Diagnosis of double hit lymphoma

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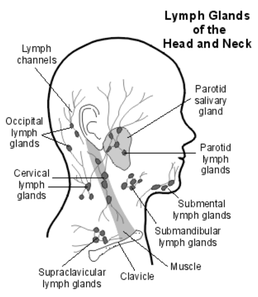
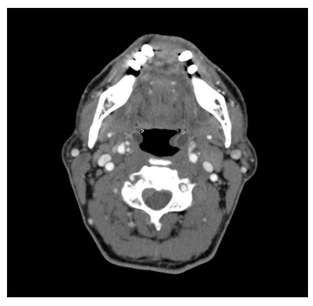
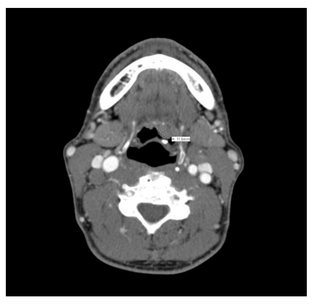
Initial Presentation

The patient went to sees his PCP for a chief complaint of “neck lumps”, is found on physical exam to have firm R supraclavicular mass. Given he was a former smoker (15 pack year smoking history, quit in 1987), he was sent for CT scan of the neck which showed mild bilateral cervical lymph node enlargement, right side greater than left with the largest node measuring 12 mm in the short axis in the lower right neck.

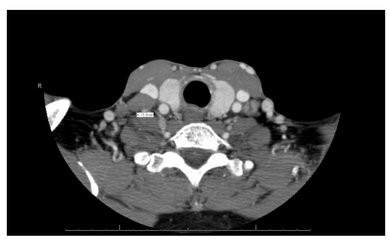


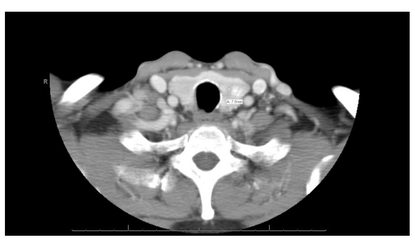


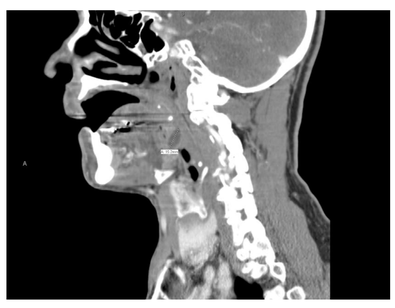


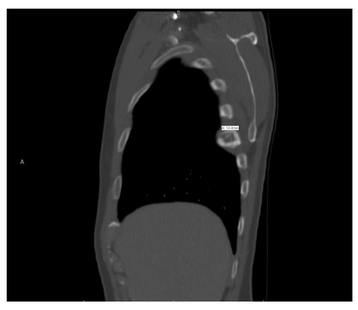
Clinical Course – 1 week later, CT chest

The patient receives CT scan of the chest given neck CT findings. This scan shows lytic and sclerotic lesion in the right posterolateral 7th ribs with an adjacent smoothly marginated pleural/subpleural soft tissue mass measuring 1.7 x 0.6 x 1.8 cm concerning for a malignancy arising from within the pleural/chest wall soft tissues or within the bone.



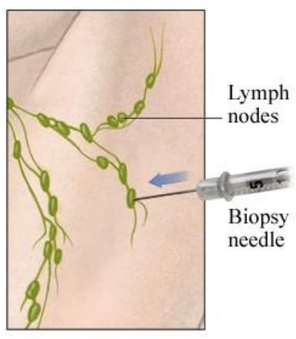






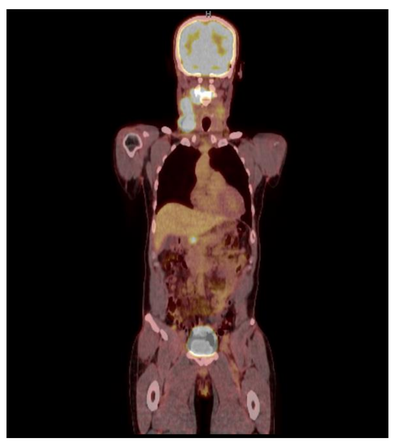
U/S guided biopsy - 2 weeks after initial presentation

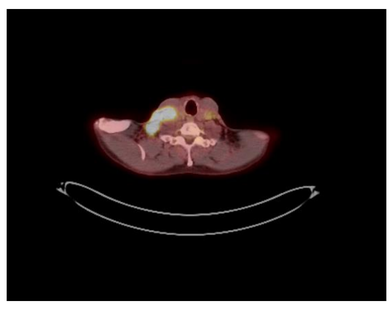
An ultrasound guided R cervical lymph node biopsy is performed. Pathology reveals a mixed population of CD20 positive B cells and CD3 positive T cells with a negative pancytokeratin stain. Flow cytometry of the sample shows “no malignant population of lymphocytes” however specimen is identified as hypocellular and additional tissue sampling is recommended if there is high clinical suspicion for malignancy.



