Outline

- Background
- Common presentations
- Diagnosis/workup
- Staging
- SBP, EMP
- Studies
Definition

- Discrete, solitary mass of neoplastic plasma cells
- Two subtypes of solitary plasmacytoma
  - Solitary Plasmacytoma of Bone
  - Extramedullary Plasmacytoma
Solitary Bone Plasmacytoma

Epidemiology

- <5% of plasma cell neoplasms
  - 1-2% of all US cancers are plasma cell tumors
- M>F (3-4:1)
- Median age at dx: 50 – 55 years old
  - About 10 years younger than MM
- Most common in the axial skeleton
  - Especially thoracic spine (13/46 in one study)
Solitary Bone Plasmacytoma
Clinical Presentation

- Bone pain – most common presentation
- Pathologic fractures
  - Vertebral -> severe back pain, spasms, cord compression
  - Rib, clavicular -> pleuritic pain
Solitary Bone Plasmacytoma
Patient workup

- Labs
  - CBC w/diff
  - Calcium
  - Creatinine
  - Beta-2 microglobulin, LDH, CRP reflective of tumor burden
- SPEP/UPEP, immunofixation
- Bone marrow aspirate and bx
Solitary Bone Plasmacytoma
Patient workup

- Skeletal survey
- CXR
- MRI
  - Assess presence of multiple lesions
  - Detect early associated MM
Solitary Bone Plasmacytoma Diagnosis

- Single bone lesion with biopsy-proven clonal plasma cells
- Rule out MM
  - Normal bone marrow (<10% plasma cells)
  - Otherwise negative skeletal survey
  - Absence of anemia, hypercalcemia, or renal impairment
  - Low/no M ptn on SPEP, UPEP and immunofixation
  - MRI
## Solitary Bone Plasmacytoma Staging (Drurie-Salmon Myeloma Staging)

<table>
<thead>
<tr>
<th>Stage</th>
<th>HgB (g/100 mL)</th>
<th>Serum Ca (mg/100 mL)</th>
<th>IgG (g/100 mL)</th>
<th>IgA (g/100 mL)</th>
<th>UPEP (g/24h)</th>
<th>other</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (all)</td>
<td>&gt; 10</td>
<td>≤12</td>
<td>&lt; 5</td>
<td>&lt; 3</td>
<td>&lt; 4</td>
<td>XR survey nl or SBP only</td>
</tr>
<tr>
<td>III (≥1)</td>
<td>&lt; 8.5</td>
<td>&gt; 12</td>
<td>&gt; 7</td>
<td>&gt; 5</td>
<td>&gt; 12</td>
<td></td>
</tr>
</tbody>
</table>
II: not I or III

subclassification (renal function)

- A: serum Cr <2 mg/100 mL
- B: serum Cr >2 mg/100 mL
I: serum beta-microglobulin < 3.5 mg/L, serum albumin ≥ 3.5 g/dL
- MS: 62 mos

II: not one or three
- MS: 44 mos

III: serum beta-microglobulin ≥ 5.5 mg/L
- MS: 29 mos
# STAGING SYSTEMS FOR MULTIPLE MYELOMA

<table>
<thead>
<tr>
<th>Stage</th>
<th>Durie-Salmon Criteria¹</th>
<th>ISS Criteria²</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>All of the following:</td>
<td>Serum $\beta_2$-microglobulin &lt; 3.5 mg/L</td>
</tr>
<tr>
<td></td>
<td>• Hemoglobin value &gt; 10 g/dL</td>
<td>Serum albumin ≥ 3.5 g/dL</td>
</tr>
<tr>
<td></td>
<td>• Serum calcium value normal or ≤ 12 mg/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Bone x-ray, normal bone structure (scale 0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Low M-component production rate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• IgG value &lt; 5 g/dL;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• IgA value &lt; 3 g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Bence Jones protein &lt; 4 g/24 h</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Neither stage I nor stage III</td>
<td>Neither stage I nor stage III</td>
</tr>
<tr>
<td>III</td>
<td>One or more of the following:</td>
<td>Serum $\beta_2$-microglobulin ≥ 5.5 mg/dL</td>
</tr>
<tr>
<td></td>
<td>• Hemoglobin value &lt; 8.5 g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Serum calcium value &gt; 12 mg/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Advanced lytic bone lesions (scale 3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• High M-component production rate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• IgG value &gt; 7 g/dL;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• IgA value &gt; 5 g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Bence Jones protein &gt; 12 g/24 h</td>
<td></td>
</tr>
</tbody>
</table>

| Subclassification Criteria |  |
|---------------------------|  |
| A Normal renal function (serum creatinine level < 2.0 mg/dL) |  |
| B Abnormal renal function (serum creatinine level ≥ 2.0 mg/dL) |  |
Solitary Bone Plasmacytoma
Natural History

