Soft Tissue Tumors and Malignancies

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Agenda

• Look at basics of tumors and diagnosis
• Look at some important literature and concepts
• Look at common F&A soft tissue tumors
Good news

• ST lesions more common than osseous lesions, benign tumors more common than malignant tumors.
  – P. Ferguson, OKU F&A 3, 2003

Good news

• Lesions of the F&A tend to present early in their course due to thin overlying soft tissue
Good news

• Primary malignant neoplasia of the F&A are rare
• Secondary malignancies and metastatic disease are also uncommon
• Benign processes outnumber malignant processes possibly 100:1

Zeytoonjian FAI 2004

• 25 years
• 175 sarcomas of the F&A vs 2367 other areas
  – Synovial sarcoma
  – Osteosarcoma
  – Ewing’s
• F&A sarcoma mortality 10% vs 27% remaining areas
• “It seems to be far safer to have a high-grade tumor of the distal leg, ankle, or foot than in other parts of the body…”
The “Great Trap”

“Although the rarity of malignant diseases [in the F&A] is encouraging, unfortunately it carries the potential for misdiagnosis and increased morbidity in Pts who do have a malignancy. The onus thus falls upon the treating physician to maintain respect for all foot and ankle lesions.” –Arthur Walling, MD, Florida

The “Great Trap”

“F&A tumors are rare in comparison with other common traumatic and overuse foot and ankle disorders… Delayed, incorrect diagnosis, or inappropriate surgery for malignancy can produce devastating results and make limb salvage impossible.” –Peter Ferguson, MD, Toronto
So what to do?

- Thorough H&P
- Plain radiographs
- CT
- MRI
- Bone Scan
- Labs (CBC, ESR, CRP, blood cultures, Ca, PO4, PSA, LFTs, SPEP/UPEP)
- New Patient This routine will give correct Dx ~85% of the time.
  - *Skeletal metastases of unknown origin. A prospective study of a diagnostic strategy.* Rougraff BT. JBJS 75(9), 1993
- **ONLY** when ALL of this has been done, should you proceed to biopsy!

Documentation of the lesion

- Size
  - Rate of growth
- Symmetry
  - Borders
  - Colors
- Elevated?
- Fixed?
- Pulsations?
- Tenderness
- Transillumination
Biopsy

• Fine needle
• Core needle
• Punch
• Incisional
• Excisional

Biopsy principles

• Incision that can be incorporated into definitive resection
• Minimal soft tissue dissection and plane development to avoid contamination
• Incisions longitudinal when possible
• Avoid exposure of major neurovascular structures
• Achieve strict hemostasis
• If drain used, position so it can be excised at definitive surgery
• Excisional biopsy can be performed for presumed benign lesions or lesions small enough (2cm diameter or less) to include a cuff of normal tissue
• Use tourniquet without exsanguination
• Same surgeon should perform biopsy, definitive resection
Margin excision

• Intra-lesional excision
  – Plane of dissection passes thru the tumor
• Marginal excision
  – Plane of dissection is thru the reactive zone. Can have planned marginal margins (eg-spinal cord)
• Wide excision
  – Surgical plane thru completely normal tissue outside the reactive zone. Wide resection in the foot is very challenging due to proximity of NV structures and paucity of ST coverage
• Radical excision
  – Entire compartment. Bones of the hindfoot, individual tarsal bones, and individual rays should all be considered their own compartments

“Unplanned excision”

• Poor pre-operative planning
• Improper imaging
• Improper biopsy
• Inadequate margins
Why are malignant soft tissue tumors so difficult in the F&A?

• Difficult to obtain adequate resection
• Makes it hard to obtain clean margins and maintain function at the same time
• Problems with soft tissue coverage
• Lack of good anatomic compartments
  – Easy to cross contaminate
• Many times STS will necessitate amputation

“The Hazards of Biopsy”

• 1982 JBJS study based on survey of MSTS membership
• 20 members asked to submit records on 20 consecutive pts with biopsy and subsequent treatment for malignant primary bone or soft tissue tumor
• 329 Pts
  – 222 bone, 107 soft tissue
“The Hazards of Biopsy”

- 18.2% major errors in diagnosis
- 10.3% technically poor or inadequate biopsies
- 18.2% major change in treatment plan due to problems with biopsy
- 4.5% unnecessary amputations
- Complications 3 - 5x more frequent when performed at referring institution rather than center of definitive treatment
- CONCLUSION: Refer Pts to treating center before performing a biopsy!

