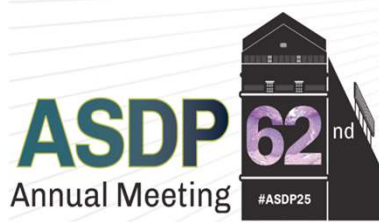


Primary Cutaneous Presentation of Nodal T-Follicular Helper Cell Lymphoma, Angioimmunoblastic Type, with Associated EBV-positive B-cell Lymphoproliferative Disorder

Yazan Alhalaseh, MD
Hematopathology Fellow
Cleveland Clinic
November 7th, 2025



1

Disclosures

- I do not have any financial relationships to disclose



2

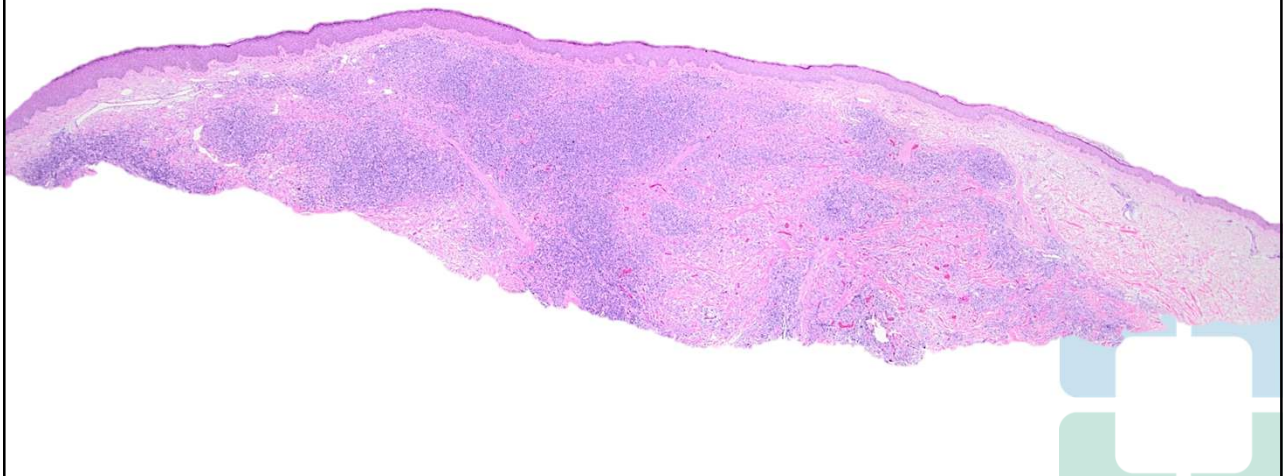
Case presentation

- 71-year-old gentleman who presents with
 - 2.5 cm erythematous nodule with arborizing vessels
 - Posterior aspect of the left upper arm
 - Recent camping
 - Clinical differential arthropod bite reaction

