EHA-TSH Tutorial on Follicular Lymphoma

Tutored Clinical Case 1

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Clinical history

- A 46-year-old man with no significant past medical history presents to the hematology clinic as he noticed left-sided submandibular lymphadenopathy

- He reports slight weight loss over the past two months

Physical Exam

- Temperature 36.7°C,heart rate 72/min, blood pressure 120/70 mm Hg
- He has non-tender and mobile left submandibular lymphadenopathy which measured 2x2 cm
- There was no organomegaly

Laboratory

- WBC: 9.0 x 10^9/l
- Hct: 36%
- Hb: 120 g/l
- Platelets: 220 x 10^9/l

- LDH: 204 U/l (N<225)
- ALT: 20 U/l (3-36)
- AST: 19 U/l (0-35)
- Uric acid: 4.6 mg/dl (3-7)
- Urea: 44 mg/dl (7-22)
- Creatinine: 0.81 mg/dl (0.56-1)

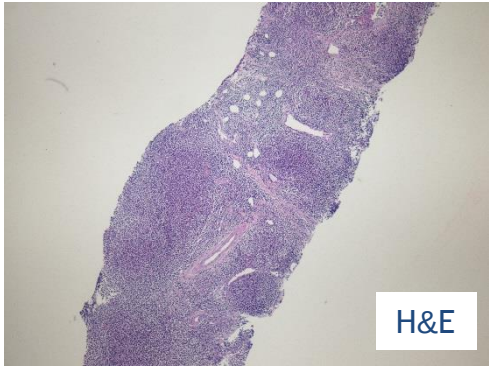
Laboratory

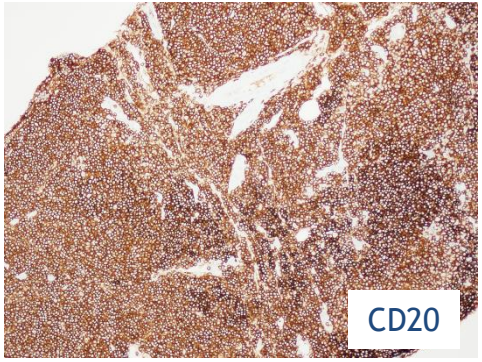
- Thorax and abdomen CT showed supraclavicular, superior mediastinal, mesenteric, and retroperitoneal lymphadenopathy. His largest lymph node is 2.8 cm.

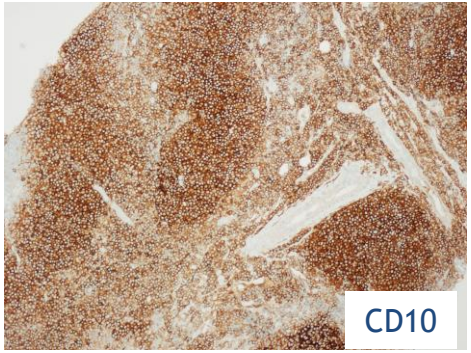
- Excisional lymph biopsy showed grade 2 follicular lymphoma that was positive for CD20, CD10, Bcl-6 and Bcl-2 co-expression; Ki-67 15%

