



# Multi-Institutional Hematopathology Interesting Case Conference

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Hematopathology Fellow (PGY-5)

12/17/25



EMORY  
UNIVERSITY  
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MEDICINE

Department of  
Pathology and  
Laboratory Medicine

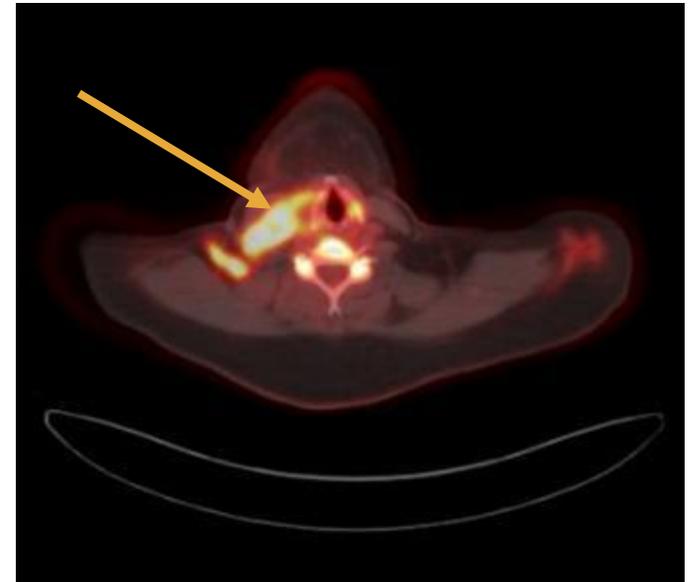
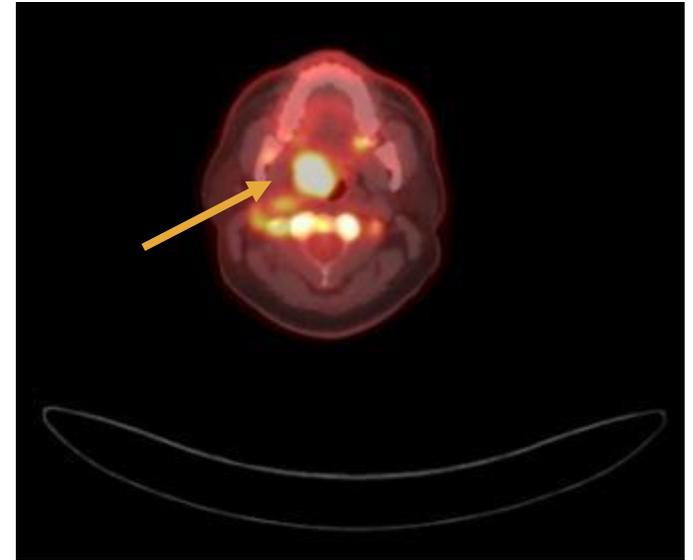
# DISCLOSURE

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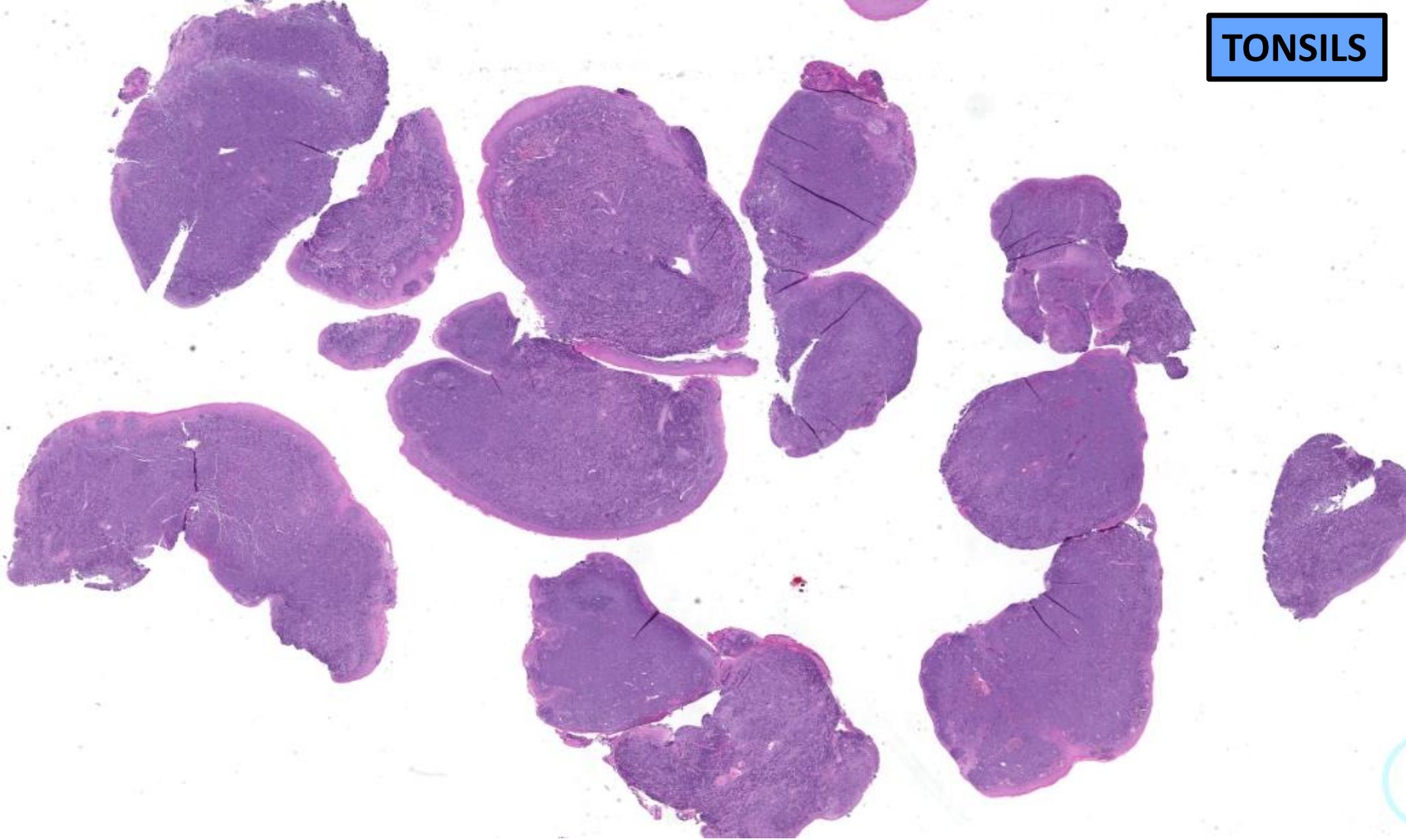
**“I have no financial relationships or conflicts of interest to disclose.”**

