Thymoma: new findings

Thoracale Oncologie
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TOGA symposium « triple T » 28 oktober 2011

ITMIG www.itmig.org

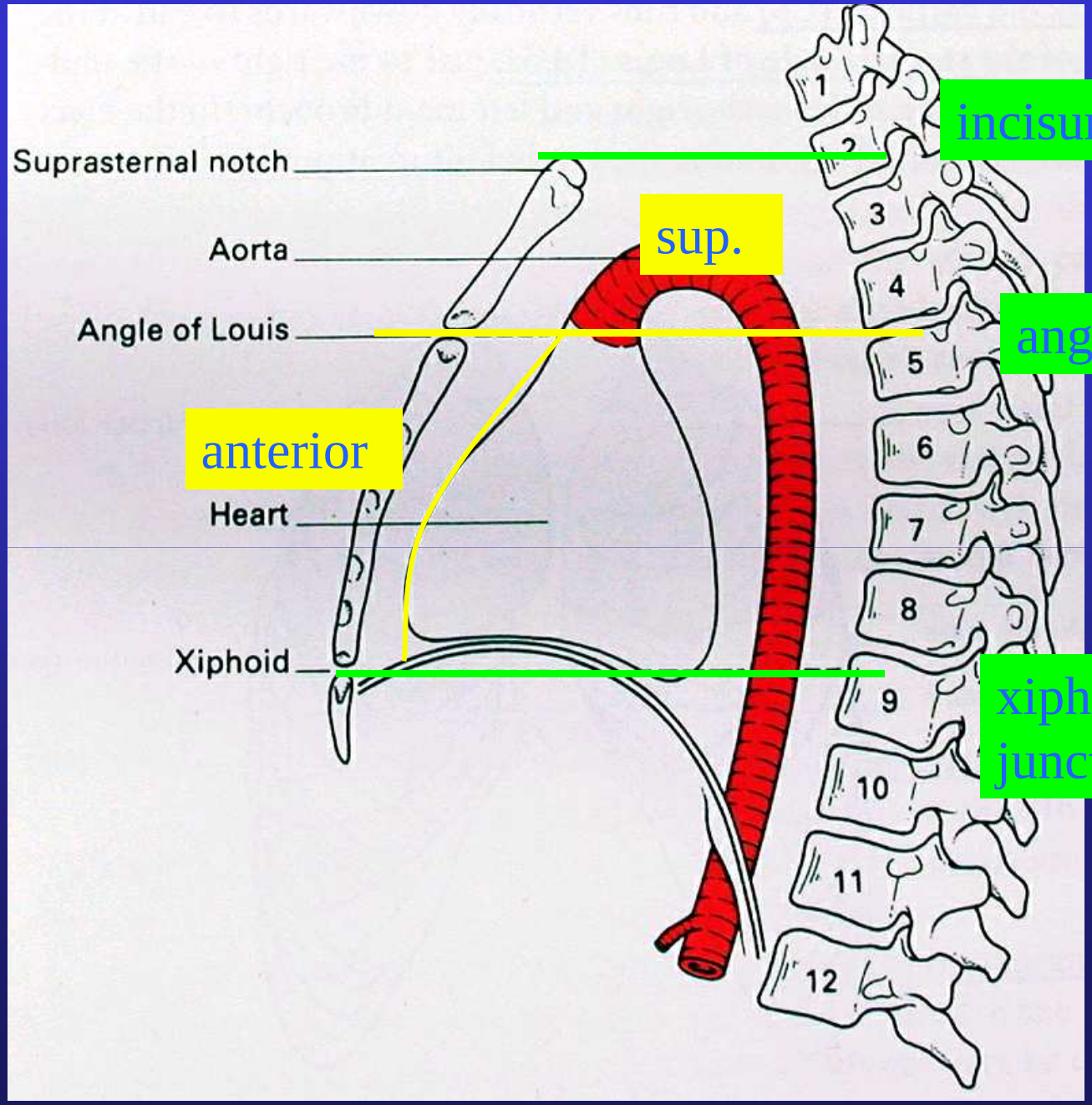
International THYMIC MALIGNANCY Interest Group

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

Thymic malignancies and other mediastinal tumors

Introduction

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


Suprasternal notch
Aorta
Angle of Louis
Heart
Xiphoid
1
2
3
4
5
6
7
8
9
10
11
12
incisura jugularis
sup.
angulus sterni
anterior
xiphosternal junction

Thoracic wall
Anatomical references

- Suprasternal notch — T2/3
- Angle of Louis (angulus sterni) — T4/5
  - ✓ 2nd costal cartilage
  - ✓ superior and inferior mediastinum
  - ✓ upper border of heart
  - ✓ origin and end aortic arch
  - ✓ tracheal bifurcation
- Xiphosternal junction — T9

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

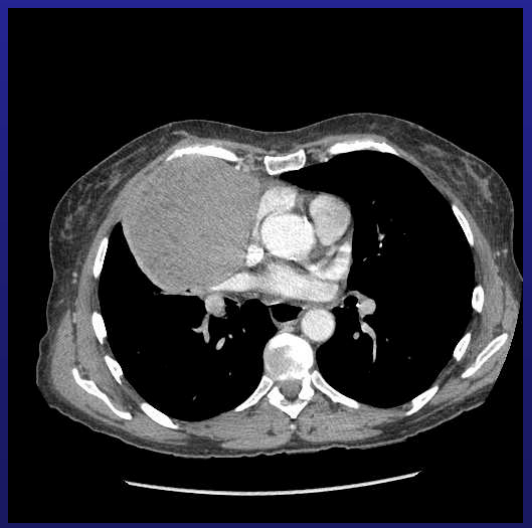
  59 anterior mediastinum
  29 middle
  16 posterior

Davis RD Jr et al. Ann Thorac Surg 1987; 44:229-37

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

4 x T !