“The Hazards of Biopsy – Revisited”

- 1996 JBJS article
- Looking at 1992 data of same MSTS - based study as 10 years prior
- 25 MSTS members submitted 597 Pts
  - 362 bone, 235 soft tissue
“The Hazards of Biopsy – Revisited” JBJS 1996

• 17.8% major errors in diagnosis
  – 18.2% in ‘82 study
• 8.4% technically poor or inadequate biopsies
  – 10.3% in ‘82 study
• 19.3% major change in treatment plan due to problems with biopsy
  – 18.2% in ‘82 study
• 3% unnecessary amputations
  – 4.5% in ‘82 study
• Complications 2 - 12x more frequent when performed at referring institution rather than center of definitive treatment
  – 3 - 5x in ‘82 study

• CONCLUSION: We haven’t learned our lesson! Refer the Pt BEFORE biopsy!

Soft Tissue Sarcomas of the Foot and Ankle: Impact of Unplanned Excision, Limb Salvage, and Multimodality Therapy

• 52 consecutive pts with sarcomas
• Unplanned excisions 56% of the time
• After treatment, 7 had recurrence
  – 5 of these had unplanned excision prior
• More free flaps for unplanned group
• Conclusion: unplanned excisions required more aggressive treatment and radiotherapy but does not seem to effect functional outcomes
**Sarcoma v Carcinoma**

- Malignant cancer of the supportive tissue, mesoderm origin
  - Bone, cartilage, fat, muscle, blood vessel
  - Connective tissue

- Malignant cancer of epithelial origin
  - Skin, glands
  - Lining of internal organs
Metastasis

Common Distant Metastatic Sites

<table>
<thead>
<tr>
<th>Site</th>
<th>Tumor Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>Breast, Colon, Prostate, Kidney, Thyroid, Stomach, Cervix, Rectum, Testis, Bone, Skin (Melanoma), and Ovaries</td>
</tr>
<tr>
<td>Liver</td>
<td>Lung, Breast, Colon, Pancreas, Ovaries, and Stomach</td>
</tr>
<tr>
<td>Bone</td>
<td>Breast, Lung, Prostate, Kidney, and Thyroid</td>
</tr>
<tr>
<td>Brain</td>
<td>Breast, Lung, and Melanomas, Leukemias and Lymphomas</td>
</tr>
</tbody>
</table>
**Metastasis**

<table>
<thead>
<tr>
<th>Primary site</th>
<th>Metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Where the cancer starts)</td>
<td>(Where it often spreads to)</td>
</tr>
<tr>
<td>Breast</td>
<td>Lymph nodes (underarm), lung, bone, liver, brain</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>Lymph nodes (next to bowels), liver, lung, bone</td>
</tr>
<tr>
<td>Lymph nodes (next to kidney)</td>
<td>Lymph nodes (next to lungs), other lung, adrenals,</td>
</tr>
<tr>
<td>Liver, bone, brain</td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td>Lymph nodes (in pelvis), liver, lung</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Lymph nodes (in abdomen), liver, lung, bone, brain</td>
</tr>
<tr>
<td>Prostate</td>
<td>Lymph nodes (in pelvis), bone, lung, liver</td>
</tr>
<tr>
<td>Soft tissues (sarcomas)</td>
<td>Lungs, bone, lymph nodes, brain</td>
</tr>
<tr>
<td>Stomach</td>
<td>Lymph nodes (in abdomen), liver, lungs, brain</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Lymph nodes (in neck), lungs, liver, bone</td>
</tr>
</tbody>
</table>

**Benign v aggressive**

- Non-malignant characteristics
- Slow growing
- Well-demarcated
- Homogenous

- Malignant characteristics
- Faster growing
- Not well-demarcated
- Heterogenous
- Invasive/reactive
- May be more painful
Which do you want?

