Atlas of Findings for Diffuse Large B Cell Lymphoma

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Goals

- Understand the pathophysiology and anatomy of lymphadenopathy
- Learn the menu of imaging tests for lymphoma
- Learn how to interpret the most common imaging studies for lymphoma with accurate terminology
- Learn the differential diagnoses for different types of lymphadenopathy and bowel wall thickening
Outline

- Patient presentation
- Radiologic imaging
- Relevant pathophysiology
- Relevant anatomy
- Menu of tests
- Differential diagnosis based on imaging findings
- Patient outcome
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Previously healthy 75yo F presenting with 8 pound weight loss and fatigue over the past 4 months.

PMH, meds, allergies, social history noncontributory

Family History:
- Sister – thyroid cancer
- Son – skin cancer
- Older half brother – prostate cancer
- Older half brother – mesothelioma
- Aunt – leukemia
- Uncle – gastric cancer
- Uncle – pancreatic cancer
Our Patient: Physical Exam and Labs

- Pertinent physical exam findings
  - Fullness at base of the sternocleidomastoid on the L side
  - Mobile 2cm L axillary node

- Labs
  - Elevated Beta-2 microglobulin at 5.4mg/L (normal: 0.8–2.2 mg/L)
  - CBC w/diff, renal function, LFTs, calcium, albumin, UA grossly normal.
Outline

- Patient presentation
- **Radiologic imaging**
- Relevant pathophysiology
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Our Patient: Imaging Studies

- Given mobile 2cm left axillary node physical exam finding, bilateral diagnostic mammogram was performed showing a 3 cm hypervascular solid mass in the lower left axilla suspicious for malignancy.
- CT Thorax and Abdomen (imaging will be reviewed in upcoming slides)
We will now review the pertinent findings from the CT thorax and abdomen C+. 
Our Patient: Soft Tissue Mass on CT Thorax

AXIAL CT Thorax C+
Soft tissue mass displacing trachea to the right and compressing left thyroid lobe. Left subclavian vein.
Our Patient: L Axillary Lymph Node on CT Thorax

AXIAL CT Thorax C+

Left axillary lymph node containing an area of low attenuation in its lateral portion most consistent with a focus of necrosis.
Our Patient: L Axillary Lymph Node on CT Thorax (Magnified)

AXIAL CT Thorax C+

Left axillary lymph node containing an area of low attenuation in its lateral portion most consistent with a focus of necrosis.
Our Patient: Multiple Liver Lesions on CT Abdomen

*AXIAL CT Abdomen C+*

*Multiple low-attenuation areas* in the liver parenchyma that are too small to characterize. The *largest lesion* of the liver is measured as shown. The *spleen* is at the upper limit of normal size. Together with other findings, this is suggestive of multifocal malignancy.
Our Patient: Retroperitoneal Soft Tissue Mass on CT Abdomen

AXIAL CT Abdomen C+ at the level of the aortic diaphragmatic hiatus

Bulky retroperitoneal soft tissue mass measuring 3.5x5.5x7.5 cm (coronal not shown). The mass displaces the abdominal aorta and IVC anteriorly. Inferior splenic pole low attenuation focus could be a small hemangioma or a metastasis.
Our Patient: Bowel Wall Thickening on CT Abdomen

AXIAL CT Abdomen C+
Numerous non continuous segments of bowel with abnormal mural thickening.
Our Patient: Enlarged Mesenteric Lymph Node on CT Abdomen

Numerous enlarged mesenteric lymph nodes. Largest node shown above.
Our Patient: More Enlarged Mesenteric Lymph Nodes on CT Abdomen

AXIAL CT Abdomen C+
Numerous enlarged mesenteric lymph nodes.
Our Patient: Summary of CT Thorax and Abdomen Findings

Radiology Report:

1. “L lower cervical mass with tracheal displacement”
2. “Retroperitoneal soft tissue mass at the level of the aortic [diaphragmatic] hiatus displacing the aorta and IVC anteriorly”
3. “Non contiguous segments of bowel wall thickening and luminal dilatation with associated mesenteric lymphadenopathy”
4. “Multiple hepatic low–attenuation lesions which are too small to characterize”