WHO histological typing of tumors of the thymus

1. epithelial tumors

1.1. thymoma

type	A	spindle cell, medullary
	AB	mixed
	B1	lymphocyte-rich, lymphocytic, predominantly cortical, organoid
	B2	cortical
	B3	epithelial, squamoid, well-differentiated thymic ca.

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.

Rosai J. Histological typing of tumors of the thymus. 2nd ed. Springer, Berlin, 1999

WHO histological typing of tumors of the thymus

3. germ cell tumors
4. lymphoid tumors
5. stromal tumors
6. tumor-like lesions (thymic hyperplasia, thymic cyst)
7. neck tumors of thymic or related branchial pouch derivation (ectopic hamartomatous or cervical thymoma)
8. metastatic
9. unclassified

Rosai J. Histological typing of tumors of the thymus. 2nd ed. Springer, Berlin, 1999

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

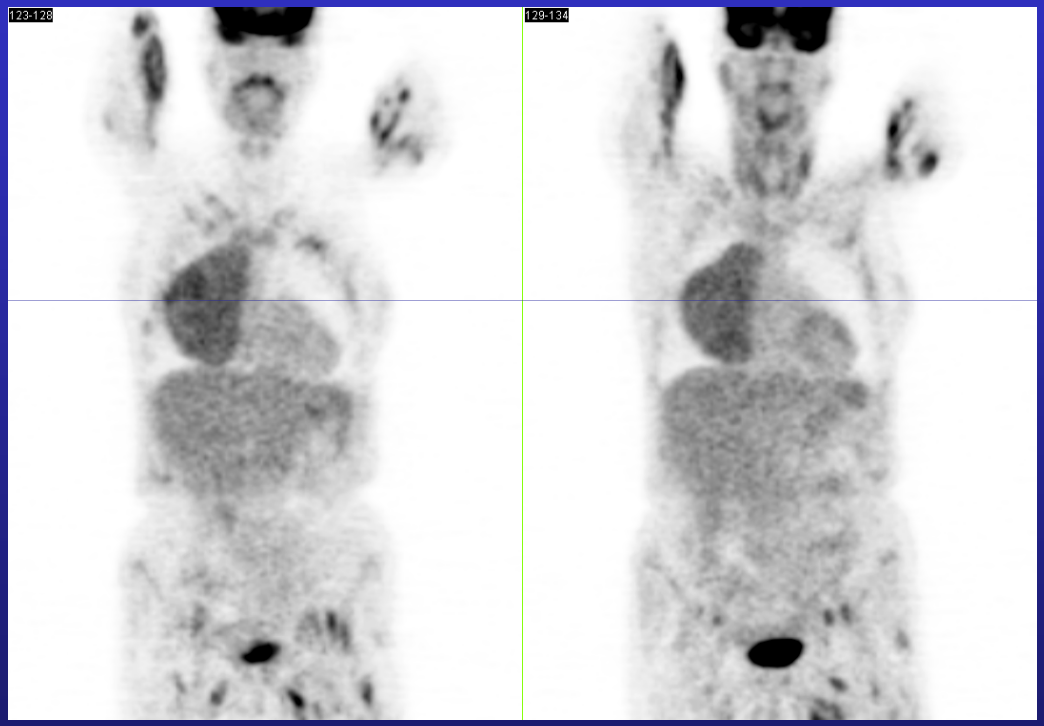
- 30 – 50 years, ♂ = ♀
- 50% symptomatic — myasthenia gravis
  dyspnea, cough, substernal pain
- myasthenia gravis — 60-70 % thymic hyperplasia
  10-12 % thymoma
- invasive thymoma: symptoms due to local compression

