Diagnostic Radiology and Nuclear Medicine Imaging in Hodgkin’s Disease

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March 2001
Agenda

- Introduction to radiological regions of the mediastinum.
- Differential diagnosis of an anterior mediastinal mass.
- Brief review of Hodgkin’s disease.
- Radiological imaging for Hodgkin’s disease.
  - Menu of tests
  - Diagnostic potential and limitations of tests
  - Role in treatment monitoring and follow-up
  - Introduction to gallium scanning
Patient Clinical History

• A previously healthy 26-year-old white male was referred to the BIDMC infectious disease department for evaluation of:
  – Anorexia with weight loss of 173 to 148 pounds over 8 months
  – Occasional headaches
  – Nonproductive cough
  – Prolonged unexplained fevers to 103\(^\circ\)
  – Worsening drenching night sweats

• Entire infectious disease work-up was negative.
Done as part of the FUO work-up and revealed:
- A right mediastinal opacity.
- Obliteration of the retrosternal clear space.
Areas of the Mediastinum

- **Anterior**: Bounded by the clavicles, diaphragm, sternum, and the pericardium and trachea.
- **Middle**: Between the anterior and posterior mediastinum. Includes the heart, great vessels, and pulmonary roots.
- **Posterior**: Bounded by the thoracic inlet, diaphragm, vertebral bodies/paravertebral gutters, and the pericardium.

Regions of the Anterior Mediastinum

- Region I
- Region II
- Region III

Differential Diagnosis: Adult Anterior Mediastinal Mass

- **Region I**
  - Retrosternal goiter
  - Tortuous innominate artery
  - Lymph nodes
  - Thymic tumors
  - Ascending aortic aneurysms

- **Region II**
  - Germ cell neoplasms
  - Thymic tumors
  - Sternal tumors (usually mets)

- **Region III**
  - Pericardiac fat pad
  - Diaphragmatic hump
  - Morgagni hernia
  - Pericardial cysts

Definitive Diagnosis

- A Chamberlain procedure (mediastinotomy) was performed.
- Multiple biopsies of the large anterior mediastinal mass were taken.
- Histology and flow cytometry revealed Hodgkin’s Disease, nodular sclerosing type.
Hodgkin’s Disease

- 7500 new cases per year.
- 20% of all lymphomas.
- Mean age of diagnosis is 32.
- Arises in a single node and spreads characteristically to anatomically contiguous nodes.
**Hodgkin’s Disease**

- Often associated with distinctive “B symptoms”:
  - Unexplained fevers > 38°C.
  - Drenching night sweats in past month.
  - Weight loss >10% over 6 months.

- Histology: Reed-Sternberg cell admixed with a variable inflammatory infiltrate.

Imaging in Hodgkin’s Disease

- Staging is of utmost clinical importance because therapy, prognosis, and clinical course are all intimately related to the distribution of disease.

- Diagnostic radiology and nuclear medicine play a pivotal role in:
  - Initial staging.
  - Intra-treatment surveillance.
  - Post-treatment surveillance.
Hodgkin’s Disease Staging

Ann Arbor Classification

Radiographic work-up in initial staging

• Mandatory radiological work-up includes:
  – Chest PA/lateral
  – CT of thorax
  – CT of abdomen and pelvis (replaces Bipedal lymphangiogram)
CT Scan

- Done with IV contrast, early phase imaging, 1 cm slices.
- Detects intrathoracic disease not detected on CXR in 20% of patients.
- Between 10-60% of patients have management change post-CT.
- Sensitivity of abdominal node detection equal to bipedal lymphangiography and is noninvasive and gives added information.
Characteristics

CT findings:

General rule: nodes >1 cm are concerning.
- Often see Asymmetric, anterior mediastinal soft tissue mass.
- Pleural effusions in 30% of cases (lymphatic/venous obstruction).
- Benign pericardial effusions common.
Out Patient: Chest CT

- Large, well circumscribed anterior mediastinal mass.
Out Patient: Chest CT

- Small pericardial effusion.
- Small right pleural effusion.
Radiographic work-up in initial staging – optional tests

- Liver and spleen ultrasonography
  - If clinical suspicion for involvement.
  - Specificity & sensitivity similar to CT or MRI.

- Technetium bone scanning
  - If bony pain, questionable lesions on other studies.

