Sarcoma

Sarcoma

SARCOMA = any tumor of mesenchymal origin

Tissue of Origin	Common Sarcomas
Soft Tissue	
Fat	Liposarcoma
Fibrous tissue	Fibrosarcoma
Smooth muscle	Leiomyosarcoma
Skeletal muscle	Rhabdomyosarcoma
Connective Tissue	
Bone	Osteosarcoma
Bone	Ewing's Sarcoma
Bone	Giant Cell Sarcoma
Cartilage	Chondrosarcoma
Fibrous	Desmoid
GI Visceral	GIST: gastrointestinal stromal tumor
Dermal/Visceral	Kaposi's Sarcoma
Vascular	Angiosarcoma

Benign vs. Malignant

Some sarcomas behave as benign rather than malignant tumors.

They are locally invasive but don't metastasize

Ex: desmoid tumors, giant cell tumors of bone

Sarcoma

Principles of Treatment:

If LOCALIZED disease →
surgical resection with wide margins

If ADVANCED disease →
often anthracycline-based chemotherapy

Prognosis for Malignant Tumors:

If LOCALIZED disease = CURABLE

If ADVANCED disease = POOR PROGNOSIS
If metastatic likely aggressive variety w/ survival on order of months

Sarcoma: GIST

General:
- Most common sarcoma of GI tract
- From interstitial cells of Cajal
- Stomach (70%), SI (20%) & anywhere in GI
  Stomach = best prognosis

Mutations:
- **KIT (85%) or PDGFR (10%) mutations**
- KIT/PDGFR WT = SDH, NF1, BRAF, etc

IHC:
- CD117 (KIT)
- DOG ("discovered on GIST")
- CD34+ (stem cell marker)

Grading:
Low Grade: < 5 mitoses/5 mm2
High Grade: > 5 mitoses/5 mm2

LOCALIZED THERAPY
- Observe if small (< 3 cm)
- Surgery if large
- Consider adjuvant therapy if high risk
  High risk = size > 5 cm OR high mitotic rate
  Imatinib 400 mg QD x 3Y

SYSTEMIC THERAPY

KIT/PDGFR TKIs
- 1st line: **Imatinib** (400 mg QD → 800 mg QD)
- 2nd line: Sunitinib
- 3rd line: Regorafenib
- 4th line: Ripretinib

KIT/PDGFR specific mutation subsets
KIT Exon 11 = good response to imatinib (11 is heaven)
KIT Exon 9 = poor response to imatinib (9 is not fine). Try 800 mg.
KIT Exon 17 = resistance to imatinib/sunitinib **(17 is mean)**
PDGFR D824V = resistance to imatinib **(use avapritinib)**

KIT/PDGFR Wild Type
- Check for SDH, NF1 mutations = resistant to TKIs above

Sarcoma: Kaposi's Sarcoma

General:
- Associated with **HIV**
- Cause by **HHV8**
- Post-transplant

Staging:
- Skin or LN
- Visceral organs (GI tract, heart)

LOCALIZED THERAPY

- Observation if asymptomatic
- Topical creams
  - Alitretinoin gel
  - Imiquimod cream
- Other: RT, cryotherapy, laser

SYSTEMIC THERAPY

HIV ART
- Often only treatment needed if pt not previously on ART
- IRIS can cause flair of KS

Chemotherapy
- Needed if symptomatic or visceral disease
- Doxorubicin or Paclitaxel monotherapy

Relapsed/Refractory
- Pomalidomide

Sarcoma: Soft Tissue

Soft Tissue	
Fat	**Liposarcoma**
Fibrous tissue	**Fibrosarcoma**
Smooth muscle	**Leiomyosarcoma**
Skeletal muscle	**Rhabdomyosarcoma**

EARLY STAGE TREATMENT

- **Surgical wide resection +/- RT**
  RT indicated for intermediate/high grade or large tumors (>5 cm)

- Consider Neoadjuvant/Adjuvant chemo in: high grade or large tumors (>5 cm)
  Ex: AIM (doxorubicin, ifosfamide/mesna)

SYSTEMIC THERAPY

- Consider metastasectomy if oligometastatic

- **Anthracycline based singlet or doublet chemotherapy**
  Ex: Anthracycline/ifosfamide
  Histology specific

- **Second/Third Line Therapies**
  Trabectedin (liposarcoma/leiomyosarcoma)
  Pazopanib
  Larotrectinib (NTRK mutation)
  Checkpoint inhibitors (MSI-high)

Sarcoma: Connective Tissue

Osteosarcoma

GENERAL

- Most common bone sarcoma
- Bimodal age incidence
- Occurs in bone metaphysis (neck)
- Mixed lytic/blastic appearance
- Periosteal reaction causes codman triangle on x-ray

TREATMENT:

- Neoadjuvant/adjuvant chemotherapy
  Doxorubicin/cisplatin +/- MTX
  Osteo (dOx) sarC (Cis) oMa (MTX)
- Adjuvant RT if positive margins
- **Metastasectomy of pulmonary mets**

Ewing's Sarcoma

GENERAL

- Commonly in children
- From primitive neuroectodermal tumor
- Occurs in bone diaphysis (shaft)
- Onion-skinning pattern on CT

DIAGNOSIS

- IHC: CD99, nuclear factor FLI-1
- Molecular: EWSR1/FLI-1 = t(11;22)

TREATMENT:

- Neoadj chemotherapy → surgery → Adj chemo
  VDC/IE
  VDC = vincristine, doxorubicin, cyclophosphamide
  IE = ifosfamide/etoposide (* IE not needed stage IV)
- Adjuvant RT if positive margins

Sarcoma: Connective Tissue

Desmoid Tumor (Aggressive Fibromatosis)

General
- Commonly of young adults
- Connective tissue tumor
- Locally aggressive, rarely metastasize
- Majority: CTNBB1 mutations
- Associated with Gardner's syndrome (FAP: APC gene)

Treatment:
- Observation if asymptomatic & no FAP: can have spontaneous remission
- Surgical resection if localized
- TKIs: **Sorafenib**, pazopanib
- Chemo: Doxil or Doxorubicin +/- decarbazine
- Other (slower options): NSAID, imatinib, IFN, tamoxifen

Chondrosarcoma

GENERAL
- From cartilage
- Older patients (age >60), Indolent growth
- Mutations in IDH1/2

TREATMENT:
- **Surgical resection with wide margins**
- **NO role for chemotherapy or RT (*unless higher grade mesenchymal sub-type)**

Giant Cell Sarcoma of Bone

General
- Benign but destructive, rarely metastasizes
- Malignant cells secrete RANK ligand → lytic destruction

Treatment
- Resectable: Surgical resection
- **Unresectable/Metastatic: Denosumab**, RT, IFN