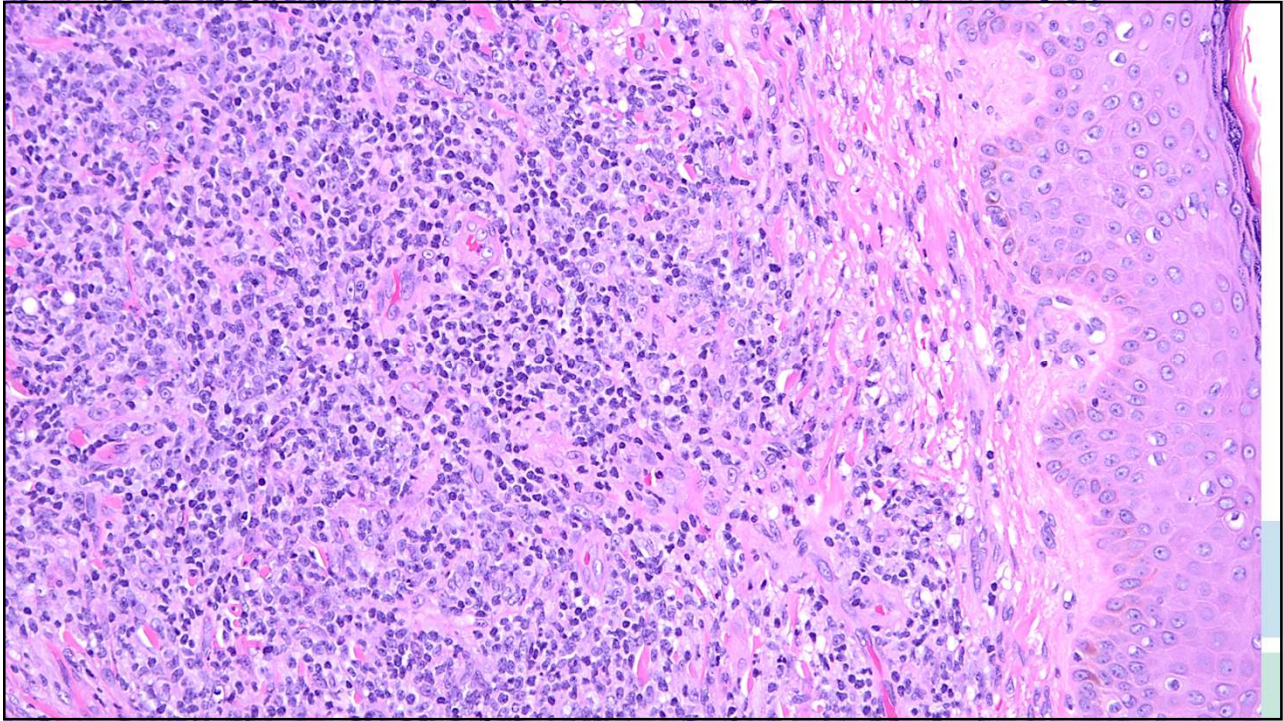


3

A shave biopsy is taken of the lesion



4



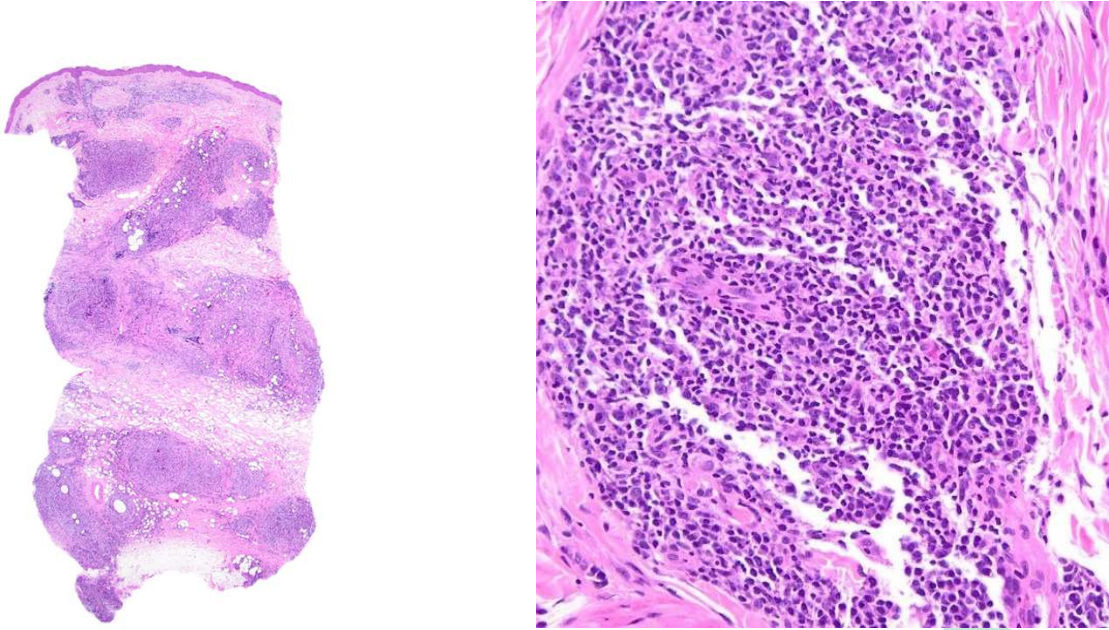
5

Three months after

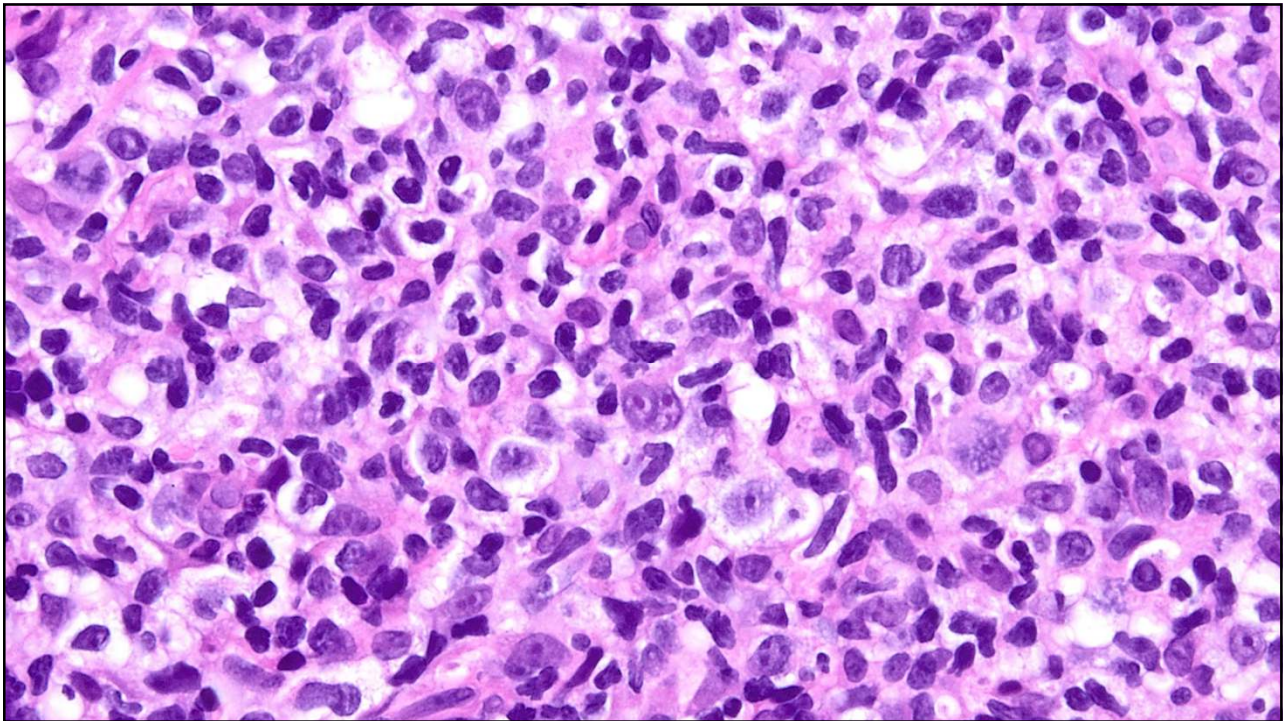


6

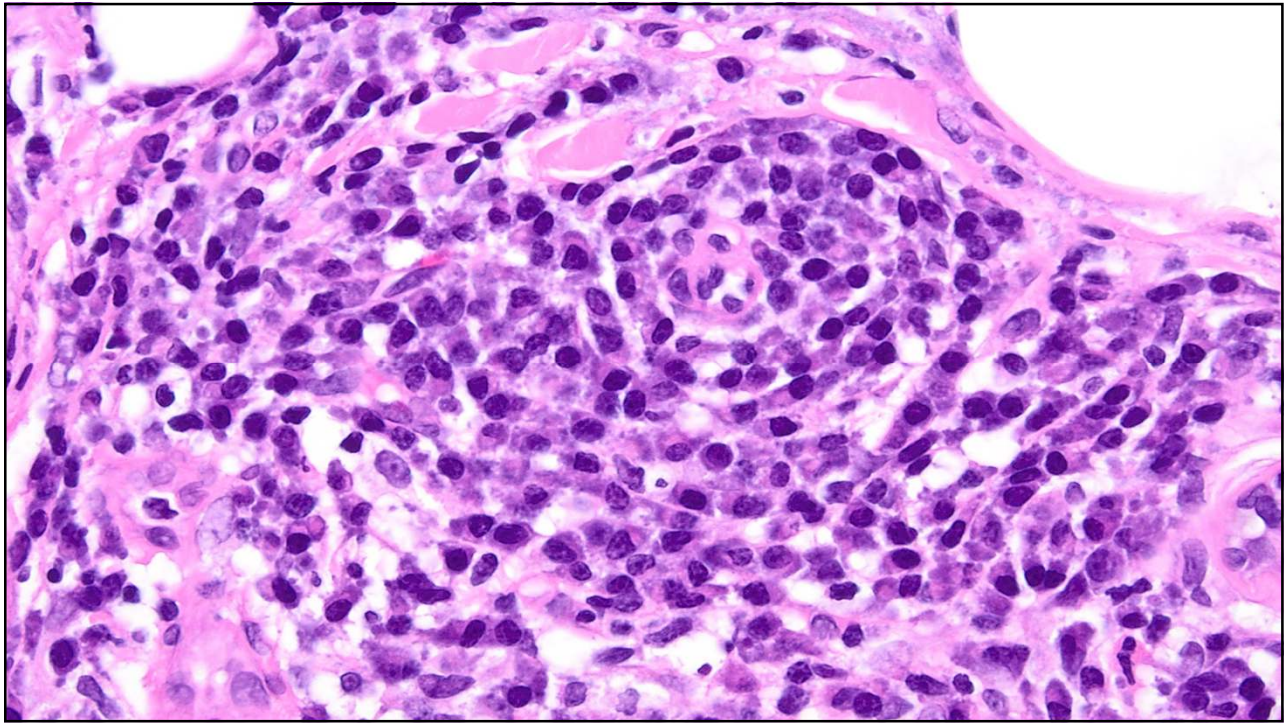