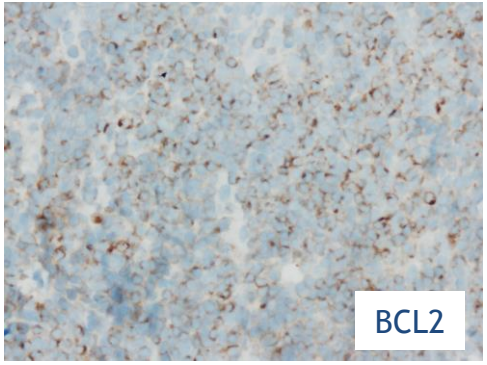
- Bone marrow biopsy was negative

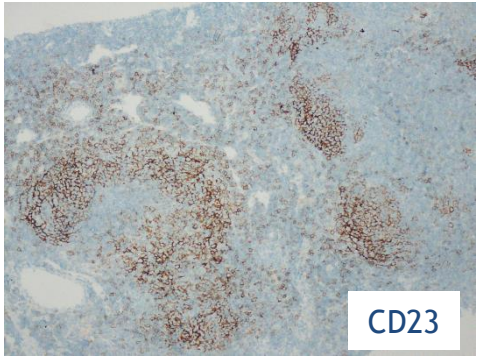
Lymph node biopsy



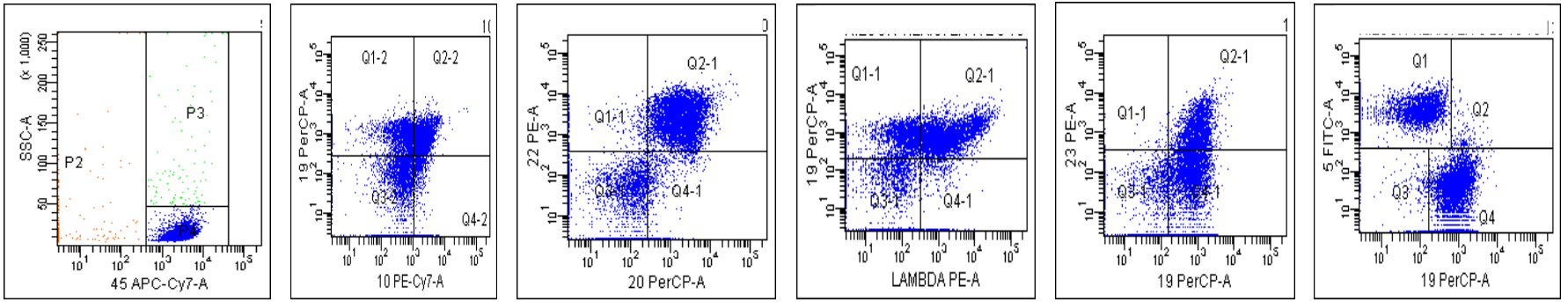








Flow cytometry



Lymphocytes 98%, B cells 60%, T cells 38%, NK cells 2%
Surface Ig light chain – predominantly lambda type
CD10 (60%) and CD23(33%) positive

Treatment

Which treatment option would you recommend for this patient ?

- Stage III FL, low tumor burden
- Advanced stage FL patients with low tumor burden do not require immediate treatment unless they have symptomatic nodal disease, compromised end organ function, B symptoms, symptomatic extranodal disease or cytopenias

Dreyling M, et al. Ann Oncol 2016;27(suppl 5):v83.

What I did

- I proceeded with watchful waiting

January 2012

- Submandibular adenopathy
- Dx: Stage III FL
- Watch & wait

February 2016

Bilateral inguinal adenopathy

Laboratory

- PET/CT showed supraclavicular, superior mediastinal, mesenteric, and retroperitoneal lymphadenopathy (SUVmax: 3.0-7.6). His largest lymph node is 10.4 cm

Discussion

What is the risk of histologic transformation into aggressive lymphoma in FL patients ?

- Risk of HT into DLBCL is 3% per year during the first ten years.

- "Advanced stage" at diagnosis has been reported as the only predictor of future transformation in a multivariate analysis.
  - Median OS after transformation was <2 years

Pavanello F, et al. Mediterr J Hematol Infect Dis 2016; 8:e2016062.
Al-Tourah AJ, et al. J Clin Oncol 2008;26:5165.

Discussion

What is the risk of histologic transformation into aggressive lymphoma in FL patients ?

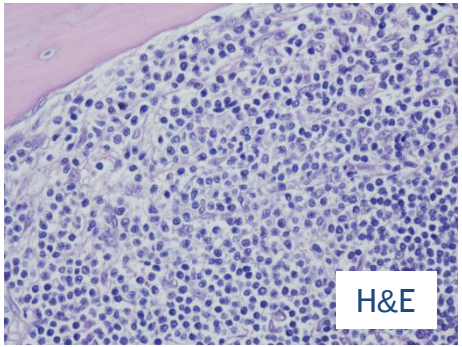
- FDG-PET/CT imaging can be an effective tool to detect histological transformation.
- Emergence of a focal lymphoma site with SUVmax 3 times higher or more than the others on a single scan, or that has tripled its uptake on serial scans, raises suspicion of HT and should be biopsied.

