Thymomas and Thymic Carcinoma

**Introduction:** Thymic tumors are rare neoplasms that arise in the anterior mediastinum, and account for about 20% of mediastinal masses. Median age of onset are between 40 and 60 years of age, and similar incidence in men and women.

**Risk Factors:** No known risk factors. A strong association with myasthenia gravis.

**Biology:** Undefined

**Clinical Presentation:**
1) Anterior mediastinal mass
   - Thymomas → local compression, e.g. hest pain, shortness of breath, cough, phrenic nerve palsy
   - Thymic carcinoma → more local invasive, distant metastasis is rare.

2) Paraneoplastic symptoms
   - Myasthenia gravis
   - Pure red cell aplasia
   - Hypogammaglobulinemia/immmunodeficiency

**Diagnosis:**
A. Mediastinal Mass:
   - CT chest with contrast
   - Serum β-HCG, AFP, LDH
   - PET-CT scan optional
   - TSH, T3, T4 level
   - Pulmonary function tests (PFTs)
   - MRI chest

**Pathology:**
A. IHC: Epithelial cells + lymphocytes + Cytokeratin

**UpToDate:** Sutent and mTOR inhibitor may have activities in thymic carcinoma.

B. WHO Types:
1) Type A thymoma: medullary thymoma (9%).
2) Type AB thymoma: mixed thymoma (24%).
3) Type B
   - B1: 13%, predominantly cortical thymoma, lymphocyte rich
   - B2: 24%
   - B3: well-differentiated thymic carcinoma, 15%.
4) Thymic carcinoma:

In general, encapsulated tumors (type A and AB) are associated with stage I or II disease, whereas types B1, B2, and B3, and thymic carcinoma are more frequently associated with invasion into adjacent organs or with disseminated disease (stages III and IV).

**C. Staging**
Prognosis:

1) Thymomas are slow-growing, and the presence of invasion is an important adverse prognostic marker. Thymic carcinomas are more aggressive and have poorer prognosis.

2) Prognostic factors: stage + histology + complete resection status + size
   - Negative prognostic factors:
     * Tumor >10cm
     * Extent of the surgical resection
     * Tracheal or vascular compromise at presentation
     * Age <30yrs
     * Presence of hematologic paraneoplastic syndromes

Tx Principle:

A. Surgically resectable:

1) Total thymectomy → remove all thymic tissue, not just tumor tissue (standard care).
   → √ serum anti-acetylcholine receptor antibody before surgery (myasthenia gravis leads to respiratory failure during surgery).
   → If complete resection is NOT possible, debulking with subtotal resection, followed by RT (improve survival)
   → Although thymomas is chemo-sensitive, chemo dubulking is still invastigational.

2) Post-op treatment: adj Therapy
   - R0 resection → observe for stage I thymoma (completely encapsulated)
   - R0 resection → post-op RT for all other thymomas (stage II-IV) or thymic carcinoma with capsular invasion present
   - R1 resection → post-op RT (thymoma) or "post-op RT + chemo" for thymic carcinoma
   - R2 resection → "RT + chemotherapy" for both thymoma and thymic carcinoma

B) Locally advanced, unresectable:

1) Locally advanced: neoadj chemotherapy → re-staging → surgical resection, followed by post-op RT (optional)
   - If remains unresectable after neoadj chemo → RT +/- chemotherapy

2) Metastatic disease:
   - Isolated solitary met: → surgical resection → post-op chemo or RT
   - Distant mets: → chemotherapy

C. Chemotherapy choices.

1) 1st line:
   - CAP (cisplatin/doxorubicin/cyclophosphamide) for thymoma
   - Carbo/Taxel for thymic carcinoma

2) 2nd line:
   - Etoposide
Follow-Up:  
- Patients with thymoma are at risk for the development of second malignancies.
- Annual chest CT