“Overall constellation of findings is most in keeping with lymphoma with left axillary, retroperitoneal, small bowel and mesenteric nodal involvement. Lesions in the liver remain indeterminate.”
Given that our patient’s imaging findings were concerning for lymphoma, the left axillary node was biopsied for confirmation.
Our Patient: Pathology Report of Left Axillary Node

- Pathology Report:
  - “The combined morphological and immunophenotypical findings are consistent with a large B cell lymphoma with aggressive features.”
Given the diagnosis of lymphoma, the patient therefore underwent FDG Tumor Imaging (PET–CT) for staging.
Our Patient: Left Cervical Node on PET

AXIAL FDG–PET
A 5.1 x 3.2 cm left cervical nodal conglomerate is markedly FDG avid (SUVmax 30.4). There is no abnormal FDG uptake elsewhere in the head or neck.
Our Patient: Left Axillary Node on PET

AXIAL FDG–PET
2.8 x 1.6cm left axillary lymph node is FDG avid (SUVmax 34.1).
Our Patient: Left Lateral Chest Wall Node on PET

AXIAL FDG–PET
Slightly more inferior on the left lateral chest wall is a 0.6 x 0.4cm FDG avid node (SUVmax 6.9).
Our Patient: Left Retrocrural Mass on PET

AXIAL FDG–PET

A 5.8x3.3cm retrocrural mass is markedly FDG avid (SUVmax 35.1).

Hypodensities in liver are not FDG avid.
There are multiple FDG-avid mesenteric masses that are difficult to separate from the FDG-avid thickened bowel wall.
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Definition of Lymphoma

- Neoplasm derived from cells that normally develop into T lymphocytes (cytotoxic T lymphocytes, helper T lymphocytes, or regulatory T lymphocytes) or B lymphocytes (including plasma cells)

Freedman et al., 2014 C
WHO Classification of Lymphoma

- Mature B–cell neoplasms
  - Diffuse large B–cell lymphoma
- Mature T–cell and NK–cell neoplasms
- Hodgkin’s lymphoma
- Histiocytic/dendritic cell neoplasms
- Posttransplantation lymphoproliferative disorders
## Cotswold–Modified Ann Arbor Classification of Lymphoma

### Table 1. Cotswold-modified Ann Arbor classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>Involvement/features</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Single lymph node region (I) or one extralymphatic site (IE)</td>
</tr>
<tr>
<td>II</td>
<td>Two or more lymph node regions, same side of the diaphragm (II) or local extralymphatic extension plus one or more lymph node regions same side of the diaphragm (IIIE)</td>
</tr>
<tr>
<td>III</td>
<td>Lymph node regions on both sides of the diaphragm (III), which may be accompanied by local extralymphatic extension (IIIE)</td>
</tr>
<tr>
<td>IV</td>
<td>Diffuse involvement of one or more extralymphatic organs or sites</td>
</tr>
</tbody>
</table>

### Suffix

<table>
<thead>
<tr>
<th>A</th>
<th>No B symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Presence of at least one of the following: unexplained weight loss &gt;10% baseline during 6 months before staging; recurrent unexplained fever &gt;38°C; recurrent night sweats</td>
</tr>
<tr>
<td>X</td>
<td>Bulky tumor is defined as either a single mass of tumor tissue exceeding 10 cm in largest diameter or a mediastinal mass exceeding one-third of the maximum transverse transthoracic diameter measured on a standard posterior-anterior chest radiograph</td>
</tr>
</tbody>
</table>

Kwee et al., 2008
Outline

- Patient presentation
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Head and Neck Lymph Node Anatomy

Lymph nodes of the head and neck

- Posterior auricular
- Occipital
- Superficial cervical
  - Lower ear and parotid
- Deep cervical
  - Other nodes of head and neck, occipital scalp, ear, back of neck, tongue, trachea, nasopharynx, nasal cavities, palate, esophagus
- Posterior cervical
- Supraclavicular
  - Thorax and abdomen
- Preauricular
- Parotid
- Tonsillar
  - Jugulodigastric
- Submental
  - Lower lip, floor of mouth, apex of tongue
- Submandibular
  - Cheek, side of nose, lower lip, gums, anterior tongue

