Case 4
Soft Tissue Mass in the Left Submandibular Region

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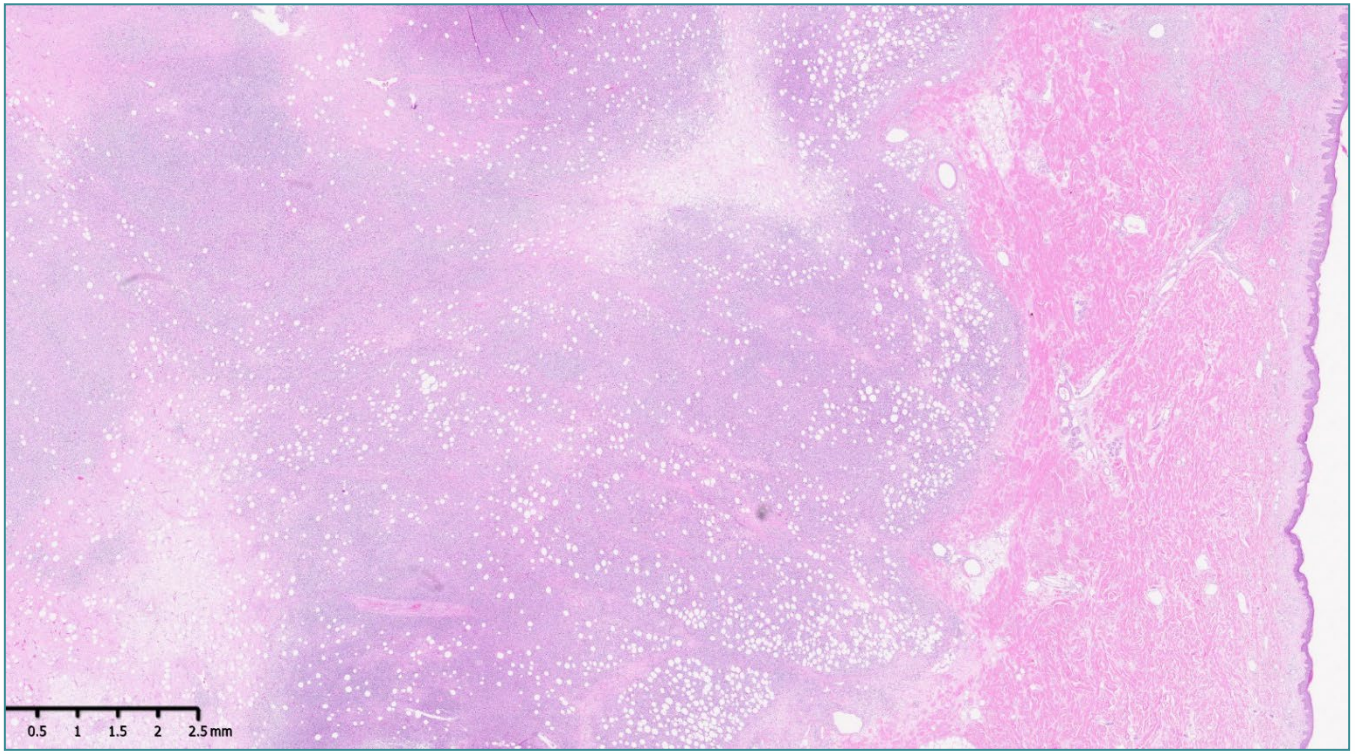
Patient History

65-year-old female with a history of diabetes, hyperlipidemia, depression, GERD and hypothyroidism.

Following cholecystectomy, the patient presented with a mass in the abdominal wall at the incision site that failed to heal. Biopsy of the mass led to a diagnosis of possible anaplastic large cell lymphoma, ALK, negative. PCR for TRG was negative. NGS was indeterminate.



Patient History

- 6 months later, the patient noticed a firm, large mass on the left side of her jaw. With complaint of 3-day history of dizziness, double vision and gait instability, patient presented to OSH.

- Denied any fevers, night sweat and body weight loss.