# Clinical History

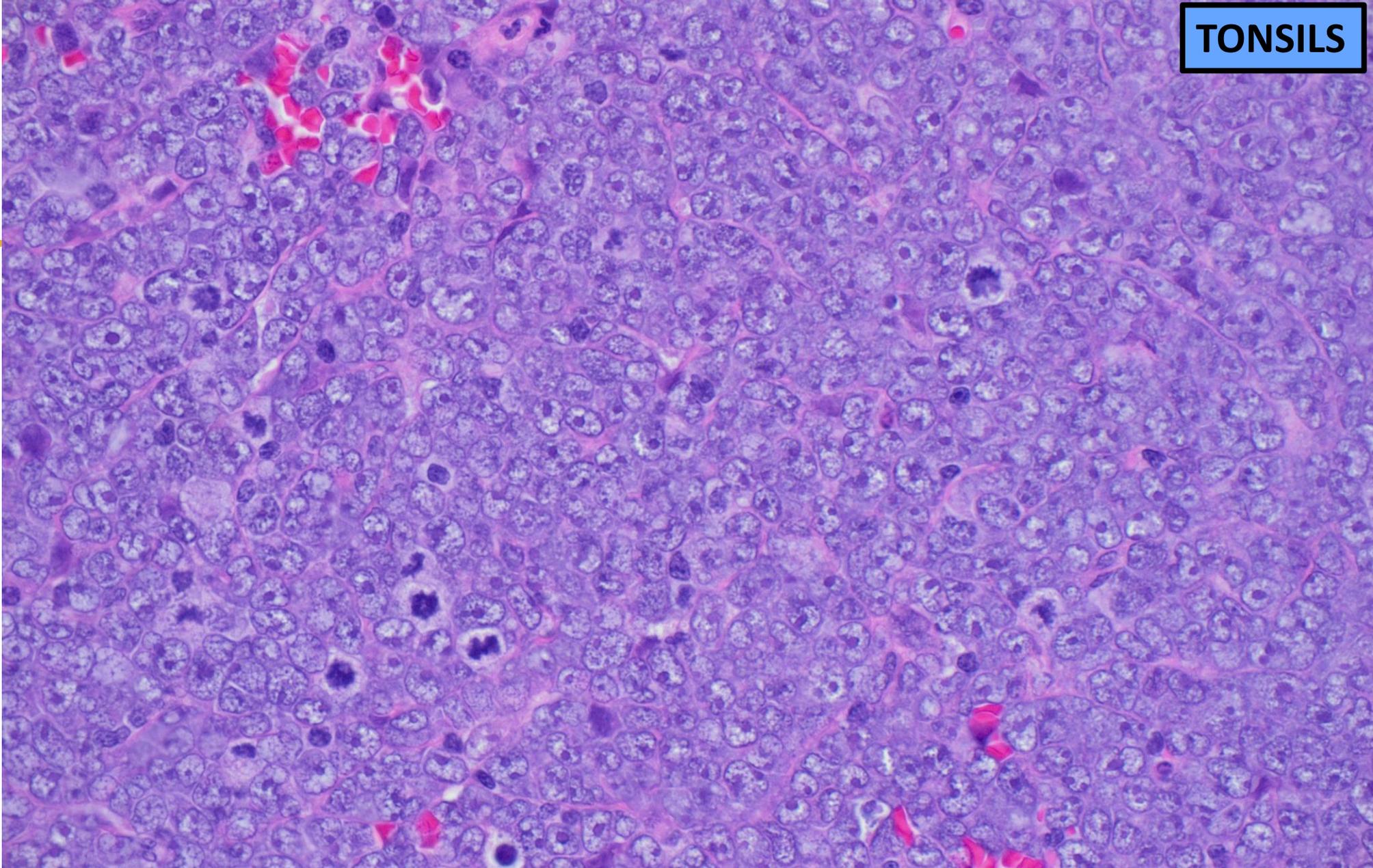
- 33y old man, no significant PMH
- Worsening neck swelling and pain despite antibiotics.
- PET/CT Scan
  - Exophytic large pharyngeal mass concerning for squamous cell carcinoma.
  - Right side of the mandible, SUV of 8.4.
  - Right axillary lymphadenopathy, SUV of 15.4.



**TONSILS**



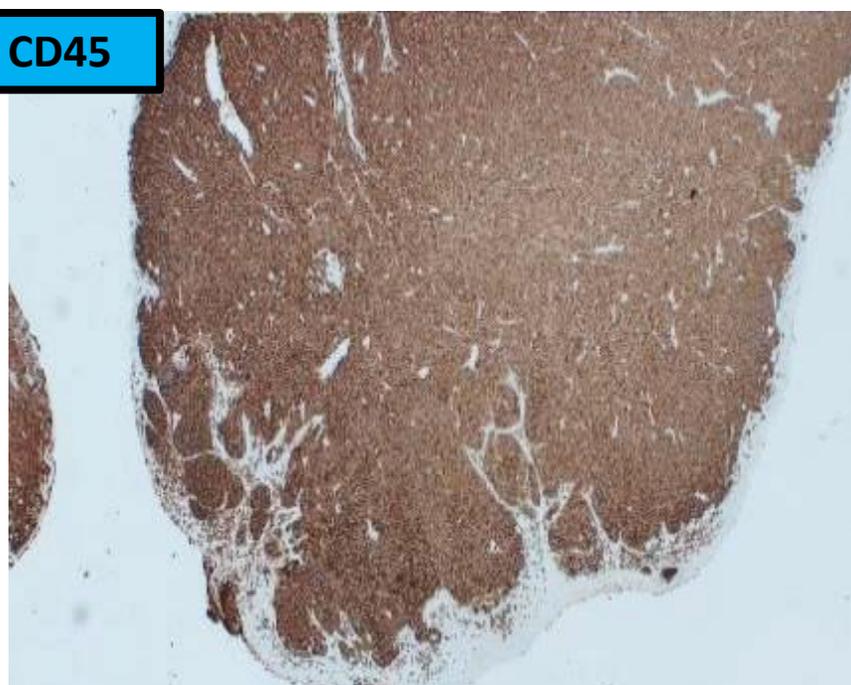
**TONSILS**



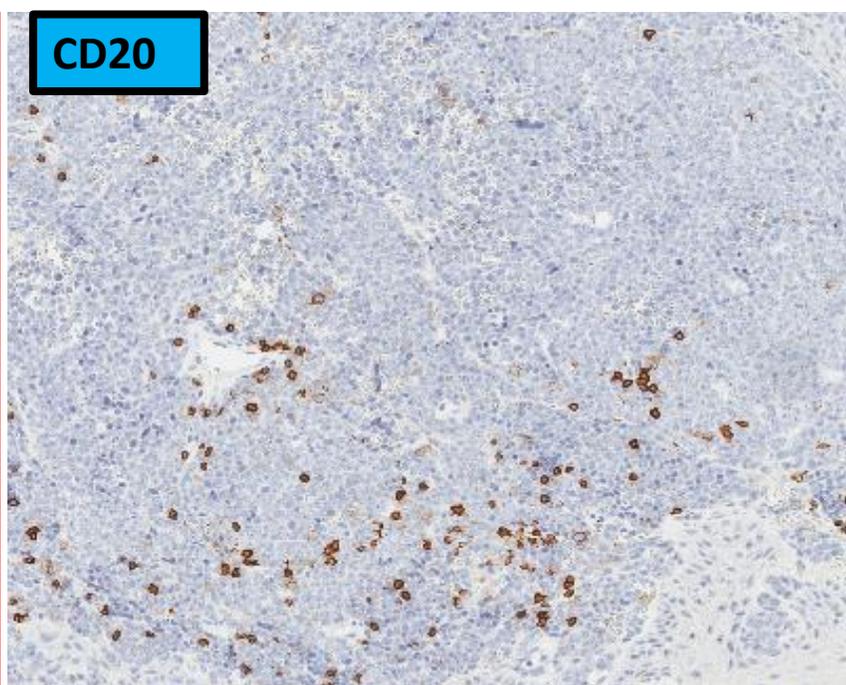
# Differentials?

