Desmoid Tumors: Understanding Treatment Options in 2019

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A real desmoid story...

- 35 year old female physician who noted abdominal cramping and pain in her mid abdomen and a palpable mass in August 2018
- She performed an ultrasound on herself in the ER which showed a 4.5 x 4.5 cm mass in her mid abdomen
- CT scan showed a mesenteric mass that was wrapped around and blocking the inferior mesenteric vein with multiple satellite nodules/lymph nodes.
- Biopsy confirmed the diagnosis of desmoid tumor
A real desmoid story...

- Mother had a neuroendocrine cancer in the appendix, father had Hodgkins lymphoma
- The patient had a negative colonoscopy for any polyps
- She had no other medical problems but has three children, with the last baby born 4 months prior to her symptoms. This most recent baby was conceived with in vitro fertilization.
Tumor board discussion...

- Ongoing pain likely related to venous outflow obstruction (confirmed on colonoscopy as well)
Treatment options in 2019...

- Watch and Wait
- Attempt Surgery
- Radiation
- Chemotherapy (IV)
- Targeted treatments (chemo pills)
- Estrogen-blocking Treatments
- Ablation IRE/Nanoknife/HIFU

- Doxorubicin/Dacarbazine
- MTX/vinblastine
- Doxil
- Sorafenib
- Imatinib
- Pazopanib
- Nirogacestat
- Tegavivint (IV)
- Tamoxifen +/- sulindac
- Aromatase inhibitors
- Celebrex
Choosing a treatment approach

- Symptoms
- Location
- Risk to surrounding structures and organs
- Growth pattern over time
- Obvious estrogen exposure (pregnancy)
- Personal preferences (oral drugs vs. IV, particular side effect profiles)
- Other medical conditions

- Anxiety over “doing nothing”
- How long is acceptable to wait for a response?
- Can shrinkage or necrosis create a more definitive option? (surgery, electroporation?)
- What is the expected function or appearance after my desmoid surgery?
- Am I a candidate for any clinical trials?
Our patient’s case

- Pain and vascular congestion
  - Unlikely to get negative margins
  - Major risks
    - *Maybe later

- Secondary cancers in a 35 year old
  - *Maybe later

- A little big
  - Discrete tumor boundaries
    - *Maybe later

- Chemotherapy (IV)
  - Doxorubicin/Dacarbazine
  - MTX/vinblastine
  - Doxil

- Targeted treatments (chemo pills)
  - Sorafenib
  - Imatinib
  - Pazopanib
  - Nirogacestat

- Estrogen-blocking Treatments
  - Tamoxifen +/- sulindac
  - Aromatase inhibitors
  - Celebrex

- IRE/Nanoknife
  - HIFU

- Radiation

- Attempt Surgery
Our patient’s case

**Risks of therapy**

**Tamoxifen/Sulindac**
- 15-20% shrinkage
- 25-30% symptom improvement
- Maybe higher for our pt with recent pregnancy/IVF

**Sorafenib**
- 33% shrinkage
- 70% symptom improvement
- Risky for our patient with impaired bowel blood flow

**Doxorubicin/dacarbazine**
- 66% shrinkage
- 80% symptom improvement
- Chemo side effects

**Doxil**
- 36% shrinkage
- 92% symptom improvement
- Slow (6 months)

**Nirogacestat**
- Would have to wait for tumor progression

**Chances of tumor shrinkage**

Brooks et al, Eur J Cancer, 1992
Hansmann et al, Cancer 2004
Gounder et al, NEJM 2018
Constantinidou et al, Eur J Cancer 2009
Patel et al, Cancer 1993
Our patient’s course

- Completed 3 cycles of treatment before having this scan
- Pain resolved
- Significant side effects - nausea/vomiting, low blood pressure
- Adjusted treatment for cycle 4 but still toxic - stopped treatment
Genetic Mutations as a Biomarker

Increased risk of recurrence with S45F relative to T41A (and probably S45P)

S45F present in 29% of desmoids in this series (others ranging from 9-45%)

- B-catenin (95% sporadic desmoids)
- APC (inherited desmoids, a few sporadic)

S45F, T41A, S45P

“always on”

Does mutation status predict response to chemotherapy or hormonal therapy?

Image - quora.com; Lazar et al, Am J Pathol 2008

HR 4.28 [95% CI 1.75-10.48, p= 0.0015]
Historical desmoids treated with chemotherapy

- **All patients (n=201)**
  - Excluded for insufficient clinical data
    - N=50

- **MDACC – N=126**
- **UM – N=68**
- **Sinai – N=7**

- **Total number of Treatment Episodes N=409**
  - Surgery alone - 3 (2%)
  - Systemic therapy alone - 55 (38.4%)
  - Surgery + Systemic – 59 (39.1%)
  - Radiation + Systemic – 8 (5.3%)
  - Surgery + Radiation + Systemic – 26 (17.2%)

- **b-cat Mutation Testing**
  - Completed (n=91)
  - Pending (n=27)
  - Not Available (n=33)

- **Episodes with Mutation Data and Clinical Outcomes**
  - Clinical PFS (n=224)
  - Time to Next Treatment (n=211)
  - RECIST responses (n=127)

- **Episodes with b-Cat Mutations (n=316)**
- **T41A 41 (45.1%)**
- **S45F 27 (30.0%)**
- **S45P 1 (1.1%)**
- **Negative 22 (24.2%)**
Historical responses to chemotherapy - by mutation status

Unpublished data
Historical responses to chemotherapy - by mutation status

- Overall no dramatic differences in response to traditional treatments (surgery, chemotherapy or tamoxifen) by specific mutation status
- Too few patients with S45F to look at sorafenib/imatinib, but adding additional patients
- Final results at fall meeting

Unpublished data
Summary

- Overall, many different options for treatment in today’s day and age
- Selection of appropriate treatment requires multidisciplinary input, and consideration of each’s patient unique circumstances and preferences
- Chemotherapy with doxorubicin/dacarbazine and methotrexate/vinblastine highly effective regardless of mutation for durable tumor growth arrest/shrinkage
- We are still in need of better biomarkers to predict patients with more aggressive disease
- Hopefully newer treatments will lead to similar benefit as chemotherapy with less side effects

Thank you! Questions?

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