Imaging Non-Hodgkin’s Lymphoma

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Harvard Medical School Year III
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Our Patient: Ms. M

- Ms. M: 24 year old female
- Chief Complaint: stabbing chest pain, SOB
- Review of Systems: no fevers, sweats, chills, or weight loss
- Past Medical History: status post appendectomy one year prior; EBV infection two years prior
- Social History: past cocaine use
- Family History: diabetes, heart disease
- Physical Examination: unremarkable
Chest X-ray Findings

PA

Trachea

Silhouetting out of right heart border

Lateral

Soft-tissue density in retrosternal area

PACS, BIDMC
Lobular soft tissue mass in anterior mediastinum with mass effect on heart.

LV, left ventricle
RV, right ventricle
Aorta
Anterior Mediastinal Anatomy

Clemente CD. Anatomy: A Regional Atlas of the Human Body. Fig. 152.
Mediastinal Lymph Nodes

Superior Anterior Mediastinal Lymph Nodes: 34% involvement in NHL

Clemente CD. Anatomy: A Regional Atlas of the Human Body. Fig. 187.
Differential Diagnosis

- Thymoma
- Thyroid Mass
- Teratoma
- Lymphoma
Patient 2: Thymoma

- Most common anterior mediastinal mass in adults

- 40% present with parathymic syndromes: myasthenia gravis, aplastic anemia, red cell aplasia

- Features
  - Asymmetric location on one side
  - Homogenous density
  - Some have cystic components
  - 20% have calcifications

Thoracic CT

Courtesy of Fabio Komlos, MD, BIDMC
Thyroid Mass

- Well defined mass contiguous with cervical thyroid

- Tracheal displacement common on CXR

- Heterogenous density on CT with marked contrast enhancement
Patient 3: Thyroid Mass

Thoracic CT

- Well defined mass contiguous with cervical thyroid
- Tracheal displacement common on CXR
- Heterogenous density on CT with marked contrast enhancement

www.medscape.com/.../ 91/449156/449156_fig.html
Teratoma

- 20% malignant; all are surgically removed
- Typically present as large mass lesions
- Variable tissue content: calcification in 30%, fat or fat-fluid levels, cystic areas, soft tissue
Patient 4: Teratoma

Thoracic CT

- Calcific density
- Fat & soft-tissue densities
- Notice the size!

Courtesy of Fabio Komlos, MD, BIDMC
Lymphoma

**Hodgkin’s**
- Reed-Sternberg cells
- 90% originate in lymph node
- 95% superior mediastinal nodal
- Contiguous progression
- Incidence: 1:50,000
- Bimodal age distribution: 30 & 70

**Non-Hodgkin’s**
- Heterogeneous group
- 60% originate in lymph nodes
- 85% from B cells; 15% from T cells
- Occurs in all age groups (mean age 50 years)
- Increased incidence in patients with altered immune status
Mediastinal Mass Biopsy

- Median sternotomy procedure
- 3-4 cm incision through the skin and subcutaneous tissue
- To the right of the sternum, between the first and second ribs

www.mrcmedical.it/aemедical.htm
Tissue Histology

- Uniform, small undifferentiated cells with basophilic cytoplasm
- Tingible-body macrophages: starry-sky pattern

Diagnosis: Burkitt’s Lymphoma
WHO Classification of the Non-Hodgkin's Lymphomas
According to Clinical Aggressiveness

The indolent lymphomas

**B-cell neoplasms**
- Small lymphocytic lymphoma/B-cell chronic lymphocytic leukemia
- Lymphoplasmacytic lymphoma (Ex Waldenstrom's macroglobulinemia)
- Plasma cell myeloma/plasmacytoma
- Hairy cell leukemia
- Follicular lymphoma (grade I and II)
- Marginal zone B-cell lymphoma
- Mantle cell lymphoma

