MRI and PET Imaging of Thymic Malignancies

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OBJECTIVES

To discuss:
• The role of MRI in imaging thymic malignancies
• The role of PET-CT in imaging thymic malignancies

ANTERIOR MEDIASTINAL MASS

Role of imaging:
• Is the mass physiologic?
• Is the mass a malignancy?
• Is it a primary thymic malignancy?
• Is it localized early disease, locally infiltrative or disseminated?
• Is there disease recurrence?

MRI

• Used for tumor evaluation in patients with iodine allergy or renal failure
• No radiation risk

MRI: Is the mass physiologic?

• Rebound hyperplasia
• Lymphoid hyperplasia
• Lymphoid hyperplasia in patients with myasthenia gravis

MRI

• Multiplanar imaging, though multidetector CT reformations produce diagnostic images comparable to MR
Hyperplastic thymus

- Chemical shift technique is useful in differentiating thymic hyperplasia from thymoma
- 25 year old woman with myasthenia gravis and lymphoid hyperplasia

MRI: Is the mass a malignancy?

- MRI provides improved contrast resolution
- Low attenuation: cystic change
- Mural soft tissue nodules: characteristic of cystic thymoma rather than a congenital cyst

MRI: Is it a primary thymic malignancy?

- Representative anterior mediastinal tumors:
  - Thymoma
  - Thymic Carcinoma
  - Neuroendocrine cancer
  - Thymic Cyst
  - Mature teratoma
  - Malignant germ cell tumor
  - Lymphoma

MRI: Is it localized? Disseminated?

Masacka-Koga Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Macroscopic and microscopic description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Completely encapsulated</td>
</tr>
<tr>
<td>II (a)</td>
<td>Microscopic invasion into capsule</td>
</tr>
<tr>
<td>II (b)</td>
<td>Macroscopic invasion into surrounding fatty tissue or grossly adherent but not breaking through mediastinal pleura or pericardium</td>
</tr>
<tr>
<td>III</td>
<td>Macroscopic invasion into neighboring organ (i.e., pericardium, great vessels, lung)</td>
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<tr>
<td>IV (a)</td>
<td>Pleural or pericardial dissemination</td>
</tr>
<tr>
<td>IV (b)</td>
<td>Lymphogenous or hematogenous metastasis</td>
</tr>
</tbody>
</table>

- 127 patients with anterior mediastinal tumors: thymoma, thymic carcinoma, thymic cyst, mature teratoma, malignant germ cell tumor, lymphoma
- Correct first choice diagnosis
  - By CT 61%
  - By MRI 56%
  - By CT+MRI 86%
- CT was equal or superior to MRI in the diagnosis of all anterior mediastinal tumors except for thymic cysts

Tomiyama, Eur J Radiol 2009
MRI: Is it localized? Disseminated?

• Need to identify patients to be treated with chemotherapy prior to surgery (stages III and IVa)

• Identify non-operable candidates (stage IVb)

• Local invasion is often microscopic, underestimated by CT and MRI

STAGING: MRI

Obvious MRI Findings associated with Stage III/IV

• Vascular involvement
  - Irregular luminal contour
  - Endoluminal soft tissue
  - Vascular encasement

• Pleura – Ipsilateral pleural nodules

STAGING: MRI

Indirect signs for advanced disease

• No MRI studies correlating imaging findings to stage III-IV Masaoka staging

• 17 thymomas (5 stage I; 12 stage II-IV)

• Invasive: 92% heterogeneous, 50% lobulated internal architecture caused by fibrous septa

• Stage I: none lobulated but all heterogeneous

Sakai, AJR 1992

STAGING: MRI

Indirect signs for advanced disease

• MRI studies correlate imaging findings to WHO classification

• However, higher stages are more commonly found at presentation with B3 Thymoma and thymic cancer

Sadohara, Eur J Radiology 2006

STAGING: MRI

Indirect signs for advanced disease

• Thymic carcinoma more likely to have
  - Irregular contours
  - Necrotic or cystic components
  - Heterogeneous contrast enhancement
  - Lymphadenopathy

• More indolent thymomas compared to thymic cancer:
  - Almost complete capsule
  - Septum
  - Homogenous enhancement

Sadohara, Eur J Radiology 2006

STAGING: DYNAMIC MRI

To identify if time to peak enhancement can differentiate between:

- Thymoma and other anterior mediastinal tumors
- Stage I+II from III thymoma

• 59 patients:
  - Thymoma (n=31)
  - Thymic carcinoma (n=14)
  - Lymphoma (n=7)
  - Malignant germ cell tumor (n=4)
  - Thymic carcinoid (n=3)

Sakai Acta Radiologica 2002
Can MRI Replace CT in the Evaluation of Thymoma?