McClain et al., 2014
Radiologists often group lymph nodes into levels. This is helpful in terms of staging certain cancers, such as squamous cell carcinomas.
Head and Neck Lymph Node Levels

Lymph nodes of the head and neck

- **Posterior auricular**
- **Occipital**
- **Superficial cervical**
  - Lower ear and parotid
- **Deep cervical**
  - Other nodes of head and neck, occipital scalp, ear, back of neck, tongue, trachea, nasopharynx, nasal cavities, palate, esophagus
- **Submandibular**
  - Cheek, side of nose, lower lip, gums, anterior tongue
- **Supraclavicular**
  - Thorax and abdomen
- **Preauricular**
- **Parotid**
- **Tonsillar**
  - (Jugulodigastric)
- **Submental**
  - Lower lip, floor of mouth, apex of tongue

Lymph node levels

- **II**
- **Ib**
- **Ia**
- **III**
- **IV**
- **Vla**
- **Vb**
- **VI**
- **VII**

Background image is from (with modifications) the 20th U.S. edition of Gray's Anatomy of the Human Body, originally published in 1988 and therefore落入 the public domain.

McClain et al., 2014

Daeubler et al., 2014
Lymph Node Regions in the Body

<table>
<thead>
<tr>
<th>Node group, number</th>
<th>Drainage</th>
</tr>
</thead>
</table>
| Supraclavicular (2-4) | Right side: Mediastinum, lungs  
Left side: Abdomen |
| Deltoplectoral (1-2) | Arm |
| Axillary (20-30) | Arm, breast, thorax |
| Epitrochlear (1-2) | Medial side of arm below elbow |
| Inguinal (12-20) | Lower extremity, genitalia, buttock, and abdominal wall below umbilicus |
| Popliteal (6-7) | Lower leg |
From the lymph nodes, lymphatic vessels carry lymphatic fluid or lymph towards lymphatic ducts in the pattern of lymphatic drainage areas.
Lymphatic Drainage Areas

Right drainage area

Left drainage area
When the lymph reaches the lymphatic ducts, the lymph drains into veins
Lymphatic Drainage Connections to Veins

**Lymphatic Ducts**

- Right Lymphatic Duct empties at junction of right internal jugular and right subclavian veins
- Thoracic Duct - empties into junction of left internal jugular and left subclavian veins
- Cisterna Chyli – most inferior part of thoracic duct
Clinical lymphadenopathy = palpable enlargement (>1cm) of one or more lymph nodes.

Radiologically, lymphadenopathy size thresholds (always measured in short axis) vary depending on the region.
- Most cervical nodes: 10mm
- Submental, submandibular: 15mm
- Retropharyngeal: 8mm
- Mediastinal: 10mm
- Mesenteric: 3mm (up to 5mm in some hospitals)

Douketis, 2012
Gerstenmaier et al, 2014
Pathogenesis of Lymphadenopathy

Cancer cells, infectious microorganisms, antigens, foreign particles enter lymphatic vessels

Lymph nodes filter lymphatic fluid

3 Possible Outcomes:
A) Antigens presented to lymphocytes within nodes → proliferation (reactive lymphadenopathy)
B) Microorganisms directly infect nodes (lymphadenitis)
C) Cancer cells lodge in and proliferate in the nodes
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- Radiologic imaging
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- Relevant anatomy
- **Menu of tests**
- Differential diagnosis based on imaging findings
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CT and/or PET are imaging modalities of choice to establish baseline prior to treatment and for staging.

PET
- Gallium scan used to be gold standard for cancer diagnosis and staging, but is non-specific as it can indicate new or old infection, inflammation, or malignancy.
- FDG is currently used as radiotracer as it is more specific and lymphoma is typically FDG-avid.
- Current research into potential as a biomarker of response to chemotherapy.

When available, combined PET-CT to measure disease activity.