- 
- Hematolymphoid neoplasm
    - B- cell neoplasm
      - Large B-cell Lymphoma
      - B-ALL/LBL
      - Burkitt lymphoma
      - Blastoid/pleomorphic MCL
    - T-cell neoplasm
  - Carcinoma
  - Melanoma

CD45



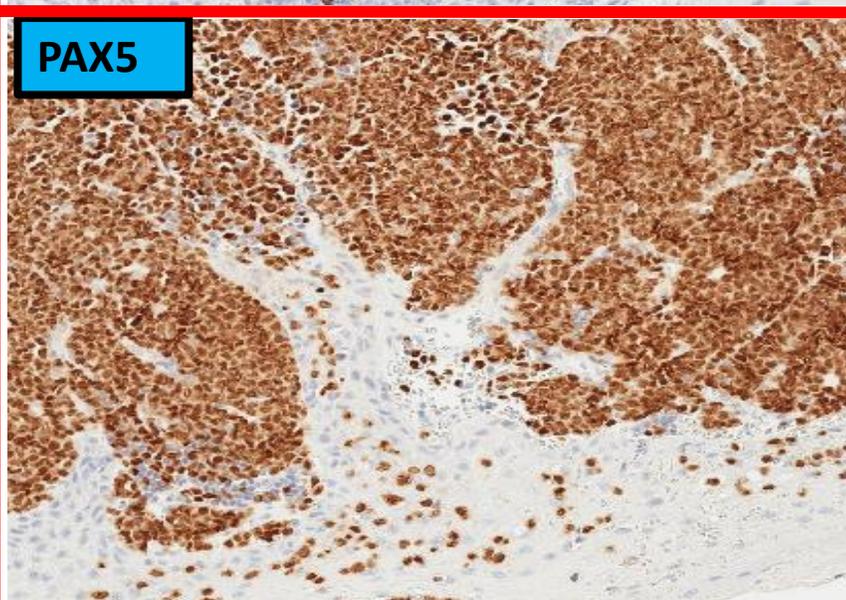
CD20



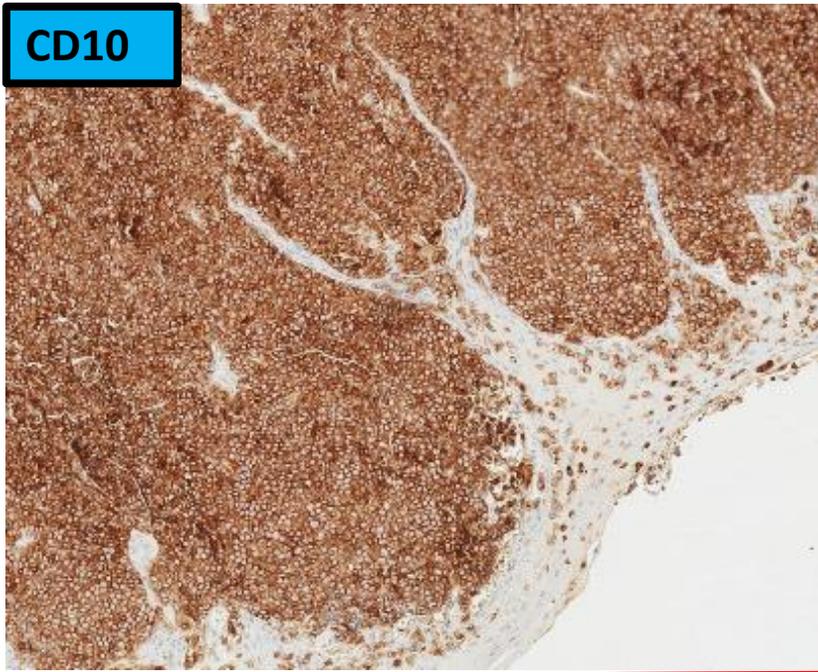
CD19



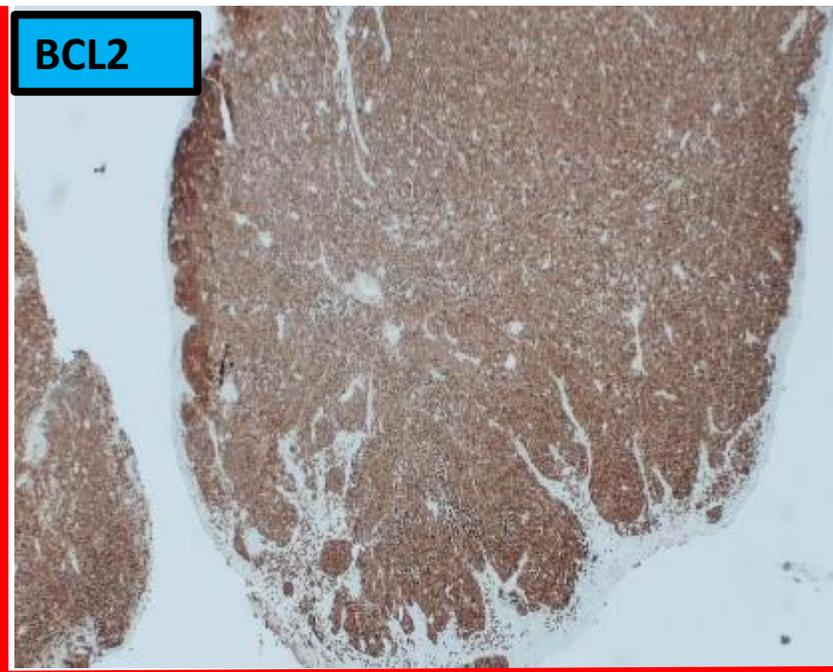
PAX5



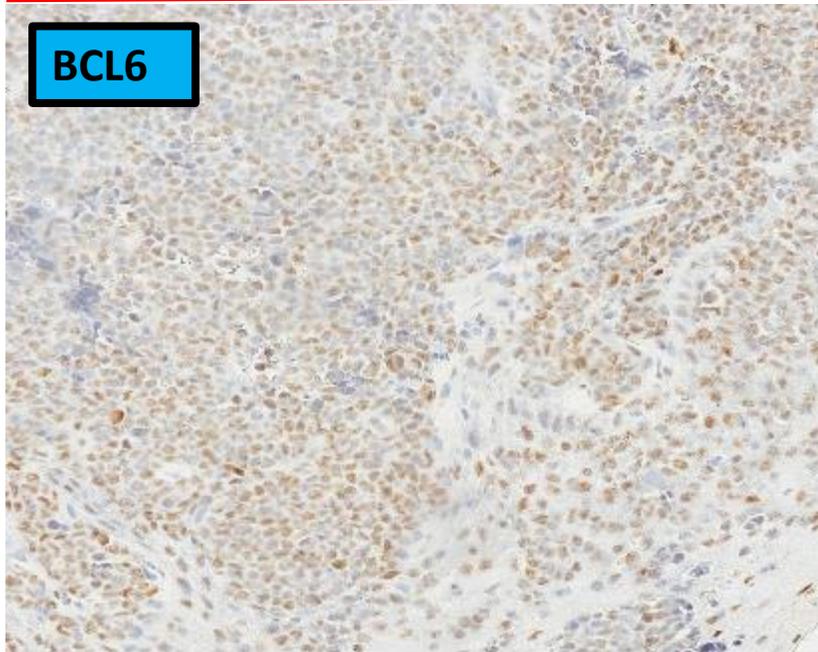
CD10



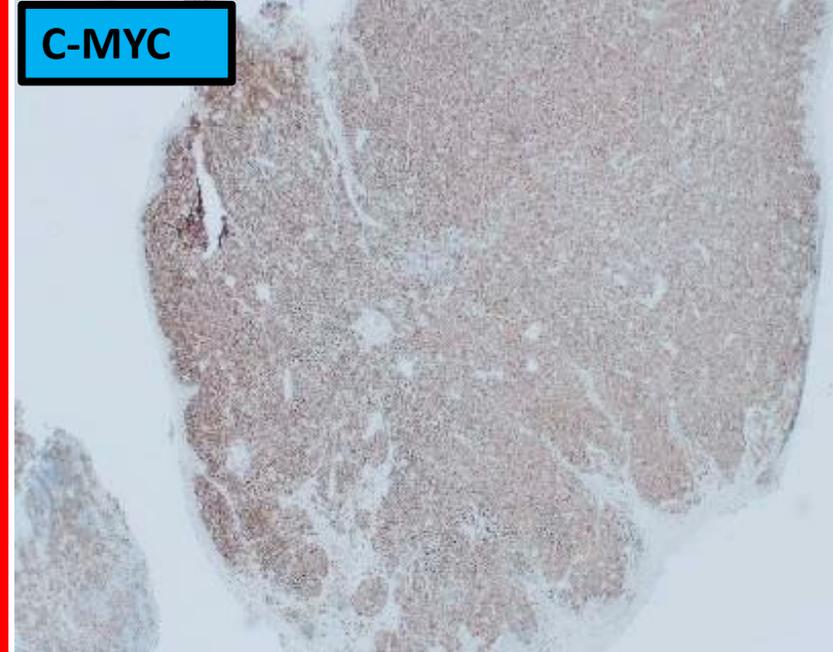
BCL2



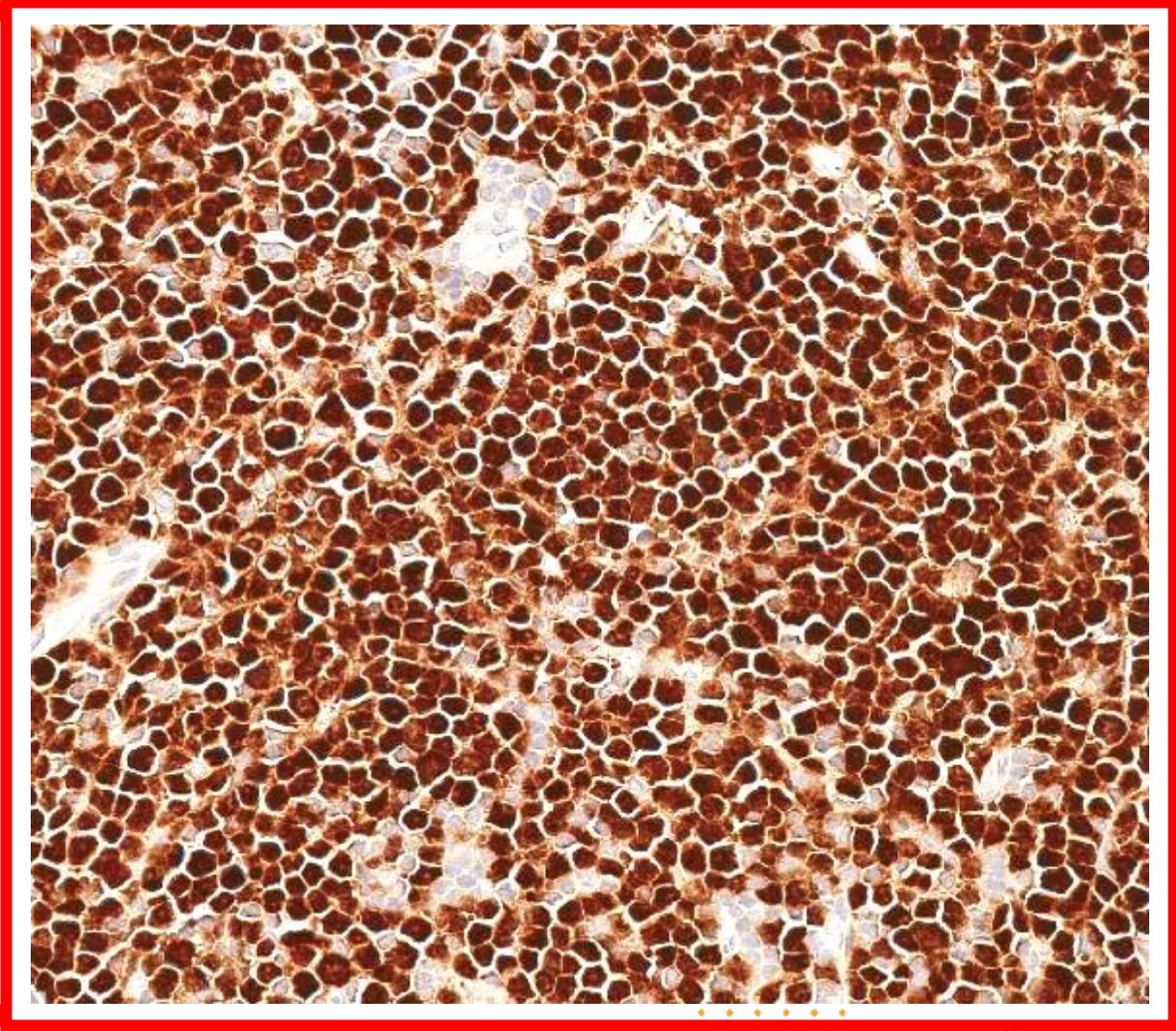
