Thymoma: new findings

Thoracale Oncologie
Groep Antwerpen

Paul Van Schil
UZ Antwerpen

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ITMIG www.itmig.org

Announcement

International THYMIC MALIGNANCY
Interest Group

7 and 8 July 2011
following the IASLC meeting
NH-Hotel Barbizon Palace,
Amsterdam, The Netherlands

Introduction

- difficult anatomy
- several compartments
- no uniform definitions
- variety histologic tissues
- pluripotent cells
- access controversial
- multiple incisions
- minimally invasive techniques

Thymic malignancies and other mediastinal tumors

Thoracic wall

Anatomical references

- Suprasternal notch
- Angle of Louis (angulus sterni)
- 2nd costal cartilage
- superior and inferior mediastinum
- superior border of heart
- origin and end aortic arch
- tracheal bifurcation
- Xiphosternal junction

Anterior mediastinal – anterosuperior compartment

- anterior to pericardium
- includes: lymphatic tissue, thymus, extrapericardial aorta + branches, great veins
- masses more likely to be malignant
- 400 pts mediastinal tumors
  malignant 59 anterior mediastinum
  29 middle
  16 posterior

Case 1: anterior mediastinal tumor

61-year-old ♀
- emergency department: fatigue, diffuse muscular complaints, ↓ exercise tolerance
- history: hiatal hernia, varicectomy, 20 pack years, hypercholesterolemia

Anterior mediastinal tumors

- Thymoma
- Lymphoma (T-cell lymphoma)
- germ cell tumors
  - benign teratomas
  - seminomas
  - embryonal, nonseminomatous germ cell tumors
- mediastinal cysts
  - pericardial
  - enterogenous (bronchogenic + enteric)
  - thymic
  - thymic, parathyroid tissue

WHO histological typing of tumors of the thymus

1. epithelial tumors
   1.1. thymoma
      - type A: spindle cell, medullary
      - type B: lymphocyte-rich, lymphocytic, predominantly cortical, organoid
      - type B1: lymphocytic, predominantly cortical
      - type B2: epithelial, squamoid
      - type B3: epithelial, squamoid, well-differentiated
   1.2. thymic carcinoma (type C thymoma)
      - low- (well-differentiated) and high-grade (undifferentiated)

2. neuroendocrine tumors
   - carcinoid, small cell ca, large cell neuroendocrine ca.

Thymoma

“Thymomas are fascinating tumors because of their multifaceted clinical presentation, including an unrivaled frequency of associated paraneoplastic autoimmune diseases and an astounding histologic heterogeneity.”

Muller Hermelink HK, Curr Opin Oncol 2000; 12:426-33

- most common ant. mediastinal primary neoplasm in adults, rare in children
- 20% of all mediastinal neoplasms in adults
- most common neoplasm affecting thymus

Thymoma

- 30 – 50 years, ♂ =
- 50% symptomatic myasthenia gravis
dyspnea, cough, substernal pain
- myasthenia gravis 60-70 % thymic hyperplasia
- 10-12 % thymoma
- invasive thymoma: symptoms due to local compression
Case 1: anterior mediastinal tumor

- 61-year-old ♀
- Cardiac ultrasound: no invasion, hypertrophic left ventricle, good systolic function
- EMG: strongly suggestive of myasthenia
- PET scan: slight uptake ant. mediastinal tumor
diffuse tracer uptake skeletal muscles: paraneoplastic?

Paraneoplastic symptoms

- Autoimmune SLE, sarcoidosis
- Endocrine disorders Addison
- Hematologic PRCA, hypogammaglobulinemia
- Neuromuscular myasthenia gravis
- Miscellaneous hypertrrophic pulmonary osteoarthropathy

Paraneoplastic syndromes

Thymoma

Diagnosis - staging

- CT, MRI
  - Encapsulated, smaller lesions that are resectable: no puncture or biopsy (leave capsule intact!)
- Staging
  - Invasive thymoma: at time of surgical resection - considered malignant because of their invasive potential
  - Masaoka – Koga staging system

Masaoka - Koga staging system

- Stage I: grossly and microscopically completely encapsulated tumor
- Stage IIa: microscopic transcapsular invasion
  - b: macroscopic invasion into thymic or surrounding fatty tissue, or greatly adherent to but not breaking through mediastinal pleura or pericardium
- Stage III: macroscopic invasion into neighboring organs, i.e. pericardium, great vessels or lung
- Stage IVa: pleural or pericardial metastases
  - b: lymphogenous or hematogenous metastases