Mean peak time

- Thymoma 1.5min vs. non-thymoma 3.2 min
  \( p<0.0001 \)
- Stage I+II 1.3min vs. stage III 2.5 min
  \( p=0.02 \)

Sakai Acta Radiologica 2002

Comparative study:

- CT
- MRI
- Fluoroscopy- sniff test

Can MRI Replace CT in the Evaluation of Thymoma?

Early results

- CT and MRI are quite similar
- Both have under and over diagnosis of pleural metastases

MRI: Is there disease recurrence?

- Differentiating early disease recurrence is difficult after therapy
- No MRI studies published

THYMOMA- NUCLEAR MEDICINE

- Nuclear medicine is rarely used for evaluation of thymoma
- CT has now replaced Thallium\(^{201}\) for evaluation of thymus
- Indium\(^{111}\) Octreotide shows uptake in thymoma and is used to identify patients who may respond to treatment with octreotide
- The amount Indium\(^{111}\) Octreotide uptake is variable and does not correlate with tumor size, histological type, staging, clinical behavior or prognosis


THYMOMA- NUCLEAR MEDICINE

- A series of 18 patients showed uptake in all patients with thymoma, thymic ca, thymic carcinoid and no uptake in lymphangioma and thymic hyperplasia
- Both planar imaging and SPECT imaging only detect deposits >1.5cm and miss pleural and pericardial disease readily identified by CT and MRI
- In a series assessing 29 patients with recurrence of thymoma, indium\(^{111}\) Octreotide was only positive in 27%

Rosati, abstract 2004, 2005 ASCO meeting
**PET**

- Improved resolution
- Not routinely used
- Most common agent FDG

**ANTERIOR MEDIASTINAL MASS**

Role of PET:
- Is the mass physiologic?
- Is the mass a malignancy?
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**FDG PET: Is the mass physiologic?**

Physiologic FDG uptake is seen in the normal thymus
- 73% of up to 13 year old children
- 8% of 30-40 year olds

*Jerushalmi J Nucl Med 2009*

**FDG PET: Is it a primary thymic malignancy?**

- Although small studies have shown that SUV is lower with thymic hyperplasia as compared to thymoma, significant overlap in SUV is seen in a much larger study

*P<0.01* to thymoma, significant overlap in SUV is seen in a much larger study
23 patients: age 13-58
5 thymic hyperplasia
14 thymoma
4 thymic cancer
*n=23*  
*Kumar Ann Nucl Med 2009*

**FDG PET: Is the mass a malignancy?**

Whether the increased FDG uptake is physiologic or malignant depends on:
- CT appearance
- Focality of FDG uptake
- History

*Jerushalmi J Nucl Med 2009*
FDG PET: Is it a primary thymic malignancy?

- 19 patients with anterior mediastinal mass
  - low risk thymic tumors A, AB, B1 (n=6)
  - high risk thymic tumors B2, B3 thymic cancer (n=7)
  - lymphoma (n=3)
  - other primitive thymic tumors (n=3)
- SUV of low risk thymoma was lower than high risk thymoma and lower than lymphoma
- SUVmax >5 requires presurgical biopsy to identify tumors that should be treated with upfront chemotherapy

Luzzi Eur J of Cardiothoracic Surg 2009
Terzi Lung Cancer 2011

FDG PET: Is it a primary thymic malignancy?

- There is overlap of FDG SUVmax in patients with high risk thymic epithelial tumors, lymphoma, paraganglioma and non seminomatous germ cell tumor

Luzzi Eur J of Cardiothoracic Surg 2009

FDG PET: Is it a primary thymic malignancy?

- SUV uptake is higher in thymic cancer (n=4)
  as compared to thymoma (n=14):
  Thymic cancer mean SUVmax 7 (range 4.3-9.2)
  Thymoma mean SUVmax 2.3 (range 0.8-3.9)
- SUV cannot differentiate between WHO classification (A, AB, B1 vs B2, B3)

Kumar Ann Nucl Med 2009

FDG PET: Is it a primary thymic malignancy?

- SUVmax is significantly higher in thymic cancer (n=16) as compared to thymoma (n=17)
- SUVmax cannot distinguish between WHO classification of thymoma

Sung J Nucl Med 2006

FDG PET: Is it localized? Disseminated?

- When studies mix thymic cancer with thymoma increased SUVmax appears to be associated with stage III/IV disease as compared to stage I/II

Igap Eur J cardiothoracic Surg 2011
Luzzi Eur J of Cardiothoracic surg 2009
FDG PET: Is it localized? Disseminated?

- However, this may be a thymic cancer effect skewing the data as thymic cancer has higher SUV\textsubscript{max} and tends to present as more advanced disease.

Luzzi Eur J of Cardiothoracic surg 2009

FDG PET: Is it localized? Disseminated?