Laboratory data:

- WBC: 3.60 [3.98-10.04 k/mcl]
- HGB: 11.1 [11.2015.7 g/dL], MCV: 92.4 [79.4-94.8 fL]
- Platelets: 225 [173-369 k/mcl]

- LDH: 469 [125-220 U/L]
- ALP: 328 [40-150 U/L]
- HTLV-I/II Ab: Negative

- Bone marrow biopsy: Not Done.

Laboratory Data

- CSF:
  - Albumin: 32 [9-34 mg/dL]
  - Glucose: 74 [40-70 mg/dL]
  - RBC count: 0 mm^3
  - WBC count: 0 mm^3
- CSF flow:
  - No diagnostic evidence of T-cell lymphoma.

    (A limited panel was performed due to low cellularity. Only a focused T-cell panel was performed.)

Image Studies

- Neck CT scan:
  - 6.6 cm ill-defined soft tissue mass within the left submandibular region, infiltrating the surrounding fat.
  - Probable bony erosion/bony destruction in the region of the left mandible.
- Brain MRI:
  - Abnormal signal present within several right frontal sulci, suggesting leptomeningeal disease.
  - Marrow infiltrate was also suspected.

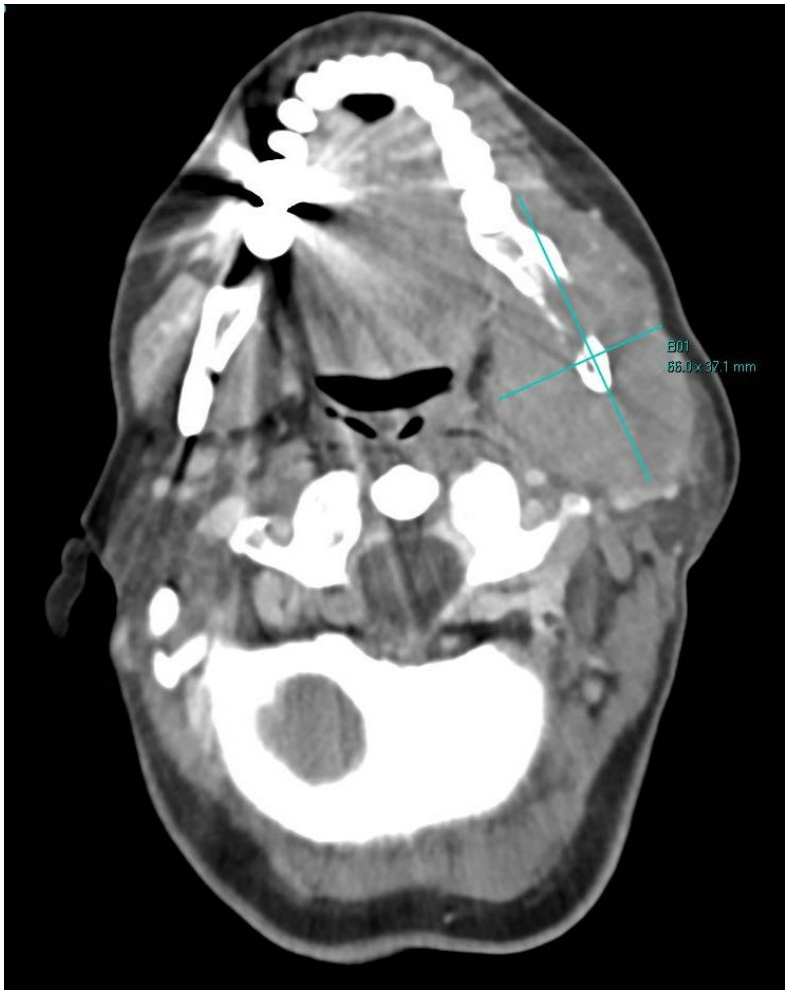
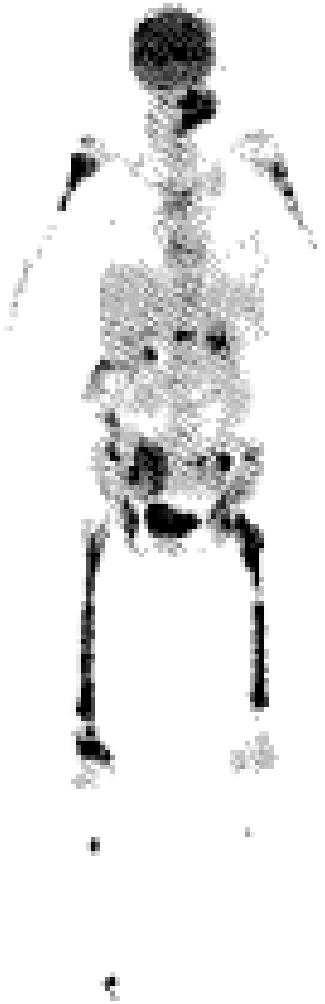


