CASE STUDY IN NON-HODGKIN LYMPHOMA

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Disclosures

• Dr. Raziya Mia
  • None

• Dr. Diego Villa
  • Honoraria and advisory boards for: Lundbeck, Abbvie, Celgene, AstraZeneca, Gilead, Novartis, Seattle Genetics, and Roche.
Non-Hodgkin Lymphoma (NHL)
Learning Objectives

At the end of this session participants will be able to:

• Recognize criteria for the diagnosis of NHL
• Describe key patient care issues in the management of NHL
• Identify therapies available in the management of NHL
NHL Facts

• Diverse group of hematologic malignancies
  • Arise from lymphocytes at various stages of development
  • Involve lymph nodes and/or lymphatic tissue in organs
  • ~85% B-Cell
  • ~15% T-Cell or NK-Cell
  • Disease characteristics reflect the cell of origin
NHL Facts

• In 2017 (Canadian Cancer Society Statistics)
  • 8300 Canadians were diagnosed with NHL
    • 4600 men and 3700 women
  • 2700 Canadians died from NHL
    • 1500 men and 1200 women
• Incidence increases with age to 120/100,000 and peaks at ages 80-84 (National Cancer Institute 2016)
• Uncommon in children
NHL Facts

- There are more than 60 Subtypes
  - Common subtypes number far fewer
- Histology
  - Aggressive (eg. Diffuse Large B-Cell Lymphoma)
  - Intermediate
  - Indolent (eg. Follicular Lymphoma)
- Indolent NHL can transform into aggressive NHL
- NHL can cause many complications and oncologic emergencies
NHL Facts

• Cause unknown but there are risk factors
  • Immune suppression
  • Treatments for autoimmune diseases
  • Infectious exposures associated with NHL
    • EB Virus (Burkitt’s Lymphoma)
    • HTLV-1 (Type of T-cell Lymphoma)
    • HIV/AIDS
    • H. Pylori (MALT Lymphoma)
    • Hepatitis C (Splenic Marginal Zone Lymphoma)
  • Genetic syndromes
Treatment Options

- Wait and watch
  - Asymptomatic indolent lymphoma
- Immediate Treatment
  - Curable subtypes
  - Symptomatic
- Systemic Therapy
- Radiation Therapy
- Stem Cell Transplant
- Emerging Therapies
Mr. LG - 2010

• Age – 65 years
• Low grade right inguinal discomfort x1 yr
  • Mentioned during routine examination with his family physician in November 2010
• PMHx: Hypertension managed with Quinapril and HCTZ
• Weight 64.7 kg, Height 171 cm
• Otherwise healthy, fit, never smoker, occasional alcohol use, with no significant occupational exposures
• Ultrasound
  • Prominent bilateral groin lymph nodes up to 3.9 cm

• CT
  • Lymphadenopathy in inferior mediastinum, retrocrural space, and anterior cardiophrenic space up to 1.7 cm
  • Massive retroperitoneal, mesenteric, and pelvic/inguinal lymphadenopathy up to 3 cm
  • Distal ureters partially encased by retroperitoneal nodal complexes bilaterally, with mild prominence of collecting systems but unremarkable kidneys
  • Normal spleen size of 10.6 cm
Mr. LG – 2011

- FNA Requested

IS THIS A USEFUL TEST IN THIS CLINICAL SCENARIO?
Mr. LG – 2011

• FNA
  • Mixed Lymphoid population
    • ?Reactive Lymph Node
    • ?Low grade Lymphoma
• Excisional Biopsy R. Groin
  • Path: Follicular B Cell Lymphoma, grade 1-2
• Flow Cytometry
  • Immunophenotypically abnormal B cell population
  • DNA PCR showed presence of a monoclonal B Cell population
Assessed at BCC in March 2011

- Hx: Night sweats 3-4x/week x 1 yr
- Px: Palpable axillary lymph nodes and healing incision R. inguinal area
- Hgb 162, WBC 5.6, ANC 3.7, platelets 157
- Cr 87, Ca 2.38, LD 222 (normal < 220), TSH 2.99, normal LFT's
- Hepatitis B/C/HIV tests negative
- Normal SPEP and SFLC
What Specifically Defines B Symptoms?
B Symptom Criteria

- Fever > 38°C
- Drenching Night Sweats
- Unexplained Loss of >10% Body Weight over 6 months
NHL Symptoms

- None
- Painless Lymph Node Swelling
- Unexplained Fever
- Drenching Night Sweats
- Persistent Fatigue
- Anorexia
- Unexplained Weight Loss
- Cough, Chest Pain
- Abdominal Pain, Bloating, Fullness
- Pruritis
- Rash
Mr. LG - 2011