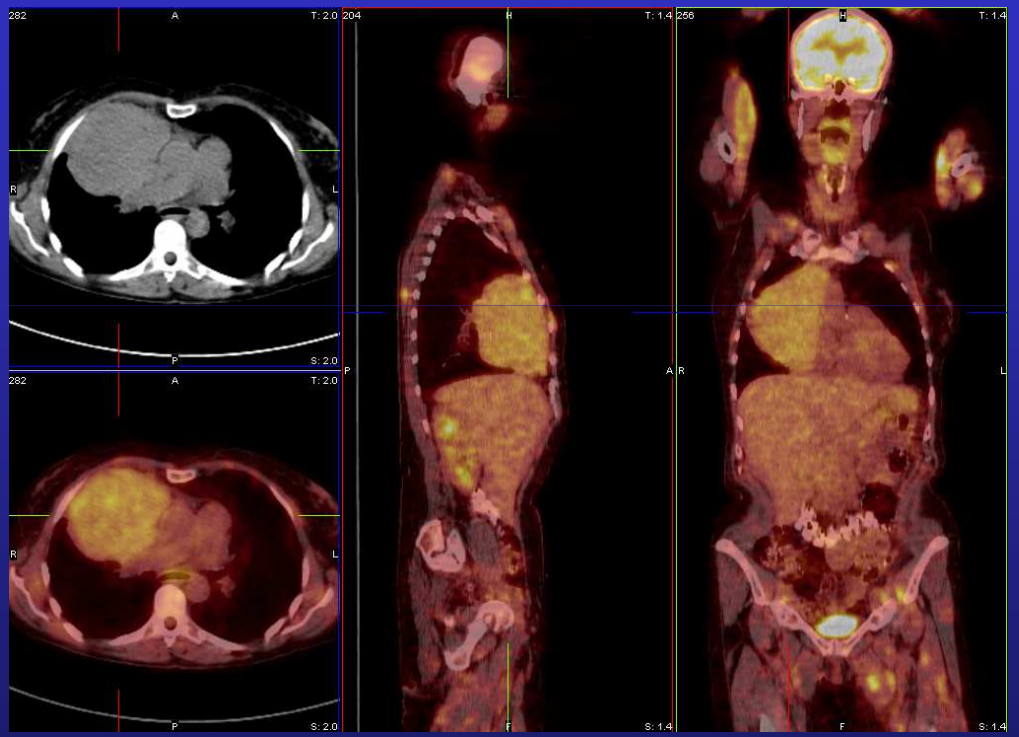
Case 1: anterior mediastinal tumor

61-year-old ♀

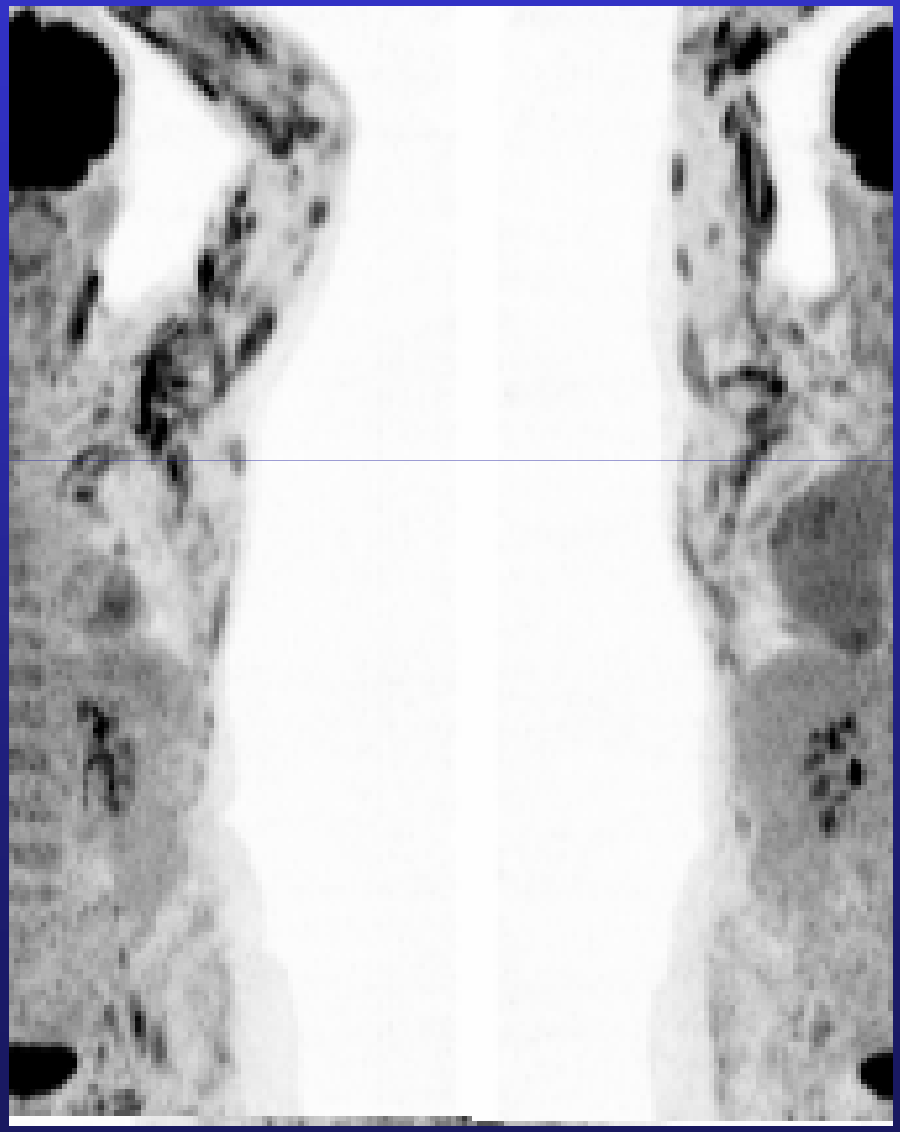
- **cardiac ultrasound: no invasion, hypertrophic left ventricle, good systolic function**
- **EMG: strongly suggestive of myasthenia**
- **PET scan: slight uptake ant. mediastinal tumor**
  diffuse tracer uptake skeletal muscles: paraneoplastic?