BCL6

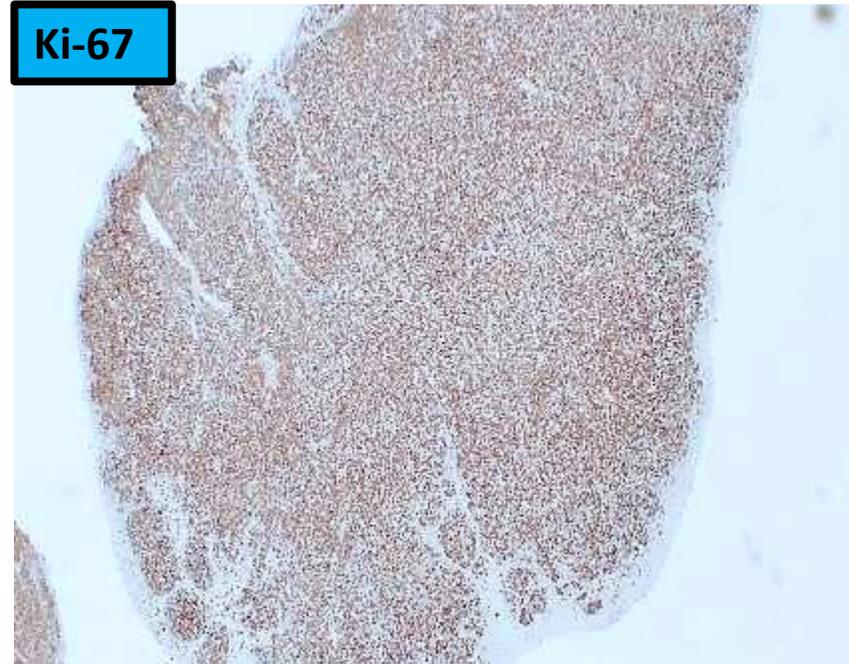
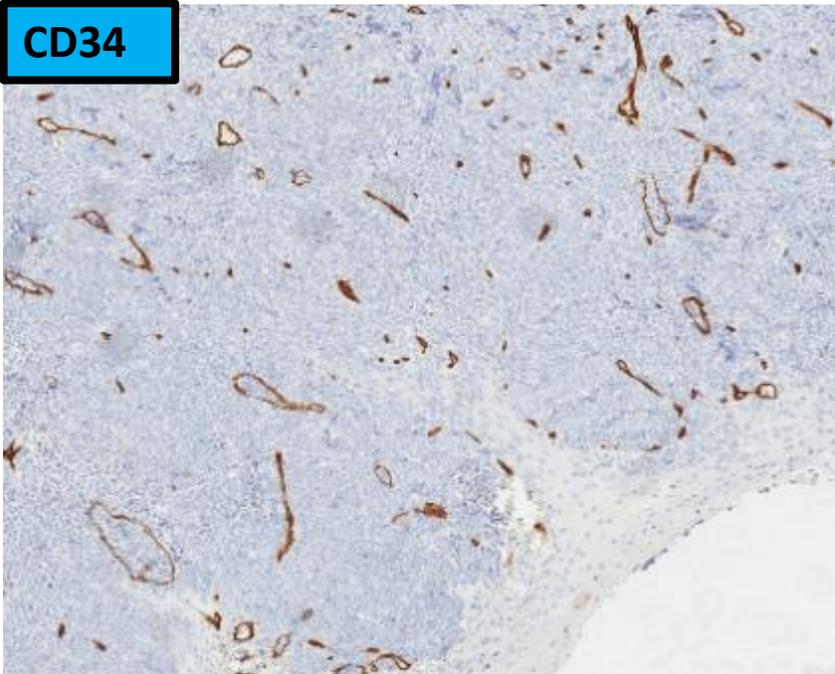


C-MYC



TdT





# SUMMARY

## POSITIVE

PAX5, CD19, CD22, CD79a, CD10, BCL6, CD43, CD45, BCL2, MYC

TDT

Ki-67 (70-80%)

## LINEAGE

B cell

T cell

Myeloid

NK / Cytotoxic

Immature / Lymphoblastic

Activation / Anaplastic

Viral

Neuroendocrine

Epithelial

Others

## NEGATIVE

CD20, MUM1

CD3, CD4, CD5, CD8, CD43

CD13, CD33, CD34, CD117, MPO

CD56

CD1a

CD30, ALK1

EBER, HHV8