Any further investigations?
• Bone Marrow Biopsy - positive for marrow involvement

How Would You Stage Mr. LG?
Lymphoma Staging

• Stage I – Involvement of 1 lymph node or a group of adjacent nodes
• Stage II – Involvement of 2 or more lymph node regions on the same side of the diaphragm
• Stage III – Involvement of 2 or more lymph node regions above and below the diaphragm
• Stage IV – Extranodal Involvement
Lymphoma Staging

- Unlike staging of solid tumours
- Reflects areas of lymphoma involvement
- Stage IV disease may respond well to treatment
Lymphoma Staging Alphabet Soup

- A – No symptoms
- B – B symptoms
- E – Extranodal site
- S – Splenic Involvement
- X – Bulky disease
NHL Score
The International Prognostic Index (IPI)

• Risk factors:
  • Age greater than 60 years
  • Elevated serum LDH
  • ECOG performance status >1
  • Stage III or IV disease
  • Extranodal involvement in 2 or more sites
IPI 5-Year Survival > 60

1 point each:
• Age > 60
• Increased LDH
• ECOG >1
• Stage III or IV
• > 1 site of extranodal involvement

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<th>Risk</th>
<th>Points</th>
<th>5 Year Survival</th>
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<tr>
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<td>2</td>
<td>51%</td>
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<tr>
<td>High Intermediate</td>
<td>3</td>
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### IPI 5-Year Survival <60 yrs

- Increased LDH
- ECOG > 1
- Stage III or IV

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<td>69%</td>
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<td>46%</td>
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<tr>
<td>High</td>
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Follicular Lymphoma International Prognostic Index (FLIPI)

1 point each:
• Age > 60
• Increased LDH
• Hemoglobin < 120 g/L
• Stage III or IV
• > 4 LN groups

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<th>Points</th>
<th>5 - Year Survival</th>
<th>10 - Year Survival</th>
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<tbody>
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<td>91%</td>
<td>71%</td>
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<tr>
<td>Intermediate</td>
<td>2</td>
<td>78%</td>
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<tr>
<td>High</td>
<td>3-4</td>
<td>52%</td>
<td>35%</td>
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Back to Mr. LG - 2011

• Diagnosis
  • Stage IVB Follicular Lymphoma
  • FLIPI Score 4: Age 65, LD 222, Stage IV, > 4 LN groups

• Prognosis
  • 5-Year Survival ~ 52%
  • 10-Year Survival ~ 35%
Mr. LG

First line treatment recommendation?
Mr. LG - 2011

CVP-R (Cyclophosphamide, Vincristine, Prednisone, Rituximab)

Would treatment choice differ in 2018?
Mr. LG

- Tolerated Cycles 1-4 CVP-R well
  - Resolution of axillary lymphadenopathy
- Post Cycle 4 CT scan showed significant interval improvement
- LD decreased to 153
- Minimal peripheral neuropathy with no function impairment cycles 5-8
- No dose reductions needed
Mr. LG – 2011-2013

- Post treatment CT scan
  - Further debulking of lymphadenopathy
- Treatment resulted in at least a very good partial response
- Proceeded to 8 cycles of maintenance Rituximab between December 2011 and August 2013
- CT scan showed no evidence of lymphoma recurrence
- Active surveillance arranged
Lymphoma surveillance

• History
• Physical

• Investigations
  • Hematology panel
  • Creatinine
  • LD
  • LFT’s
  • Imaging only when clinically indicated
Footnote: Mrs. G - 2015

- Diagnosed with Ovarian Cancer and undergoing chemotherapy
Mr. LG – 2015

• Presents in August 2015 with recurrence of night sweats
• Lymphadenopathy palpable in supraclavicular and axillary areas
• Hgb 155, WBC 8.4, ANC 6.9, Platelets 219
• Cr 90, Ca 2.38, LD 200, LFT’s normal
• CT scan
  • Recurrent bulky disease
  • Encasement of the ureters by lymphomatous tissue
  • Extrinsic compression of both ureters > on left
What is the next line of treatment?
Mr. LG - 2015

- Fludarabine + Rituximab x6 cycles between September 2015 and January 2016
- Well tolerated
- Post treatment CT scan
  - Decreased lymphadenopathy
  - Hydronephrosis improved
Mr. LG - 2016

