Carcinoma of the Thymus

General Clinical Features

- No apparent gender predilection
- Age range of 35-75 yrs.
- Tumors present as incidental masses, or with cough or chest pain; no association with myasthenia gravis, pure red cell aplasia, or hypogammaglobulinemia
- Distant metastases involve lung, liver, bones, and other sites
- Overall survival at 5 yrs. is < 20%; cases with diffuse growth, invasive margins, and > 10 mitoses/10 HPF have a particularly adverse evolution
CARCINOMA OF THE THYMUS
General Histological Features

- Tumor may have a misleadingly “pushing” margin; some are even apparently encapsulated
- Overt variations on the themes of squamous or glandular differentiation are seen in only a minority of cases
- Vesicular or hyperchromatic nuclei with prominent nucleoli
- Obvious mitotic activity
- Neutrophils and eosinophils may be numerous in the stroma in some cases, leading to diagnostic confusion
- Foci of spontaneous necrosis are common
- Rare cases arise in transition from “ordinary” thymoma

HISTOLOGIC TYPES OF THYMIC CARCINOMA

- Squamous carcinoma
- Basaloid carcinoma
- Lymphoepithelioma-like carcinoma
- Clear-cell carcinoma
- Neuroendocrine carcinoma
- Papillary adenocarcinoma
- Mucinous (colloid) carcinoma
- Macropapillary carcinoma
- Adenosquamous carcinoma
- Sarcomatoid carcinoma
- Anaplastic carcinoma
- Micronodular carcinoma
- Rhabdoid carcinoma
CARCINOMA OF THE THYMUS
Immunohistological Features

- Keratin+ (with “interlocking” cellular pattern in LELC)
- PAX-8 & Epithelial membrane antigen +/-
  - Vimentin -
  - CD45-
- SYN/CGA+ in neuroendocrine CA
- CD5, CD117, GLUT-1 +/-
- Intratumoral lymphocytes are CD99-
Weissferdt-Moran TNM Staging System for Thymic Carcinoma

**Description**

- **T1**: Tumor limited to thymus gland
- **T2**: Tumor invading visceral pleura, lung, pericardium, great vessels, chest wall, or diaphragm
- **T3**: Direct extrathoracic tumor extension, beyond thoracic inlet (consisting of the manubrium, the first thoracic vertebra, & the first ribs and their cartilage) or diaphragm
- **N0**: No lymph node metastasis
- **N1**: Lymph node metastasis to intrathoracic lymph nodes
- **M0**: No distant metastasis
- **M1**: Distant metastasis (indirect tumor spread, including metastasis to extrathoracic lymph nodes)

**Stage Groupings**

- **Stage I**: T1N0M0
- **Stage II**: T2N0M0
- **Stage III**: T3N0M0
- **Stage IV**: Any T, N1, M0
- **Stage IVa**: Any T, any N, M1

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**Proposed stage T1, tumor limited to the thymus gland:**

- **Proposed stage T2, tumor limited to the thymus gland:**
- **Proposed stage T3, extrathoracic tumor extension:**

**Survival curves for 33 patients with thymic carcinoma according to the Weissferdt-Moran staging system:**

- Kaplan-Meier.
**Differential Diagnosis of Carcinoma of the Thymus**

- **Metastatic carcinoma**
- Large cell non-Hodgkin lymphoma
- “Syncytial” Hodgkin lymphoma
- “Solid” embryonal carcinoma of the thymus
- Metastatic melanoma

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**THYMIC NEUROENDOCRINE NEOPLASMS**

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**THYMIC NEUROENDOCRINE CARCINOMAS**

- Rosai et al. described 8 cases of thymic tumors in 1972 (in *Cancer*) under the rubric of “mediastinal endocrine neoplasm, of probable thymic origin, related to carcinoid tumor;” this name was very quickly abbreviated to “thymic carcinoid”
- In another publication in the same issue of *Cancer*, Rosai et al. documented the association between thymic carcinoids and MEN type I
THYMIC NEC: Clinical Presentation

• Male to female ratio of 3:1; median age 43 yr.
  • Approximately 30% of patients are asymptomatic; another 20% have cough, chest pain, or SVC syndrome
  • Approximately 50% have functional tumors, producing an endocrinopathy (Cushing’s syndrome, SIADH) or MEN type I
  • Other associated conditions may include myopathy, neuropathy, Eaton-Lambert syndrome, and hypertrophic osteoarthropathy
THYMIC NEC: Histological Variants

GRADE I:
• Organoid ("conventional")
• Diffuse (lymphoma-like)
• Sclerotic
• Oncocytic
• Spindle-cell
• Pigmented (melanotic & lipofuscinoid)
• Mucinous
• Angiectatic
• Medullary carcinoma-like/amyloidotic

GRADE II
GRADE III:
• Pure small-cell neuroendocrine carcinoma
• Pure large-cell neuroendocrine carcinoma
• Mixed small- and large-cell neuroendocrine CA

Grading of Neuroendocrine Carcinomas of the Thymus

• Outlined by Klemm & Moran (Semin Diagn Pathol 1999; 16: 32-41)
• Grade 1-- Organoid growth, nuclear uniformity, ≤3 mitoses per 10 HPF, and only punctate, if any, necrosis
• Grade 2-- Areas of confluent sheet-like growth, noticeable nuclear pleomorphism, > 4 but <10 mitoses per 10 HPF; obvious areas of necrosis
• Grade 3-- Images identical to SCNC or LCNC of the lung (in part or globally), with geographic necrosis & mitotic activity ≥ 10 per HPF

Grading of Neuroendocrine Carcinomas of the Thymus: Comments

• In fact, there appears to be a two-tiered biological grading “scheme” for thymic NEC; grade I tumors have a relatively long evolution, and even patients with distant metastases may live for 10+ years; on the other hand, grades II and III tumors behave similarly (…aggressively)
• However, grade II and grade III tumors are more common than grade I in the thymus, by far
WHENCE THE “ATYPICAL CARCINOID?”

• “Atypical carcinoid” is no longer a useful clinicopathologic designation, because pathologists have, over the past 20 years, used this term as a wastebasket for pulmonary tumors with a variety of morphologic patterns (e.g., high-grade large-cell NEC, “intermediate cell” variant small-cell NEC, and organoid non-endocrine carcinomas of the lung)

• Treatment data on this entity are therefore hopelessly polluted

LARGE CELL NEUROENDOCRINE CARCINOMAS

• Formerly grouped with “atypical carcinoid” or with large cell carcinoma, not further specified; thymic neoplasms with such characteristics have been reported

• Those nosological inaccuracies have adverse treatment-related impact, in that the behavior of large cell NECs is most like that of small cell NECs, and patients with the former neoplasms may benefit from chemotherapy that is directed at the latter tumors.
Small-Cell Thymic Neuroendocrine Carcinomas

- Uncommonly seen in “pure” form—they are most often admixed with another variant of neuroendocrine carcinoma, or with a non-neuroendocrine carcinomatous component
- Behavior may be somewhat better than that of pulmonary small-cell carcinomas, but that point is uncertain
- Thymic SCNC is TTF-1- negative
• Complete resection of tumor is possible in only roughly 50% of cases; however, thymic NEC may also be paradoxically encapsulated
• Aggressive surgical attempts at extirpation should be recommended; irradiation and chemotherapy are not particularly effective for thymic NEC
• Lymph nodal metastases in the chest are seen in ~70% of cases; 40-50% of patients develop extrathoracic metastases (to bone, liver, brain, lungs, & skin)
• Overall mortality at 10 years' followup is approximately 50%; death is due to intractable local recurrence or metastasis