Paraneoplastic symptoms





Paraneoplastic symptoms



Thymoma
Paraneoplastic syndromes

• autoimmune	SLE, sarcoidosis
• endocrine disorders	Addison
• hematologic	PRCA, hypogammaglobulinemia
• neuromuscular	myasthenia gravis
• miscellaneous	hypertrophic pulmonary osteoarthropathy

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

Thymoma
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 grossly 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

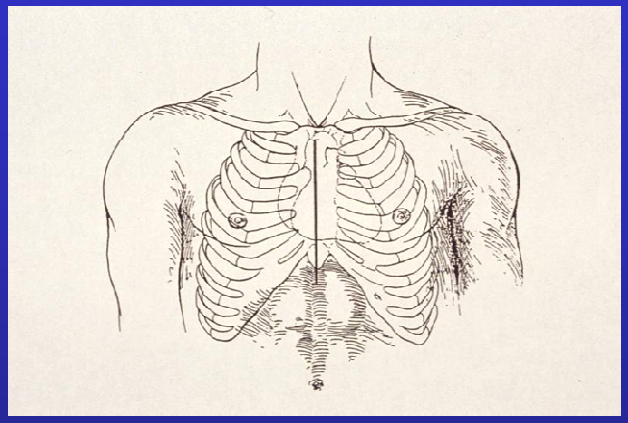
Masaoka A et al. Cancer 1981; 48:2485-92
Koga K et al. Pathol Int 1994; 44:359-67
Muller Hermelink HK. Curr Opin Oncol 2000; 12:426-33

Thymoma - treatment

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

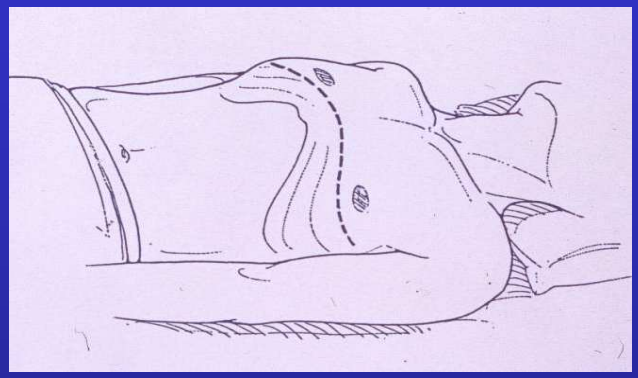
locally advanced, unresectable malignant thymoma: **induction chemotherapy, surgery, PORT**

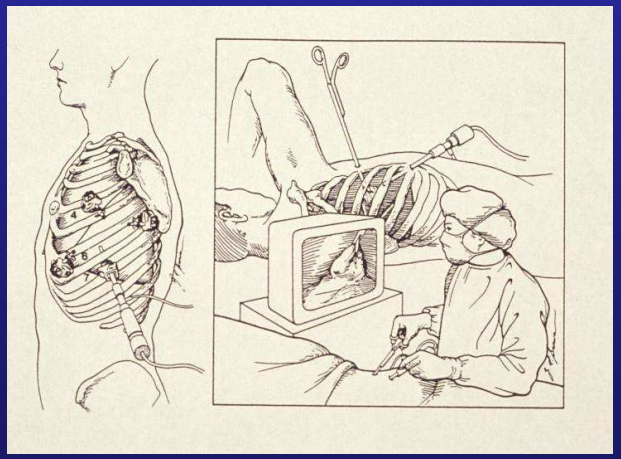
Thymectomy - approach



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

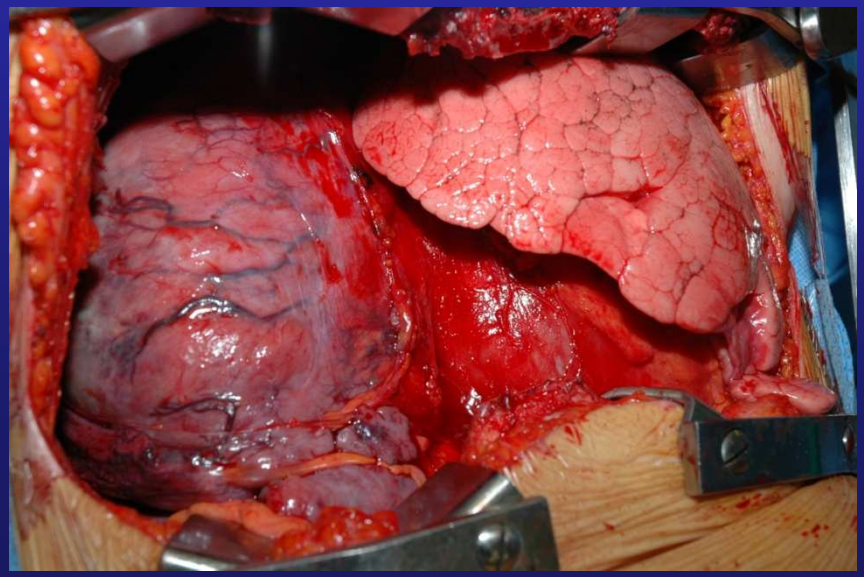
  if both invaded: one resected, one dissected off tumor