- 50-60% progress to MM
- Median time to progression is 2-3 years
- Median overall survival is 10 yrs
- Some postulate it is part of the MGUS – MM continuum
Solitary Bone Plasmacytoma
Predictors of Progression to MM

- Tumors >4-5 cm
- ≥ 60 years old
- High M protein levels (1g/dL)
- Persistence of M protein after treatment
- Spine lesions
Solitary Bone Plasmacytoma

Treatment

- Definitive XRT
- $\geq 45 \text{ Gy}$
- Involved bone with 2-3 cm margin
- Chemotherapy and surgery usually not indicated
  - Chemo reserved for systemic disease
  - Orthopedic surgery may be indicated
- LC 80-90%, better if $<5$ cm
Solitary Bone Plasmacytoma
Monitoring for recurrence

- Labs (every 3-6 months for 1 year then annually)
  - Measure frequently early on to confirm radiosensitivity of tumor
    - SPEP/UPEP, immunofixation
    - CBC
    - Calcium
    - Creatinine

- Skeletal survey or MRI
  - Every 6 months for 1 year, then as clinically indicated
Multiple Myeloma

CLINICAL PRESENTATION

Solitary Osseous
Solitary Extraosseous

PRIMARY TREATMENT

RT (≥ 45 Gy) to involved field
RT (≥ 45 Gy) to involved field and/or surgery

FOLLOW-UP/SURVEILLANCE

- CBC
- Serum chemistry for creatinine, albumin, LDH, calcium, beta-2 microglobulin
- Serum quantitative immunoglobulins, serum protein electrophoresis (SPEP), serum immunofixation electrophoresis (SIFE)
- Consider serum free light chain assay
- 24 h urine for total protein, urine protein electrophoresis (UPEP), urine immunofixation electrophoresis (UIFE)
- Consider bone marrow biopsy as clinically indicated
- Consider bone survey as clinically indicated or annually
- Consider MRI and or CT and or PET/CT as clinically indicated or every 6-12 mo

Primary progressive or Response followed by progression
Restage with myeloma workup
See Active _symptomatic_ myeloma (MYEL-3)

See Response Criteria for Multiple Myeloma (MYEL-C).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
Solitary Bone Plasmacytoma
Dimopoulos et al, JCO 1992

- Retrospective study
  - 45 patients with SBP
  - Minimum dose 30 Gy
- Single institution - MDACC
45 patients with SBP treated with XRT from 1966-91

Minimum dose of 30 Gy

Diagnosis
- Bone marrow (<5% plasma cells), skeletal survey, SPEP/UPEP, quantitative Igs
- 93% had preserved uninvolved Igs
## Solitary Bone Plasmacytoma

*Dimopoulos et al, JCO 1992*

<table>
<thead>
<tr>
<th>Dose (Gy)</th>
<th>Patients</th>
<th>Local Control Rate</th>
<th>MM Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-45</td>
<td>18</td>
<td>89% <em>(Local Control not achieved in 2 patients)</em></td>
<td>12 (67%)</td>
</tr>
<tr>
<td>46-55</td>
<td>18</td>
<td>100%</td>
<td>8 (44%)</td>
</tr>
<tr>
<td>&gt;55</td>
<td>9</td>
<td>100%</td>
<td>3 (33%)</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>96%</td>
<td>23 (51%)</td>
</tr>
</tbody>
</table>
Solitary Bone Plasmacytoma
Dimopoulos et al, JCO 1992

- Median survival 13 years
- MM progression
  - 23 patients (51%)
  - Median: 20 months
  - 68% within 3 years
9/30 pts had disappearance of M- rtn after XRT
- These 9 remained disease free

21/30 patients had persistent M- rtn
- 64% of these progressed to MM

Remission >10yrs
- 9/9 patients whose M- rtn disappeared with tx
- 15% of those whose M- rtn didn’t disappear or who had non-secretory disease
Conclusions

- In SBP patients, involved field XRT + disappearance of M-protein predicted long-term disease free survival.
- Nonsecretory disease and persistent myeloma protein after treatment were adverse prognostic factors.