Synaptophysin, Chromogranin

P40

CD99, CyclinD1

# FLOW CYTOMETRY

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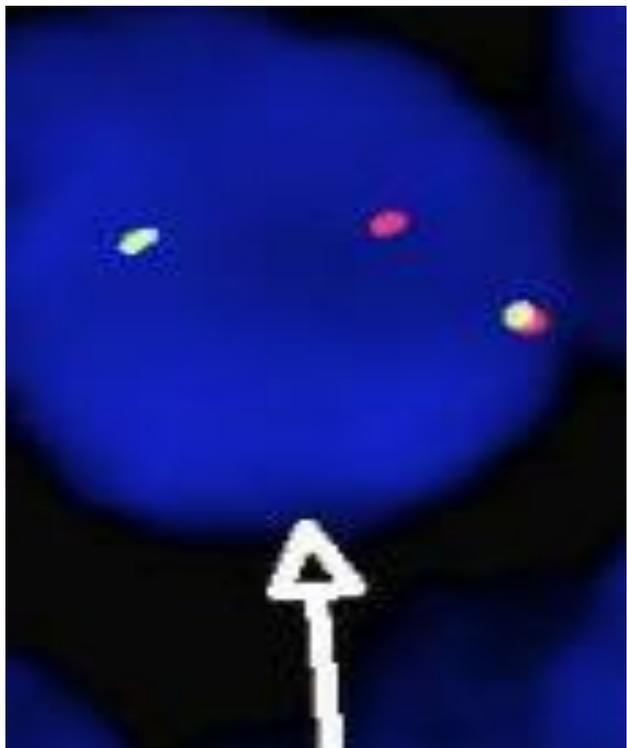
- **TONSIL:** CD10 positive B cell population, negative for CD20 and surface light chain expression.
  
- **CSF :** No evidence of B-cell neoplastic population

# Differentials?

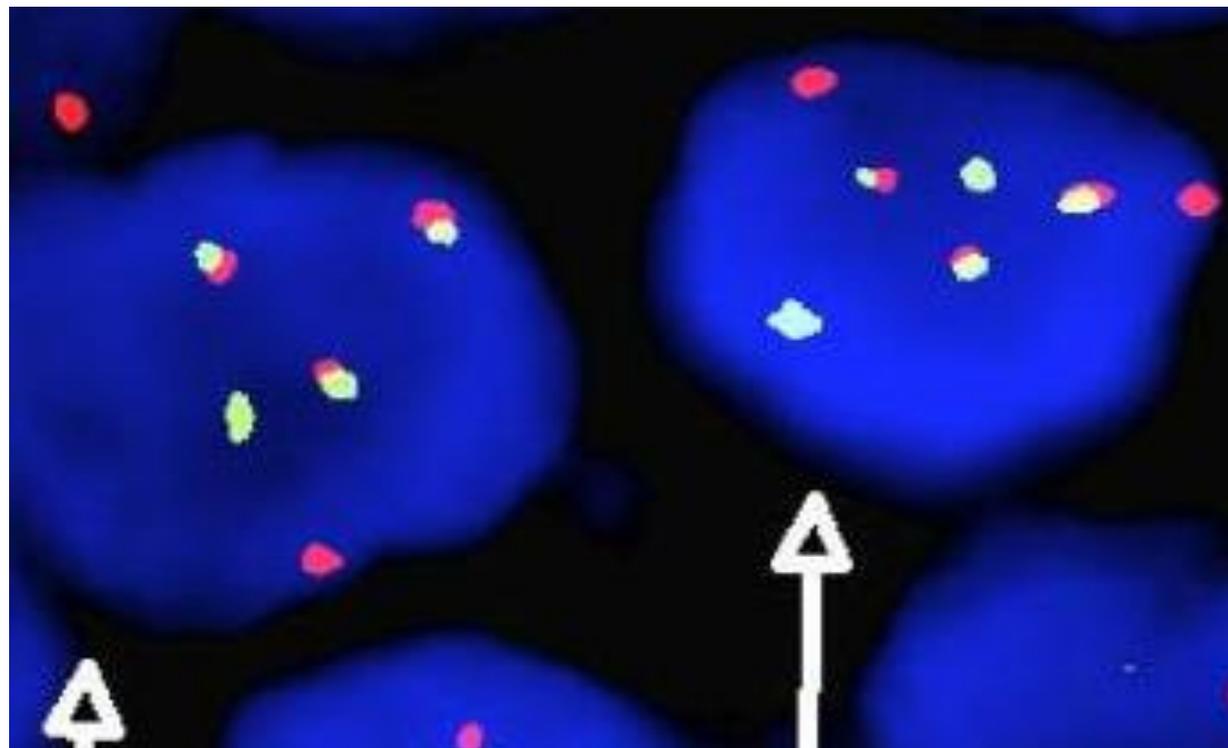
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    - ~~T-cell neoplasm~~
  - ~~Carcinoma~~
  - ~~Melanoma~~