Benign lesions are hypocellular, well-differentiated, little cellular atypia, zero mitotic figures.

Malignant lesions are hypercellular, anaplastic, disorganized, numerous mitotic figures.

What makes it bad?
### TUMOR GRADING/STAGING - AJCC STAGING PROTOCOL FOR SOFT TISSUE SARCOMAS

<table>
<thead>
<tr>
<th>STAGE</th>
<th>GRADE</th>
<th>PRIMARY TUMOR</th>
<th>REGIONAL NODES</th>
<th>DISTANT METS</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>1 (Well-Diff’d)</td>
<td>5 cm or less</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>IB</td>
<td>1 (Well-Diff’d)</td>
<td>Over 5 cm</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>II A</td>
<td>2 (Mod Diff’d)</td>
<td>5 cm or less</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>IIB</td>
<td>2 (Mod Diff’d)</td>
<td>Over 5 cm</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>IIIA</td>
<td>3 (Poor Diff’d)</td>
<td>5 cm or less</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>IIIB</td>
<td>3 (Poor Diff’d)</td>
<td>Over 5 cm</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>IVA</td>
<td>Any</td>
<td>Any Size</td>
<td>0-1</td>
<td>Yes</td>
</tr>
<tr>
<td>IVB</td>
<td>Any</td>
<td>Any Size</td>
<td>0-1</td>
<td>Yes</td>
</tr>
</tbody>
</table>


### Benign F&A soft tissue tumors

- Ganglion
- Morton’s Neuroma
- Fibroma
- Plantar Fibromatosis
- Desmoid
- Glomus Tumor
- Hemangioma
- Lipoma
- Schwannoma
- Neurofibroma
- Leiomyoma
- Pigmented Villonodular Synovitis (PVNS)
- Synovial Chondromatosis
**Ganglion**

- Extremely common
- 11% of all ganglions
- Second to the hand
- May arise from joint capsules, tendon sheaths, ligaments, menisci, labra, and aponeuroses

**Ganglion**

- Clinically, can appreciate mobile, superficial mass which will transilluminate
- MRI shows well-defined mass with signal intensity equivalent to water
Ganglion

• 70% recurrence rate with simple aspiration
• Excision should include entire cyst wall and degenerative capsule or tendon sheath
• Recurrence rate ~10% 

Neuroma

• Perineural fibrosis of a plantar digital nerve
• Most commonly found in the 2nd or 3rd (75%) intermetatarsal spaces
• Most common in females, 5th & 6th decades
• On MRI, well-demarcated round or dumbbell-shaped lesions centered in NV bundle on the plantar side of the transverse metatarsal ligament
• Isointense to muscle on T1, hypointense to fat on T2
Plantar Fibromatosis

- Generally found 20s-50s
  - Dupuytren’s contracture, Peyronie’s
- M>F
- Bilateral in 10-50%
- Malignant degeneration is unknown
- Causative cell=myofibroblast
- Firm, fixed to plantar fascia
- Growth is slow

Nonsurgical TX with shoe modifications, NSAIDs
- “Surgical resection is best avoided”
  - Coughlin & Mann
- Wide excision
- Large margins
- Complications
  - skin necrosis
  - delayed wound healing
  - recurrence

- 18 pts with surgical excision
- 1.5 cm margins
- NWB incisions
- 2 recurrences
- 54% delayed wound healing


- Grading System
  - Grade I = Focal disease isolated to a small area on the medial and/or central aspect of the fascia. No skin adherence, no deep extension to flexor sheath.
  - Grade II = Multifocal disease with or without proximal or distal extension. No adherence to the skin. No deep extension to flexor sheath.
  - Grade III = Multifocal disease with or without proximal or distal extension. Either adherence to skin or deep extension to the flexor sheath.
  - Grade IV = Multifocal disease with or without proximal or distal extension. Adherence to skin and deep extension to flexor sheath.
Glomus Tumor

- Benign vascular tumor in Pts 20-40 years old
- M:F 1:3
- Typically present with bright-red or bluish discoloration beneath nail bed
- Usually less than 1cm in diameter
- X-rays may show well-margined bony erosion over dorsal surface of distal phalanx
- Tx = marginal excision
- Recurrence is unusual
- Beware melanoma in pigmented lesions under the nail!


