Vesalius SCALpel™ : Sarcoma (see also: soft tissue/sarcoma folios)

1% of adult malignancies, 15% of pediatric
multimodality Rx the rule
    ext pre 55Gy or post 65Gy -> 90% control
circumferential and tissue plane growth, pseudocapsule
1/3 of pts. asymptomatic
lymphatic spread rare
    exceptions: epitheliod, rhabdomyo, clear cell, angio
predisposition:
    genetic:
        VonRecklinghausen neurofibromatosis: 10% neurofibrosarcoma
        LiFraumeni (P53): rhabdomyosarcoma, early breast cancer
        retinoblastoma (Rb)
        FAP
        Gardner's: desmoid (aggressive fibromatosis)
        somatic p53 mutation found in 30-60% of soft tissue sarcomas
    radiation: 8-50X increased incidence
    lymphedema, lymphangiosarcoma, 3% of all sarcomas, 10y average delay
        after axillary lymph node dissection = Stewart-Treves syndrome
    chemical:
        PVC: aggressive hepatic angiosarcoma
        phenoxyacetic acid herbicides: dioxin, agent orange
        arsenic
        hemochromatosis
    trauma: postpartum
molecular markers
    leiomyosarcoma: RB1
    synovial: SYT-SSX 1,2 fusion products
    malignant fibrous histiocytoma (MFH): P53
    neurofibromatosis: S-100
    angio: factor VIII
    rhabdo: myoglobin (alveolar histology worst)
types: 20% lipo-, 19% leiomyo-, 18% malignant fibrous histiocytoma (MFH, all hi grade, spindle cell, cartwheel pattern), 10% fibro-, 7% synovial, 32%, other (45 other types)
age: child small blue cell, embryonal rhabdomyoSA (H&N, GU, extremity; favorable prognosis <10yo)
    young adult: synovial
location:
    50% extremities (lipo, MFH, Ewing's)
    40% trunk/retroperitoneum (lipo,leio)
    10% head and neck
Dx
    painless mass, frequent delay diagnosis
    Bx: > 5cm, new, increasing size, symptomatic
        core Bx 90% accurate, replacing incisional Bx

retroperitoneal mass assume sarcoma, operate without Bx
4% LN mets, 25% distant mets (hematogenous)
visceral spread to liver
extremities spread to lung
grade, not size most important staging criterion (one of few tumors grade is important in staging)
I, II lo grade, III, IV hi grade
I well differentiated, II moderately well, III poorly, IV undifferentiated
based on: mitosis, cellularity, necrosis, differentiation, stromal content
size: T1 < 5cm (a superficial, b deep [deep/investing fascia]), T2 > 5cm (a, b)
T1 better prognosis
N & M 0 and 1
no adequate staging retroperitoneal, visceral
5y survival by stage:
I 95%, II 80, III 50, IV 15
overall 50%

surgery
margins 2-3cm ideal, outside pseudocapsule
< 2mm 100% recurrence
90% limb-sparing successful, 10% recurrence, rare amputation
Moh's surgery (successive frozen section of margins) for well differentiated in critical areas
leave clips for adjuvant radiation
amputation only if recurrent and can't be reexcised without severe loss of limb function
salvage amputation improves Karnofsky score and quality of life
radiation: adjuvant increases local control (external beam and brachytherapy)
< 5cm with negative margins no RT, even for hi grade
chemo little benefit
doxocycline, ifosfamide may improve local recurrence, survival
hi grade, > 5cm 20% response
isolated hyperthermic limb perfusion with melphalan & ifosfamide in selected cases
chemoradiation neoadjuvant may shrink large tumor; 25% wound complications
hi risk
local recurrence: age > 50, recurrent, positive margin, fibroSA, malignant peripheral nerve SA
distant recurrence: > 10cm, recurrent, deep, hi grade, leiomyoSA, non-lipoSA
recurrence
recurrence directly related to grade, nerve sheath worst
local recurrence most significant factor for overall survival
most recur < 2y, older patients more local recurrence
retroperitoneal scan: hi recurrence rate (30-50%)(hard to get negative margin)
30% recurrence < 2y, limb salvage still possible
head and neck hi recurrence (48%), hard to get margins
resect isolated recurrence, 2/3 long term benefit
predictors of survival after recurrence: extent, length of disease-free interval, older
distant mets: 25% 1y survival

chemo: doxocycline, ifosfamide, dacarbazine
up to 47% response rate, 10% complete response
lung met resect. (even bilat.) if primary controlled, no mediastinal involvement, no extrathoracic disease, medically fit
20-50% 5y survival
benefit of resecting hepatic met unclear

retroperitoneal
15% of all sarcomas, 55% of retroperitoneal tumors
vague symptoms, present late: abdominal mass, wt. loss, pain, early satiety, nausea/vomit
only 50% negative margins
common location for recurrence (50%), die of local disease
CT/RT little benefit

GIST
interstitial pacemaker cells of Cajal
markers:
CD34: hematopoietic progenitor cell antigen
CD117: C-kit protein: membrane receptor with tyrosine kinase component
C-Kit proto-oncogene (tyrosine kinase receptor) mutation/overexpression
also PDGFR alpha (another tyrosine kinase receptor)
most common mesenchymal tumor of the GI tract
frequently benign, can be malignant (> 5cm)
5 mitoses/10 HPFs
malignant changes highest in stomach
hi recurrence, lo lymph node mets so no lymph node dissection
recurrence common on peritoneal surface of liver
65% stomach, 25% small bowel, 5% colon, 5% esophagus
presentation: 60% pain, 35% bleeding
Rx: resect with negative margin, no node dissection
50% cure with complete resection, 50% overall 5y survival
imatinib mesylate/gleevac selective inhibition tyrosine kinase receptors
50% partial response unresectable disease, 31% stable
sunitinib more powerful for inatinib resistant
role as adjuvant Rx under investigation
endoscopic, CT f/u

desmoid
like low grade sarcoma, women, multiple recurrences
no metastatic potential
resect with clear margin
sulindac, TAM may prevent recurrence
increased incidence in FAP

bone sarcoma
osteosarcoma most common
childhood and adolescence
painful mass
CT/MRI, incisional Bx
induction/pre-op/neoadjuvant chemo helps limb-sparing (Ewing's)

- 25% develop pulmonary mets

childhood sarcoma
- small blue cell most common (70%)
- rhabdo-, Ewings (musculoskeletal, 25% mets @ Dx, favorable prognosis)
- chemo/rad pre-op, incisional Bx
- respond better than adult

head and neck
- 4% of all sarcomas, 1% of head and neck cancers
- XRT may be some benefit, no role for chemo
- 45-68 overall 5y

neurofibromatosis
- peripheral/type1 (VonRecklinhausen) most common; central neurofibromas
- 3-15% lifetime risk neurofibrosarcoma
    - large, rapid growth
    - high uptake PET/FDG (fleurodeoxyglucose) suggests malignancy
    - complete resection with margins +/- RT

mesothelioma
- asbestos
- pleura, peritoneal, tunica vaginalis
- usually late Dx
- palliative Rx, 0% 5y survival

vascular
- 4% of all soft tissue sarcomas
- no Bx, causes bleeding
- excise with negative margin
- XRT depending on location

chemo main benefit for bone and child