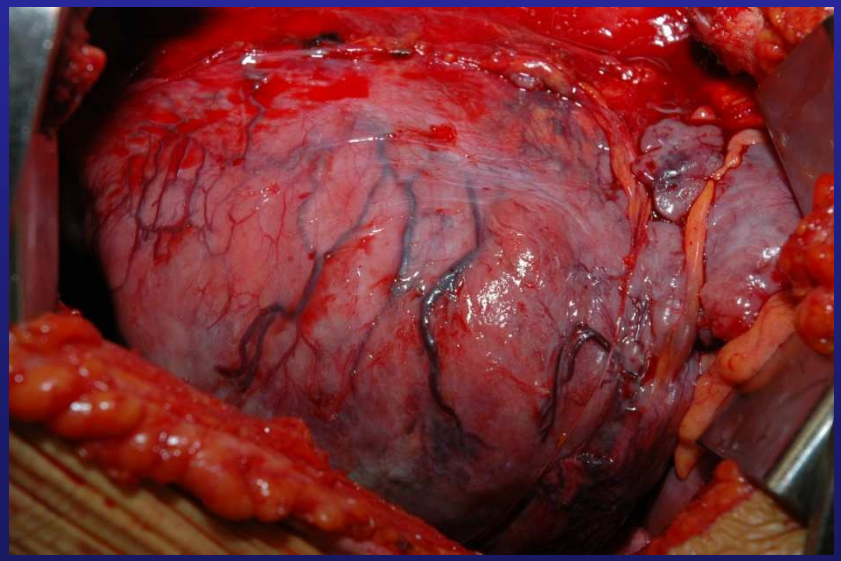
- invasive tumors: debulking acceptable + PORT or chemoradiotherapy

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**

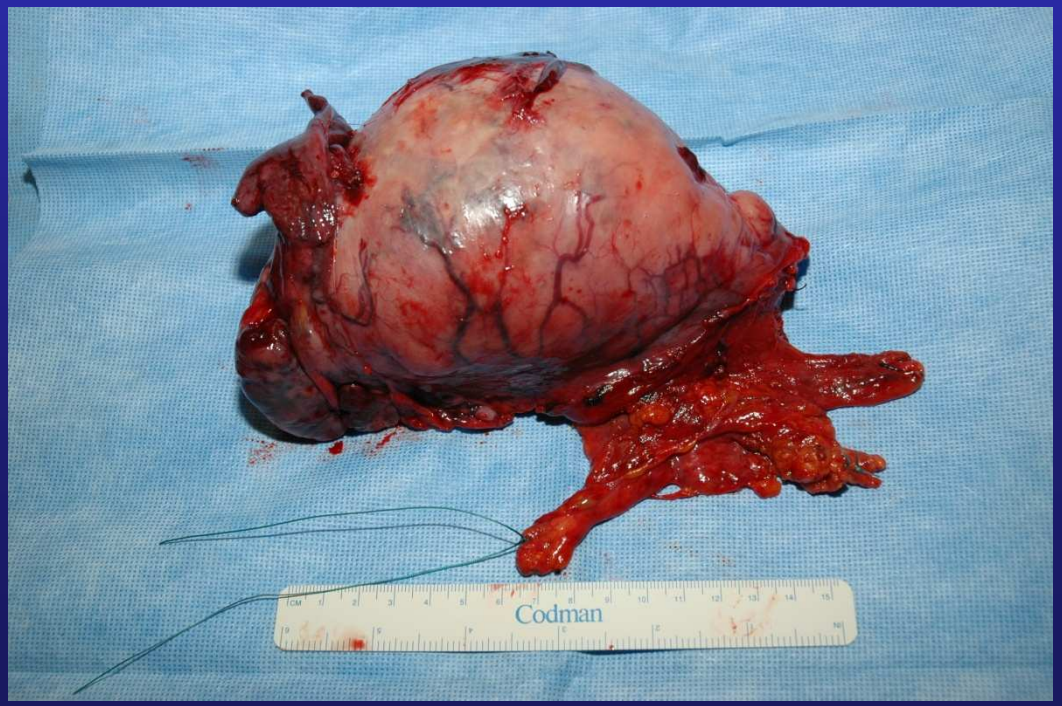




Case 1: anterior mediastinal tumor

61-year-old ♀

- **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%

Maggi G et al. Ann Thorac Surg 1991; 51:152-6

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 ca.) 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 79%

Kim ES et al. Lung Cancer 2004; 44:369-79

Thymoma - chemotherapy

- thymoma: chemotherapy-sensitive

induction chemotherapy

- locally invasive tumors (particularly thymic ca.) or large bulky masses
- cisplatin-based regimen + resection ± PORT
- 30 pts induction CT: 3 cycles cisplatin, epirubicin, etoposide
- 2 CR , 20 PR, 8 SD
- all pts operated no † 23 complete resections
- postop. RT 21 pts, CT-RT 8 , CT 1
- 10-year survival stage III 86% stage IVA 76%

