Evaluation of the Anterior Mediastinal Mass

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Disclosure

• Consultant (Physicians’ Advisory Board), Medtronic
Objectives

• Describe the most common anterior mediastinal problems
• Review current clinical standards for evaluation of anterior mediastinal abnormalities
The Mediastinum

• Anterior
  – Borders:
    • Thoracic inlet
    • Diaphragm
    • IMAs / phrenic
    • Sternum
    • Pericardium
  – Contains thymus, IMAs, lymph nodes, connective tissue, fat
The Anterior Mediastinum

• Includes
  – Thymus, IMAs, lymph nodes, connective tissue, fat

• Masses
  – Thyroid
  – Thymus
  – Teratoma
  – “Terrible” Lymphoma
Case Presentation

- 83-year old woman, previously healthy, who presents with 2 month h/o DOE (SOB when walking stairs)
- PMH: spinal stenosis, hypercholesterolemia, s/p TAH/BSO, s/p knee arthroscopy
- Social HX: never smoker; non-drinker. Former real estate agent

- Diagnostic evaluation?
• Chest CT
  – 3.9 cm anterior mediastinal mass
  – Cystic and solid in nature

• PET
  – Mild hypermetabolic activity in lesion
  – No other sites

• Diagnostic options
  – TTNA
  – Surgical bx/resection
When to Biopsy an Anterior Mediastinal Mass?

Biopsy strategies
1. Needle (FNA, core)
2. Surgical (Chamberlain, VATS)

When to proceed straight to resection?
1. Imaging shows features consistent with teratoma
2. Patient > 40 years old, AND
   1. $\beta$-HCG and $\alpha$-FP are normal, AND
   2. No clinical s/sx of lymphoma
3. Patient has a diagnosis of MG
Case Presentation

- Cardiac evaluation negative
- Surgery: Robot-assisted thymectomy, uncomplicated post-op course
- Pathology
  - Cortical thymoma, WHO B1 type, 3.9 cm
  - Focal microscopic capsular invasion
Which of the following is most commonly associated with an anterior mediastinal mass?

a. Substernal or ectopic thyroid
b. Ectopic parathyroid gland
c. Thymus
d. Lymphoma
e. Germ cell tumor
Which of the following is most commonly associated with an anterior mediastinal mass?

a. Substernal or ectopic thyroid
b. Ectopic parathyroid gland
c. Thymus – accounts for 50% of anterior mediastinal masses
d. Lymphoma
e. Germ cell tumor
Thymic Masses

- Thymoma
- Thymic cyst
- Thymic carcinoma
- Ectopic parathyroid gland
• Arises from 3rd pharyngeal pouches at 6th week of gestation
• Development of cellular immunity (T lymphocytes)
• After 1st year of life, decreases in size and mass at a steady rate until middle age
• May harbor ectopic parathyroid tissue
• Arterial supply is via IMA’s
• Venous drainage into innominate vein
A 34-year old man presents with this mass. On further questioning, he reports a 6-month h/o diplopia, difficulty swallowing, and weakness of torso and thighs. Sx’s are typically worse later in the day and evening. Appropriate tests for his w/u include each of the following EXCEPT?

A. Brain CT  
B. Deep tendon reflexes  
C. Edrophonium chloride injection  
D. Serum acetylcholine receptor antibody assay  
E. Single-fiber EMG
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Thymoma and Myasthenia Gravis

- 50% of patients with thymoma have MG
- 10-15% of patients with MG have thymoma
- 70% of patients with MG have thymic hyperplasia

- MG Presentation: Weakness in specific muscle groups
  - Ocular sx’s: diplopia, ptosis
  - Craniofacial sx’s: difficulty chewing or swallowing, slurred speech, voice changes
  - Dz progression is descending (craniocaudal) direction
Workup for Myasthenia Gravis

- Tensilon Test: IV injection of edrophonium chloride results in immediate improvement of muscle weakness
- Serum testing for antibodies to acetylcholine receptor (AchR) is pathognomonic
  - Normal levels of AChR do not exclude the dx of MG
- Single-fiber EMG is useful when the clinical picture is not clear and there are not antibodies
  - With MG there is increased neuromuscular jitter
- Brain imaging not necessary
Thymoma

- Occur in patients of all ages; peak is 35-70 years
- Staging – TNM, WHO, Masaoka
- Surgery is the mainstay of treatment
Thymoma