A punch biopsy is taken of the lesion



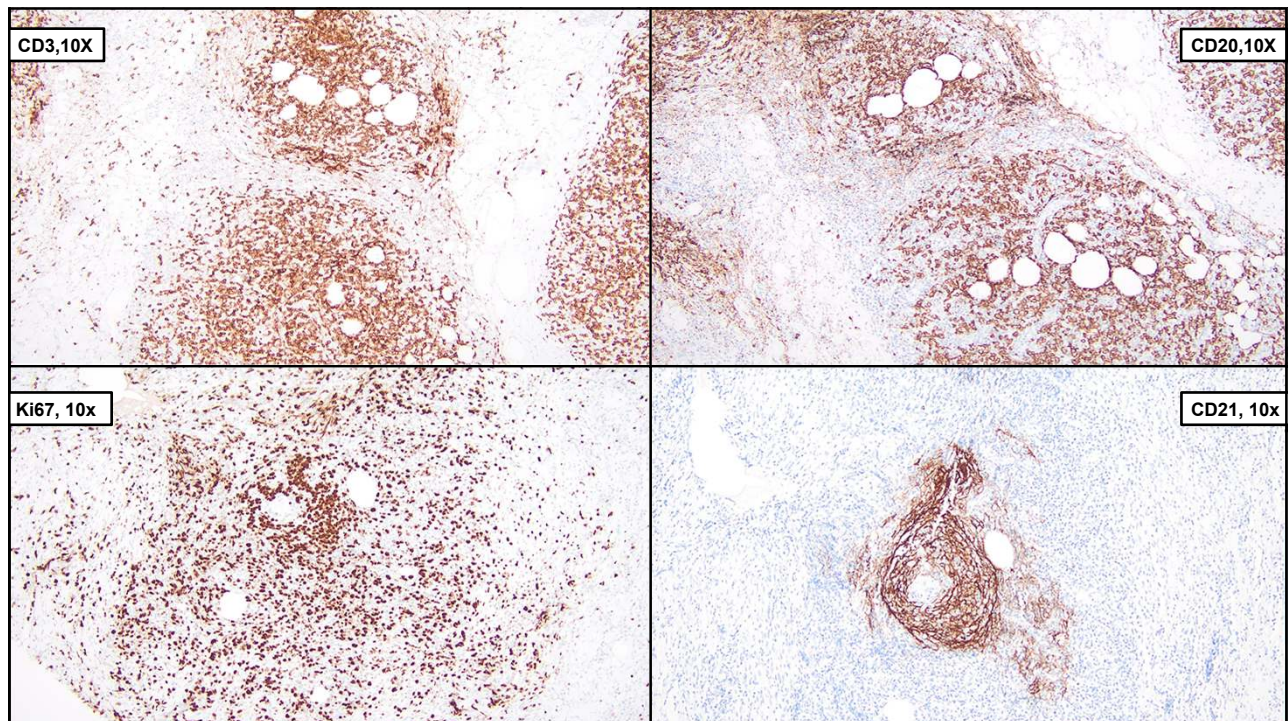
7



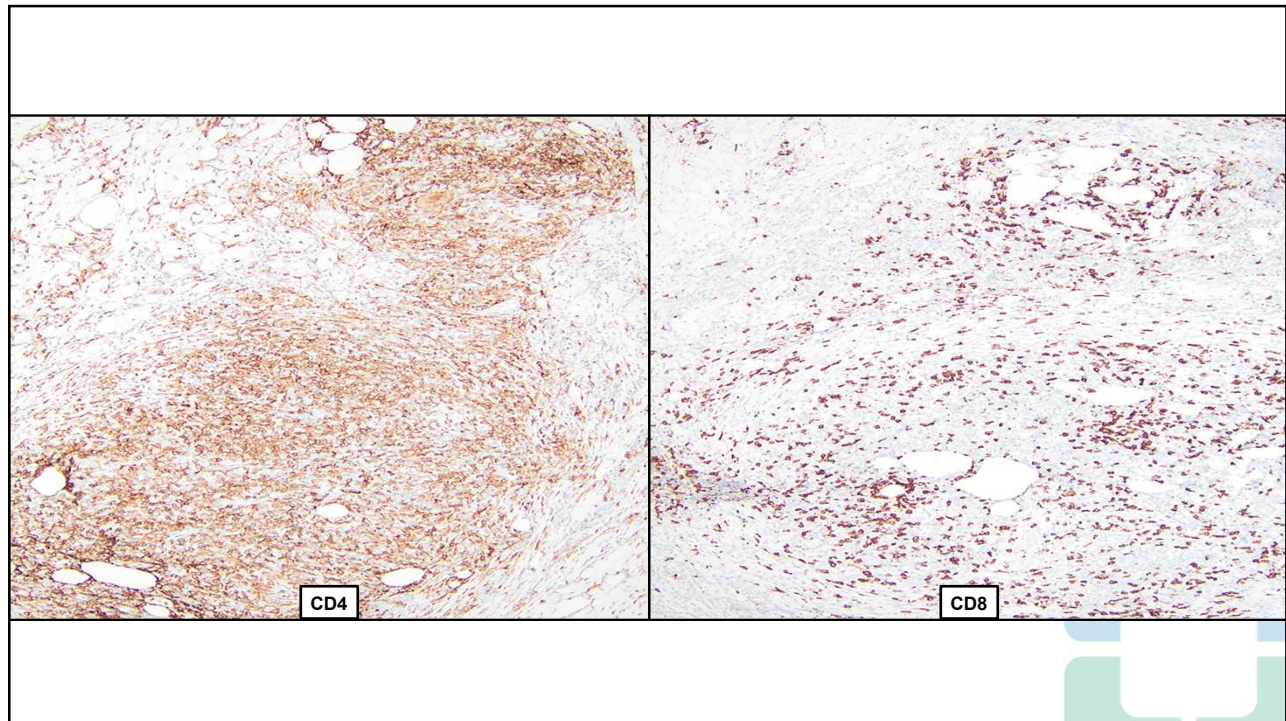
8



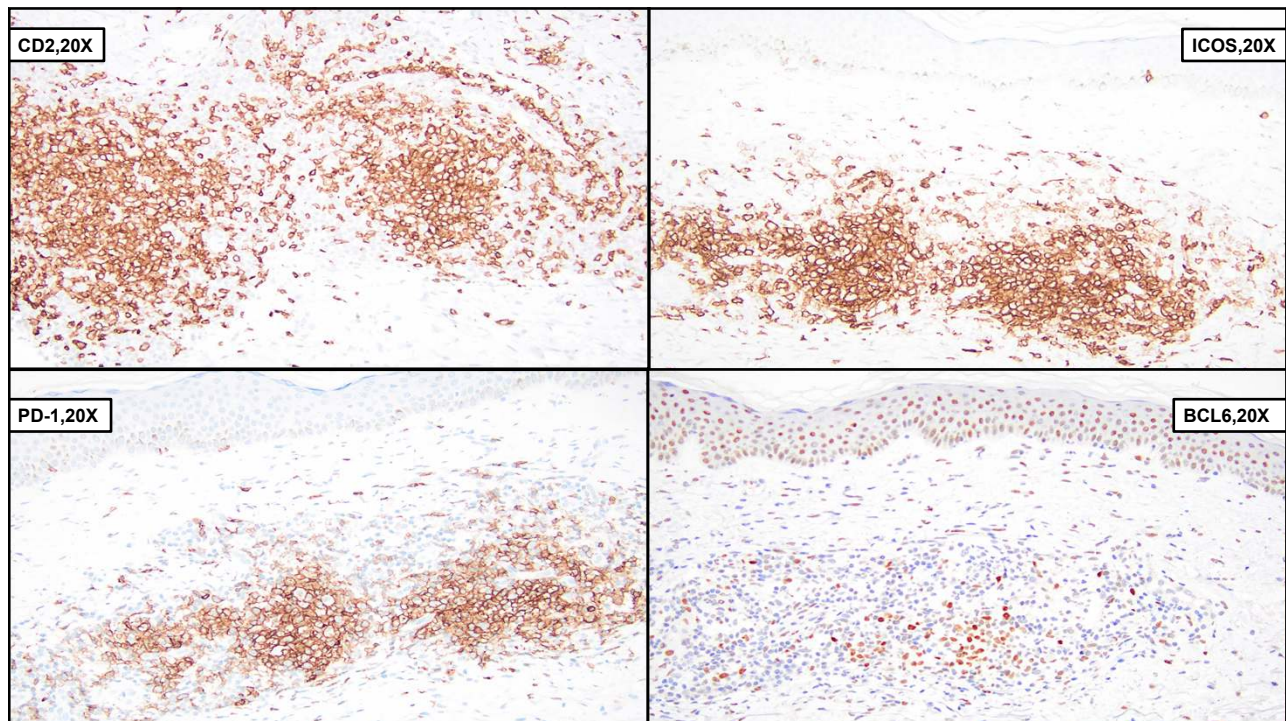
9



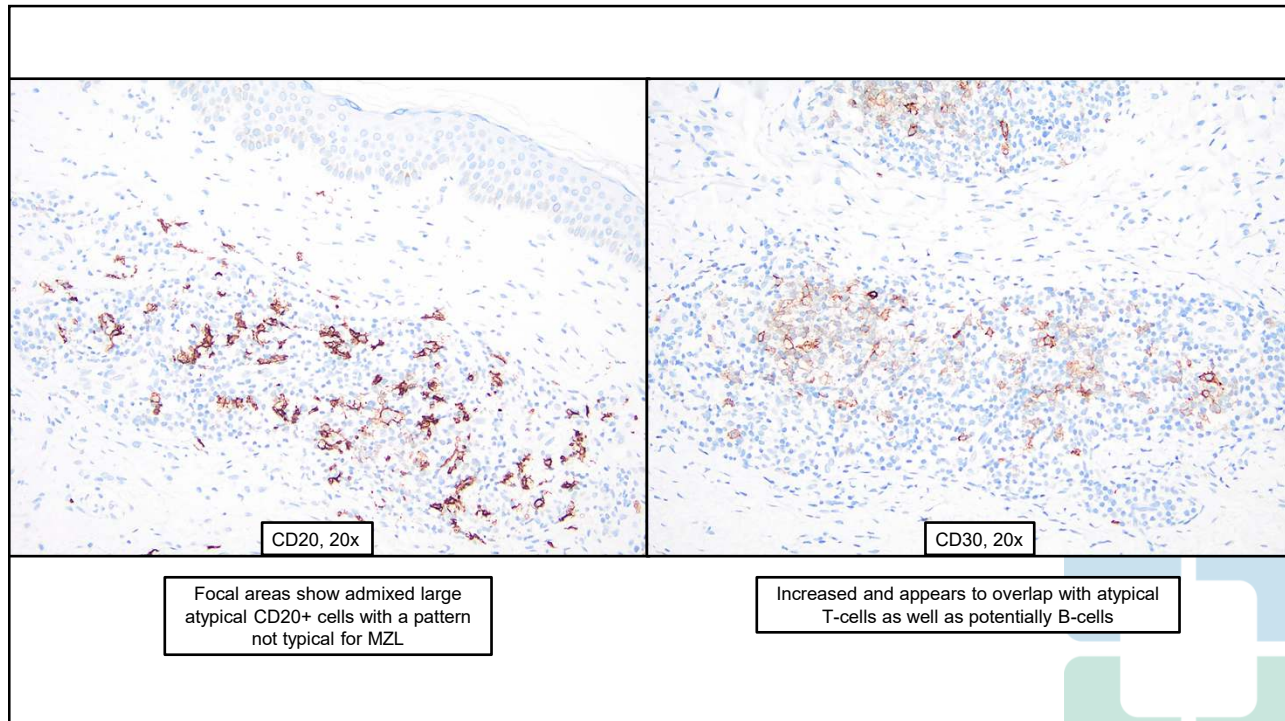
10