# FISH RESULT

POSITIVE for translocation of 8q24 *MYC*

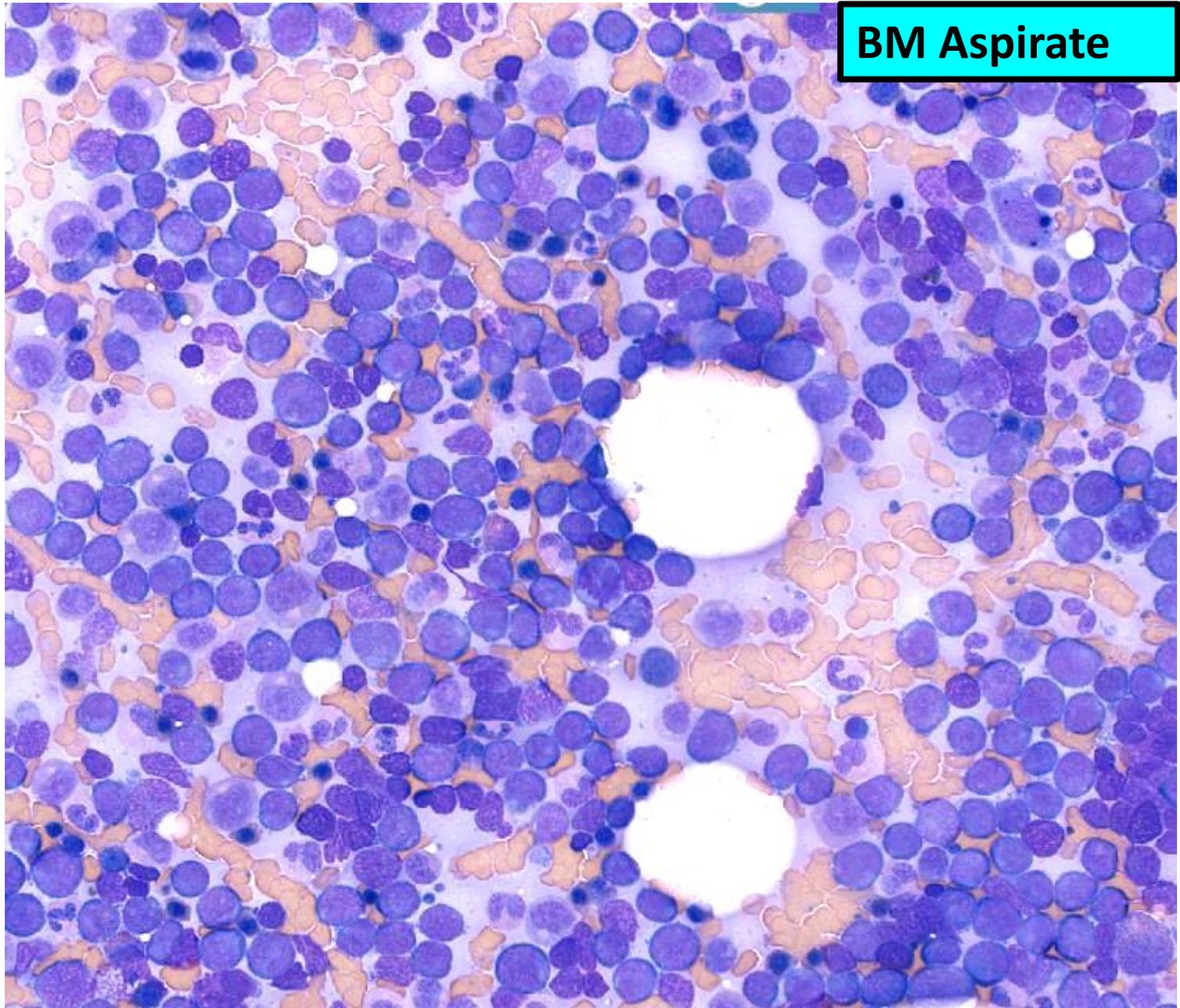
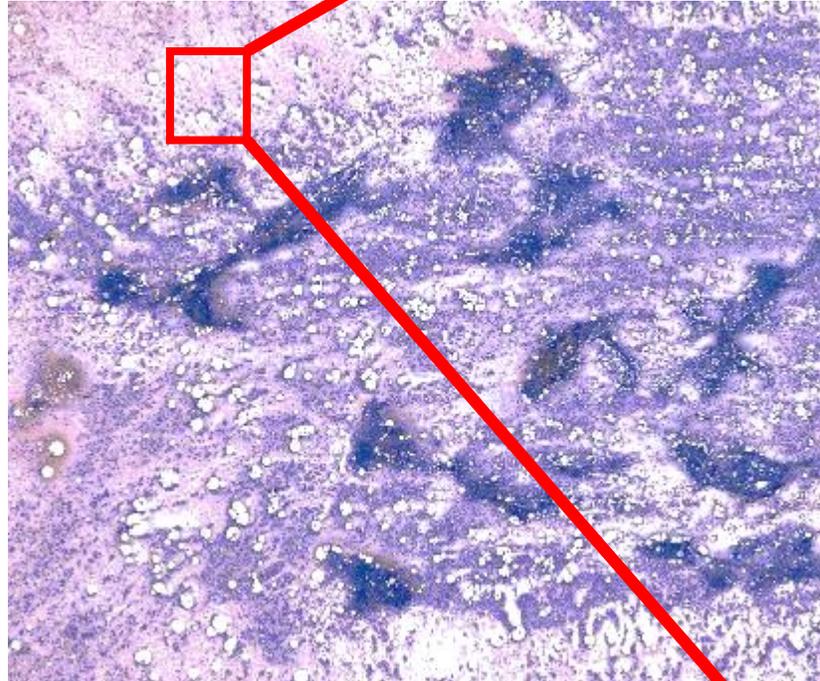


POSITIVE for typical and variant t(14;18)



