Primary Lymphoma of Bone (PLB)

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11/22/2013
63 year old female

- CC: Two month LBP and hip pain
- MRI L-S spine 12/17:
  - metastatic disease L2-S2
  - path fx L5, L iliac, L pubic ramus, L ischial tuberosity, L femoral head
- CT C/A/P:
  - right atrial mass 5cm
  - right renal lesion, concern for mets
- Brain MRI: negative
- CT-guided biopsy of L5: nondiagnostic, crush artifact, necrosis
ROS: low grade fever, night sweat and weight loss of 30lb/2mons

PMH:
- Hypothyroidism
- Asthma
- Obesity
- Pyelonephritis
- Urinary incontinence s\p bladder sling

Allergy: erythromycin, penicillins, sulfa drugs, Cipro, Keflex, Levaquin, Bactrim, Zithromax Z-Pak, Percocet, Symbicort
FH

- Father died of lymphoma at age 68
- Paternal and maternal aunts with lung cancer, smoking hx
- Paternal GM died of colon cancer
- Brother with hypercoag state, thromboses
SCCA 1/11/2013: Dr. Goulart

- DD:
  - Metastatic ca. of unknown primary
  - Metastatic ca. of unknown primary, will identify on further study
  - Multiple myeloma: SPEP, immunofixation negative
- Consider second biopsy of sacral bone
- PET/CT scan
- Pain control
UWMC 1/15-18 for worsening pain

- PET/CT 1/18:
  - Large focus of intense FDG uptake in the right atrium
  - Numerous abnormal FDG uptake throughout the skeleton
  - No LAP or HSM
DD per radiologist:

- primary cardiac sarcoma with bone metastases
- Primary bone process like multiple myeloma with a cardiac plasmacytoma
- Lymphoma is a possibility although lack of nodal involvement argues against it
- Melanoma could present similarly, however, there is no area of uptake to suggest a primary melanoma
Labs:

- Unremarkable
- Normal CBC with diff
- Normal chemistry, electrolyte
- LDH 561, uric acid 4

PE:

- No LAP, no HSM
- Focal tenderness at vertebrae and hip
► Left sacral bone biopsy 1/18, then D/C
► Readmitted on 1/25 for worsening pain
  ▪ Biopsy: DLBCL, positive for CD20, CD56, CD10, Bcl-2 and Bcl-6
Bone marrow left posterior iliac crest:

- Dry tap
- Small piece of core
- Marrow is entirely replaced by CD20+ B cell infiltrate w/o normal marrow component
- However, diffuse marrow involvement vs. local tumor extension can’t be differentiated based on current material
R-CHOP started

Tolerated well, no evidence of TLS

Cardio consulted, telemetry, concern for tumor thrombosis from atrial mass

IR for LP and intrathecal MTX
  - CSF negative for tumor involvement
F/U Dr. Orozco at SCCA
PR (PET) after 6 cycles of R-CHOP
Atrial mass resolved
Unfortunately, developed asymptomatic isolated CNS relapse
Underwent surgical resection
Chemo with HD MTX per Dr. Chamberlain
Primary lymphoma of bone (PLB)

- Solitary or multiple, destructive bone lesions
- Less than 2% of all lymphomas in adults
- Pediatric, 3-9%, treatment different
- PLB accounts for 3% primary bone tumor
- M:F 1.2-1.8
- >30yo (92%) and >60yo (56%)
Clinical presentation

- Bone pain not relieved by rest
- Palpable mass from soft tissue extension
- Swelling
- Pathological fracture
- Cord compression
- B symptoms
- Axial: appendicular (63% vs. 37%)
Pathology

- Vast majority are DLBCL (>80%)
- Indolent lymphoma
  - Follicular
  - SLL
  - MZL
- Aggressive lymphoma
  - Burkitt
  - LL
Imaging

- **Plain film**
  - Lytic lesion, path fracture
  - Mixed lytic-sclerotic

- **CT or MRI**
  - Bone lesion and soft tissue involvement
  - MRI: bone marrow involvement

- **PET/CT**
  - Extent of LN involvement
  - Distant disease
Differential diagnosis

- Chronic osteomyelitis
- Primary bone sarcoma
- Leukemic infiltrate
- Small blue round cell tumors
  - Ewing sarcoma/primitive neuroectodermal tumor
  - Rhabdomyosarcoma
  - Metastatic neuroblastoma
  - Small-cell osteosarcoma
- Metastatic sarcomas
- Mesenchymal chondrosarcoma
- Metastatic carcinoma
Treatment

► RCT unavailable due to rarity of disease
► Historically, radiation alone 87-100% local control, but distant relapse rate high
► Currently, chemo w/wo radiation, 5-year survival 70%
SEER analysis

- 1500 PLB from 1973-2005
- OS at 5 and 10 years 58% and 45%
- Younger age and localized disease, independent predictors of survival
- Five-year survival
  - 87% <30
  - 74% 30-59
  - 45% >60

Jawad et al, Cancer 2010; 116: 871
► Multiagent chemo w/wo radiation
  - CHOP w/wo R
  - Involved-field radiotherapy in patient with unifocal disease
BC Cancer Agency 131 patients with PLB

- median age of 63
- 1/3 long bone, 1/3 spine
- 80% DLBCL, 78% advanced disease
- 79% CHOP, 21% R-CHOP

In 103 patients with DLBCL:

- 5-year OS 62%, 10-year OS 41%

Three-year PFS:

- 52% CHOP vs. 88% R-CHOP

Cumulative survival
Retrospective Rare Cancer Network study

- 116 patients with PLB from 1987-2008
- Stage IE (80%), IIE (20%), 78% DLBCL
- ChemoRT (75%), RT (13%), chemo (12%)
- CHOP or CHOP like w/wo Rituxan
- Median f/u 41 months
  - 5-year OS 76%, 10-year OS 72%
- Multivariate analysis, factors associated with improved 5-year survival
  - IPI score <2 (84 vs 59%)
  - Radiation dose >40 Gy (95 vs. 66%)
  - At least six cycles of chemo (81 vs. 69%)

Multivariate analysis, 5-year survival

(a) Overall survival
   - IPI 0,1
   - IPI ≥ 2
   - P=0.009

(b) Overall survival
   - RT dose > 40 Gy
   - RT dose ≤ 40 Gy
   - P=0.0054

(c) Overall survival
   - CXT cycles ≥ 6
   - CXT cycles < 6
   - P=0.01

(d) Overall survival
   - CR
   - No CR
   - P<0.0001
Univariate analysis, Lymphoma specific survival (LSS) and local control (LC)
Another large series of 82 patient
- DLBCL (80%), stage I or II (81%)
- ChemoRT (57%), RT (14%), chemo (30%)
- Median f/u of 67 months
  - Free from treatment failure 81%
  - Median OS 88%
- Multivariate analysis for favorable outcome
  - Age <40
  - Combined modality therapy

Beal et al, Cancer 2006; 106: 2652
Freedom from treatment failure by treatment type

Beal et al, Cancer 2006; 106: 2652
Follow-up

- PET/CT as post-treatment imaging study
  - Size, activity of residual mass, distinction between active disease/fibrosis
  - Six weeks after chemo or 12-weeks after radiation
  - Biopsy of PET+ area required prior to additional therapy
Conclusions

- PBL is rare, over 80% is DLBCL
- RT has good local control
- CMT with chemoRT, 70% 5-y survival
- CHOP +/- Rituxan commonly used