**T-cell neoplasms**
- T-cell large granular lymphocyte leukemia
- Mycosis fungoides
- T-cell prolymphocytic leukemia

**Natural killer cell neoplasms**
- Natural killer cell large granular lymphocyte leukemia

The aggressive lymphomas

**B-cell neoplasms**
- Follicular lymphoma (grade III)
- Diffuse large B-cell lymphoma

**T-cell neoplasms**
- Peripheral T-cell lymphoma
- Anaplastic large cell lymphoma, T/null cell

The highly aggressive lymphomas

**B-cell neoplasms**
- Burkitt's lymphoma
- Precursor B lymphoblastic leukemia/lymphoma

**T-cell neoplasms**
- Adult T-cell lymphoma/leukemia
- Precursor T lymphoblastic leukemia/lymphoma

*Editor's note*: Subclassification of the non-Hodgkin's lymphomas according to their clinical aggressiveness (i.e., indolent, aggressive, highly aggressive) is not a part of the WHO classification system, and is used by UpToDate to consolidate the general discussions concerning treatment approaches to these NHL variants.

Burkitt’s Lymphoma

• Endemic (African) and non-endemic (American) forms
• Most often in children and immunocompromised hosts
• Tumors originate from EBV-infected B cells
• t(8,14) translocation and activation of \( c-myc \)

Patient 5: Endemic Burkitt’s

Patient 6: Non-endemic Burkitt’s

Burkitt’s lymphoma Lobulated, ulcerated protuberances seen on retroflexed view during endoscopy in a patient with abdominal pain. Biopsy revealed them to be Burkitt’s lymphoma. Courtesy of Eric D Libby, MD.

http://individual.uptodateonline.com/application/topic/print.asp?file=lymphoma/14479&type=A&selectedTitle=1~17
NHL: Epidemiology & Risk Factors

- **Epidemiology**
  - Incidence: 15.1 per 100,000 persons per year in U.S.
  - 73% increase since 1970’s
  - Steady increase due in part to AIDS pandemic
  - Subtypes differ in frequency between age groups

- **Risk Factors**
  - Transplant patients
  - AIDS
  - Congenital immunodeficiency
  - Collagen vascular diseases: RA, SLE
  - Infectious agents: EBV, *H. pylori*

*Grainger, p. 1401*
## Staging Non-Hodgkin’s Lymphoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Site of Involvement</th>
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<tbody>
<tr>
<td>I</td>
<td>Single lymph node region (I) or single extralymphatic organ or site (IE)</td>
</tr>
<tr>
<td>II</td>
<td>Two or more lymph node regions on the same side of the diaphragm (II) or one or more lymph node regions plus and extralymphatic site (IIE)</td>
</tr>
<tr>
<td>III</td>
<td>Lymph nodes of both sides of the diaphragm</td>
</tr>
<tr>
<td>IV</td>
<td>One or more extralymphatic organs with or without lymph node involvement</td>
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</table>
Imaging Modalities: Lymphoma

- Plain film
- CT
- MRI
- Ultrasound
- Nuclear Medicine (Gallium Scanning & FDG-PET)
- Fusion Imaging (PET-CT)
Plain Film

- 25-40% of NHL patients present with thoracic node involvement

- Pulmonary parenchymal abnormalities: alveolar opacities & peribronchial disease

- Skeletal imaging indicated for bony pain or if pathological fracture is suspected

- Bony lesions are mostly osteolytic
Computed Tomography

- Modality of choice for staging and follow-up

- Ability to demonstrate enlarged lymph nodes throughout the body

- Detection of soft tissue pathology

- Limitation: distinguishing active tumor from fibrotic mass
Computed Tomography

Scout view of Ms. M

Ms. M’s Abdomen

No evidence of abdominal lymphoma

Aorta

Liver

Spleen

Pancreas

Kidneys

PACS, BIDMC
Metastasis to Liver & Spleen

- Note the size of liver and spleen
- Nodular low-density mass in spleen
- B-cell lymphoma

- Nodular infiltration of liver
- Diffuse large B-cell NHL

http://individual.uptodateonline.com/application/topic/print.asp?file=lymphoma/13075&type=A&selectedTitle=1~203
Magnetic Resonance Imaging

- Modality of choice to evaluate CNS involvement

- Extremely sensitive in detecting bone marrow involvement

- Lymph nodes are low-intermediate attenuation on T1 and intermediate-high on T2
Ms. M’s Brain MRI