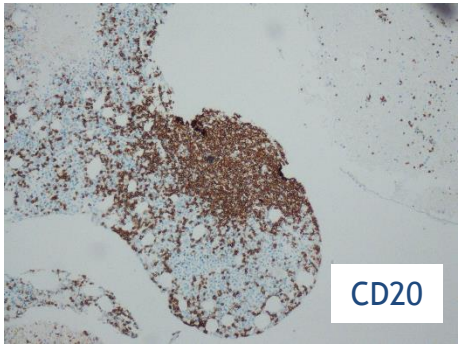
Pavanello F, et al. Mediterr J Hematol Infect Dis 2016; 8:e2016062.
Karam M, et al. Nucl Med Commun, 2011; 32: 177.

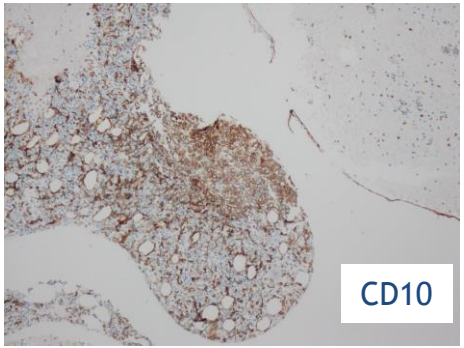
Laboratory

- Lymph node biopsy was pursued at that time confirming grade 2 follicular lymphoma

Laboratory







- Bone marrow biopsy showed 60% involvement with FL.

Treatment

Which treatment option would you recommend for this patient ?

- Relapsed Stage III FL, high tumor burden
- For advanced stage patients with high tumor burden FL, rituximab in combination with chemotherapy such as CHOP or bendamustine are recommended.

Hiddemann W, et al. Blood 2005; 106: 3725.
Rummel M, et al.Lancet2013; 381:1203.

What I did

- Rituximab 375mg/m2, D1 + bendamustine 90 mg/m2, D1-2, every 21 days for 6 cycles was given.

- PET/CT imaging at end of therapy was consistent with “complete remission”.

Discussion

Is there a role for rituximab maintenance for FL patients responding R-Benda?

- Based on the results of the PRIMA study, maintenance therapy with rituximab (375mg/m2 every 8 weeks) up to 2 years is recommended for patients responding to first-line chemoimmunotherapy with R-CVP, R-CHOP or R-FCM.

- The role of maintenance with regimens besides R-CHOP or R-CVP remaines uncertain.

Salles G, et al. Lancet 2011;377:42-51.

January 2012

- Submandibular adenopathy
- Dx: Stage III FL
- Watch & wait

February 2016

- Bilateral inguinal adenopathy
- 6 X R-Benda

November 2016

- Bilateral inguinal adenopathy

Laboratory

- PET/CT showed conglomerated paraaortic, aortocaval, mesenteric, lymph nodes measuring up to 14.4 cm; inguinal and iliac lymphadenopathy (SUVmax: 3.0-7.6).

Treatment

Which treatment option would you recommend for this patient ?

- Early Relapsed Stage III FL
- High-dose chemotherapy with autologous stem cell transplantation (ASCT) is an appropriate consolidative treatment in patients progressing within 24 months of initial chemoimmunotherapy (“early treatment failure”).

Montoto S, et al. Haematologica 2013; 98: 1014.

What I did

- DHAP 3 cycles, followed by autologous SCT

  - Conditioning regimen: BEAM (carmustine, etoposide, cytarabine,melphalan)
  - CD34+ cell count: 5.2 x10^6/kg
  - Engraftment: Neutrophil on day +11; Platelet on day+ 16

Discussion

What is the value of PET/CT in FL ?

- Consensus guidelines of the ICML Imaging Working Group and Lugano Classification recommend that PET-CT rather than contrast-enhanced CT scanning should be considered as a new standard for initial staging and response assessment of FL.

- Response assessment with PET/CT has been found to be an independent prognostic factor for FL progression and overall survival.

Barrington SF, et al. J Clin Oncol 2014;32:3048.
Cheson BD, et al. J Clin Oncol 2014;32:3059

Trotman J, et al. J Clin Oncol 2011;29:3194.
Luminari S, et al. Ann Oncol 2014;24:442.
Dupuis J,et al. J Clin Oncol 2012;30:4317.

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Thanks for your attention