Positive for *MYC* and *BCL2* rearrangement

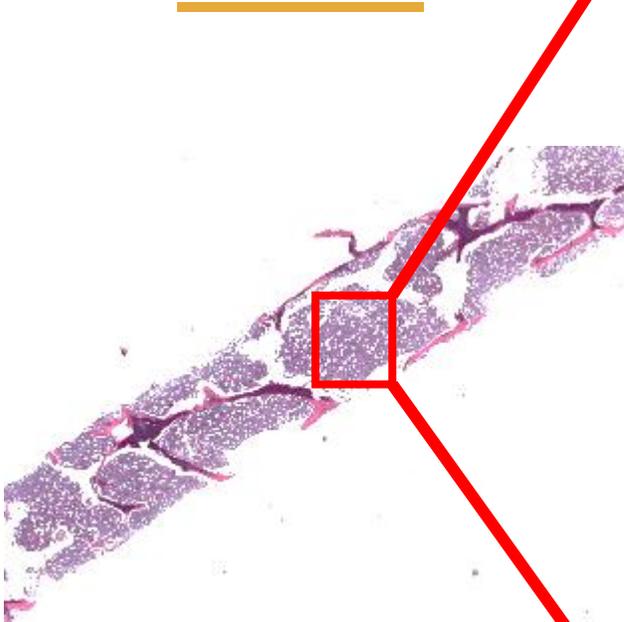
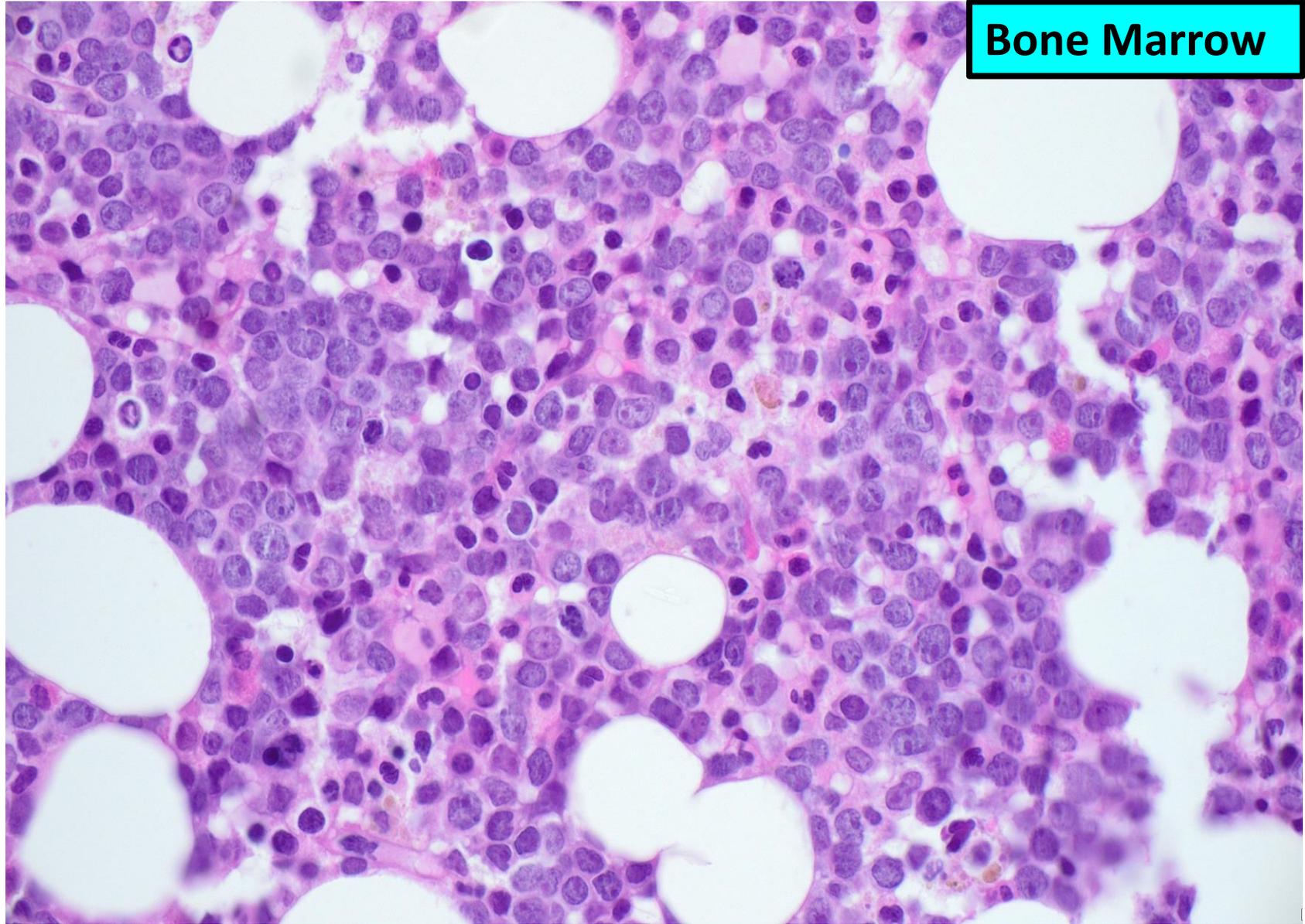




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**Bone Marrow**



# Chromosome analysis

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- 51,X,-Y,+1,+2,der(2)psu,dic(1;2)(p13;p23),+5,+7,**der(8)t(8;22)(q24.1;q11.2),t(14;18)(q32.3;q21.3)**,+17, add(17)(q24),+18,der(22)t(8;22)add(22)(q11.2),+r[10]/46,XY[10]

# CASE SUMMARY

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- A 33-year-old male with pharyngeal mass and bone marrow involvement
- **Morphologic & Immunophenotypic Profile:**
  - Atypical lymphoid cells with blastoid features
  - B cell markers
  - **CD20 negative, Surface Ig negative**
  - **TdT positive and CD34 negative**
  - Ki-67 (70-80%), C-myc +
- **Cytogenetics/FISH:**
  - Complex karyotype with **MYC** and **BCL2** rearrangement

# Classification Dilemma: TdT<sup>+</sup> Lymphoid Neoplasm

## B-Acute Lymphoblastic Leukemia/Lymphoma

- Strong, uniform TdT expression
- CD20 negativity
- Lack of surface immunoglobulin
- Blastoid morphology

## High Grade B cell lymphoma Double- Hit Lymphoma

- *MYC* + *BCL2* rearrangements
- CD34 negative
- Strong CD45 expression
- Complex karyotype



