Stanford Desmoid Tumor Board

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Case 1

- 26 year old male presents with soft tissue mass over the spine

Past Medical History:

-Age 12, Soft tissue mass over the dorsum of right foot; biopsy showed desmoid; resection of mass

-Age 15, Screening colonoscopy showed numerous polyps

-Age 25, Total colectomy with ileorectal anastomosis, pathology showed multiple adenomatous polyps

Familial Adenomatous Polyposis

- Multiple colorectal adenomatous polyps (typically more than 100)
- 3 cases per 100,000 individuals, accounts for less than 1 percent of all colorectal cancers in the United States
- Caused by germline mutations in the tumor suppressor gene, Adenomatous Polyposis Coli (APC), located on chromosome 5q21-q22
- Autosomal dominant pattern of inheritance with nearly complete penetrance of colonic polyposis but variable penetrance of the extracolonic manifestations of the disease
- Up to 25 percent of FAP cases are due to new or de novo APC mutations

APC gene

- More than 1000 different mutations of the APC gene associated with FAP
- Colorectal cancer occurs in nearly 100 percent of individuals with FAP if untreated, with an average age of 39 years at cancer diagnosis
- Desmoid tumors occur in 10 to 15 percent of FAP patients
- Desmoids are most commonly located in the abdomen
- 10 percent of cases will have a rapidly progressive course. This may result in pain, bowel obstruction, ureteral obstruction, and vascular compromise

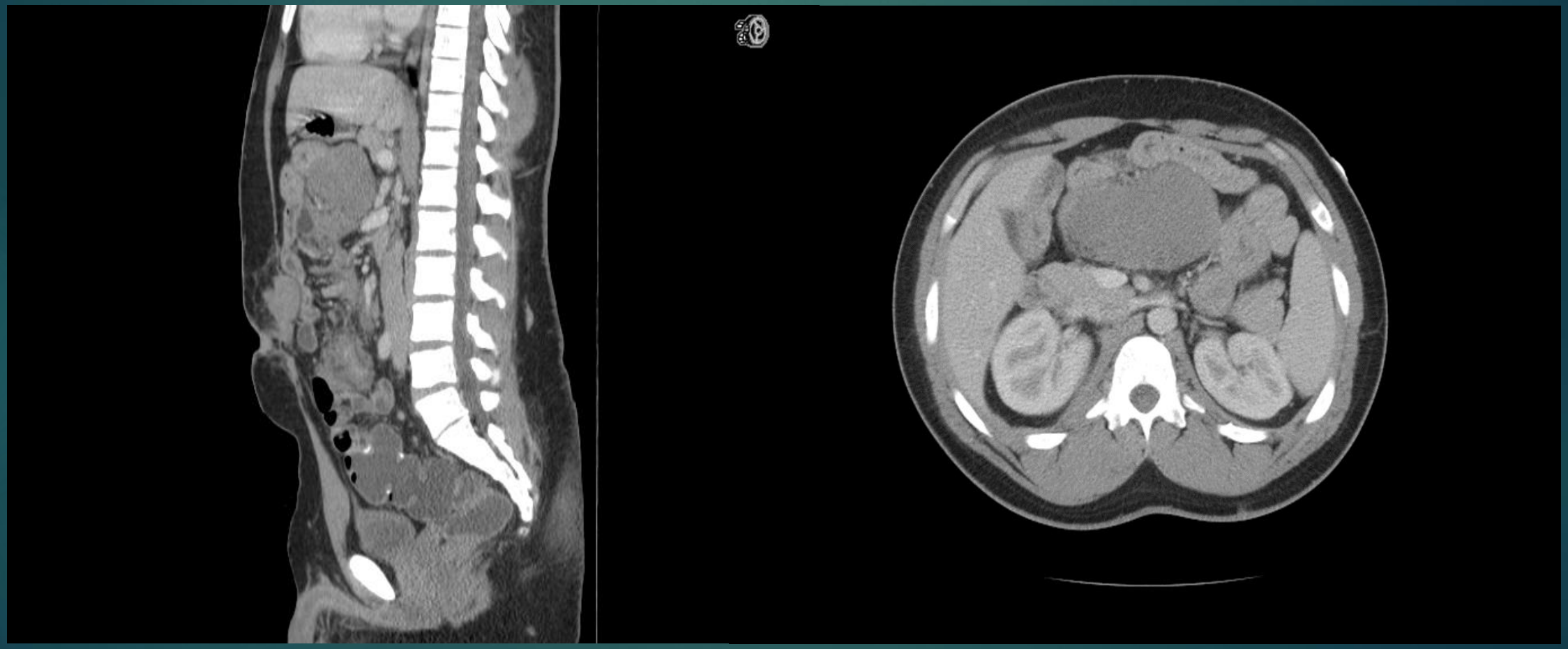
APC mutations

- A normal APC protein prevents the accumulation of beta-catenin by mediating its phosphorylation and resultant degradation.
- Mutations in the APC gene lead to premature truncation of the APC protein and loss of the beta-catenin regulatory domain. This allows beta catenin to accumulate, bind to, and activate the transcription factor tcf-4