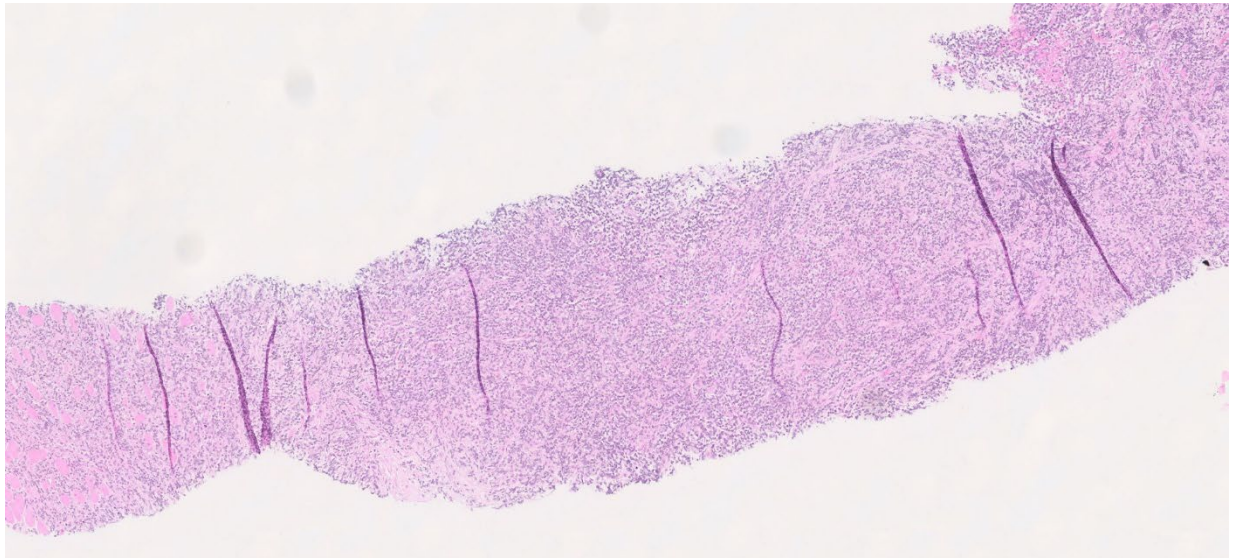
Image Studies

- PET/CT:
  - Hypermetabolic erosive mass in the left mandible.
  - Extensive malignancy throughout the entire central marrow spaces and marrow of the proximal long bones.



