Thymic Tumors

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Case

**HPI**
53 yo man referred from OSH for anterior mediastinal mass. Initially presented with leg weakness and back pain for 2 months. Decreased sensation in both legs.

**PM/SH:** skin graft over RLE

**Meds:** motrin

**Social Hx:** Ex-5 pack-yr smoker, construction worker
Preop Work-up

• **LP**: negative

• **Serology**
  • acetylcholine receptor binding antibody – negative

• **MRI C/L spine**: diffuse enhancement of nerve roots in lumbar spine and cauda equina

• **CT chest**: homogenous anterior mediastinal mass, no evidence of SVC invasion. No adenopathy

• **Biopsy**: high grade carcinoma vs. thymoma—types B2 and AB with neuroendocrine features
Operation

Median sternotomy, complete excision of thymus with tumor, ligation of left innominate vein, right phrenic nerve, partial resection of SVC with Dacron patch reconstruction

EBL 1 L
Pathology

- Thymic carcinoma—squamous cell. 9 cm. Infiltrating into pericardium. Resection margin positive. Lymph nodes negative X2. No lymph-vascular invasion.
- Masaoka stage III
- WHO classification C
Course

• POD 1 Extubated, aspirin started
• POD 2 Respiratory distress, swelling in head, upper body. Reintubated. CT chest: thrombosis of SVC. Full anticoagulation started.
• POD 3 Stent to SVC by IR
Course

• POD 5 Extubated. Desat to 80’s then bradycardic, unresponsive. Attempted reintubation unsuccessful. Cricothyroidotomy. Lost vitals. ACLS X 10 minutes. Anticoagulation held
• POD 7 tracheostomy and bronchoscopy
• POD 8 anticoagulation resumed
• Currently in SICU, awake, recovering from anoxic brain injury, awaiting transfer to rehab facility
Thymus
Anatomy

• Arises primarily from the third pharyngeal pouches
• 15 gm at birth → 40 gm puberty → atrophy
• Arterial supply: internal mammary a, inferior thyroid a
• Venous drainage: posterior venous trunk → left innominate vein
Anterior Mediastinal Tumors

- Thymic tumors (~50%)
- Lymphoma (25%)
- Germ cell tumors (20%)
- Thyroid, parathyroid tissues
- Duplication cysts
- Hemangioma
- Lipoma
Thymic Tumors

• 4 major types
  – Epithelial cell (thymomas, thymic carcinomas)
  – Neuroendocrine (carcinoid, small cell carcinoma)
  – Thymolipomas
  – Rare tumors (neuroblastoma, ganglioneuroblastoma, etc)
Thymomas

- Most common thymic tumor
- Encapsulated (40-70%) or invasive (30-60%)
- Derived from thymic epithelial cells
Presentation

- Age > 40 years
- ~50% asymptomatic
- Local symptoms: pain, dyspnea, cough, hoarseness

Parathymic syndromes
  - Myasthenia Gravis
  - Other diseases: cytopenias, nonthymic malignancies, hypogamaglobulinemia, SLE, polymyositis, RA, UC, thyroiditis
CT chest with contrast
- Solid
- *No cystic, low-density areas* – teratoma
- Calcifications – also in teratoma

MRI
- Vascular invasion
- Defining fluid or fatty component of the mass

PET
- Role not defined
Serum Studies

- AFP
- β-hCG
- LDH
- Work up for myasthenia
To biopsy or not to biopsy…

Resection, No Biopsy
- Imaging diagnostic of small thymoma
- Assoc. with MG
- >40 yrs, no symptoms of lymphoma, normal β-HCG and AFP

Biopsy First
- Cannot distinguish b/t lymphoma, teratoma, or thymoma
- Extensive thymoma: neoadjuvant therapy
**Staging—Degree of Invasion**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>Encapsulated, tumor may invade into, but not through capsule microscopically.</td>
</tr>
<tr>
<td>Stage II</td>
<td></td>
</tr>
<tr>
<td>IIa</td>
<td>Macroscopic invasion into thymus or fat or adherent to but not through pleura or pericardium</td>
</tr>
<tr>
<td>IIb</td>
<td>Microscopic trans-capsular invasion</td>
</tr>
<tr>
<td>Stage III</td>
<td>Macroscopic invasion of neighboring organs (pericardium, great vessels, lung)</td>
</tr>
<tr>
<td>Stage IV</td>
<td></td>
</tr>
<tr>
<td>IV A</td>
<td>Pleural or pericardial dissemination</td>
</tr>
<tr>
<td>IV B</td>
<td>Lymphogenous or hematogenous mets</td>
</tr>
</tbody>
</table>

TNM stage NOT USED!!!
Histologic Classification

**WHO**

- Type A (spindle cell, medullary)
- Type AB (mixed)
- Type B
  - B1 (lymphocyte-rich, predominantly cortical)
  - B2 (cortical)
- B3 (epithelial, well-differentiated thymic carcinoma)
- Type C (thymic carcinoma)

**Benign thymomomas:**
Indolent, but malignant degeneration, recurrences, metastasis can occur.

**Well-differentiated thymic carcinomas:**
MG present in majority

**Thymic carcinomas:**
Worst prognosis
Disease Course

• Thymomas are generally indolent
• Spread mostly by local extension
• Can metastasize to distant sites (+ lymph nodes)
Treatment

• **Surgical resection**
  – Mainstay of treatment
  – Achievement of a complete resection, including en bloc, is paramount to oncologic outcomes
  – Different approaches

*FIGURE 131-6* Overall survival of patients with thymoma by Masaoka stage and by completeness of resection.²⁴
Overall Survival After Complete Resection

Graph showing survival rates for different stages of disease.

