Presenter Disclosure

- Faculty / Speaker’s name: Dr. Pamela Skrabek

- Relationships with commercial interests:
  - Grants/Research Support: none
  - Speakers Bureau/Honoraria: none
  - Consulting Fees: Celgene, Bristol Myers Squibb
  - Other: none
Mitigating Potential Bias

• I will not be discussing pharmaceuticals
Learning Objectives

1. To be able to determine if splenomegaly is concerning
2. In a patient with splenomegaly know clinical context where Hematology referral is beneficial
3. When a patient has lymphadenopathy outline an approach to investigation and understand when to suspect lymphoma
Introduction

• Enlarged lymph nodes & splenomegaly common
• Wide differential diagnosis for both
• Clinical or diagnostic significance of a spleen that is modestly enlarged on scan but is not palpable (ie, "scanomegaly")\(^1\) is uncertain

Spleen Function

• Immune organ
• Phagocytosis of erythrocytes
• Site of hematopoiesis
• Blood reservoir
Spleen Size

• Normal is actually hard to define
  – Varies by height, gender, race
• A palpable spleen is usually enlarged
• Ultrasound Length > 13 cm
• CT normal volume from 107 to 315 cm³,
  – One study correlates this to maximum length of 10 cm*

* Bezerra A et al. AJR:184, May 2005
Causes Splenomegaly

Infection – most common viral
Autoimmune disorders
Sarcoidosis
Hemolysis
Hematological malignancy - Myeloproliferative neoplasms, lymphoma
Obstructive disease - blood flow - cirrhosis, portal vein thrombosis

Splenomegaly Referral

Consult Service: Hematology / CCMB

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<th>Level of Urgency:</th>
<th>Reasons for Consultation:</th>
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<td>☐ Emergent* (patient to be seen within &lt; 1 hr)</td>
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* Requires Attending MD to Attending MD phone call/conversation

Key Features Relevant to Question: 53 y/o F with History of Diabetes Mellitus, Cancer, and Surgery, presenting with weight loss (44) / height (65) (85) kg, 2015. Enlarged spleen.

FINDINGS:

Examination was performed without the benefit of IV contrast due to a high serum creatinine. This limits assessment of solid organs. Allowing for this:

Images of the lung bases demonstrate a trace right pleural effusion. Heart is enlarged.

There is minimal ascites adjacent to the liver. Spleen is enlarged measuring approximately 15.1 cm in length. No gross focal splenic lesion. The gallbladder is present. Liver, pancreas, adrenals and kidneys appear grossly unremarkable. There appears to be circumferential urinary bladder wall thickening. A small amount of free fluid is present within the pelvis. No pathologically enlarged intra-abdominal or pelvic lymph nodes by CT criteria. No gross bowel abnormalities although endoscopy is more sensitive for detection of GI pathology including malignancy.

IMPRESSION:
Splenomegaly

Define Splenomegaly: Palpable, > 13 cm on ultrasound
Platelet count < 75 x 10^9/L, or WBC count < 3 x 10^9/L may be less likely attributed to portal hypertension
Splenomegaly Referral

Weight loss, fatigue, petechiae legs, low grade fevers. Bioprosthetic pulmonlyar valve. Exam with spleen tip palpable, 1.5 cm inguinal LN, petechiae/ some large more like purpura
Normally 1/3 platelets sequestered in spleen, hypersplenism can be up to 90%, "apparent thrombocytopenia". Splenic "metastasis" usually hematological

Acute Mono - Young adult with fever, sore throat, splenomegaly.

In registry study ½ with hepatic splenomegaly had hepatomegaly, signs of chronic liver disease or thrombocytopenia.

Splenic "metastasis" usually hematological.
Splenomegaly Referral 2

Nothing on exam or history that was concerning only iron deficiency anemia. Significant patient post partum, no other change.

CT mild splenomegaly, fatty liver.
Practice Points

• Radiology does not always give measurement or degree of variation from upper limit normal

• If non palpable spleen and patient is well without abnormalities on CBC
  – No need for referral, follow clinically & with imaging repeat in 6 months
Learning Objectives

1. To be able to determine if splenomegaly is concerning
2. In a patient with splenomegaly know clinical context where Hematology referral is beneficial
3. When a patient has lymphadenopathy appreciate an approach to investigation and when to suspect lymphoma
Suspicion of lymphoma

• Most patients initially present to primary care provider

• >30% patients with NHL and > 40% HL have more than 3 visits to Primary Care before investigations/ referrals

• No symptom signature

Suspicion of Lymphoma

• lifetime probability NHL 2 %
• very few factors greatly increase risk
  • Primary Immune Disorders (incidence lymphoma 12-25%)
  • Autoimmune Disease, Organ Transplant, HIV, Drugs that modulate immune system
Suspicion of Lymphoma

