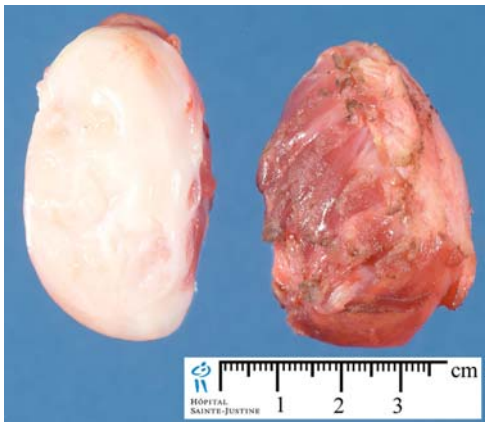
DESMOID TUMORS AND FAMILIAL ADENOMATOUS POLYPOSIS

Familial Adenomatous Polyposis

- 1% of the new cases of colorectal cancer of the inherited polyposis syndromes
- germline mutation in APC gene (tumor suppressor on chromosome 5q21)
  - carries 100% lifetime risk of developing colorectal cancer
- ▪three phenotypic variants of FAP
  - Gardner's Syndrome
    - associated with multiple soft tissue and bony abnormalities including:
      - ocular lesions
      - desmoid tumors
      - osteomas
      - supernumerary teeth
      - fibromas
      - epidermal cysts
      - congenital hypertrophy of pigmented retinal epithelium
      - adrenal adenomas
      - periampullary adenocarcinoma
      - cholangiocarcinoma
      - thyroid malignancy
      - gastric adenomas
  - Turcot's Syndrome
    - Rarer
    - associated with CNS tumors such as medulloblastomas
  - Attenuated FAP
    - manifests later in life, typically after 50
    - usually present with <100 polyps
    - typically more proximal
- classic definition requires presence of >100 colorectal polyps, although typically presents with hundreds to thousands
  - 50% develop adenomas by age 15
  - 95% by age 35
  - 100% by age 40
  - nearly all affected with develop colorectal cancer by fifth decade
- member of kindred with FAP or who have first-degree relatives with spontaneous mutations should seek genetic testing and screening sigmoidoscopy or colonoscopy as early as age 10 and no later than puberty
- presentation
  - rectal bleeding and diarrhea most common
  - changes in bowel habits
  - weight loss, anemia, and abdominal pain
  - 2/3 with symptomatic disease already have a carcinoma
- Surgical intervention
  - in adolescents colectomy usually deferred until 17-18
  - if >20 then colectomy as soon as possible
  - Options:

        - total proctocolectomy and end ileostomy
        - total colectomy and ileorectal anastomosis
        - total proctocolectomy without mucosectomy and stapled ileal pouch-anal anastomosis
        - total proctocolectomy with mucosectomy and hand-sewn IPAA reconstruction
- Extracolonic Manifestations
    - gastric polyps:
        - if located in fundus tend to be benign hamartomatous or hyperplastic polyps
        - if located in antrum tend to be dysplastic and predisposed to malignant degeneration
    - duodenal cancer
        - leading cause of death in FAP patients after colectomy performed and risk of colorectal cancer eliminated:
        - need regular EGD surveillance

Colon of affected FAP patient



Desmoid Tumor

<u>Desmoid Tumors</u>

- mesenchymal neoplasms
- rare, benign, nonmetastasizing but locally invasive neoplasms consisting of well-differentiated, proliferating fibroblasts
- affect up to 13% FAP patients with 20% lifetime risk
- tumor growth unpredictable: most slow, but 10% aggressive
- complications:
    - SBO and perforation, intestinal hemorrhage, DVT
- ~3/4 are intraabdominal, in mesentery of small bowel
- also occur with equal frequency in abdominal wall or extraabdominally with equal frequency
- 3rd most common cause of death in FAP pts after colorectal and duodenal ca
- greatest risk factor for development of desmoids: prior surgery
- commonly develop within 5 years of initial surgery for FAP
- other risk factors:
    - pregnancy
    - females

    - family history
    - desmoids
    - specific mutation in APC
- Diagnosis:
    - CT, MRI, ultrasound, but excisional biopsy usually required
- Medical management
    - first line: NSAIDS (sulindac) then Antiestrogen (tamoxifen or toremifene) or both concurrently
    - ~30-50% respond within 2 wks to 3-6 months but may take up to 2 yrs
    - surveillance CT/ clinical exam at 6-12 month intervals
    - Chemotherapy in aggressive desmoids whom medical therapy has failed (doxorubicin, dacarbazine, carboplatin)
    - Radiotherapy for treatment of nonresectable extraabdominal or abdominal wall tumors, or as adjuvant therapy of tumors after resection with positive margins but risk of radiation enteritis
- Role of Surgery
    - intraabdominal desmoids that are symptomatic due to mass effect, are causing intestinal or ureteral obstruction or perforation, or those found at colectomy or are recurring after primary resection
    - difficult to resect because of location at root of mesentery
    - preferred treatment for extraabdominal tumors or tumors located in abdominal wall
    - Recurrence rates reported as high as 85%
    - multiple SB resections may necessitate SB transplant
    - Ideal treatment?

Knudsen et al. 2002

- review of literature regarding treatment of desmoid tumors in FAP
- concluded first-line treatment, regardless of tumor size, should be sulindac 200mg qd in combination with tamoxifen 20-40mg qd or toremifene 180mg qd
- if tumor continues to grow, sulindac increased to 400mg qd and tamoxifen is replaced with toremifene.
- surgery for well-defined desmoids without involvement of vital structures that are symptomatic:
- if SBO or ischemia immenent, bypass
- chemo first line for desmoid involving larger vessels or vital organs without signs of obstruction or ischemia

Hansmann et al. 2003

- 22 FAP-associated desmoid tumors and 8 patients with spontaneous desmoid tumors
- 300mg sulindac + 120mg tamoxifen or 120mg of raloxifen qd for six months
    - PD: progressive disease (25% size lesion)
    - SD: stable disease (no 25% increase or decrease)
    - PR: partial regression (25% reduction tumor size)
    - CR: complete regression (clinicoradiologic)
- FAP-associated desmoid tumors who had prior desmoid surgery and were given medical treatment: 4/4 recur, ¾ PD, ¼ PR

- FAP-associated desmoid tumor given medical therapy: 10/13 with cessation of growth, PR or CR, 3/13 SD
- FAP-associated desmoid tumor not given medical therapy: 5 patients with small, slow growing tumor, 2 spontaneous CR, 1 PD after surgery then SD, 1 CR after radiation therapy, 1 lost to f/u
- sporadic desmoid tumor given medical therapy: 5/8 had prior resection for desmoid: 4/5 recur, 1 PD, 2 SD, 1 CR
- Conclusion:
  - recommend sulindac/ tamoxifen as first line
  - if prior resection for desmoid exists then therapy less successful

References

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Amanda Kong, MD