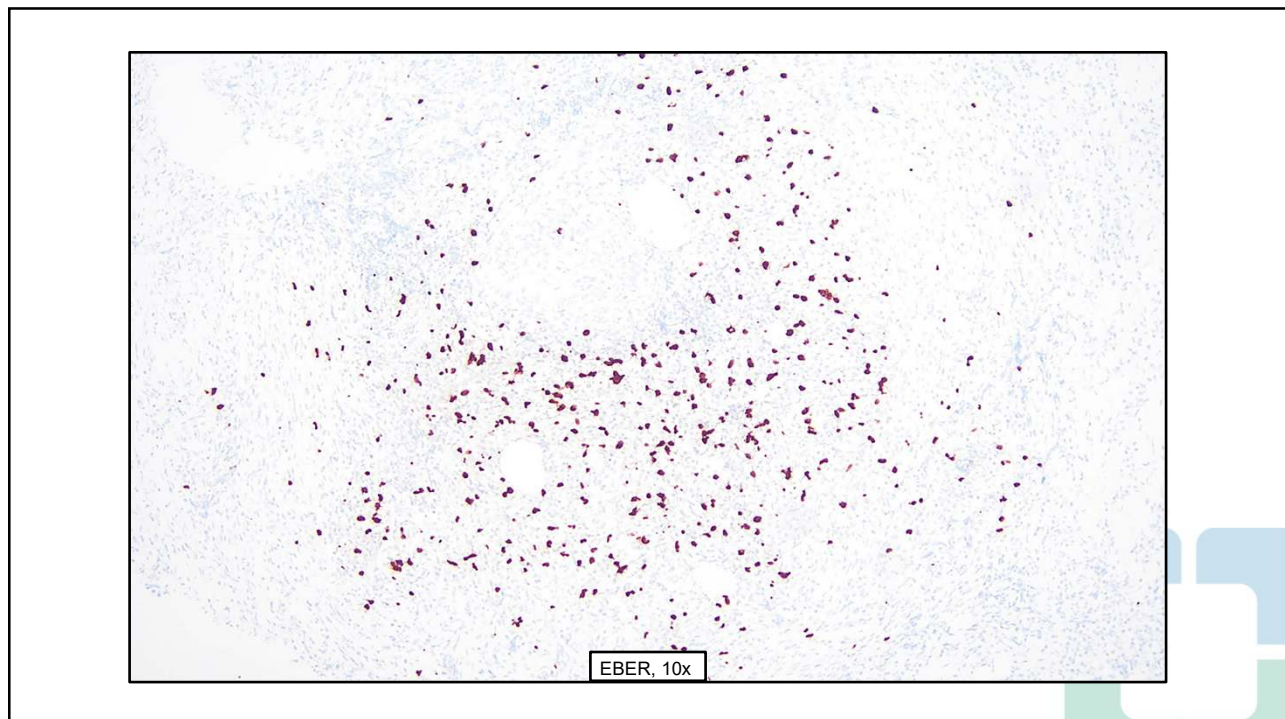
11



12

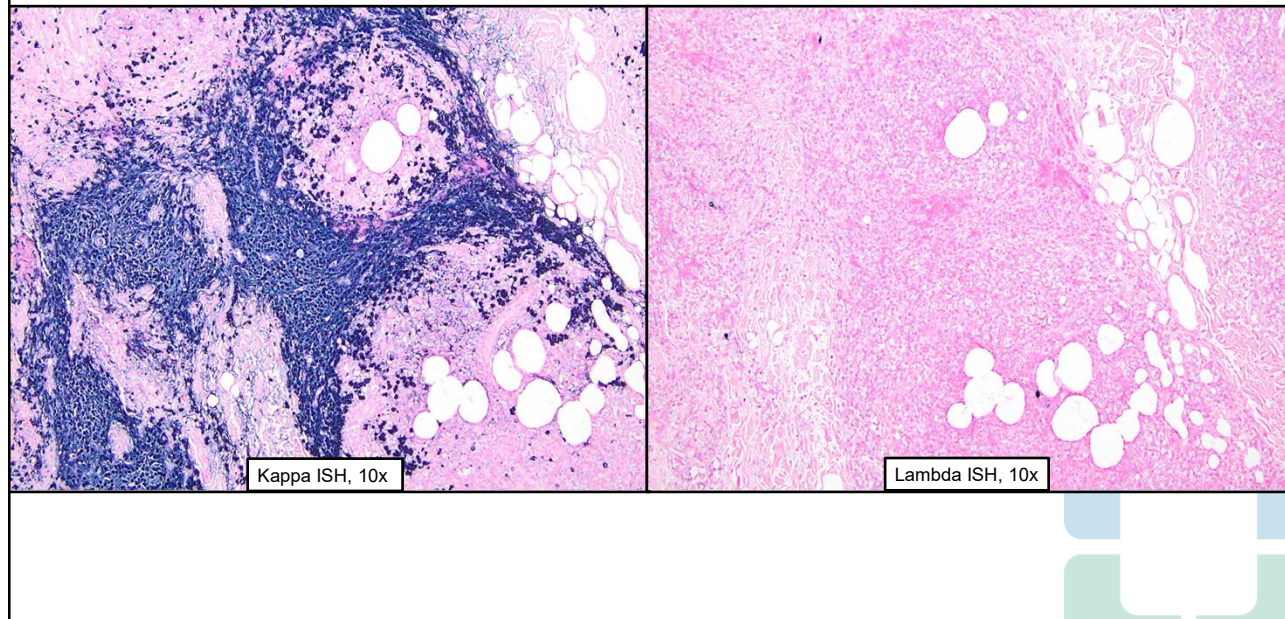


13



14

AY0



15

Differential Diagnosis

- Patient has primarily cutaneous disease with focal FDG-avid pelvic lymph nodes
 - Primary cutaneous marginal zone lymphoma/LPD
 - Primary cutaneous CD4-positive small/medium T-cell LPD
 - EBV+ polymorphic lymphoproliferative disorder
 - Cutaneous involvement by systemic T follicular helper cell lymphoma
 - Both B and T-cell lymphomas???