Picture from https://myhealth.alberta.ca/Health/pages/conditions.aspx?hwid=hw232506

PET scan – 4 weeks after initial presentation

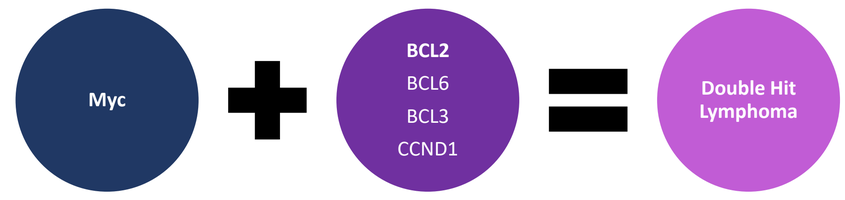




A PET/CT is performed and shows abnormal hypermetabolic foci in the posterolateral R lung, mediastinum, left hilar regions, bilateral neck, peri-caval, para-aortic region and throughout the axial and appendicular skeleton highly suspicious for a malignant or metastatic process.

Excisional biopsy – 5 weeks after initial presentation

Given high suspicion for malignancy, more tissue was needed so an excisional biopsy of the right neck lymph nodes was performed. Pathology revealed diffuse large B-cell lymphoma and flow cytometry reported a clonal B-cell population. FISH studies were positive for MYC oncogene (8q24) rearrangement in 37% of cells and BCL2 rearrangement in 54% of cells.



Chemotherapy started – 6 weeks after initial presentation

The patient is started on dose adjusted R-EPOCH chemotherapy with 6 cycles planned (one cycle every 21 days) for Stage IV double hit diffuse large B-cell lymphoma.

Wilson WH et al. J Clin Oncol. 2008;26:2717-2724

Rituximab - Day 1
Etoposide – Continuous IV on Days 2-4
Prednisone – PO on Days 1-14
Vincristine (**O**ncovin) – Continuous IV on Days 2-4
Cyclophosphamide – IV on Day 5
Doxorubicin (**H**ydroxydaunorubicin) – Continuous IV on Days 2-4

TABLE. Retrospective Studies Detailing Methods of Diagnosis and Outcomes for Patients With Double-Protein-Expressing Lymphoma

Authors	IHC Cutoff MYC+ (%)	IHC Cutoff BCL2+ (%)	N	DE (%)	Regimen	DE Impact on PFS[a]	DE Impact on OS[a]
Green et al[9]	≥40	≥70	193	29	R-CHOP	3-yr PFS 39% vs 75% (*P* <.001)	3-yr OS 43% vs 86% (*P* <.001)
Hu et al[10]	≥40	≥70	466	34	R-CHOP	5-yr PFS 27% vs 73% (*P* <.001)	5-yr OS 30% vs 75% (*P* <.001)
Johnson et al[11]	≥40	≥50	167	21	R-CHOP	5-yr PFS 21% vs 63% (*P* = .020)[b]	5-yr OS 30% vs 70% (*P* = .018)[b]
Molina et al[12]	≥40	≥70	670	21	R-CHOP/ R-miniCHOP or R-ACVBP[c]	Decreased PFS (*P* = .003)	Decreased OS (*P* = .005)
Perry et al[13]	≥50	≥30	106	44	CHOP+/-R	Independent predictor of EFS (*P* = .0017)	Independent predictor of OS (*P* <.001)
Dunleavy et al[14]	≥40	Same or more intense staining as T-cell control	66	20	R-EPOCH	10-yr PFS = 67.5%; 10-yr PFS not inferior to other groups (*P* = .5)	10-yr OS = 75%; 10-yr OS not inferior to other groups (*P* = .8)

DE indicates double protein expressor; EFS, event-free survival; IHC, immunohistochemistry; OS, overall survival; PFS, progression-free survival; R-ACVBP, rituximab, doxorubicin, cyclophosphamide, vindesine, bleomycin, prednisone; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; R-EPOCH, rituximab, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin.

[a]Compared with patients without double protein expression.
[b]Validation cohort.
[c]R-CHOP/R-miniCHOP: n = 433; R-ACVBP: n = 237.

Table from http://www.gotoper.com/publications/ajho/2015/2015apr/clinical-controversies-of-double-hit-lymphoma

Summary

Double hit lymphoma is an aggressive form of diffuse large B-cell lymphoma where MYC rearrangement is associated with either BCL2 or BCL6 rearrangement thus patients often present with a rapidly growing mass, B symptoms and extra nodal disease. Here we present a case of bilateral lymphadenopathy that was negative for malignancy via needle biopsy but positive on excisional biopsy. High clinical suspicion for malignancy should lead one to obtain additional tissue for diagnostic work-up.

References

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