- Most common thymic tumor
- Histology
  - Lymphocyte predominant – may be difficult to distinguish from lymphoma on FNA
  - Epithelial
  - Mixed
- Demographics
  - Age > 40 years
  - M = F
Thymoma and Associated Diseases

• Myasthenia Gravis
  – Up to 50% of thymoma pts will have MG sx’s
  – Up to 15% of MG patients will have thymoma

• Cytopenias (Red cell hypoplasia)
• Nonthymic malignancies
• Autoimmunie Diseases – SLE, RA, Sjogren’s, polymyositis
• Ulcerative Colitis
Management of Thymoma

- Question regarding MG sx’s / medical mgmt of MG
- Surgery for Masaoka I and II
- Surgical Approach
  - Median sternotomy
  - VATS/Robotic
  - Transcervical
- Induction therapy?
  - III and IVa
- Adjuvant XRT?
  - Incompletely resected III and IV

<table>
<thead>
<tr>
<th>Masaoka Staging System</th>
<th>Description</th>
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<tbody>
<tr>
<td>I</td>
<td>Grossly and microscopically completely encapsulated tumor</td>
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<tr>
<td>IIa</td>
<td>Microscopic transcapsular invasion</td>
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<tr>
<td>IIb</td>
<td>Macroscopic invasion into thymic or surrounding fatty tissue, or grossly adherent to but not breaking through mediastinal pleura or pericardium</td>
</tr>
<tr>
<td>III</td>
<td>Macroscopic invasion into neighboring organ (i.e. pericardium, great vessel or lung)</td>
</tr>
<tr>
<td>IVa</td>
<td>Pleural or pericardial metastases</td>
</tr>
<tr>
<td>IVb</td>
<td>Lymphogenous or hematogenous metastasis</td>
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Thyroid

- Intrathoracic mass is usually continuous with thyroid gland in neck
- Sx’s: cough, SOB, dysphagia

- Surgical Approach?
  - Transcervical (95%)
  - Intrathoracic (VATS vs. partial/median sternotomy)
Ectopic Parathyroid Gland

Exploration indicated when hyperparathyroidism sx’s persist, prior neck exploration is negative and imaging suggests intrathoracic gland.
Teratoma

Germ Cell Tumors

- Benign Teratoma*
- Malignant Germ Cell Tumor
  - Seminoma
  - Non-seminomatous GCT

*most common
Mature Teratoma

- Most common germ cell tumor arising in the mediastinum
- Generally benign; malignant transformation rare
- Contains elements of fat, fluid, bone
- Not responsive to XRT or chemotherapy
- Treatment is surgery
What is the most appropriate management for a patient who coughs up hair and is found to have a large mediastinal mass?

A. Serum tumor markers
B. Resection
C. Chemotherapy
D. Chemo/XRT

Which ones?
α-FP, β-HCG

If normal tumor markers, then what?
Resection
What is the most appropriate management for a patient who coughs up hair and is found to have a large mediastinal mass?

A. Serum tumor markers
B. Resection
C. Chemotherapy
D. Chemo/XRT

Which ones?
\( \alpha \)-FP, \( \beta \)-HCG

If elevated tumor markers?
Chemotherapy
26M with Klinefelter’s syndrome p/w 3-month h/o progressive chest discomfort. Physical exam is unremarkable. CT demonstrates an anterior mediastinal mass. What is the next step in management?

A. Anterior mediastinotomy with biopsy
B. CT-guided biopsy
C. Measurement of serum tumor markers
D. Serum acetylcholinesterase and antibody measurement
E. Wide surgical excision
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B. CT-guided biopsy
C. Measurement of serum tumor markers – α-FP and β-HCG
D. Serum acetylcholinesterase and antibody measurement
E. Wide surgical excision

* Klinefelter’s is a known risk factor for primary mediastinal NSGCT
Which of the following tumor markers would be elevated in a patient with a seminoma?

a. CEA  
b. LDH  
c. α-FP  
d. β-HCG  
e. CA 19-9  
f. All of the above
Which of the following tumor markers would be elevated in a patient with a *seminoma*?

a. CEA  
b. LDH – nonspecific; elevated in both seminoma and NSGCT  
c. α-FP  
d. β-HCG  
e. CA 19-9  
f. All of the above
Which of the following tumor markers would be elevated in a patient with a non-seminomatous germ cell tumor (NSGCT)?

a. CEA  
b. LDH  
c. α-FP  
d. β-HCG  
e. CA 19-9  
f. All of the above
Which of the following tumor markers would be elevated in a patient with a non-seminomatous germ cell tumor (NSGCT)?

a. CEA
b. LDH – nonspecific; elevated in both seminoma and NSGCT
c. $\alpha$-FP – elevated in NSGCT
d. $\beta$-HCG – elevated in NSGCT
e. CA 19-9
f. All of the above
This 26M has normal serum α-FP and mildly elevated β-HCG levels. Biopsy is required to establish the diagnosis.