- Presents in July 2016 with vague upper abdominal discomfort and change in bowel habit
- CT scan
  - Stable findings in the subcarinal, distal thoracic, left para-aortic, and mesenteric areas
  - Progression of lymph node mass in the upper aortocaval area at the level of the renal hila,
    - 6.5 x 5.8 x 3.3 cm
    - Encasement of the right renal arteries
    - Mass effect on the inferior vena cava
What is the next treatment option?
Mr. LG - 2016

- Radiation Therapy between August 24 – September 14, 2016
- By November 2016
  - Fatigue
  - Recurrent night sweats
- CT scan
  - Lymphoma progression with new involvement
    - Right upper neck
    - Right kidney
    - Right external iliac areas
What might be happening?
There is good clinical evidence of lymphoma transformation

What are the pros and cons of doing a biopsy in this setting?
What would be the next treatment of choice?
Mr. LG - 2017

- Received 5 cycles of CHOP-R between November 2016 and March 2017
- Stormy course
  - Febrile Neutropenia
  - Recurrent Clostridium difficile
    - Managed with Metronidazole, then Vancomycin
    - Ultimately required a fecal transplant
  - Neuropathy
Mr. LG - 2017

- Cycle 6 omitted due to poor tolerance
- CT scan showed a good response to treatment
- Developed Herpes Zoster infection in April 2017
  - Managed effectively with Valacyclovir
Mr. LG – 2017... 6 months later

- Disease progressed again with anteromedial right chest wall mass measuring 5.6 x 2.7 cm.

What is the next line of treatment?
Mr. LG - 2017

- Started on GDP-R chemotherapy
  - 6 cycles of treatment September 2017–February 2018

- Stormy course
  - Febrile Neutropenia
  - Pancytopenia
  - Increased Neuropathy
  - Tinnitus
  - Recurrent Herpes Zoster
Mr. LG - 2018

- Venous access issues – PICC catheter inserted in January 2018
- Complicated by catheter related thrombosis in February 2018
  - Occlusive left basilic and subclavian deep vein thrombosis
    - Rx: Dalteparin
- Completed last cycle of treatment and PICC catheter removed
Mr. LG - 2018

Post GDP-R Rx investigations March 2018

- Hgb 106, WBC 4.6, ANC 1.6, platelets 207
- Cr 87, Ca 2.25, LD 284, LFT’s normal
- CT scan
  - Mixed response to treatment
  - Significant decrease in size of right chest wall mass
- PET scan planned
Mr. LG - 2018

• April 2018 developed clinical progression
  • Night sweats
  • Clinically palpable swelling along the right sternal border
• Repeat CT Scan confirmed disease progression
  • Right parasternal conglomerate 8.4 x 5.4 cm nodal mass
  • New 2.6 x 1.3 cm mass adjacent to the right 5\textsuperscript{th} rib

Next Step?
Mr. LG - 2018

- Palliative radiation between May 16-30, 2018
  - Right parasternal region
  - Right 5\textsuperscript{th} rib
Mr. LG - 2018

• Discussion with medical oncologist
  • All standard treatment exhausted
  • Consider a clinical trial
    • None open locally
    • Patient declines consultation at Vancouver Centre
Over to Dr. Villa...

... For his opinion on treatment options if the patient had been willing to pursue a clinical trial
BC Cancer Study

Biology of Lymphoma (Bio-Lym)
RTC planned with investigations
June 11, 2018

- Hgb 127, WBC 3.6, ANC 2.6, Platelets 103
- Cr 83, Ca 2.32, Bilirubin 8, GGT 189, Alkaline Phosphatase 398, AST 63, ALT 35
- LD 2680
Mr. LG – 2018

- CT Scan June 25, 2018
  - Marked progression with multiple new pleural based nodules/masses right hemithorax
  - Right pleural effusion
  - Right paraspinal soft tissue masses into the central canal T7/T8
  - Left chest wall/2nd rib lesion
  - New abdominal and retroperitoneal lymphadenopathy
  - Compression of the IVC
  - Multiple masses in the liver
  - Suspicious areas in spleen and right kidney
Mr. LG - 2018

- June 27, 2018: Communication with family by telephone
  - Significant clinical decline
    - Anorexia, Pain, and Weakness
  - Patient wished no further treatment including radiation therapy
- Family physician involved
  - Pain and symptom management
  - Community supports in place
Mr. LG – age 73

Died peacefully on July 3, 2018
My Thoughts

• The patient and his wife were fine people who handled whatever came their way with reason, grace, and dignity

• During one visit while on GDP-R chemotherapy Mr. LG expressed the desire to stop treatment
  • He continued after discussion
  • It is my belief and hope that this increased his quality of life for the time he had remaining

• It was a privilege to be involved in the care of this courageous and inspiring gentleman