• IF first degree relative with NHL, HL or CLL
  ~1.7 fold, 3.1 fold and 8.5 fold risk respectively of same diagnosis

• Thus lifetime risk NHL ~ 3.4% even lower specific lymphoma subtypes
Suspicion of lymphoma

• Most cases NHL and HL present with lymphadenopathy (LN)
  • Positive Predictive Value [PPV] 18.6% (patients > 40)

• B symptoms - aggressive lymphomas with high disease burden
  • In isolation neither PPV or Negative Predictive Value (NPV) that high

Suspicion of lymphoma

• Other clinical signs/ symptoms in isolation low predictive value

• Increased PPV of LN for lymphoma
  • Weight loss, abdominal complaints, dyspnea
  • Leukocytosis, cytopenia, increased liver enzymes, increased inflammatory markers


Work-Up of Lymphadenopathy Suspicious for LYMPHOMA

RISK FACTORS: HIGH risk: immune deficiency (i.e. HIV or organ transplant), autoimmune disease +/- immune suppressing medications, and history of lymphoma

PRACTICE POINTS: **Consider your differential diagnosis** - reactive LN due to infection (i.e: TB) or inflammation, metastatic malignancy and autoimmune disease. This document applies to adults 17 years of age or older.

Emergent
- Airway compromise
- Superior vena cava compression
- Spinal cord compression

Send to Emergency Department

Pallpable Lymphadenopathy (LN)
- Abnormal LN: >2-3 cm, persistent enlargement & without obvious cause

Lymphadenopathy on Imaging

History & Physical Exam
**Consider your differential diagnosis**
Order CBC, HIV test, Chest X-ray

No ↑ Lymphocyte Count

High Suspicion / Concerning Features
PROCEED without delay
- HIGH Risk Patients (as above)
- LN + Abnormal Bloodwork (severe anemia, thrombocytopenia, pancytopenia)
- Widespread LN +/- splenomegaly or bulky LN (mass >6cm)
- Mediastinal mass
- LN with rapid growth
- LN & B symptoms (drenching sweats, unexplained fever, weight loss)
- Patient symptomatic from abnormal LN (i.e: short of breath, abdominal pain)

Order flow cytometry on peripheral blood (query CLL vs other lymphoma)

Positive for CLL or monoclonal lymphocyte population

REFER TO CCMB

If ANY Concerning features - Determine* best site for diagnostic biopsy
- Order URGENT CT scans if not already done, including neck, chest, abdomen & pelvis
- Preference for site of biopsy:
  - Palpable >Mediastinal > CT guided
  - Order CBC, chemistry (including Ca, LDH, Cr) and INR if not already done
*If assistance is needed contact Hematologist on call for advice

If NONE Clinical Follow up

Persistent / progressive LN
on exam (>4weeks) or imaging (after serial examination)

Continue to Diagnostic pathway
pg.2

> In Sixty timeline starts with evidence of concerning features
> In Sixty All imaging done within 2 weeks

Timeline and Legend pg.5

IN60_LYMS: 03-06-2015
Initial Steps

• History, examine all LN groups
  – Size, consistency, rapidity of growth
  – Local cause
    – Oropharynx, liver, spleen
• CBC, Chest x ray, HIV test
• CT scan is imaging test of choice in adults
Figure 1. Cervical triangle anatomy with common lymph node locations and drainage areas.
Lateral Neck Mass

• Most commonly benign - infection/ inflammation
  – odotogenic, salivary, viral or bacterial etiologies
  – Recent Ear, Nose, Throat symptoms good NPV

• More concerning for malignancy
  • Lymphoma up to 50% malignant lateral neck mass

Lymphadenopathy (LN) + HIGH Risk patient
LN + anemia, thrombocytopenia or pancytopenia
Widespread LN +/- splenomegaly or bulky LN (mass >6cm)
Mediastinal mass
LN with rapid growth or B symptoms (drenching sweats, unexplained fever, weight loss)
Patient symptomatic from abnormal LN (ie: short of breath, abdominal pain)
Work-Up of Lymphadenopathy Suspicious for LYMPHOMA

RISK FACTORS: HIGH risk: immune deficiency (i.e. HIV or organ transplant), autoimmune disease +/- immune suppressing medications, and history of lymphoma.

PRACTICE POINTS: **Consider your differential diagnosis** - reactive LN due to infection (i.e. TB) or inflammation, metastatic malignancy and autoimmune disease. This document applies to adults 17 years of age or older.

**Emergent**
- Airway compromise
- Superior vena cava compression
- Spinal cord compression

**PRACTICE POINTS:** All referrals sent within 24 hrs of visit. Provide complete information as requested to avoid delays. Ensure patient and family is well informed and receives appointment information. If patient is in distress, offer referral to local counselor. See Supporting Information for Clinicians (p. 4) for contacts and resources. Contact the Cancer Question Helpline for Primary Care for assistance.