- Originates from the glomus body, a small neuromyoarterial apparatus in the capillary, regulates local blood flow and temp
- Temp sensitivity
- MRI findings of a well-delineated masses dark on T1, bright on T2
- Excision provides reliable relief
Lipoma

- Most common benign ST tumor, common in ages 40-60y
- Displaces rather than invades local structures
- Consist of mature adipocytes
- Mostly subcutaneous, but can be intramuscular, intermuscular, in tendon sheath, in nerve
- Present as asymptomatic, slow-growing round or ovoid masses having a soft or doughy consistency
- Signal characteristics on MRI must match sub-Q fat on ALL sequences
- Tx = marginal excision
- Extremely low recurrence

Hemangioma

- Benign vascular tumor common in 1st 3 decades of life
- Can be superficial, subfascial, or both
- When superficial, can have bluish discoloration and soft, doughy texture
- Most foot hemangiomas are clinically asymptomatic
Hemangioma

- Small calcifications (phleboliths) on plain XR are pathognomonic
- On MR the lesions consist of multiple lobules, tubules, and septations with irregular margins
- Low on T1, very high on T2, marked contrast enhancement
- Tx should be conservative as recurrence rate is high
- Compression and treatment of symptoms

Schwannoma

- AKA neurilemmoma
- Benign peripheral nerve sheath tumor
- Age 30-40y
- Slow-growing lesions within epineurium
- Usually solitary < 2cm
- Mass may be painful, have + Tinel’s sign
- On surface of nerve
- Well encapsulated
Schwannoma

• Grossly arises as an eccentric growth from the nerve.
• Encapsulated by a fibrous connective tissue layer and there are no neural elements within the tumor.
• Do NOT undergo malignant degeneration, as do neurofibromas.
• MRI demonstrates relationship b/t lesion and peripheral nerve. Low on T1, high on T2.

Schwannoma

• Tx = careful dissection of tumor from nerve fascicles
• Frequently can be accomplished without damage
• Recurrence and decreased nerve function are rare
Neurofibroma

- Benign tumor of peripheral nerves
- 90% solitary
- 10% associated with von Recklinghausen’s
- Firm, nontender, well-circumscribed masses arising from cutaneous nerves
Neurofibroma

- NOT well-circumscribed
- Do NOT have a distinct capsule
- Do infiltrate surrounding nerve fibers
- No clear plane of dissection
  - Makes impossible to excise without damaging nerve
- 5% transform to neurosarcoma
- Tx = benign neglect
  - Choose between disability caused by lesion and that which will result from resection

Desmoid

- Locally aggressive myofibroblastic lesion
- High recurrence rate after resection
- Most common between puberty and age 40
- Foot is a common site of involvement
- Can grow quickly to great size
- Arises from muscle, myofascia or aponeurosis
- Presents in the foot as a ST mass deep, rock hard, painless mass in the plantar arch
- Not superficial like plantar fibromatosis
- More common in females
**Desmoid**

- Low on T1, low on T2
- MR reveals intermuscular mass which tends to grow along fascial planes
- Can displace, entrap, or invade adjacent structures
- Histologically have abundant bundles of collagen, uniform spindle cells
- Tx = Wide excision, high recurrence rate which may necessitate eventual amputation
- XRT for recurrent lesions, some reports of low dose chemotherapy.