- MRI
  - If suspected occult liver, spleen, thymus, bone marrow lesions.
  - Specificity & sensitivity similar to CT for liver or spleen involvement.

- Gallium scanning
  - Useful in differentiating scarring from active mediastinal lymphoma.
Gallium radionuclide tumor imaging

• **Main indication:**
  – Staging of lymphomas, assessment of their response to therapy, and relapse detection.

• **Technique:**
  – $^{67}$Ga-citrate administered I.V.
  – Acquire delayed images.
  – SPECT = rotation of a photon detector array around the body to acquire data from multiple angles.
  – Determines position and concentration of radionuclide distribution.

• **Imaging Mechanism**
  – Rough surrogate marker for tumor metabolic activity.
  – Increased permeability of tumor vessels
  – Large extracellular fluid space
  – Tumor up-regulation of iron-binding proteins such as ferritin
Gallium radionuclide tumor imaging

- **Contraindications:**
  - None.

- **Radiopharmaceutical:** \(^{67}\text{Ga}-\text{Gallium citrate}
  - 8-10 mCi, \(\gamma\)-emitter.
  - Half-life = 78 hours.
  - Binds to transferrin (in plasma), lactoferrin (in tissue), and ferritin.

- **Equipment:**
  - Gamma camera w/ whole body and tomographic abilities, medium or high energy collimator, imaging computer.

- **Patient Preparation:**
  - Bowel regimen may be given after injection to clear activity.
Gallium radionuclide tumor imaging

• Images:
  – Acquired at 48 and 72 hours.
  – Sensitivity for detecting HD is about 85%, specificity of 90%.
  – Sensitivity for mediastinal disease is 95%, specificity of 90%.

• Aftercare:
  – None.

• Complications:
  – None.

• Cost:
  – The cost of SPECT imaging is around $700.
Gallium radionuclide tumor imaging

- Normal gallium activity:
  - Renal cortex: First 24 hours.
  - Liver: Greatest uptake of gallium.
  - Spleen.
  - Bone marrow & blood pool: behavior as an iron analog.
  - Skeleton: Incorporated into the Ca-hydroxyapatite crystal as a Ca$^{2+}$ analog.
  - Children: physeal and thymic activity.
  - Glands: Nasopharynx, salivary & lacrimal.
  - Bowel: 1st colonic activity on delayed images.
  - Breasts & breast milk.
  - External genitalia.
Our Patient: SPECT Imaging

- Large area of intense tracer accumulation in anterior mediastinum.
- Consistent with history of mediastinal lymphoma.
Patient Treatment

- Chemotherapy: 5 cycles of ABVD
- Radiation therapy: Modified mantle
Radiographic intra-treatment surveillance

- Repeat studies with detectable lesions at presentation.
- Determines therapeutic response, therapy modification.
- Follow:
  - Tumor volume decrease.
  - New lesions.
  - Therapy-induced lesions.
Our Patient: Chest P A and Lateral

- Large right mediastinal mass has resolved.
Frontal CXR Comparison

Pre-treatment

Intra-treatment
Lateral CXR Comparison

Pre-treatment

Intra-treatment
Our Patient: Chest CT

- Homogeneous soft tissue mass in the anterior mediastinum
- 3.6 x 2.4 cm
Chest CT Comparison

Pre-treatment

Intra-treatment
Radiographic intra-treatment surveillance

- Residual fibrotic mass often visible on CXR and CT.
- Further investigations determine nature of residual abnormality.
- Gallium imaging after 3 cycles of chemotherapy is an excellent prognostic indicator of clinical outcome.
- A complete response is achieved in 70% of patients.
  - Longer disease free survival.
  - Lower mortality.
Our Patient: SPECT Imaging

- No abnormally gallium-avid region in the anterior mediastinum.
SPECT Comparison

Pre-treatment

Intra-treatment
Radiographic post-treatment surveillance

- Repeat investigations that were abnormal at presentation.
- 25% of relapses occur at new sites.
- Regression of disease may be slow.
- Residual fibrotic mass may still be visible on chest radiograph and CT.
- Further investigations may be necessary to define nature of residual abnormality, can also follow over time.
References

The End!
Acknowledgements

- Beverlee Turner for her support and PowerPoint expertise
- Larry Barbaras and Ben Crandall our Web Masters