- Retrospective
- 57 patients with SBP treated with XRT at MDACC
  - 1965 – 1996
LC achieved in 55/57 (96%) of patients

- Median time to MM progression: 1.8 years
  - Dimopoulus: 20 mos

- Median survival: 11 years
11 patients had disappearance of M-ptn following XRT
- All had ≤1.0 g/dL initially (total: 22)
- 2 relapsed (at 4 and 12 years)

17/30 (57%) with a persistent protein peak relapsed
Patients with thoracolumbar disease

- 7/8 patients diagnosed with plain films alone developed MM
- 1/7 diagnosed with MRI of the spine + plain films developed MM
Conclusion

- Precise staging including MRI of the spine is necessary for patient selection for definitive XRT
- Disappearance of M-protein following XRT represents a high likelihood of cure
Extramedullary Plasmacytoma
Characteristics

- Plasmacytoma outside of bone marrow
- Often associated with IgA monoclonal ptn
- Predominantly in the upper respiratory tract
Extramedullary Plasmacytoma
Epidemiology

- 3-4% of plasma cell malignancies
- Median age of diagnosis 60 yo
- M>F
- About 85% in upper aerodigestive tract (UAD)
  - GI tract 2nd MC
  - May also involve lung, bladder, thyroid, testis, ovary, tonsil
Extramedullary Plasmacytoma
Clinical presentation

- Upper respiratory tract
  - Epistaxis
  - Increased nasal discharge
  - Obstruction

- Other sites produce localized symptoms
Extramedullary Plasmacytoma

Diagnosis

- Biopsy-proven extramedullary monoclonal plasma cell tumor
- No evidence of bone destruction or occult disease elsewhere
10-40% progress in 10 years
- Much less common than SBP patients
10 year OS 40-90%
LC ≥ 80%
Extramedullary Plasmacytoma Treatment

- **Definitive XRT**
  - 45-50 Gy/4-5 weeks
  - Consider covering primary draining nodes

- **Surgery may be considered for GI disease**
  - Alexiou et al showed no difference between surgery, XRT, or combined modality tx for sites other than H&N

- **Adjuvant chemo doesn’t lower relapse rate or increase DFS**

- Literature search
  - MEDLINE, Index Medicus, Deutsches Institut fur Medizinische Dokumentation und Information, reference lists from respective publications
  - Reviewed 400+ publications between 1905-97
Extramedullary Plasmacytoma
Alexiou et al (Cancer 1999)

- 869 patients with EMP treated with surgery, XRT, or combined modality tx
- 82.2% in UAD, 43.8% in nasal cavity or paranasal sinuses
### Extramedullary Plasmacytoma
Alexiou et al (Cancer 1999)

- UAD: increased median OS or recurrence free survival with combined tx

<table>
<thead>
<tr>
<th>Treatment</th>
<th>XRT (n=290)</th>
<th>Surgery (n=143)</th>
<th>Combined (n=176)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median OS</td>
<td>144 mos</td>
<td>156 mos</td>
<td>&gt;300 mos</td>
</tr>
<tr>
<td>% conversion to MM</td>
<td>17.5</td>
<td>6.3</td>
<td>13.5</td>
</tr>
</tbody>
</table>
Non-UAD: no survival difference between tx arms

Low rate of LN involvement: 7.6% in UAD, 2.6% non-UAD
Conclusions

- Surgery alone gives the best results in EMP if resectability is good
- If not feasible, combined therapy is indicated

- Retrospective review at PMH
- 1960 – 2000 (68 patients)
- Median follow up 8 years
Extramedullary Plasmacytoma

- Median age at dx: 60
- M>F (3:1)
- Sinonasal tract most common location (35%)
- LC
  - 81% at 5 years, 79% at 10 years
- DFS
  - 52% at 5 years, 41% at 10 years
### Extramedullary Plasmacytoma


<table>
<thead>
<tr>
<th>Treatment</th>
<th>n</th>
<th>LR</th>
<th>MM</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>3</td>
<td>1 (33.3%)</td>
<td>0</td>
</tr>
<tr>
<td>Chemo</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>XRT</td>
<td>39</td>
<td>5 (12.8%)</td>
<td>7 (18%)</td>
</tr>
<tr>
<td>XRT+chemo</td>
<td>3</td>
<td>2 (66.7%)</td>
<td>2 (66.7%)</td>
</tr>
<tr>
<td>Pre-op XRT</td>
<td>4</td>
<td>2 (50%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Surgery only</td>
<td>8</td>
<td>1 (12.5%)</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>Post-op RT</td>
<td>10</td>
<td>2 (20%)</td>
<td>2 (20%)</td>
</tr>
</tbody>
</table>
Conclusions

- XRT is the treatment of choice for EMP
- Surgery is reserved for large tumors and extensive bone destruction
Solitary Plasmacytoma summary

- Plasmacytoma is a rare disease
- Treatment study consists mainly of retrospective reviews
- Based on retrospective data, XRT is the treatment of choice in SBP
- For EMP, there is conflicting data. However, based on the radiosensitivity of plasma tumors, XRT is accepted as the treatment of choice