**Pigmented Villonodular Synovitis (PVNS)**

- Benign proliferative disorder of the synovium that can affect joints, bursae, tendon sheaths (giant cell of tendon sheath)
- Unknown etiology
- Most common 3rd-4th decade
- Ankle is the 3rd most common site after knee and hip
- Monoarticular swelling
- Recurrent bloody effusion on joint aspiration
Pigmented Villonodular Synovitis (PVNS)

- Periarticular erosions involving both sides of the joint
- MR is very heterogeneous on both T1 and T2
- Histo = fibrous stroma with monocytes, giant cells, xanthoma cells, hemosiderin deposits
- Tx = open synovectomy
- Recurrence is high 40%, may use adjuvant XRT
• Review of 10 cases

Synovial Chondromatosis

• Chondral metaplasia within the synovium produces numerous ovoid osteocartilagenous bodies embedded in synovium and/or floating in joint
• 2:1 M:F ratio, 3rd-5th decades
• Malignant transformation is very rare
• Symptoms
  − limitation of motion, joint pain, swelling
Synovial Chondromatosis

- X-rays are diagnostic, but MR can help delineate ST extent
- Low on T1, high on T2 “Rings and arcs”
- Peaks in early adulthood, 2:1 M:F
- ~50% of cases involve the knee but also occurs in ankle
- Tx= open synovectomy, recurrence is rare

Malignant F&A soft tissue tumors

- Synovial Sarcoma
- Clear Cell Sarcoma
- Malignant Melanoma
- Kaposi’s Sarcoma
Synovial Sarcoma

- Most common sarcoma of F&A
- Named for its resemblance to developing synovial cells
- But VERY rare within a joint
- Occurs in para-articular regions of the extremities (tendon sheaths, bursae, joint capsules)
- Usually flexor surfaces
- 15 - 40y with slight male predominance
- 50% present with mass, 50% present with mass and pain
- t(X:18) creates STT/SSX fusion gene
- Most common site of synovial sarcoma mets is to lung

30% of cases have stippled ST calcifications on xray
- On MR the lesions appear well-defined, intermuscular, clearly differentiated from surrounding tissues, demonstrate intense enhancement with contrast
- Histologically biphasic with epithelial-like and spindle-like cells
- Epithelial cells are large, round/oval, with abundant pale cytoplasm. Arranged in cords, whorls
- Fibrous cells are large, plump spindle cells with scant cytoplasm and darkly staining nuclei
- Tx = wide resection with XRT
**Synovial sarcoma of the foot and ankle.**
Scully SP, CORR 1999.

- 14 Pts reviewed at Duke, Walter Reed
- Avg age = 28y, duration of symptoms 14 months
- Tenderness, edema, enlarging mass
- 3 had no pain
- 6 had initial diagnoses of benign entities
- 10/14 had report of prior trauma which confounded diagnosis
- Only 2 had attempts at limb salvage, all others had TTA or partial foot amputation
- 1/14 had local recurrence
- 8/14 had pulmonary metastases. All pts with pulmonary disease died
- No difference in survival between limb salvage, amputation
- Tumor size was not predictive of prognosis in this study
- Late recurrences (up to 8 years after diagnosis) were noted

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**Clear Cell Sarcoma**

- AKA malignant melanoma of the soft parts
- Only ~50% produce melanin, has also been called amelanotic melanoma
- Rare malignant neoplasm of uncertain origin
- Usually affects pts 20-40 years old, F&A represent 43% of cases
- Unlike melanoma, CCS is a relatively deep lesion that develops in intimate association with tendon, fascia, and rarely involves the skin
Clear Cell Sarcoma

- Well-defined and homogenous on MR, so often mistaken as benign lesions
- Composed of well-defined nests or fascicles of uniform cells with clear cytoplasm separated by fibrocollagenous stroma
- Characteristic t(12;22) translocation
- High recurrence and metastasis rate make prognosis poor-55% 5-y DFS
- Tx=wide resection, XRT. Chemo is ineffective

Melanoma

- Many types
- 5 types of malignant melanoma
  - Superficial spreading
  - Nodular melanoma
  - Acral lentiginous
  - Amelanotic
  - Lentigo
**Superficial spreading**

- Most common
- Fair skinned
- # of sunburns
- Slow growing, flat, solitary lesion
- Best prognosis