B-LBL with *MYC* + *BCL2* rearrangements

OR

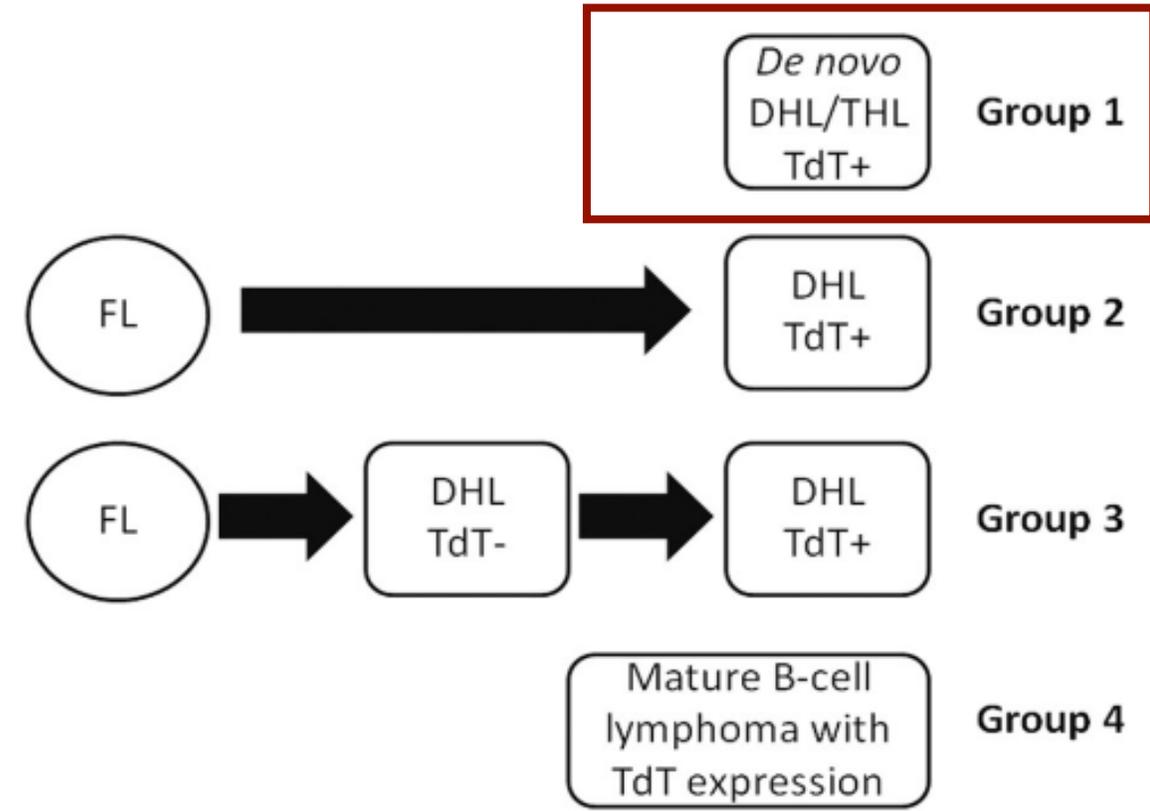
HGBL-DH with TdT expression



## High-grade B-cell lymphomas with TdT expression: a diagnostic and classification dilemma

Chi Young Ok<sup>1</sup>, L Jeffrey Medeiros<sup>1</sup>, Beenu Thakral<sup>1</sup>, Guilin Tang<sup>1</sup>, Nitin Jain<sup>2</sup>, Elias Jabbour<sup>2</sup>, Sherry A Pierce<sup>2</sup>, Sergej Konoplev<sup>3</sup>

- TdT-positive HGBL-DH represents a distinct entity.
  - Double-hit genetics are extremely rare in de novo B-LBL.
  - Its clinical behavior and prognosis align with HGBL, not B-LBL.
- Recognizing these rare tumors improves prognostication and supports development of targeted therapies.



**“High-grade B-cell lymphoma with TdT expression (cytogenetically defined)”** to clearly reflect the biology and avoid misclassification as B-ALL

# TdT+ Large B- cell Lymphomas

- Only 2% of 258 LBCLs showed >10% TdT positivity, all CD34–.
- Most from transformed FL or prior TdT– LBCL.
- Genetic profile matched GCB-DLBCL not B-LBL with uniform MYC rearrangement.
- Demonstrated DH signature, very high proliferation (>75%), and complex karyotypes.
- Median survival was 2 months

ORIGINAL ARTICLES

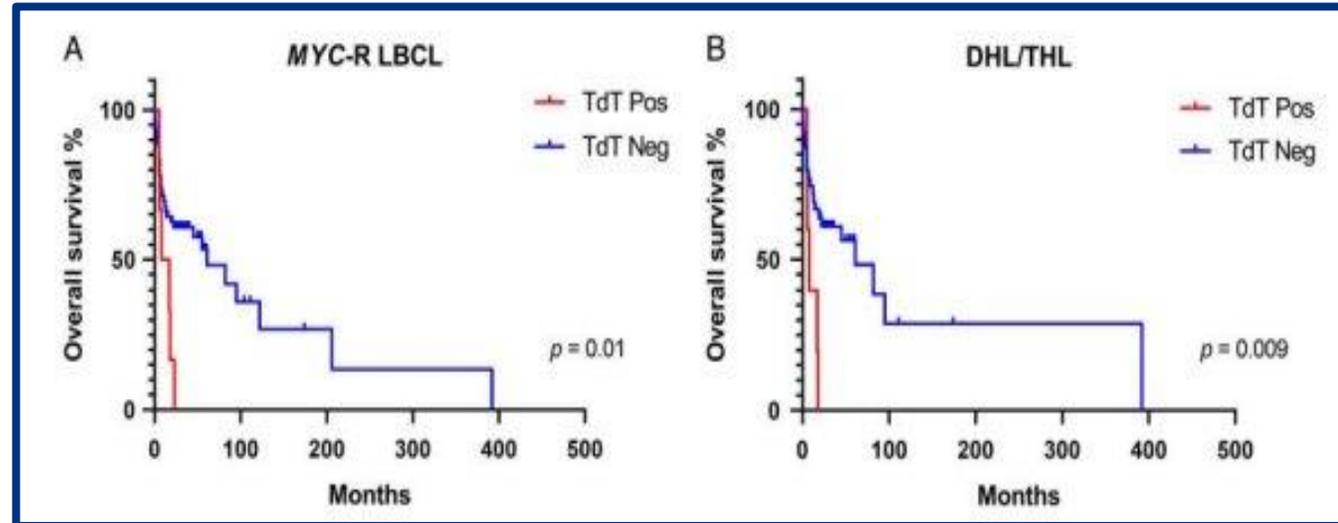
## Mutational Landscape of TdT<sup>+</sup> Large B-cell Lymphomas Supports Their Distinction From B-lymphoblastic Neoplasms

### A Multiparameter Study of a Rare and Aggressive Entity

Bhavsar, Shweta MD<sup>\*</sup>; Liu, Yen-Chun MD, PhD, MS<sup>†</sup>; Gibson, Sarah E. MD<sup>‡</sup>; Moore, Erika M. MD<sup>‡</sup>; Swerdlow, Steven H. MD<sup>†</sup>

Author Information

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These cases are best identified using a multiparameter approach (morphology, IHC, cytogenetics, molecular data).



# Diagnosis

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- **High-grade B cell neoplasm with *MYC* and *BCL2* rearrangements**
  - **Features that support B-LBL** blastoid morphology, lack of CD20 expression, absence of surface light chain expression, and strong TdT expression are features that support B-LBL
  - **Findings that favor HGBL** including the absence of CD34 expression, strong CD45 expression, the presence of *MYC* and *BCL2* rearrangements, and a complex karyotype.

# Clinical Course

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- Treated with dose-adjusted EPOCH-R × 2 cycles;
- Tumor progressed rapidly despite therapy.
- Bone marrow was negative for lymphoma
- Cervical lymph node showed persistent high-grade B-cell neoplasm
- NGS panel requested

# NGS Findings

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- NGS detected a ***BRAF V600E*** mutation (VAF 31%).
- Characteristic of Hairy cell leukemia but rare in other B cell lymphomas.
- BRAF V600E mutation is used for targeted therapy in various malignancies.
- Its role in high-grade B-cell lymphoma is unclear

# Clinical progression

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- **Follow-up:** PET/CT revealed new hypermetabolic lesions and peripheral blood showed numerous atypical mononuclear cells.
- **Treatment:** inotuzumab plus R-GDP as a bridge to CAR-T consideration.
- **Clinical course:** rapid progression, and multiorgan decline.
  - Eliminated further disease-modifying options and led to transition to hospice care, passed away days later.

# Conclusion

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- A diagnostically challenging de novo high-grade B-cell neoplasm with MYC/BCL2 rearrangements and strong TdT expression.
- TdT in mature B-cell lymphomas is rare and significantly complicates classification.
- Descriptive terminology (e.g., “High-grade B-cell lymphoma with TdT expression”) is recommended to avoid misclassification as B-ALL/LBL.
- A high-VAF BRAF V600E mutation was identified, an unexpected finding that may offer a potential therapeutic target.
- Prognosis is extremely poor, supporting referral to novel therapies and clinical trials whenever feasible.

# REFERENCES

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THANK YOU

