Desmoid Tumors

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Case Presentation

• 49F who presented with epigastric abdominal pain
• Pain intermittent and colicky
• Associated with soft bowel movements
• Denied fever/chills, nausea/vomiting
• Colonoscopy performed 1 year ago showing diverticulosis
Case Presentation

- **PMHx**: HTN, DM, ESRD (MWF), glaucoma, leiomyomatous uterus
- **PSHx**: Debridement of Right Heel Ulcer, C-sections x 3, Tonsillectomy, LUE AV Fistula creation, Open Cholecystectomy
- **FHx**: unremarkable
- **SHx**: denies T/E/D
- **Ax**: Penicillin
Case Presentation

• Vitals: Stable
• Gen: AAOx3, legally blind
• Abd: well-healed surgical scars, no masses, non-distended, soft, slightly TTP in epigastrium, no rebound/guarding
• Ext: good bruit at LUE AVF site
• Labs: unremarkable
Case Presentation

• CT Abdomen/Pelvis: well circumscribed small tissue mass measuring 4.4 x 5 cm abutting the small bowel, diverticulosis
Intervention

- Diagnostic Laparoscopy, Exploratory Laparotomy, Small Bowel Resection, Mesenteric Mass Excision
Postoperative Course

- POD 0: Transferred to floor from PACU
Postoperative Course

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• POD 1: Tolerated regular diet
Postoperative Course

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• POD 3: Discharged home
Postoperative Course

• POD 0: Transferred to floor from PACU
• POD 1: Tolerated regular diet
• POD 3: Discharged home

• Pathology
  • Well circumscribed mass lesion measuring 6.5 x 5.6 x 5 cm attached to the serosal side of bowel
  • Spindle cell lesion with poorly defined interface with intestinal muscularis propria microscopically
  • Strongly positive for β-Catenin, negative for CD117
  • Fibromatosis, margins negative
Questions?
Overview

- Definition
- History
- Epidemiology
- Presentations
- Diagnostic Tests
- Treatments
- Surveillance
- Outcomes
Definition

• World Health Organization
  • “Clonal fibroblastic proliferations that arise in the deep soft tissues and are characterized by infiltrative growth and tendency toward local recurrence but an inability to metastasize”

• Synonyms
  • Aggressive Fibromatosis
  • Deep Musculoaponeurotic Fibromatosis
  • Well Differentiated Nonmetastasizing Fibrosarcoma
  • Fibrosarcoma Grade I of the Desmoid Type
History

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• 1883: “Desmoid” is coined by Müller from “Desmos”
• 1951: Gardner describes associated findings of “conspicuous surface lumps or tumors” in all family members diagnosed with Familial Adenomatous Polyposis

Epidemiology

• Incidence: 2.4 – 4.3/1,000,000 cases/year
• 0.03% of all neoplasms
• 3% of all soft-tissue tumors
• Median age 30 years
• Female to Male ratio of 2:1

Pathophysiology

• β-catenin dysregulation implicated
  • CTNNB1
  • Levels controlled by adenomatous polyposis coli (APC)

• Key mediator in Wnt signaling pathway
  • Wnt targets include c-Myc
  • Wnt also implicated in development of colorectal and other GI carcinomas

• Additional mutations in the pediatric population

Presentations

- Sporadic
- Gardner Syndrome
- Pregnancy
Sporadic

- Most common presentation
- Somatic APC mutations
- Activating mutations of CTNNB1
- Most commonly associated with Desmoid tumors of the extremities
  - Limb girdles
  - Proximal extremities

Extremity Desmoids

Head and Neck Desmoids

Gardner Syndrome

• 5 – 15% of patients with Desmoid tumors also have a diagnosis of Familial Adenomatous Polyposis (FAP)
• 10 – 20% of FAP patients have Gardner Syndrome
• Mutation in adenomatous polyposis coli (APC) gene (5q21-22)
• More commonly associated with intra-abdominal Desmoid tumors
• Often unresectable
• Cause of death in approximately 11% of patients

Intra-abdominal Desmoids: FAP

Mesenteric Desmoids: FAP

Pregnancy

- Estimated to be 8 – 18% of all Desmoid tumors
- Most commonly associated with Desmoid of abdominal wall
- Thought to be associated with high estrogen state
- Associated with good outcomes
- Not associated with increased obstetric risk


Abdominal Wall Desmoids

Intra-abdominal Desmoids: Pregnancy

Diagnosis

• CT
  • Preferred for intra-abdominal lesions

• MRI
  • Preferred for extremities, head/neck, abdominal/thoracic walls
    • Cannot predict clinical behavior based on imaging

• Biopsy
  • Confirms the diagnosis

• Endoscopy
  • Suspected FAP
Treatment

• Extra-abdominal/Abdominal Wall
• Intra-abdominal
Extra-abdominal/Abdominal Wall Desmoids