Lucchi M et al. J Thorac Oncol 2006; 1:308-13

Rajan A, Giaccone G. Thorac Surg Clin 2011; 21:107-114

Thymoma - chemotherapy

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; 22:293-9

Rajan A, Giaccone G. Thorac Surg Clin 2011; 21:107-114

Thymoma - survival

- overall 5-year survival 70% with local invasion 50%
  without 75%
- overall 10-year survival 50% with local invasion 30%
  without 60%
- 5-year survival Masaoka stage

I	94 - 100%
II	86 - 95%
III	56 - 69%
IV	11 - 50%

Masaoka A et al. Cancer 1981; 48:2485-92

Thymoma - survival

WHO classification

	5-year	10-year DFS
A	100%	95%
AB	93	90
B1	89	85
B2	82	71
B3	71	40
C	23	

Rena O et al. Lung Cancer 2005; 50:59-66

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)

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

Engels EA et al. Int J Cancer 2003; 105:546-51

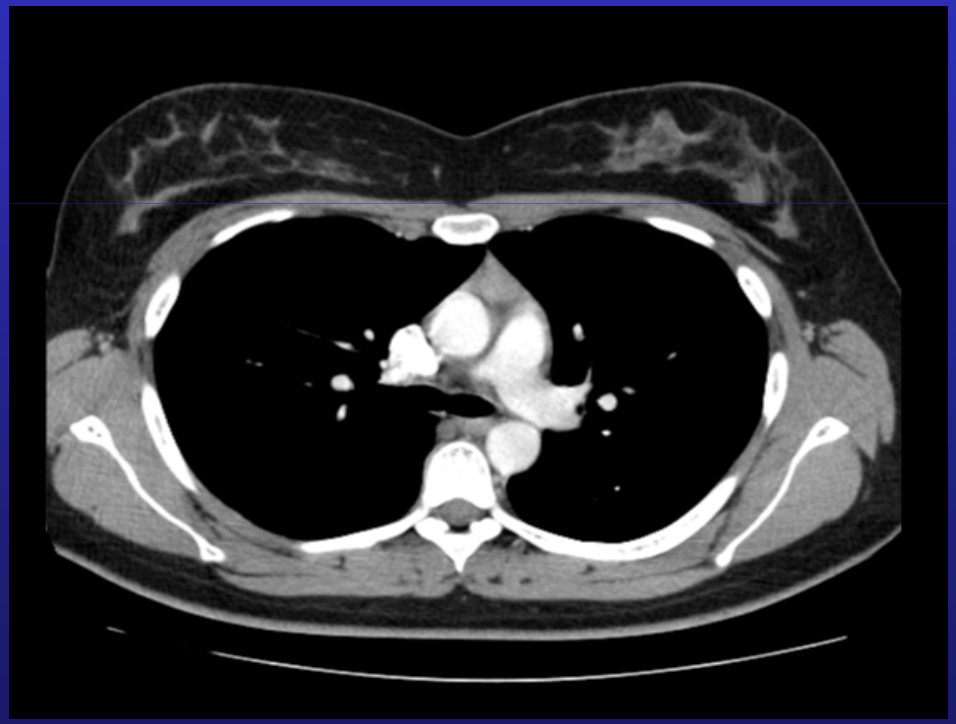
Welsh JS et al. JAMA 200; 283:1142-3

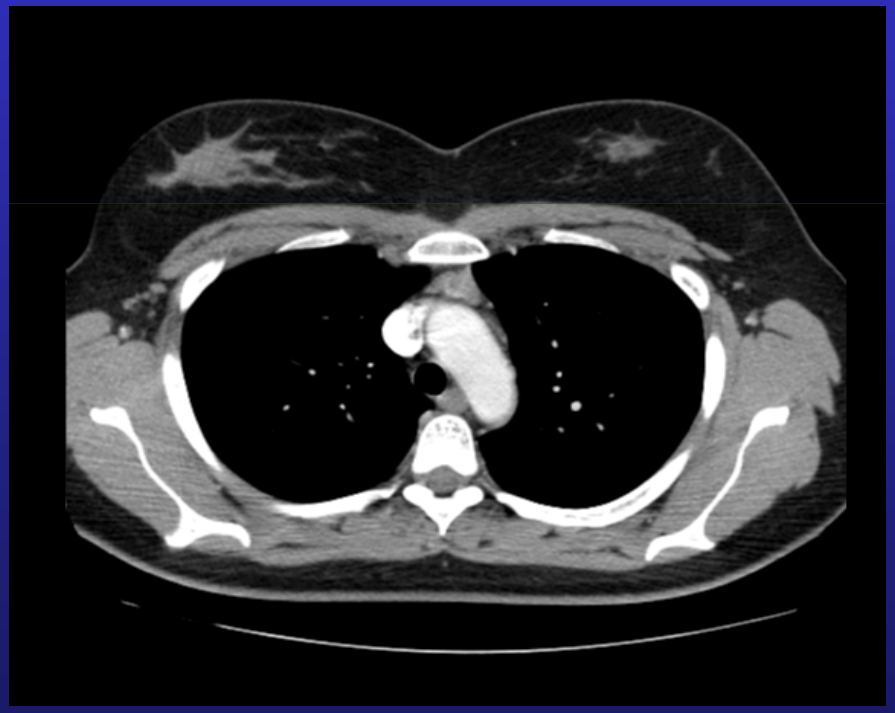
Case 2: thymic hyperplasia, nodule

28-year-old ♀

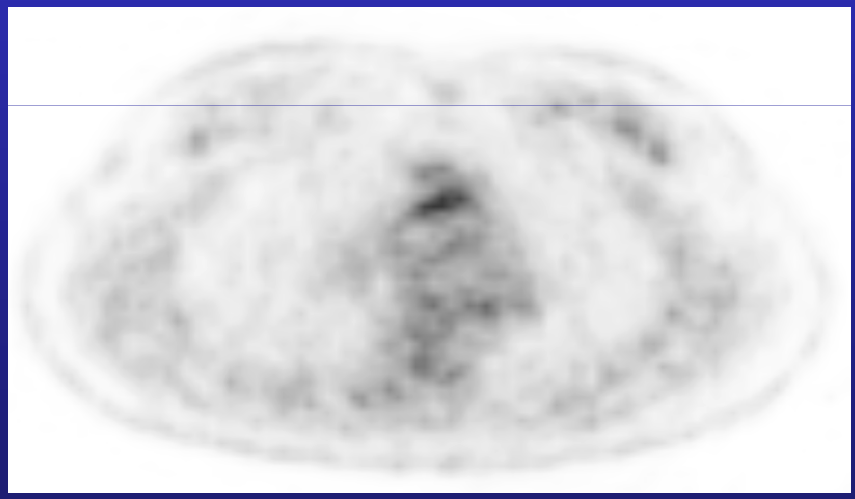
- **investigated diplopia**
- **possible ocular myasthenia, anti-ACH receptor antibodies -**
- **CT chest: thymic hyperplasia, nodule 1.6 cm**
- **PET scan: slight uptake nodule, small thymoma?**

