></td>
<td></td>
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</tbody>
</table>
Disease-free survival according to the quality of surgery

Bonvalot et al. EJSO 2008
Soft tissue sarcomas: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

P. G. Casali¹, L. Jost², S. Sleijfer³, J. Verweij⁴ & J.-Y. Blay⁵
On behalf of the ESMO Guidelines Working Group

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desmoid-type aggressive fibromatosis

Standard treatment for primary disease, if amenable to surgery without significant functional losses, is wide excision [IV, B]. In those cases in which only marginal excision can be performed, postoperative radiation therapy is an option, after sharing the decision with the patient in conditions of uncertainty, considering the possible occurrence of radiation-related high-grade sarcomas in a non-metastasizing disease. Observation is another option in selected cases, after shared decision-making with the patient, taking into account the indolent natural history of some clinical presentations.

For primary disease only amenable to surgery with significant functional losses, wide excision is an option, along with radiation therapy, observation, isolated limb perfusion (if the lesion is confined to an extremity) or systemic therapy (see below) [V, D]. The same applies to recurrent disease.

For the inoperable disease, radiation therapy, ILP (if the lesion is confined to an extremity), and systemic therapies are options, along with observation [V, D]. Systemic therapies include: hormonal therapies (tamoxifen, toremifene, Gn-RH analogs) ± NSAIDs; low-dose chemotherapy, such as methotrexate + vinblastine or methotrexate + vinorelbine; low-dose interferon; imatinib; full-dose chemotherapy (using regimens active in sarcomas). It is reasonable to employ stepwise the less toxic therapies before the more toxic.
Desmoid Tumors

WORKUP

- All patients should be managed by a multidisciplinary team with expertise in sarcoma
- H&P including evaluation for Gardner's Syndrome (See NCCN Colorectal Screening Guidelines)
- Chest imaging
- Appropriate imaging of primary site with CT or MRI as clinically indicated

PRIMARY TREATMENT

Resectable → Surgery^b^ → R1 → Observation or Consider postoperative RT if large tumor
Consider reresection or RT, if no prior RT or Observation

Resectable → Surgery^b^ → R1 → Observation

Unresectable or surgery would be unacceptably morbid

Biopsy^a^ → Observation

RT or Systemic therapy^c^ or Radical surgery to be considered if other modalities fail or Observation

Evaluation for Rehabilitation (OT, PT)
- Continue until maximal function is achieved
- H&P with appropriate imaging every 3-6 mo for 2-3 y, then annually

Recurrence, treat like primary disease

^a^ May not be necessary if complete resection planned.
^b^ For desmoids, microscopic positive margins are acceptable if achieving negative margins would produce excessive morbidity.
^c^ See Principles of Systemic Therapy (SARC-Q).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
Optimizing Treatment of Desmoid Tumors

Treatment recommendations

- Based on the risk/benefit analysis for the patient

- Dependent on tumor and patient characteristics, location, and evolution

- Observation alone could be considered for primary tumors
  - if the diagnosis is confirmed (biopsy, beta-catenin)
  - located such that progression would not cause significant morbidity
DIAGNOSIS (MRI & BIOPSY) → OBSERVATION 3 to 4 months
STOP OF HORMONAL THERAPY

2\textsuperscript{nd} MRI

STABLE

SIGNIFICANT INCREASE IN SIZE

FOLLOW UP
MEDICAL TREATMENT

STABLE OR PR
SIGNIFICANT INCREASE IN SIZE

S +/- RT or RT
Role of surgery

- If surgery, then look for R0 resection
- Whether surgery at all –
  - progressing lesion
  - can be treated with acceptable morbidity
  - patient wish
- If surgery is not expected to be R0, consider radiation therapy
- IORT
- Of course, postoperative RT if a recurrence would allow re-resection with acceptable morbidity
Recommendations

- Asymptomatic patients with extra-abdominal desmoid may be observed or treated with low morbidity therapy.

- Symptomatic *abdominal* desmoids should be considered for chemotherapy.

- Formal prospective trials may help refine recommendations.