• Initial Observation
  • Stable → continue to observe
  • Progression/Symptomatic → treatment

• Radiation Therapy
  • Primary usually given as 50 – 60 Gy over 5 – 7 weeks
  • Adjuvant indicated for R2 resection
  • Adjuvant not shown to be beneficial for R0/R1 resection
  • Neoadjuvant requires more studies

Extra-abdominal/Abdominal Wall Desmoids

• Chemotherapy ± Radiation Therapy
  • Sulindac/NSAIDs
  • Tamoxifen ± Sulindac
  • Methotrexate + Vinblastine
  • Toremifene (SERM)
  • Interferon
  • Doxorubicine
  • Imatinib/Sorafenib
Extra-abdominal/Abdominal Wall Desmoids

- Surgical Resection
  - R1 resection acceptable if R0 resection will result in unacceptable morbidity

Intra-abdominal Desmoids

• Radiation Therapy
  • Generally not recommended

• Chemotherapy (FAP)
  • Inert tumors
    • No therapy
    • Sulindac
  • Slowly Growing or Mildly Symptomatic
    • Tamoxifen (80 – 120 mg/day) + Sulindac
    • Methotrexate + Vinblastine
  • Rapidly Growing
    • High-dose Tamoxifen (120 mg/day)
    • Antisarcoma-type chemotherapy

Intra-abdominal Desmoids

- Surgical Resection
  - FAP
    - Often unresectable
    - High rate of recurrence after resection
    - Resection reserved for small, well-defined tumors with clear margins
    - However may shorten mesentery
    - Prevent Ileal Pouch Anal Anastomosis for Proctectomy resulting in Ileostomy
  - Sporadic
    - Resection offered if symptomatic/threatening function

Surveillance

- History and Physical with appropriate imaging
  - Every 3 – 6 months
  - For 2 – 3 years
  - Then annually
Recurrence

• Estimated 16 – 39% recurrence rate despite R0 resection
  • Up to 50% recurrence within 5 years
• Recurrence risk likely linked to underlying biology rather than margins
• No difference in survival between R0 and R1 resection
• Aggressive resection to achieve R0 may not be beneficial
• Resection or Chemotherapy ± Radiation Therapy are options

Outcomes: Observation

- 142 patients
- 74 patients with primary tumors
- 68 patients with recurrence
- 83 (58.5%) received Wait & See
- 59 (41.5%) received hormonal + chemotherapy
- 5-year progression-free survival measured
  - 49.9% vs 58.6% for the Wait & See and medical therapy groups respectively
  - \( p = 0.3196 \)

Outcomes: Chemotherapy

• Tamoxifen
  • Use first described in 1983
  • 15 – 20% response rate
  • 25 – 30% symptomatic relief rate
  • Data from small series and case reports

• Sulindac + Tamoxifen
  • 8 sporadic Desmoids
    • 5 (62.5%) had stable disease, 1 (12.5%) had complete response
  • 17 FAP Desmoids
    • 11 (64.7%) had stable disease/symptomatic improvement

Outcomes: Surgical Resection

- 426 patients
- 376 (88.3%) received surgical resection ± radiation therapy
  - 63 (16.8%) had R2 resection
    - 42 (66.7%) had local progression
  - 323 (85.9%) had R0/R1 resection
    - 143 (44.3%) had local recurrence

Progression-Free Survival
- Age (HR 1.97 [1.36 – 2.84], p<0.001)
- Size (HR 1.67 [1.13 – 2.36], p=0.008)
- Extra-abdominal tumor (HR 2.55 [1.48 – 4.40], p<0.001)

Outcomes: Surgical Resection

- 495 patients undergoing resection (1982 – 2011)
- 15 (3.0%) patients had FAP
- 440 (89%) patients with R0/R1 resection
  - 100 had recurrence
  - 92 had recurrence within 5 years
- 53 (11%) patients with R2 resection
- 8 (1.6%) patients died after 5 years
  - All R2 resection
  - 6 had intraabdominal lesions
  - 3 had FAP

Conclusion

• Non-metastasizing, locally recurrent disease
• Heterogeneous presentation
  • Sporadic, Gardner Syndrome, Pregnancy-associated
  • Extremity, Abdominal Wall, Intra-abdominal
• R1 resection acceptable if avoiding undue morbidity
• Recurrence likely related to underlying biology and less so margins
• Trend toward less invasive approach such as observation
All of the following are true regarding sporadic desmoid tumors EXCEPT

A. Spontaneous regression may occur
B. They commonly metastasize after resection
C. Surgery is the mainstay of treatment
D. The site of tumor is associated with recurrence
E. They occur more commonly in women
Question

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