Gardner syndrome

- Describe families with colonic polyposis and extracolonic manifestations
- Extraintestinal manifestations:
  - Desmoid tumors
  - Sebaceous or epidermoid cysts
  - Lipomas
  - Osteomas (especially of the mandible)
  - Fibromas
  - Gastric fundic gland polyps
  - Juvenile nasopharyngeal angiofibromas, etc

CT scan



Treatment options

- Systemic therapy
  - Estrogen blockers: Tamoxifen
  - Anti-inflammatory medications: Meloxicam, Sulindac
  - Tyrosine Kinase Inhibitors: Imatinib, Sorafenib
  - Chemotherapy: Adriamycin/Dacarbazine
- Local therapy
  - Surgery
  - Radiation
  - Ablation

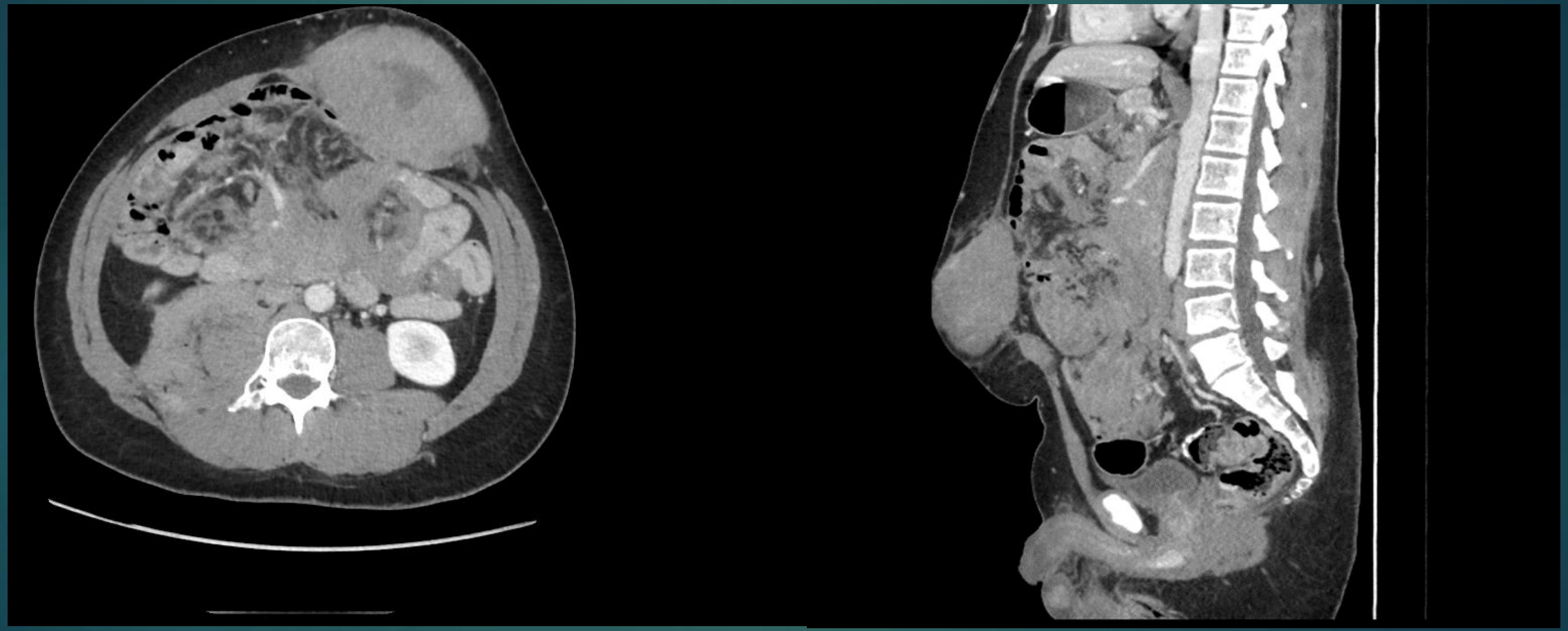
Case 1 (cont.)

- Biopsy confirmed desmoid fibromatosis
- Tamoxifen x 6 months
- Enlargement of paraspinal mass with increasing pain
- Surgical resection of paraspinal desmoid followed by radiotherapy
- Started on imatinib but had significant gastrointestinal toxicity

Case 1 (cont.)

