ARRO Case
Thymoma

Jordan Kharofa, MD
Elizabeth Gore, MD
Medical College of Wisconsin
History

HPI

• 54 yo male who presented to PCP with complaining subacute shortness of breath and chest pain.
• Pain increased after some heavy exertion.
• He described his pain as 8/10 in severity, provoked by breathing and sharp in quality.

• ROS: Negative
• Past Medical Hx: HTN
• Past Surg Hx: None
• Meds: Metoprolol

• Family Hx: Noncontributory
• Social Hx:
  – Unemployed and single.
  – One pack per week smoker over the past ten years.
  – Denied alcohol use.
Rounded density projecting over the aortic arch with corresponding oval density on the lateral CXR in ant mediastinum.

CT shows 5 x 3 cm lobular noncalcified soft tissue mass within the anterior mediastinum. PET scan was negative.
Differential Diagnosis Anterior Mediastinal Mass

• **Thymic**
  – Thymoma
  – Thymic Carcinoma
  – Thymic Cyst
  – Carcinoid
  – Thymic Lipoma

• **Germ cell tumors**
  – Seminoma
  – Non-Seminoma
  – Mixed germ Cell
  – Teratoma

• **Lymphomas**
  – Non-hodgkins
  – Hodgkins

• **Intrathoracic thyroid tissue**
Clinical Presentation of a Thymic Mass

• Many thymic malignancies present as incidental radiographic abnormalities.

• Clinical signs may include chest pain, cough, dyspnea, odynophagia.

• Phrenic nerve paralysis, or superior vena cava syndrome may suggest more invasive tumors.

• Thymomas may also present with a variety of paraneoplastic syndromes.
Paraneoplastic Syndromes- Myasthenia Gravis

- Approximately 30-50% of patients with thymomas have myasthenia gravis.

- Conversely, only 10-12% of patients with myasthenia gravis have a thymoma.

- The thymus contains a small number of myoid cells, distinguished by striations and by the presence of acetylcholine receptors on their surface.

- Patients with thymoma-associated myasthenia gravis have additional autoantibodies to striated muscle (anti-titin) in addition to the antibodies that act at the neuromuscular junction.

- Serum levels of anti-titin have been studied for detection of thymomas in patients with MG.
Other Paraneoplastic Syndromes Associated with Thymomomas

- Limbic encephalitis
- Systemic lupus erythematosus
- Polymyositis
- Myocarditis
- Ulcerative colitis
- Hashimoto's thyroiditis
- Rheumatoid arthritis
- Sarcoidosis
- Scleroderma
- Endocrine disorders
- Addison's disease
- Hyperthyroidism
- Hyperparathyroidism
- Panhypopituitarism

- T-cell deficiency syndrome
- Pancytopenia
- Erythrocytosis
- Amegakaryocytic thrombocytopenia
- Eaton Lambert syndrome
- Myotonic dystrophy
- Myositis
- Hypertrophic pulmonary osteoarthropathy
- Nephrotic syndrome
- Minimal change nephropathy
- Pemphigus
- Chronic mucocutaneous candidiasis

**Failure of Negative Selection**
-T-cells in maturation that bind too strongly to MHC antigens and self peptides are normally eliminated from the thymus via apoptosis.
-Failure to eliminate these T-cells in patients with thymoma may result in autoimmune disease.
Workup and Evaluation

- **PFTS**
- **Is a biopsy required?**
  - If clinically consistent with resectable thymic malignancy, biopsy prior to surgery not required (NCCN v2.2013).
  - If locally advanced/unresectable → core needle biopsy or open biopsy.

- **Surgery**
  - Complete En Bloc resection remains treatment of choice even in invasive lesions.

** The two most important prognostic factors in multivariate analysis are invasiveness (fat, pleura, pericardium) and completeness of resection.

- Given the prognostic implications of margin status, an aggressive surgical technique is usually performed.

- Resection of the pericardium or lung parenchyma is often required for invasive lesions.

- Clips should be placed when margins are suspected to be positive to delineate the radiation field.
Case Management

• The tumor was radiographically resectable and suspicious for thymic origin.
• Right sided VATS performed.
• Pathology consistent with mixed-type thymoma 5 x3 cm, WHO AB, with microscopic invasion into the pericapsular connective tissue.
• Margins were negative but close (<1mm).

*Masaoka Stage IIA-> Microscopic extension outside the capsule.