Kwee et al., 2008
Freedman et al., 2014 A
Freedman et al., 2014 B
Menu of Imaging Tests for Lymphoma Continued

- MRI (less often used)
  - Limited due to lengthy imaging time, limited availability, cost
  - Superior soft-tissue contrast, but staging is based on size and location criteria which can be adequately assessed on CT

Kwee et al., 2008
Freedman et al., 2014 A
Freedman et al., 2014 B
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Our patient presented with cervical lymphadenopathy, unilateral axillary lymphadenopathy, mesenteric lymphadenopathy and thickened bowel wall. Let us review the differential for each of these imaging findings.
Our Patient: DDx of Cervical Lymphadenopathy

- **Benign**
  - Infection
    - Bacteria, viral (EBV, HSV, CMV), mycobacterial (TB)
  - Kimura disease
  - AIDS–related lymphadenopathy
  - Sinus histiocytosis (Rosai–Dorfmann disease)

- **Malignancy**
  - Metastases from head and neck tumors
  - Lymphoma
  - Kaposi sarcoma
Our Patient: DDx of Unilateral Axillary Lymphadenopathy

- **Benign**
  - Mastitis
  - Infection: TB, ipsilateral arm infection (cellulitis), silicone induced granulomatous adenitis

- **Malignant**
  - Metastasis from breast malignancy
  - Melanoma
  - Primary malignancy in ipsilateral arm
  - Lymphoma: occasionally can be unilateral

Weerakkody et al., 2014 B
Our Patient: DDx of Mesenteric Lymphadenopathy

- **Benign**
  - Mesenteric Adenitis: Classically seen with Yersinia infection
  - AIDS: Secondary to TB, MAC, Kaposi sarcoma, HIV direct infection
  - Diverticulitis
  - Ulcerative colitis
  - Crohn’s disease
  - Appendicitis

- **Malignant**
  - Lymphoma
    - Most common malignant cause of mesenteric lymphadenopathy (usually Non–Hodgkins Lymphoma). Often have node enlargement in other parts of body.
  - Carcinoid tumors
  - Small bowel tumors
  - Colon cancer
  - Pancreatic cancer
Given the long differential for thickened bowel wall, we will first examine the pattern of bowel wall thickening to narrow our differential.
Thickened Bowel Wall

Bowel wall thickening

Focal
(< 5 cm)

Segmental or Diffuse
(6-40 cm) or (> 40 cm)
= Benign (except lymphoma)

Pattern of Attenuation

Stratified
Ischemia/Vasculitides
Active IBD
Infection
Other causes:
  i.e. Radiation enteritis
  Portal Hypertension
  Angioedema...

White
Ischemia
Active IBD

Gray
Ischemia
Chronic IBD or RE

Irregular, asymmetric, heterogeneous

Regular, symmetric, homogeneous thickening with no significant fat stranding

Consider small or well-differentiated adenocarcinoma

Fat stranding disproportionately more severe than wall thickening

Inflammatory
Diverticulitis;
Appendagitis; Omental infarction: Appendicitis

NEOPLASM
Primary
Secondary

Exceptions

Granulomatous disease
(i.e CD, TB)

Fig. 1  Algorithm approach to the bowel wall thickening. CD Crohn’s disease, TB tuberculosis, IBD inflammatory bowel disease, RE radiation enteritis. Adapted from the electronic poster “Bowel wall thickening—a complex subject made simple” DOI: 10.5444/esgr2011/EE-063
Lymphoma usually presents with segmental or diffuse bowel wall thickening, which is similar to the presentation of many benign etiologies. We will review the additional findings on imaging that should make us suspicious of lymphoma.
Characteristics of Lymphoma on CT Abdomen

- Segmental or diffuse bowel wall thickening with symmetric homogeneous attenuation
- Rarely obstructs the bowel lumen
- Minimal fat stranding near thickened bowel segments
- Large bulky retroperitoneal lymph nodes usually present adjacent to or in areas removed from a region of bowel wall thickening
- Associated splenomegaly
- Treated lymphoma = occasional calcifications in mesentery
Other than using the WHO classification of neoplastic diseases of the lymphoid tissue, radiologists tend to divide lymphomas by location i.e. small bowel lymphoma, mediastinal lymphoma.

As our patient presented with lymphadenopathy of multiple anatomic sites, this is consistent with diffuse lymphoma. Our patient had no history of cancer to suggest metastasis.