16

Slide 15

AYO Try to make the pictures on the same areas.

Add a high power picture of plasmacytic differentiation

Alhalaseh, Yazan, 2025-10-30T17:59:05.633

Molecular results

- Clonal B and T-cell gene rearrangements
- T-cell NGS panel
 - ***DNMT3A***: p.Arg882His (26%)
 - ***TET2***: p.Pro499Hisfs*34 (31%)



17

Final Diagnosis

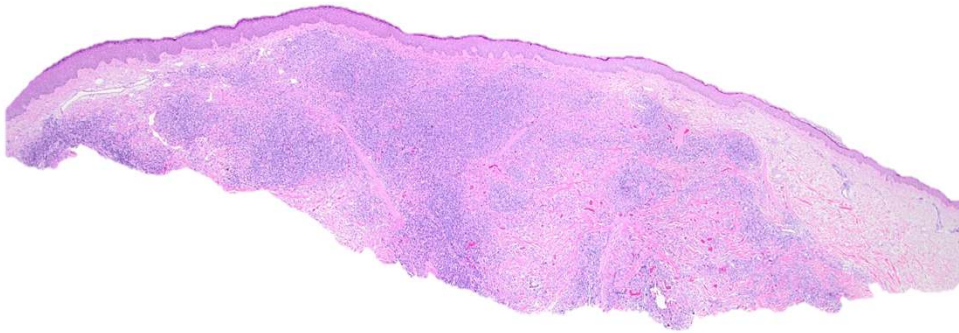
- Cutaneous involvement by
 - Nodal T follicular helper cell lymphoma, angioimmunoblastic type (WHO 5th Edition)
 - Follicular helper T-cell lymphoma, angioimmunoblastic type (ICC 2022)
 - Associated EBV+ B-cell lymphoproliferative disorder with plasmacytic differentiation