- Adriamycin/Olaratumab for 6 cycles followed by Olaratumab maintenance
- CT scan showed enlarging tumors after 18 months
- Sorafenib x 10 months
- Ct shows worsening of tumors

CT scan



Treatment Options

- Systemic therapy
  - Estrogen blockers; Anti-inflammatory medications; Tyrosine Kinase Inhibitors; Chemotherapy
  - Experimental agents
- Local therapy
  - Surgery
  - Radiation
  - Ablation

Case 2

- 29 year old female presented with swelling of left hand after traumatic injury
- MRI showed a soft tissue mass
- Biopsy showed desmoid fibromatosis

Antecedent trauma

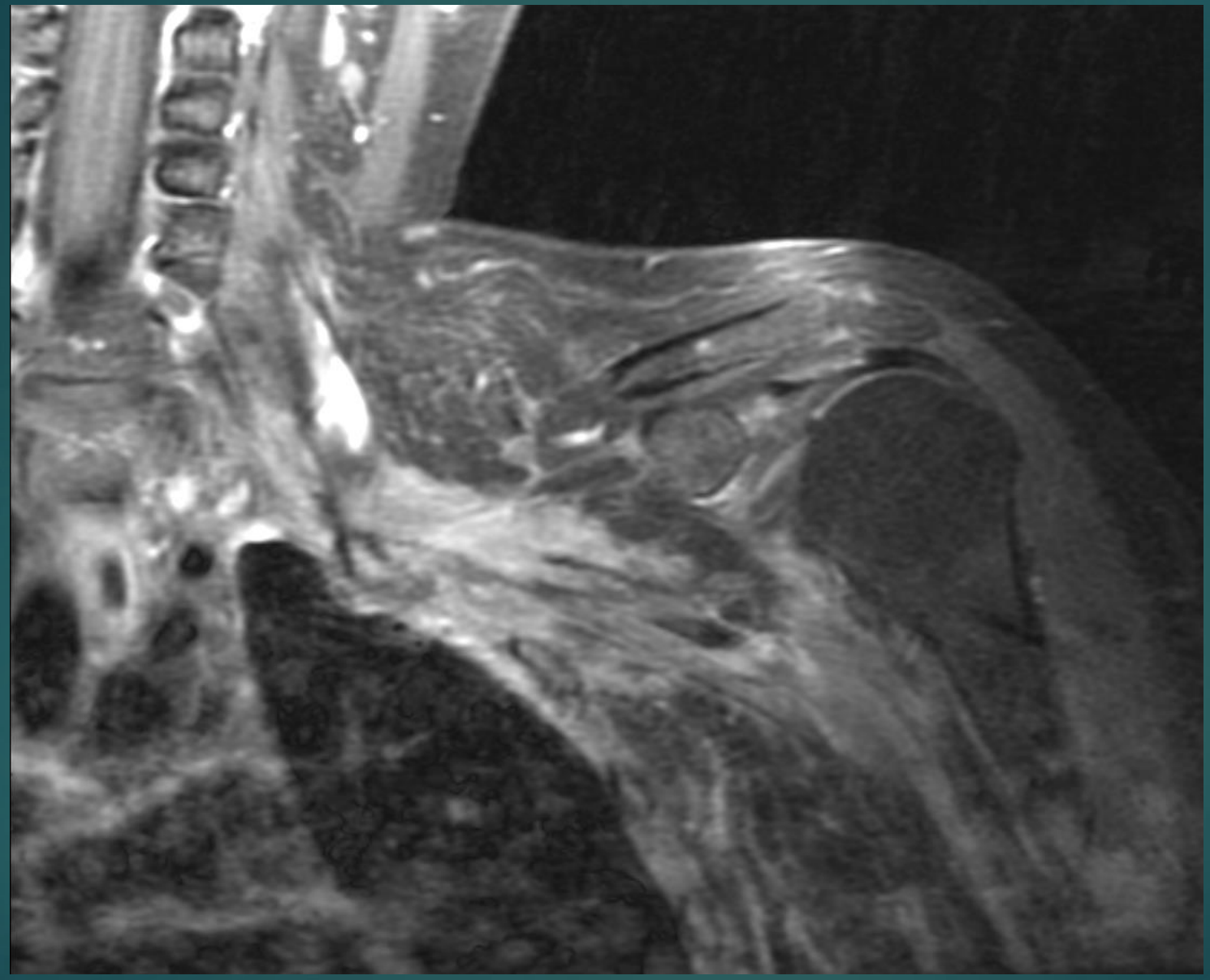
- Up to 30 percent of patients with desmoid tumors report prior trauma
- Molecular connection between wound healing processes and fibroproliferative disorders of mesenchymal tissue
- Desmoid tumors result from the growth of multipotent mesencyhmal stromal cells (MSC) in a wound healing setting that is associated with deregulated Wnt signaling due to APC loss

Treatment options

- Systemic therapy
  - Estrogen blockers: Tamoxifen
  - Anti-inflammatory medications: Meloxicam, Sulindac
  - Tyrosine Kinase Inhibitors: Imatinib, Sorafenib
  - Chemotherapy: Adriamycin/Dacarbazine
- Local therapy
  - Surgery
  - Radiation
  - Ablation

Case 2 (cont.)

- Radical resection with positive margins
- Post-operative radiotherapy
- Tamoxifen
- After 5 years, developed soft tissue mass in left neck extending down to left deltoid and brachial plexus
- Combination of imatinib, tamoxifen, meloxicam for 2 years with stable tumors
- Now with worsening tumors



Treatments options

- Cryoablation?
- Clinical trials?

Desmoid Tumor Board

- Thank you Drs. Wliky, Ghanouni, Kummar, and Million