- Stage I (n = 135): 80% (62) at 10 years, 78% (11) at 15 years
- Stage II (n = 70): 78% (16) at 10 years, 73% (30) at 15 years
- Stage III (n = 83): 47% (16) at 5 years, 30% (5) at 10 years, 30% (6) at 15 years
- Stage IV (n = 19): 8% (2) at 2 years
Thymic Carcinoma

- Poor prognosis
- Median survival 2 years
- Local symptoms
- MG and parathymic syndromes rare
- High grade (Lymphoepithelioma)
- Low grade (Squamous)
Multimodality Therapies

• Effect of radiotherapy remains controversial
  – Post operative RT is recommended only for incompletely resected stage III tumors

• Thymomas are chemosensitive
  – CAPVc regimen (cyclophosphamide, doxorubicin, cisplatin, vincristine)
Neoadjuvant Chemotherapy

• Small prospective trials
• Both resectability and survival improved in stage III, IV thymomas
### Outcomes After Preop Chemotherapy

<table>
<thead>
<tr>
<th>Study</th>
<th>No. Patients (Total)</th>
<th>No. Patients With Stage III/IV</th>
<th>Preoperative Chemotherapy</th>
<th>Adjuvant Therapy</th>
<th>% Objective Response</th>
<th>% R0</th>
<th>% Pathologic Complete Response</th>
<th>% 5-Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lucchi et al</td>
<td>36</td>
<td>25/11</td>
<td>PEEpIx3</td>
<td>RT</td>
<td>67</td>
<td>77</td>
<td>6</td>
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<td>Rea et al</td>
<td>32</td>
<td>—</td>
<td>CAPVc x3</td>
<td>RT or Ch</td>
<td>100</td>
<td>75</td>
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<td>55</td>
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<tr>
<td>Venuta et al</td>
<td>25†</td>
<td>12/13</td>
<td>PEEpIx3</td>
<td>RT/Ch</td>
<td>—</td>
<td>80</td>
<td>4</td>
<td>92/68†</td>
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<tr>
<td>Kim et al</td>
<td>22</td>
<td>11/11</td>
<td>CAPPr x3</td>
<td>RT/Ch</td>
<td>77</td>
<td>76§</td>
<td>18§</td>
<td>95</td>
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<td>Rea et al</td>
<td>16</td>
<td>13/3</td>
<td>CAPVc x3</td>
<td>RT or Ch</td>
<td>100</td>
<td>69</td>
<td>31</td>
<td>57</td>
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<tr>
<td>Macchiarini et al</td>
<td>7</td>
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<td>PEEpIx3</td>
<td>RT</td>
<td>100</td>
<td>57</td>
<td>29</td>
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<tr>
<td><strong>Average</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>89</strong></td>
<td><strong>72</strong></td>
<td><strong>18</strong></td>
<td><strong>74</strong></td>
</tr>
</tbody>
</table>

Inclusion criteria: studies of >5 patients with preoperative chemotherapy.

*Thymic carcinoma excluded.

†Only 21 of 25 patients treated with preoperative chemotherapy.

§Data for stage III/stage IV.

Data taken from an earlier full publication.161

Ch, chemotherapy; RT, radiotherapy.

Chemotherapy regimens: CAPPr, cyclophosphamide, doxorubicin, cisplatin, prednisone; CAPVc, cyclophosphamide, doxorubicin, cisplatin, vincristine; PEEpI, cisplatin, etoposide, epirubicin.
Predictors of survival in patients with locally advanced thymoma and thymic carcinoma (Masaoka stages III and IVa)

Giuseppe Cardillo a,*, Francesco Carleo a, Roberto Giunti a, Michele Giovanni Lopergolo a, Lorenzo Salvadori a, Alessia Raffaella De Massimi a, Lea Petrella b, Massimo Martelli a

61 patients with locally advanced thymoma (stage III and IVa)

Induction Chemotherapy plus Surgery (31 patients)

Surgery only (30 patients)

Adjuvant radiotherapy (34 patients)

Fig. 1. Treatment schema of this study.
<table>
<thead>
<tr>
<th>Parameters</th>
<th>HR; 95%CI</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>Complete resection</td>
<td>0.18; 0.04–0.78</td>
<td>0.02</td>
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<tr>
<td>Masaoka stage III</td>
<td>0.22; 0.05–0.81</td>
<td>0.02</td>
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<tr>
<td>Induction chemotherapy</td>
<td>0.09; 0.01–0.46</td>
<td>0.003</td>
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<tr>
<td>Histological WHO (AB)</td>
<td>0.11; 0.02–0.66</td>
<td>0.01</td>
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</table>
Summary

• Surgery is the mainstay of therapy for thymomas
• Complete resection whenever possible
• Histologic classification have minimal independent prognostic value except thymic carcinoma
• All stages and all histologic subtypes of thymomas can metastasize
• Preop chemotherapy for advanced-stage tumors improves resectability and survival
References

1. Pearson’s Thoracic and Esophageal Surgery
2. Sabiston and Spencer’s Surgery of the Chest 8e
5. Ahmad, U and Huang, J: Current Readings: The most influential and recent studies involving surgical management of thymoma. Semin Thoracic Surg 25:144-149
### Response to Chemotherapy

<table>
<thead>
<tr>
<th>Study</th>
<th>No. Patients</th>
<th>% Stage IV</th>
<th>% Thymic Carcinoma</th>
<th>Chemotherapy Regimen</th>
<th>% Objective Response</th>
<th>% Complete Response</th>
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<tr>
<td>Loehrer et al162*</td>
<td>30</td>
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<td>Bonomi et al127*</td>
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