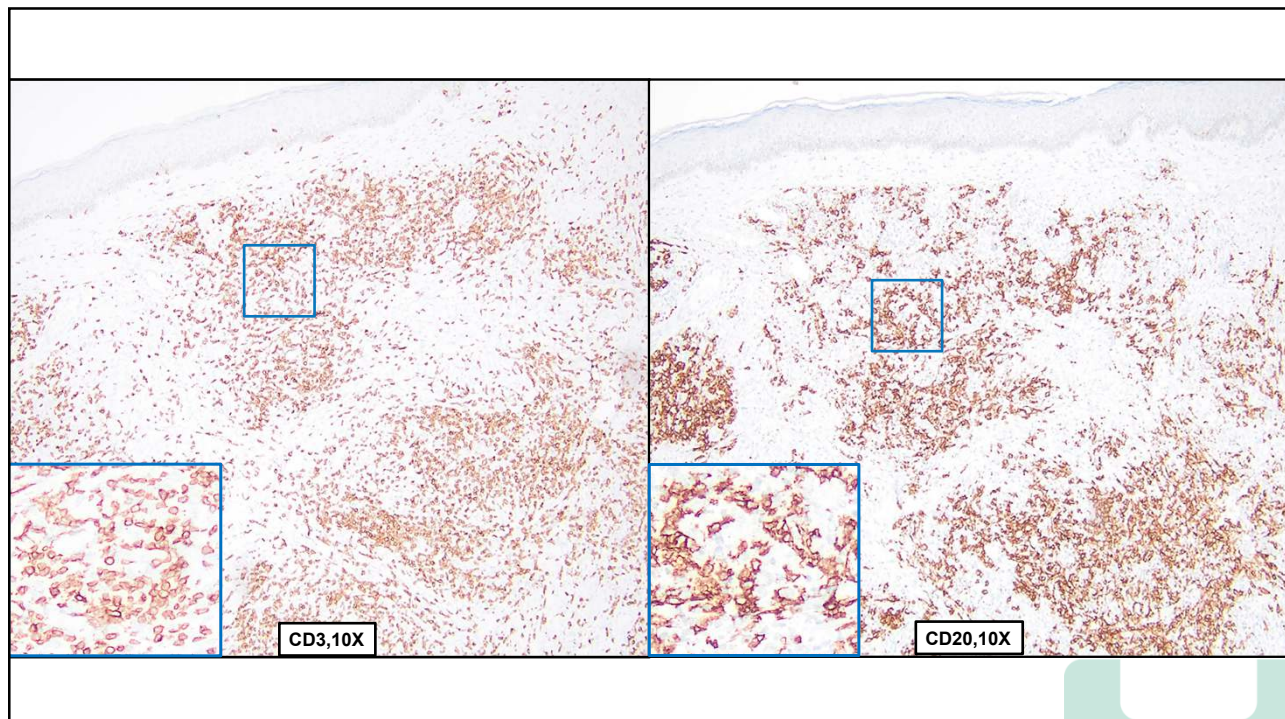
18

Revisit original biopsy

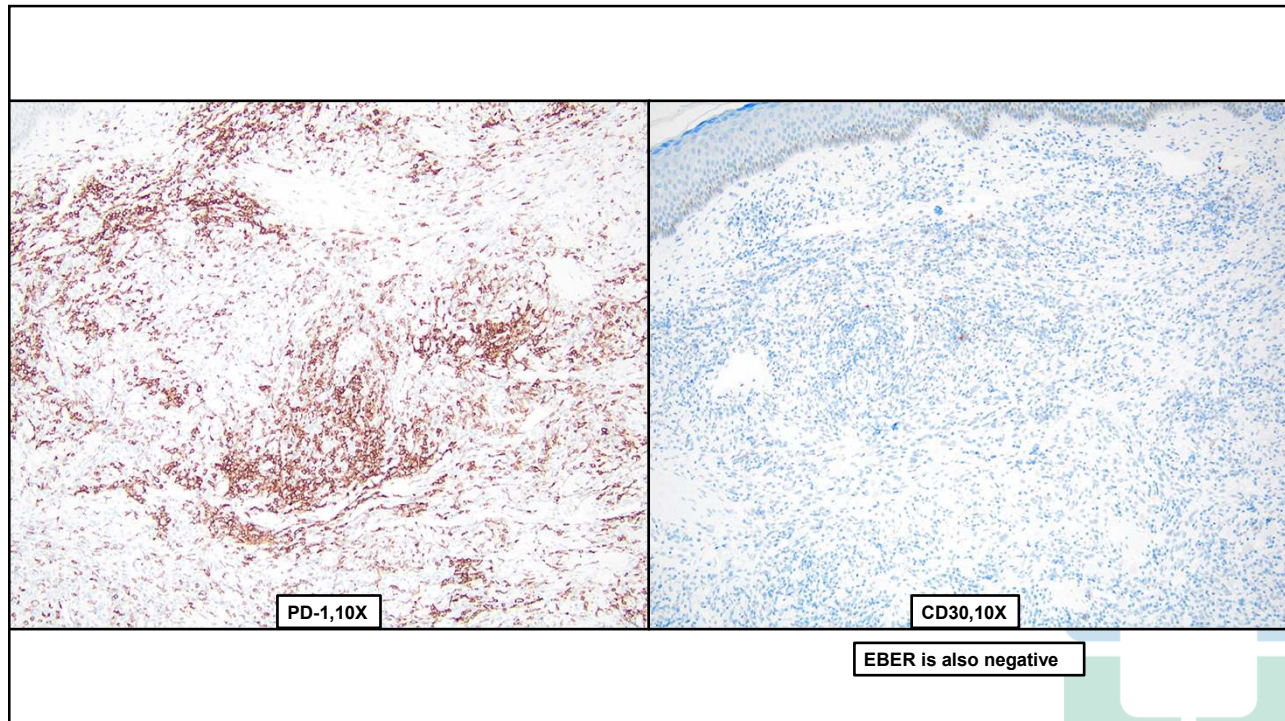
- Is there evidence of an emerging TFH lymphoma?



19

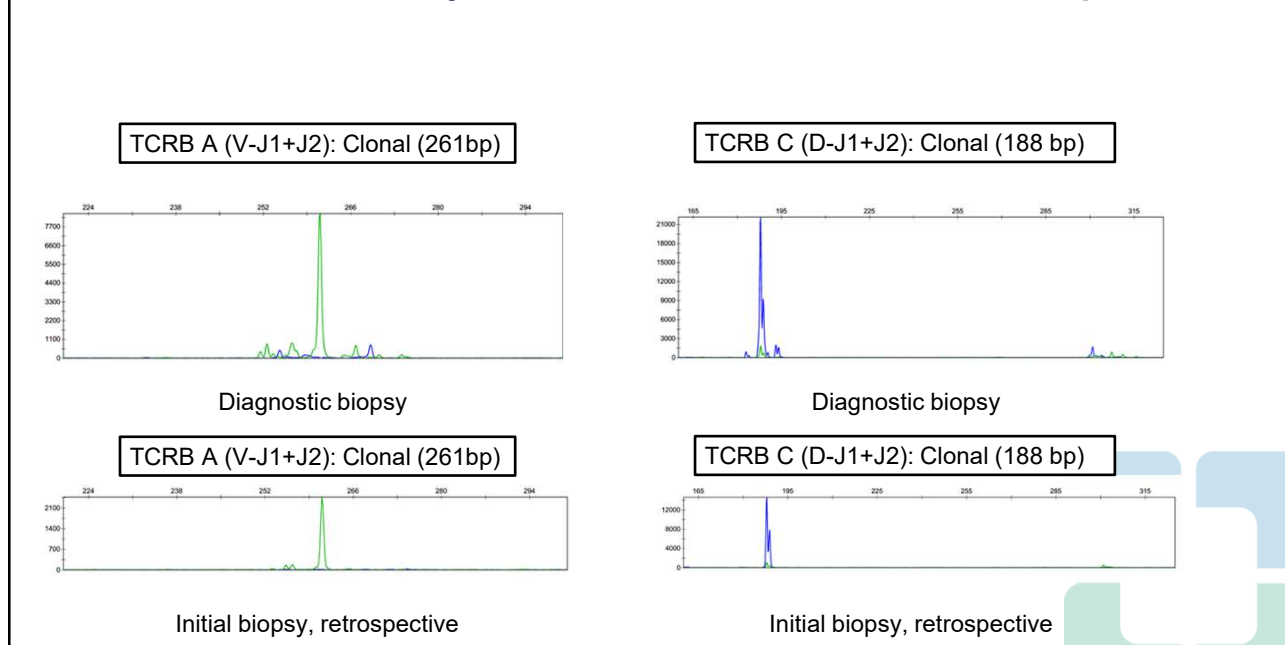


20



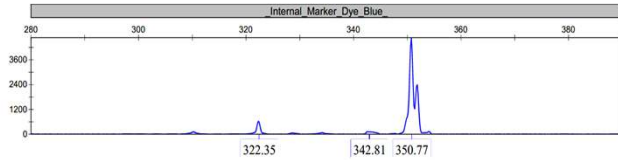
21

Molecular results yield identical T-cell clonal peaks



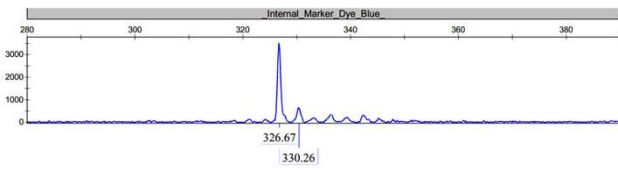
22

What about the B-cells?