Diffuse large B cell lymphoma confirmed with pathology of L axillary node biopsy.
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Our Patient: Outcome

- She received appropriate treatment. CT scan 1 year after treatment showed no evidence of lymphoma and she remains in remission.
Schedule of surveillance highly dependent on histology subtype of lymphoma and patient and provider comfort.

Relapse is much less likely to occur greater than five years after treatment.
Take-Home Learning Points

- We learned the pathophysiology and anatomy of lymphadenopathy
- We learned the menu of imaging studies for lymphoma
- We learned how to interpret the most common imaging studies for lymphoma through examining imaging studies performed on our patient
- We learned the differential diagnoses for different types of lymphadenopathy.
- We learned to classify bowel wall thickening into focal or segmental/diffuse patterns to organize our thinking of differential diagnoses. In terms of segmental/diffuse patterns, we then further examined what additional imaging findings on CT suggest lymphoma rather than a benign cause of bowel wall thickening.
The following slides are provided for your information for a more extensive differential diagnoses list based on different patterns of bowel wall thickening on imaging.
APPENDIX 1: Patterns of Attenuation in Bowel Wall Thickening

I. Homogeneous
   A. Common
      1. Submucosal hemorrhage
      2. Lymphoma
      3. Small adenocarcinoma
   B. Uncommon
      1. Infarcted bowel
      2. Pitfalls related to residual fluid
      3. Chronic Crohn’s disease
      4. Chronic radiation injury

II. Heterogeneous
   A. Stratified attenuation
      1. Common
         a. Ischemia
         b. Infectious enterocolitis
         c. Crohn’s disease, ulcerative colitis
         d. Vasculitis, lupus, Henoch-Schönlein purpura
         e. Radiation
         f. Bowel edema related to cirrhosis or low-protein state
      2. Uncommon
         a. Infiltrating scirrhous carcinoma (usually stomach or rectum)
         b. Residual fluid and contrast material
         c. Submucosal fat deposition
         d. Pneumatosis
   B. Mixed attenuation, common
      1. Large adenocarcinoma
      2. Gastrointestinal stromal tumor
      3. Mucinous adenocarcinoma
APPENDIX 2: Degree of Bowel Wall Thickening

I. Mild Thickening (<2 cm)
   A. Common
      1. Infectious enterocolitis
      2. Ulcerative colitis
      3. Crohn’s disease
      4. Radiation injury
      5. Ischemia
      6. Bowel edema in cirrhosis
      7. Submucosal hemorrhage
   B. Uncommon
      1. Adenocarcinoma
      2. Lymphoma

II. Marked Thickening (>2 cm)
   A. Common
      1. Adenocarcinoma, gastrointestinal stromal tumor, metastases, lymphoma
      2. Severe colitis
      3. Systemic lupus erythematosus
   B. Uncommon
      1. Crohn’s disease, tuberculosis, histoplasmosis, cytomegalovirus
      2. Submucosal hemorrhage

Macari et al, 2001
APPENDIX 3: Symmetry of Bowel Wall Thickening

I. Symmetric
   A. Infections of the small and large bowel
   B. Ulcerative colitis
   C. Crohn’s disease
   D. Radiation injury
   E. Ischemia
   F. Bowel edema in cirrhosis
   G. Lymphoma
   H. Submucosal hemorrhage

II. Asymmetric
   A. Adenocarcinoma
   B. Gastrointestinal stromal tumor
APPENDIX 4: Length of Bowel Wall Thickening

I. Focal (<10 cm)
   A. Common
      1. Diverticulitis, appendicitis
      2. Adenocarcinoma
   B. Uncommon
      1. Lymphoma
      2. Tuberculosis
      3. Crohn’s disease

II. Segmental (10–30 cm)
   A. Common
      1. Lymphoma
      2. Crohn’s disease
      3. Infectious ileitis
      4. Radiation
      5. Submucosal hemorrhage
      6. Ischemia
   B. Uncommon: systemic lupus erythematosus

III. Diffuse
   A. Common
      1. Ulcerative colitis
      2. Infectious enterocolitis
      3. Edema from low protein and cirrhosis
      4. Systemic lupus erythematosus
   B. Uncommon: ischemia

Macari et al, 2001
References

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