Histology

H&E



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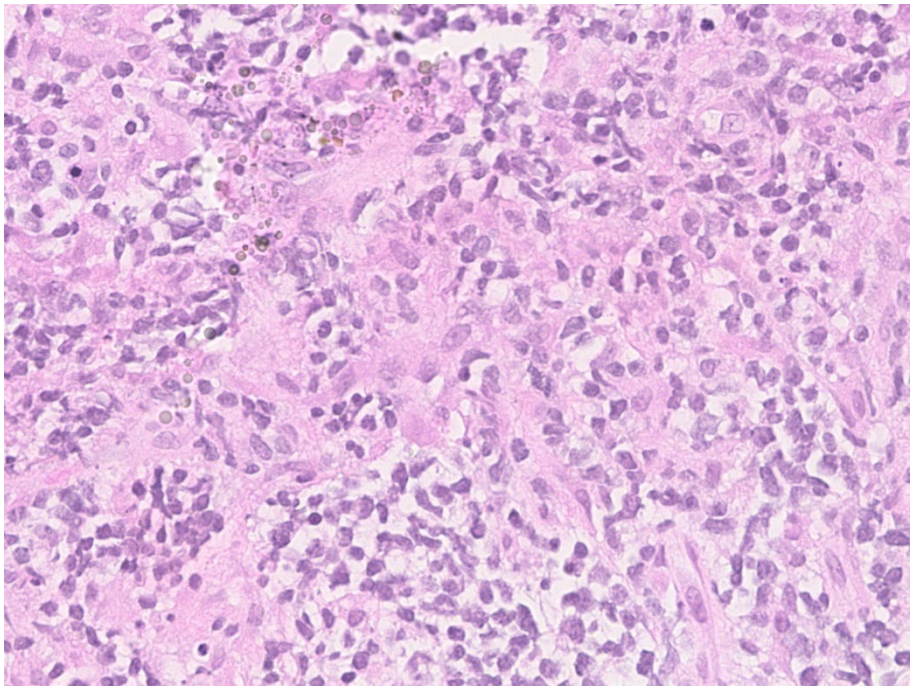
Histology

H&E



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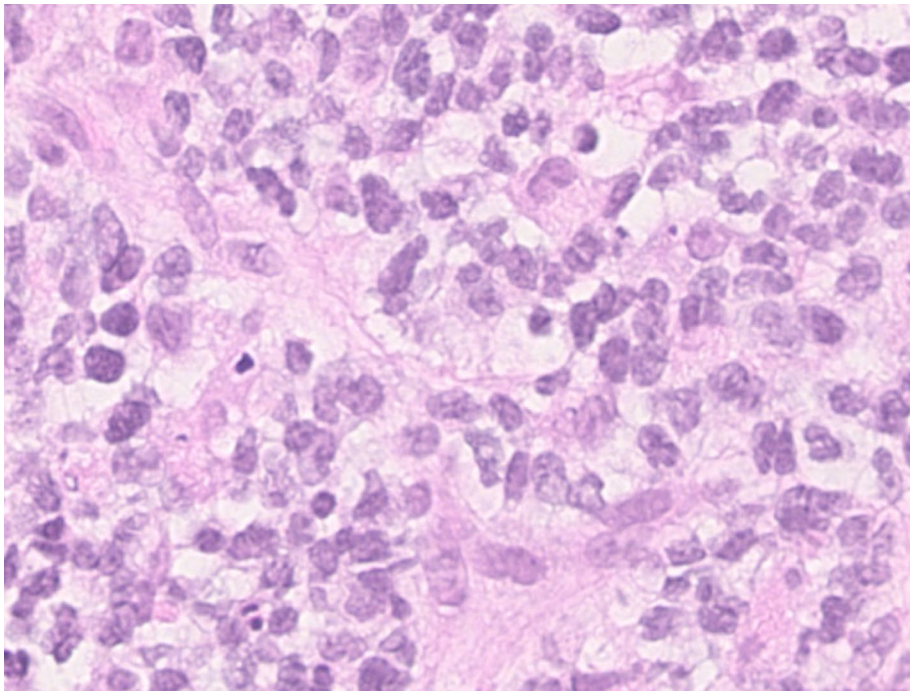