- Sagittal T1 MRI
- Axial T2 MRI

**Typical site of primary CNS lymphoma**

**Leptomeninges: common site of metastatic CNS lymphoma**

No CNS lymphoma was detected in Ms. M.
Ultrasound

- Confirming that a palpable mass is fact nodal

- Lymph node enlargement readily seen in celiac region, splenic hilum and porta hepatis

- Feature: uniform hypoechoic lobulated masses

- Detection of tumor involvement in liver, kidney, spleen or testes

- Limitations: entire retroperitoneum cannot be shown, findings are nonspecific
Patient 9: Testicular Ultrasound

Large anechoic mass

Arrows outline edge of testis

Biopsy proved to be lymphoma

Gallium Scanning

- Adjunctive for staging
- Detection of residual disease or relapse after treatment
- Sites of involvement take up Gallium and appear as bright “gallium avid” areas
- Caveat: Gallium uptake nonspecific, scan must be done before treatment, not useful in nonavid tumors
Ms. M: Gallium Scanning

Gallium avid area

- Initial whole body scan after presentation
- Five days after intravenous injection of tracer
- Intense uptake in mediastium & mildly in liver

- Three months into treatment
- Three days after injection of tracer
- Disappearance of gallium-avid disease in the thorax

Images: PACS, BIDMC
FDG-PET

- 2-Fluorine-18 Fluoro-2-Deoxy D-Glucose
- Accumulates in highly metabolic cells via glycolytic pathway
- Evaluation of residual mass during and after treatment
- Sensitivity (86%) and specificity (100%) higher than CT (86% & 67% respectively)
Fusion Imaging: PET-CT

- Integration of both biological and anatomical information during a single examination

- Role: staging, response to treatment, follow-up
Patient 10: PET-CT

- Tonsillar lymphoma in a 20-year-old male
- Secondary to Burkitt lymphoma in the abdomen
- Asymmetric signal uptake suggestive of lymphoma
- PET-CT helps localize uptake to palatine tonsils
- Physiologic uptake in tonsils difficult to distinguish from extranodal lymphoma

Images: Radiographics 2004; 24:1418.
Treated with Stanford-based regimen with high-dose CHOP

Also given allopurinol and Lupron (GnRH analog)

Responded well without major complications
Ms. M: CXR Status Post Therapy

PA Chest X-ray on admission
Six months later
Ms. M 20 Months Later...

Axial CT with contrast, on admission

Axial CT with contrast, 20 months later
Ms. M’s Prognosis...

International Prognostic Index

- Age > 60
- Serum LDH > normal
- ECOG performance status > 2
  (non-ambulatory)
- Ann Arbor Stage III or IV
- Number of extranodal sites > 1

• One point for each of the above
• Ms. M has a score of zero
**Cure Rates**

<table>
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<tr>
<th>Score</th>
<th>Risk</th>
<th>5-year Overall Survival (percent)</th>
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<tbody>
<tr>
<td>Ms. M</td>
<td>Low</td>
<td>73</td>
</tr>
<tr>
<td>0 to 1</td>
<td>Low</td>
<td>73</td>
</tr>
<tr>
<td>2</td>
<td>Low-intermediate</td>
<td>51</td>
</tr>
<tr>
<td>3</td>
<td>High-intermediate</td>
<td>43</td>
</tr>
<tr>
<td>4 to 5</td>
<td>High</td>
<td>26</td>
</tr>
</tbody>
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* Up-To-Date 2004
Take Home Points

- Lymphoma - neoplastic proliferation of lymphoid cells
- Presents as homogenous soft-tissue mass most commonly in the thorax and GI
- CT is modality of choice, critical for staging and monitoring
- Nuclear medicine: evaluation of residual masses and fibrotic tissue
References

- Freedman AS. Approach to the diagnosis; staging; and prognosis of non-Hodgkin’s lymphoma. Up-To-Date 2004.
- Freedman AS, Harris NL. Clinical and pathologic features of Burkitt’s lymphoma. Up-To-Date 2004.
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