- n=40 (37 thymoma, 3 thymic cancer)
  - SUV cannot predict invasiveness of thymomas as assessed by tumor stage.

Shibata, Cancer 2009

FDG PET: Is it localized? Disseminated?

- 33 pts: 16 thymic cancer, 17 thymoma
  - PET did not add in thymoma cases
  - In thymic cancer:
    - 2/16 LN mets detected by PET/CT not CT
    - 1/7 pts with pleural met detected by PET/CT not CT (apical)
    - No difference in extra-thoracic metastases

Sung, J Nucl Med 2006

FDG PET: Is it localized? Disseminated?

- 26 patients: 16 thymoma; 10 thymic carcinoma
  - Conventional imaging and FDG PET findings were discordant in 10 cases (23%)
  - FDG PET sensitivity 79%, specificity 100%, accuracy 85%
  - 7% PET appropriately changed patient management
  - 88% of PET scans did not influence management
  - Low FDG uptake seen in low volume and indolent disease, NPV 64%
  - PPV 100% enables appropriate modification of management in a small, but potentially important subset of patients

Lee J Med Imaging Radial Oncol 2008
FDG PET: Is there disease recurrence?

- Post treatment changes difficult to differentiate from recurrence
- FDG PET-CT improves detection of thymoma recurrence with underestimation of small volume pleural recurrence

El-Bawab Interact Cardio Vasc Thorac Surg 2010

FDG PET: Is there disease recurrence?

- Overall recurrence of thymoma
  - Sensitivity | Specificity | PPV
  - PET-CT 82% | 95% | 93%
  - CT 71% | 85% | 80%
- Anterior mediastinal recurrence of thymoma
  - PET-CT 100%
  - CT 55%

El-Bawab Interact Cardio Vasc Thorac Surg 2010

FDG PET: Is there disease recurrence?

- 40% false negative FDG PET results either due to low volume disease, indolent tumor, or post therapeutic mediastinal FDG uptake
- 5% of false negative results treatment was inappropriately altered (chemo withheld, XRT dose reduced)

Lee J Med Imaging Radiat Oncol 2008

FDG PET: Is there disease recurrence?

- FDG PET is useful for monitoring response and outcome after treatment of unresectable thymic epithelial tumors
- Results are similar though not identical to monitoring response by CT using RECIST
- It has not been established if metabolic response by FDG PET is more accurate than morphologic response by RECIST
- Metabolic response correlates with overall survival in patients with thymic cancer but not in those with thymoma

Kaira Ann Nucl Med 2011

PET: new agents

- $^{11}$C- Methionine
  - 14 thymic cancer, 9 invasive and 5 stage I thymoma
  - MET uptake similar between thymic cancer, invasive and stage I thymoma
  - FDG uptake higher in thymic cancer, similar between invasive and stage I thymoma ($p<0.01$)
  - Conclusion:
    - Use of MET PET not recommended.
    - FDG more useful as can differentiate thymic cancer from thymoma

Sasaki J Nucl Med 1999

PET: new agents

- $^{11}$C- Acetate
  - $^{11}$C- Acetate useful for non FDG avid tumors such as prostate cancer
  - Some thymomas are not FDG avid
  - 3 thymoma patients, all were $^{11}$C- Acetate avid, only 2 were FDG avid

Ohtsuka Ann Thorac Surg 2006
PET: new agents

**11C- Acetate**
- 40 patients (37 thymoma, 3 thymic cancer)
- Neither FDG nor 11C- Acetate predict Masaoka staging
- Both FDG and 11C- Acetate predict histologic type
  - All thymic cancer had FDG SUV >6.3
  - FDG-SUV <6.3 and AC-SUV ≥5.7 associated with type A/AB thymoma

Shibata Cancer 2009

**68Ga-DOTA-try-octreotide (DOTATOC)**
- Allows imaging somatostatin receptor with improved spatial resolution as compared to 111In-Octreotide scintigraphy (3–6 mm versus 10–15 mm)
- 68Ga-DOTATOC PET is superior to 111In-DTPAOC SPECT in the detection of neuroendocrine tumor deposits in the lung and skeleton and similar for the detection of NET manifestations in the liver and brain
- Only one thymoma has been tested but has not shown increased uptake (mean SUV 1.8 SUVmax 2.5)


CONCLUSION

- CT remains the primary imaging modality for evaluating patients with thymic malignancies
- CT is superior to MRI in identification of anterior mediastinal masses
- Open question: Can MRI replace CT? Staging, F/U
- Limited role for FDG PET in staging thymoma but more useful in thymic cancer and initial evaluation, prior to biopsy of the anterior mediastinal mass
- We hope a robust database will be created through ITMIG to improve our use of imaging modalities and staging predictive capability

THANK YOU