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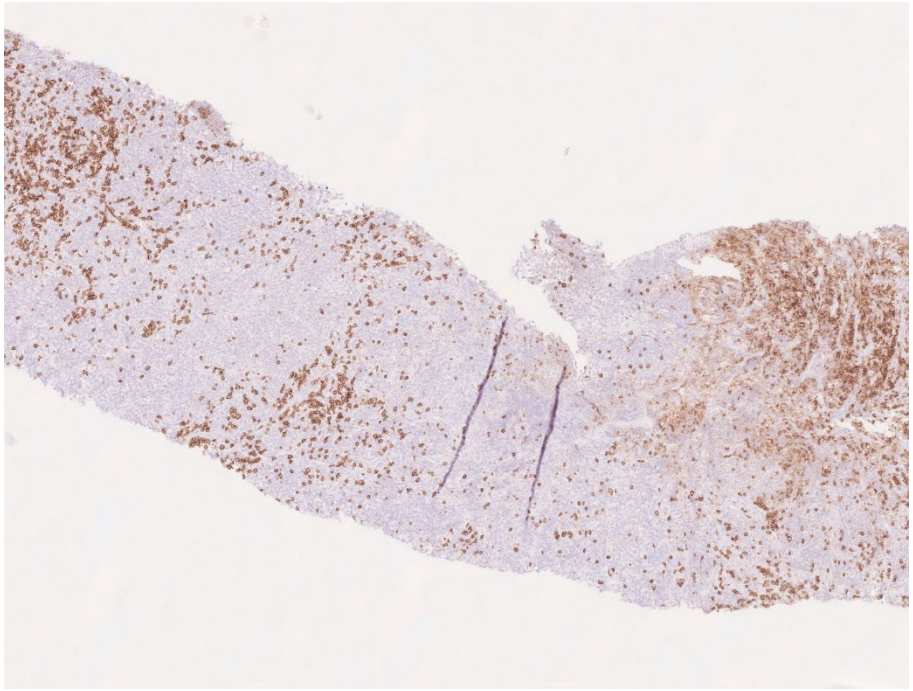
Medium-large sized tumor cells with irregular nuclear contours admixed with some small lymphocytes in a background.