Koga K et al. Pathol Int 1994; 44:359-67
Muller Hermelink HK. Curr Opin Oncol 2000; 12:426-33
**Thymoma - treatment**

- stage I resection, excellent long-term survival, recurrence 2-12%
- stages II, III resection + PORT
- stage IV chemotherapy, radiotherapy, surgery

**locally advanced, unresectable malignant thymoma:** induction chemotherapy, surgery, PORT

**Thymectomy - approach**

- median sternotomy
- clam shell incision
- VATS (thoracoscopy)
- da Vinci robotic system

**Thymoma - surgical resection**

- complete resection
- enter pericardium to evaluate extension
- cave both phrenic nerves if both invaded: one resected, one dissected off tumor
- invasive tumors: debulking acceptable + PORT or chemoradiotherapy

**Case 1: anterior mediastinal tumor**

- 61-year-old ♀
- transthoracic puncture: suggestive of cortical thymoma
- thymectomy by clam shell incision
- intrapericardial dissection; wedge excision R lung
- pathology: cortical thymoma WHO B2; capsular invasion
- uneventful postoperative recovery
- PORT

**Thymoma Surgical resection - outcome**

- depends on extent and completeness of resection
- 241 pts thymoma 7-year survival
  - complete resection 82%
  - subtotal 71%
  - biopsy alone 26%

Thymoma - radiotherapy

- usually 45-50 Gy administered
- locally advanced or metastatic unresectable disease
- micro- or macroscopic residual disease after incomplete surgical resection
- following complete resection of an invasive thymoma or thymic carcinoma (local control)
- no benefit of PORT following resection of encapsulated non-invasive tumors

Thymoma - chemotherapy

- thymoma: chemotherapy-sensitive
  - induction chemotherapy
  - locally invasive tumors (particularly thymic carcinoma) or large bulky masses
  - cisplatin-based regimen + resection ± PORT
  - 22 pts induction CT, response rate 77%
  - 21 resections attempted; 4 pCR or tumor necrosis > 80%
  - postop. RT (50-60 Gy) + 3 cycles adjuvant CT
  - 19 pts completed whole treatment
  - 7-year DFS 77% OS 78%

Kim ES et al. Lung Cancer 2006; 44:363-70

- chemotherapy for metastatic or recurrent disease
  - no large randomized trials
  - cisplatin-based combination CT (etoposide, doxorubicin, cyclophosphamide)
  - overall response rates: 70-80%
  - MST 15-38 months
  - octreotide: thymic malignancies that express somatostatin receptors → meaningful response to octreotide with addition of prednisone: RR 30%

Loehrer PJ et al. JCO 2004; 22:259-65

Thymoma - survival

- overall 5-year survival 70% with local invasion 50%
  - without 75%
- overall 10-year survival 50% with local invasion 30%
  - without 60%
- 3-year survival Masaoka stage I 94 - 100% II 84 - 95% III 56 - 69% IV 11 - 50%


- WHO classification

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Thymoma - prognosis

Adverse prognostic factors

- Invasion through the capsule into mediastinal fatty tissue, pleura or pericardium
- Extent of surgical resection (reflects invasive nature)
- Intra- or extrathoracic metastases
- Tumor size > 10 cm
- Tracheal or vascular compromise
- Age < 30 years
- Histological type (thymic carcinoma)

Case 2: thymic hyperplasia, nodule

28-year-old ♀
- Investigated diplopia
- Possible ocular myasthenia, anti-ACH receptor antibodies
- CT chest: thymic hyperplasia, nodule 1.6 cm
- PET scan: slight uptake nodule, small thymoma?

Welsh JS et al. JAMA 200; 283:1142-3

Thymoma - prognosis

- Paraneoplastic syndrome: not associated with inferior outcome
- 2nd primary cancers: 17 – 28% develop 2nd malignancies after thymectomy
- Varying histologic types: digestive system cancers, soft tissue sarcomas
- Usually outside radiation port

Welsh JS et al. JAMA 200; 283:1142-3
Anterior mediastinal tumors

Conclusions

- mediastinum: variety histologic tissues
- pluripotent cells
- thymoma
- aim: complete resection, intact capsule
- different surgical approaches
  - sternotomy, clam shell
  - minimally invasive techniques: VATS, robotic system
- unresectable tumors: combined modality therapy