*The role of adjuvant radiation in stage IIA thymoma is controversial.
WHO System for Thymomas - Current Case

WHO Histological Typing of Thymic Tumors

- **Type A** Neoplastic oval or spindle shaped epithelial cells without atypia or lymphocytes. More resemblance to medullary cells.
- **Type AB** Mixture of type A and B, with foci of lymphocytes.
- **Type B1** Resembles normal thymic cortex with areas similar to thymic medulla.
- **Type B2** Predominately cortical. Heavy population of lymphocytes. Scattered atypical cells.
- **Type B3** Predominantly polygonal epithelial cells with mild atypia. Few lymphocytes. “Well differentiated thymic carcinoma.”
- **Type C** Thymic carcinoma. These cells have cytological atypia and a cytoarchitecture resembling carcinoma.
# Masaoka's Clinical Staging - Current Case

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>5 Yr OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Macroscopically completely encapsulated and microscopically no capsular invasion</td>
<td>94-100%</td>
</tr>
<tr>
<td>II</td>
<td>Microscopic invasion into capsule (IIa) or Macroscopic invasion into surrounding fatty tissue or mediastinal pleura (IIb),</td>
<td>86-95%</td>
</tr>
<tr>
<td>III</td>
<td>Macroscopic invasion into neighboring structures, ie, pericardium, great vessels, or lung</td>
<td>56-69%</td>
</tr>
<tr>
<td>IVa</td>
<td>Pleural or pericardial dissemination</td>
<td>11-50%</td>
</tr>
<tr>
<td>IVb</td>
<td>Lymphogenous or hematogenous metastasis</td>
<td>11-50%</td>
</tr>
</tbody>
</table>
Case Management

• Following multidisciplinary discussion regarding risks/benefits of radiation, adjuvant treatment was recommended.

• CT Sim: Arms up, immobilized in vac-fix, 4-D CT obtained to evaluate respiratory motion

• CTV: included postoperative bed only.
  *No elective nodal treatment indicated.

• Radiation therapy delivered to the anterior mediastinum and postoperative bed to 50 Gy in 25 Fx.
Case Treatment

Teaching Points:
- Wedge pair → wedge heels pointed together for more homogeneous distribution

Optimal Wedge angle is:
\[ WA = 90 - \left( \frac{\text{Hinge Angle}}{2} \right) \]
*DVH- Constraints Analogous to Lung Cancer. More conservative limits are recommended when possible since patients have more longevity (NCCN 2.2013)

Combined Lung V20 <30-35%, V5 <65% (NSCLC NCCN1.2013)  
Heart V40<80%, V45<60% *Limit Dose to total heart <30 Gy (Thym NCCN 2.2013)  
Cord Max 45 Gy
Radiation Overview

• Radiation is considered in a variety of circumstances for thymic tumors:
  – Positive surgical margins or macroscopic disease left after resection regardless of stage.
  – As component of multimodality therapy in Stage III/IV unresectable tumors.
  – Adjuvant radiation following complete resection of stage II thymomas is controversial.

• Literature limited to mostly retrospective studies spanning several decades.

• The retrospective data must be considered in the context of completeness of resection and stage.
Management for Stage II

• Aggressive surgical resection.
• Adjuvant radiation for Stage II tumors is controversial.
• Recurrence is so low that the benefits of radiation are marginal after complete resection.
• Some argue for radiation since local recurrences are predominant site of failure.
  – 81% Local
  – 9% Distant
  – 11% Both
## Management By Stage Review

<table>
<thead>
<tr>
<th>Stage</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Complete resection only</td>
</tr>
<tr>
<td>II</td>
<td>Complete resection. + Adjuvant radiation for complete resection. Adjuvant radiation for +margin</td>
</tr>
<tr>
<td>III</td>
<td>Complete resection then post-op radiation. If unresectable, then trial of neoadjuvant chemo and evaluate for surgery. Otherwise, definitive chemoradiation therapy</td>
</tr>
<tr>
<td>Non metastatic IV</td>
<td>Induction combination chemo, then RT/ and or surgery</td>
</tr>
</tbody>
</table>
Radiation

**Dose (NCCN 2.2013)**
- Adjuvant treatment → 45-50 Gy, 54 Gy with + margin
- Gross disease → At least 60 Gy at 1.8-2 Gy per Fx
- Unresectable → 60-70 Gy at 1.8-2.0 Gy per Fx

**Volume**
- CTV should encompass entire thymus/operative bed and any known sites of disease. Evaluate surgical clips and discuss with thoracic surgeon.

- Thymic tumors do not routinely spread through lymphatics, thus extensive nodal irradiation is not recommended.

- Supraclavicular fields are not needed.

- AP, AP/PA, Wedge Pair arrangements often used.

- IMRT often considered if cardiac dose is high.
Chemotherapy

- Thymomas are classically chemosensitive tumors.
- Useful in metastatic or locally advanced setting.
- A clinical response is seen in roughly two-thirds of patients.
- Cisplatin containing regimens show high responses.
- Chemotherapy may be particularly useful in the neoadjuvant setting for patients with bulky masses to increase the chance of a complete resection.
- Combination chemotherapy consisting of cisplatin, doxorubicin and cyclophosphamide (PAC) is commonly used.
References


• NCCN Thymoma and Thymic Carcinoma v2.2013

Please provide feedback regarding this case or other ARROcases to arrocase@gmail.com