A. True  
B. False
This 26M has normal serum $\alpha$-FP and mildly elevated $\beta$-HCG levels. Biopsy is required to establish the diagnosis.

A. True – tissue is necessary to distinguish this seminoma from thymoma and lymphoma. CT-guided bx is preferred, but surgical bx may also be performed.

B. False 80% of seminomas stain positively for placental alkaline phosphatase.
Malignant GCTs

Seminoma

- Normal α-FP; β-HCG normal or mildly elevated
- Scrotal exam and testicular U/S – r/o testicular 1°
- Management
  - Radiation Therapy
  - Chemotherapy (Bleomycin, Etoposide, Cisplatin)
- Role for surgery?
  - Surgical excision only if residual mass is present after therapy

Duke Surgery
Seminomatous Tumors

Small encapsulated
- Surgery + XRT
- Follow

Locally advanced
- CT normal
  - Follow
- Mass on CT
  - Follow
- Growth

Distant metastasis
- Chemotherapy
- Salvage XRT, Surgery or Both
Malignant Germ Cell Tumors

Non-seminomatous GCT

• Histology
  – Yolk sac, embryonal cell, choriocarcinoma

• Males 20-40 yo

• Elevated $\alpha$-FP, $\beta$-HCG

• Management?
  – Chemotherapy (cisplatin-based)

• Indication for/timing of surgery?
  – For residual mass, after serum markers have normalized
Non-Seminomatous Tumors After Chemo

- Markers and CT normal: Observe
- Markers normal, Mass on CT: Surgery
  - Necrotic tumor: Follow
  - Viable tumor: Salvage chemotherapy
- Markers elevated: Salvage chemotherapy
Germ Cell Tumors

Malignant

Seminoma
- Normal α-FP, β-HCG
- Chemo/XRT
- Surgery only for small encapsulated or salvage for growing residual mass

NSGCT
- Yolk sac, embryonal cell, choriocarcinoma
- Elevated α-FP, β-HCG
- Chemo only
- Surgery after serum markers normalize

Benign Teratoma → Resect
A 25-year old woman with h/o nightly fevers and 10# weight loss in the last month presents with a mediastinal mass. An open biopsy is performed. The specimen is submitted entirely for frozen section and “large cell malignancy” is reported. What is the best next step in management?

a. Close the incision and draw serum markers
b. Convert the incision to anterior thoracotomy and excise the malignancy
c. Instruct the pathologist to thaw the frozen material and preserve it in formalin
d. Obtain additional tissue from permanent sections and flow cytometry
e. Request intraop consultation from gynecology
Surgical Approach?
Considerations?
A 25-year old woman with h/o nightly fevers and 10# weight loss in the last month presents with a mediastinal mass. An open biopsy is performed. The specimen is submitted entirely for frozen section and “large cell malignancy” is reported. What is the best next step in management?

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d. Obtain additional tissue from permanent sections and flow cytometry  
e. Request intraop consultation from gynecology
Lymphoma is the most common malignant tumor of the anterior mediastinum.

a. True
b. False
Lymphoma is the most common malignant tumor of the anterior mediastinum.

a. True

b. False – Lymphomas are the second most common malignancy of the anterior mediastinum; Thymomas are most common
“Terrible” Lymphoma

- Symptoms
  - Chest pain, dyspnea, wheezing, stridor, hoarseness, dysphagia, SVC syndrome

- Most common types
  - Nodular sclerosing Hodgkin’s lymphoma
  - Primary mediastinal B cell lymphoma

- Flow cytometry

- Treatment = chemotherapy

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Summary

• Evaluation of the anterior mediastinal mass must be individualized to the patient and clinical scenario
• Thymic lesions are most common, followed by lymphoma
• Role for surgery varies depending on the diagnosis
Thank you!