Diagnostic biopsy:

- EBV+, increased CD30
- Plasmacytic differentiation



Initial biopsy:

- EBV(-), CD30 (-)
- No plasmacytic differentiation

Both clonal!! ... but different B-cell clones associated with the same T-cell lymphoma at the two sites

23

Patient follow-up

- Completed 5 cycles of BV-CHP (Brentuximab Vedotin) + Cyclophosphamide + Doxorubicin + Prednisone) therapy
- Whole body PET scan no evidence of disease
- Achieved complete remission

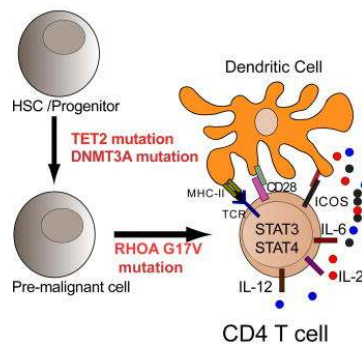
24

Nodal T-Follicular Helper Cell Lymphoma, Angioimmunoblastic Type (nTFHL-AI)

- T-follicular helper phenotype
- Lymphadenopathy and systemic disease
- 50% with cutaneous involvement
- Rarely isolated to the skin

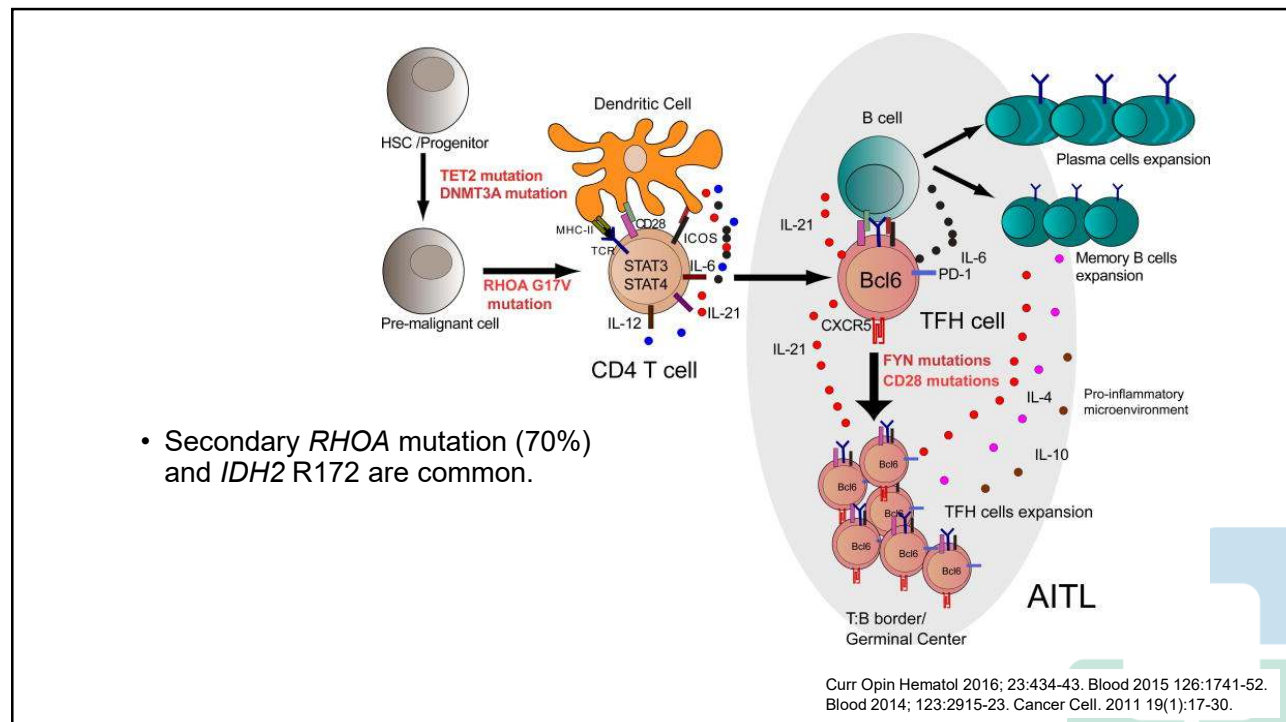
25

AITL originate from clonal hematopoiesis, particularly *TET2* or *DNMT3A* mutations



Curr Opin Hematol 2016; 23:434-43. Blood 2015 126:1741-52.
Blood 2014; 123:2915-23. Cancer Cell. 2011 19(1):17-30.

26



27

Clues to Diagnosis of Cutaneous nTFHL-AI

- Dermal atypical lymphocytic infiltrate
- TFH immunophenotype (≥ 2 markers, PD1 strong).
- Clonal TCR rearrangement and/or *TET2*, *DNMT3A*, *RHOA*, *IDH2* mutations.
- frequent EBV-positive B-cell and plasma-cell proliferation may mimic B-cell LPD
- Correlation with clinical progression and repeat biopsy often critical

28

Acknowledgement

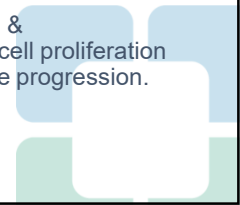
- Shira Ronen, MD
- Anthony Fernandez, MD
- Wilma Bergfeld, MD
- John McAfee, MD
- Genevieve Crane, MD, PhD



29

References

- Oishi, N., Sartori-Valinotti, J. C., Bennani, et. al. Cutaneous lesions of angioimmunoblastic T-cell lymphoma: clinical, pathological, and immunophenotypic features. *Journal of Cutaneous Pathology*, 46(9), 637-644.
- Xie, Y., & Jaffe, E. S. (2021). How I diagnose angioimmunoblastic T-cell lymphoma. *American Journal of Clinical Pathology*, 156(1), 1-14.
- Armitage, J. O. (2017). The aggressive peripheral T-cell lymphomas: 2017. *American journal of hematology*, 92(7), 706-715.
- Sandell, R. F., Boddicker, R. L., & Feldman, A. L. (2017). Genetic landscape and classification of peripheral T cell lymphomas. *Current oncology reports*, 19(4), 28.
- Kaffenberger, B., Haverkos, B., Tyler, K., Wong, H. K., Porcu, P., & Gru, A. A. (2015). Extranodal Marginal Zone Lymphoma-like Presentations of Angioimmunoblastic T-Cell Lymphoma: A T-Cell Lymphoma Masquerading as a B-Cell Lymphoproliferative Disorder. *The American Journal of Dermatopathology*, 37(8), 604-613.
- Suárez, A. E., Artiga, M. J., Santonja, C., Montes-Moreno, S., De Pablo, P., Requena, L., ... & Rodríguez-Pinilla, S. M. (2016). Angioimmunoblastic T-cell lymphoma with a clonal plasma cell proliferation that underwent immunoglobulin isotype switch in the skin, coinciding with cutaneous disease progression. *Journal of Cutaneous Pathology*, 43(12), 1203-1210.



30

Thank you