**History & Physical Exam**
**Consider your differential diagnosis**
Order CBC, HIV test, Chest X-ray

**Lymphadenopathy on Imaging**

**No Lymphocyte Count**

**Lymphocyte Count**
Order flow cytometry on peripheral blood (query CLL vs other lymphoma)

**High Suspicion / Concerning Features**
**PROCEED without delay**
- HIGH Risk Patients (as above)
- LN + Abnormal Bloodwork (severe anemia, thrombocytopenia, pancytopenia)
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  *If assistance is needed contact Hematologist on call for advice*

**Persistent / progressive LN**
If NONE Clinical Follow up

**Order flow cytometry on peripheral blood (query CLL vs other lymphoma)**

**Positive for CLL or monoclonal lymphocyte population**
REFER TO CCMB

**In Sixty**
In Sixty timeline starts with evidence of concerning features

**In Sixty**
All imaging done within 2 weeks
Referral

Dear Doctor,

I would appreciate you assessing this 23 year old male who presented to ER on March 9th with a history of shortness of breath for a few months, generalized puritis and fevers on and off. He had decreased air entry in his left lung and was found subsequently on CT to have a large mass in his left lung with mediastinal nodes and later on CT abdomen & pelvis to have an enlarged spleen. Dr

Examine patient, get CBC, biochem (including Ca, LDH), HIV, INR
Axillary LN found
Diagnostic Pathway LYMPHOMA

PRACTICE POINTS: Consultation with the Lymphoma Disease Site Group can happen earlier in the pathway if clinicians need additional support or guidance.

*Results Consistent with Lymphoma: If flow cytometry from biopsy or FNA is consistent with lymphoma, consult should be sent to CCMB Central Referral for triage by Lymphoma DSG even if final pathology report is not yet complete.

12% patients

Diagnostic Biopsy
IF THERE IS A PALPABLE MASS, DO NOT WAIT FOR CT RESULTS TO SEND CONSULT TO SURGEON:
- Order URGENT CT scans if not already done, including neck, chest, abdomen & pelvis
- Preference for site of biopsy: Palpable > Mediastinal > CT guided
- For CT-guided biopsy of intra-abdominal LN review CT Neck, Chest for alternate LN first
- Order CBC, chemistry (including Ca, LDH, Cr) and INR if not already done

FNA consistent* with Lymphoma SURGEON books Open Biopsy AND Direct Refers to CCMB Lymphoma

Biopsy (1-2 wks) sent Lymphoma protocol

Results consistent* with Lymphoma
Provider Direct Refers to CCMB Lymphoma

Clinical suspicion remains despite negative results
Refer to Lymphoma DSG for review

Negative for cancer & lymphadenopathy resolved
Send back to Primary Care Provider to inform patient of results.

Triaged by Lymphoma DSG - if Concerning features proceed with booking first appointment with hematologist when pathology anticipated to be available (~14 days after biopsy)

Mediastinal Mass: Surgeon Assessment

Intra-abdominal/retroperitoneal LN: Provider orders CT guided biopsy (no surgical referral needed)

Biopsy by mediastinoscopy (LPAC): Order (sent within 2 wks) sent

Open biopsy (same day or book O.R. within 2 weeks) sent Lymphoma protocol

FNA and core biopsies recommend 18guage or larger; sent Lymphoma protocol

Neck LN:
- Surgery Consult for Biopsy with FNA

Axillary or Inguinal LN:
Surgeon assessment

Refer to appropriate provider

Biopsy results reported within 14 days. Immediate direct referral to CCMB if suspicious of lymphoma

FNA results reported within 2 days (immediate direct referral to CCMB if suspicious of lymphoma)

Biopsy with 2 weeks of surgery consult/assessment/FNA

"In Sixty"
Diagnosis of lymphoma

• FNA – exclusion metastatic carcinoma, cannot be used for definitive diagnosis

• Open (preferred) or core biopsy required for lymphoma

  • Biopsy should be sent “LYMPHOMA PROTOCOL” if lymphoma in differential diagnosis
Practice Challenges

• Many patients with benign lymphadenopathy
• Knowing where to send patient for LN biopsy, how/when to arrange CT guided biopsy
• What to do with rapidly deteriorating patient with concerning features
Take home message(s)

• Important to rule out hepatic splenomegaly
• Infectious causes splenomegaly common especially in young patient
  – Often have fever
• algorithm helps to identify patients who most benefit from Hematology referral
  – Patients with “scanomegaly” only can be observed
Take home message(s)

• Always include physical exam (ie palpable nodes – size/ location) and whether there are concerning symptoms with consult

• In Sixty Clinical Pathway for lymphadenopathy highlights when to be most suspicious of lymphoma and approach
Thank you

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