**Nodular**

- 2nd most common
- Fast growing, elevated
- Very deep, vertical growth
- Worst prognosis
**Acral lentiginous**

- Rare
- Darker skin tones more common
- Soles/palms
- May present subungual
- Flat, slow growing
- Poor prognosis due to late diagnosis

**Amelanotic**

- Rare
- Sun exposure primary cause
- May or may not be pigmented
Lentigo

• Least common in the lower extremities
• In-situ form

Malignant Melanoma

• F&A accounts for 3-15% all melanomas
• Caucasians, 1-9% of melanomas are in the foot
• 51-82% in Asians
• 60-70% in African Americans
• Median age at diagnosis is low 40s
• Poorer survival rates reflect advanced stage and depth of lesions in F&A compared with other sites
Malignant melanoma ABCDs

- Asymmetry
- Border irregularity
- Color variation
- Diameter enlargement
  - Over 5mm should be biopsied

Malignant Melanoma

- Ominous features specific to F&A include
  1) Spontaneous nail lift-off or nail loss attributed to trauma that fails to produce a new nail
  2) Nail bed pigmentation that spills into the nail fold (Hutchinson’s sign)
  3) De Novo nail bed pigmentation that fails to migrate distally over time
  4) Non-healing ulcer in a patient is predisposing condition
- Tumor thickness, ulceration, and lung mets are most important determinants of mortality
- Tx=surgery, chemo, XRT
- Overall 5-y DFS for all sites is 80%, but F&A is only 60%, presumptively due to late detection
Diagnosis and Treatment of Malignant Melanoma of the Foot

Richard J. Gray, M.D.1, Barbara A. Pockaj, M.D.1, Miriam L. Vega, M.D.1, Suzanne M. Conolly, M.D.1; David J. DiCicco, M.D.1;
Todd A. Kiel, M.D.1, Edward W. Bechel, M.D.1

1Foot & Ankle International/Vol. 27 No. 9/September 2006

- 38 Pts with melanoma of the foot
- 26% had a plantar location
- Mean age at diagnosis 61y
- Avg time to diagnosis was 17 months
- Initial diagnosis had been considered benign in 32%
- Median thickness was 1.75 mm, and 12 Pts (34%) had ulcerations. Sentinel node biopsy showed that 16% had nodal mets at the time of surgery. Surg complications in 12 (~36%)
- All Pts underwent wide excision or Mohs technique. 8 had toe or ray amputation.
- Systemic recurrence occurred in 6
- 3 px’s had interferon, 1 had megasterol, 1 had a tumor vaccine, and 1 had XRT
- Pts with atypical nevi are at greater risk and 11% of Pts in this study reported that melanoma arose from a pre-existing lesion

Kaposi’s Sarcoma

- 1st described by Moritz Kaposi in 1872
- Renewed interest with transplant and AIDS Pts
- Approx 0.4% of transplant Pts and 30% of AIDS Pts develop KS
- Predilection for skin of hands and feet, particularly the hallux
- Present as flat, pink patches that slowly enlarge and darken
- Histo=highly vascular spindle cell lesion
- Tx=surgery, radiation and chemotherapy (injectable)
Osteomyelitis


- 7 Pts with SCC arising in F&A osteomyelitis (Marjolin’s ulcer) Avg of 27y b/t onset of draining OM and diagnosis of SCC
- All were male, mean age was 59.5y
- Development of CA is heralded by increased pain, increased drainage, bleeding, evidence of new bone destruction
- Tx of choice = amputation, performed in 6 of 7
- 1 Pt had a recurrence and required revision amputation
- 11.5-30% of Marjolin’s ulcers metastasize
- 1.6 to 23% of Pts with chronic draining OM develop SCC

SUMMARY

- Whew!! You made it!
- Refer stuff you feel uncomfortable with to your friendly neighborhood tumor surgeon (remember Uncle Henry)
- You may never see some of these diseases, but keep your mind prepared- you WILL have the opportunity to save life and limb during your career!
SOURCES