Case 2: thymic hyperplasia, nodule





Case 2: thymic hyperplasia, nodule



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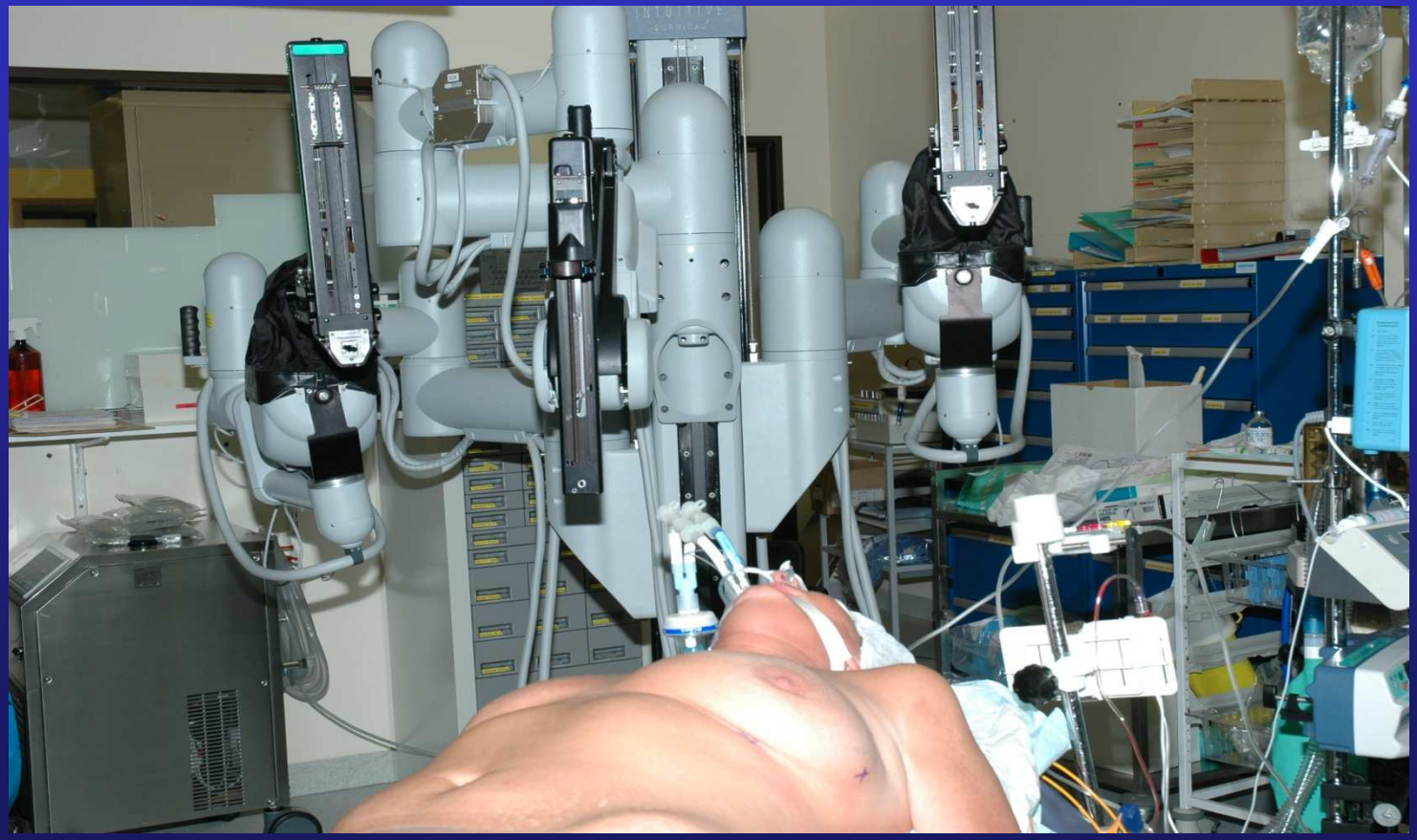
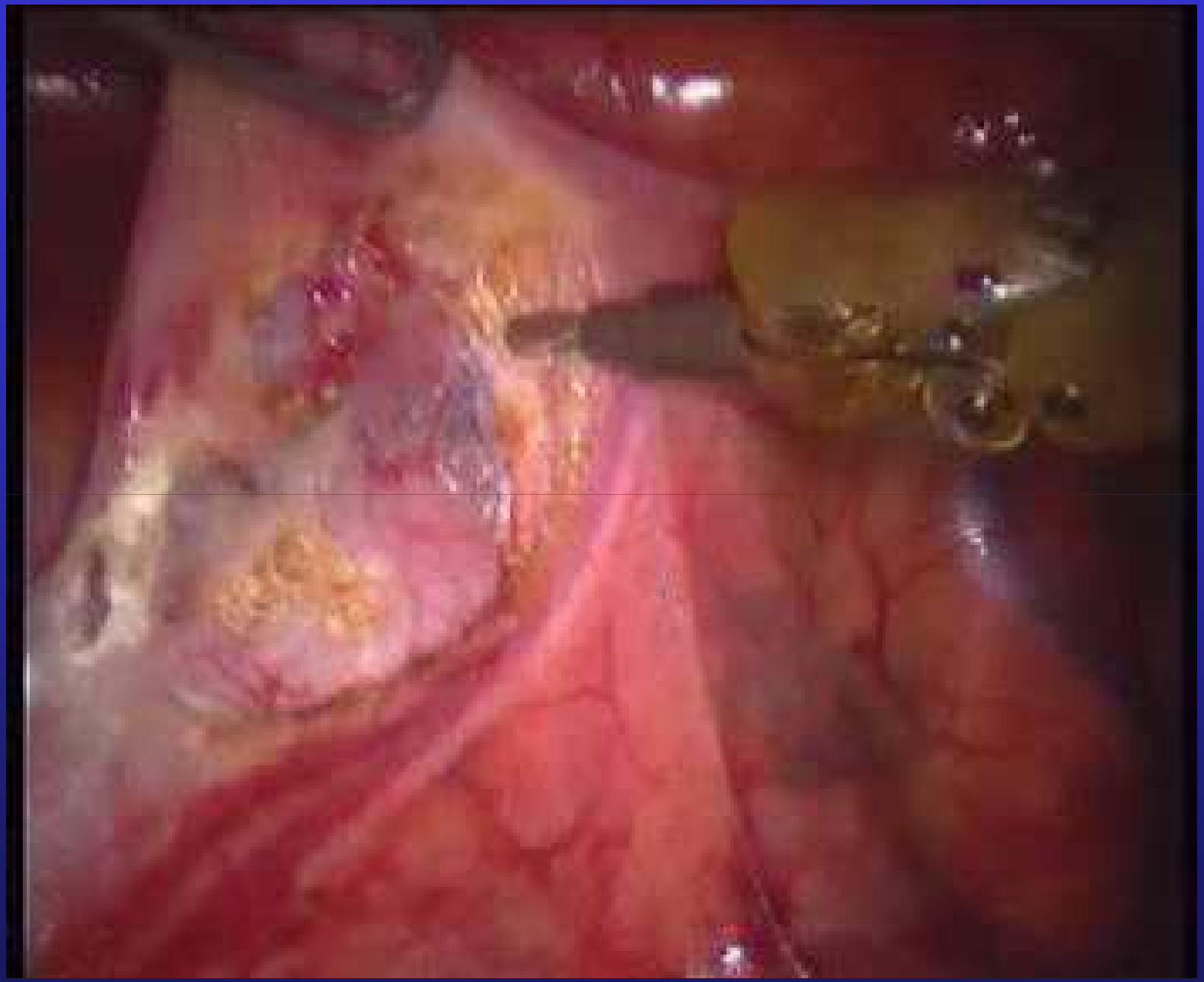


Case 2: thymic hyperplasia, nodule



Case 2: thymic hyperplasia, nodule

no postop. complications

pathology:

thymic hyperplasia
no malignancy

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