Histology

CD3



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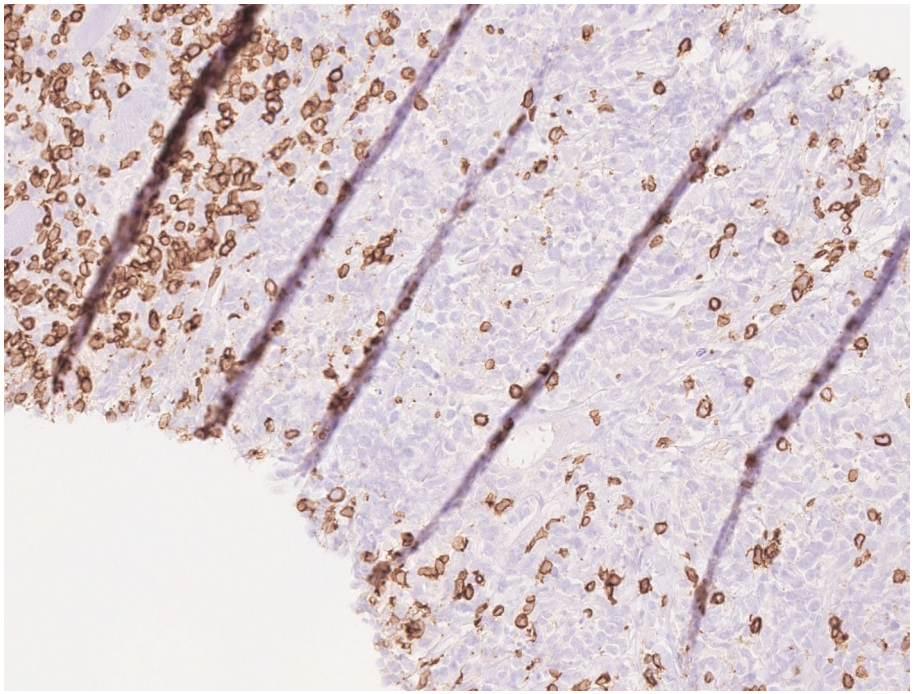
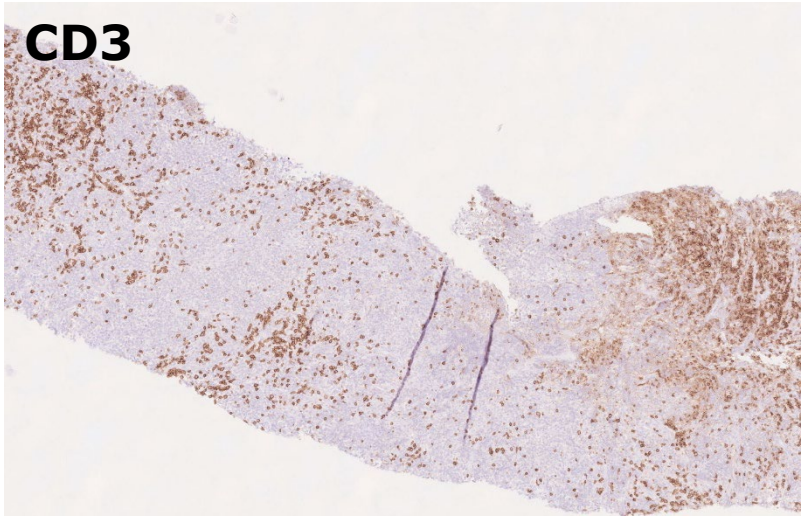
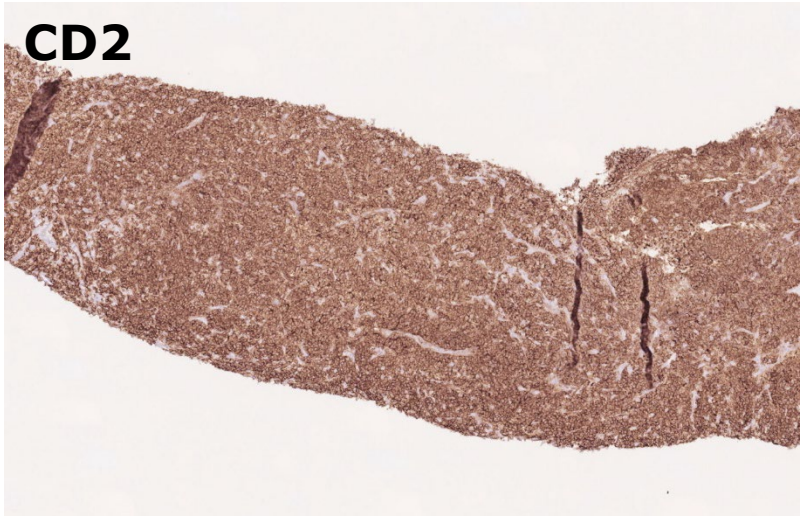
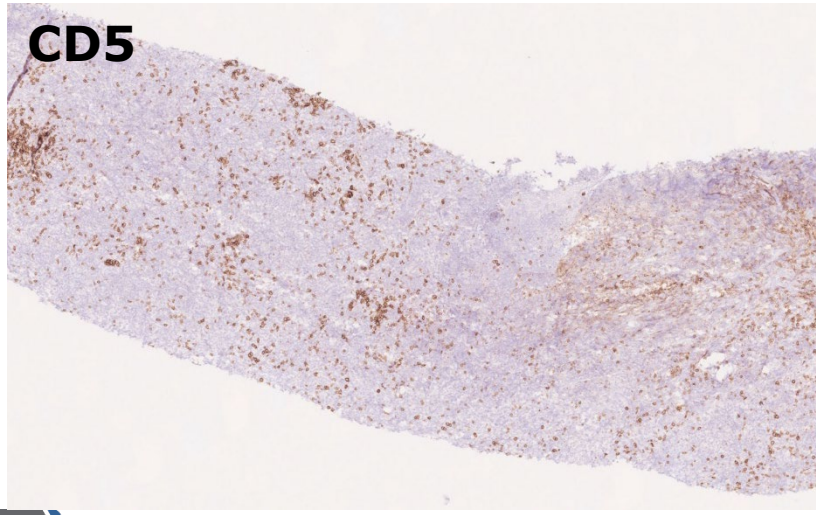


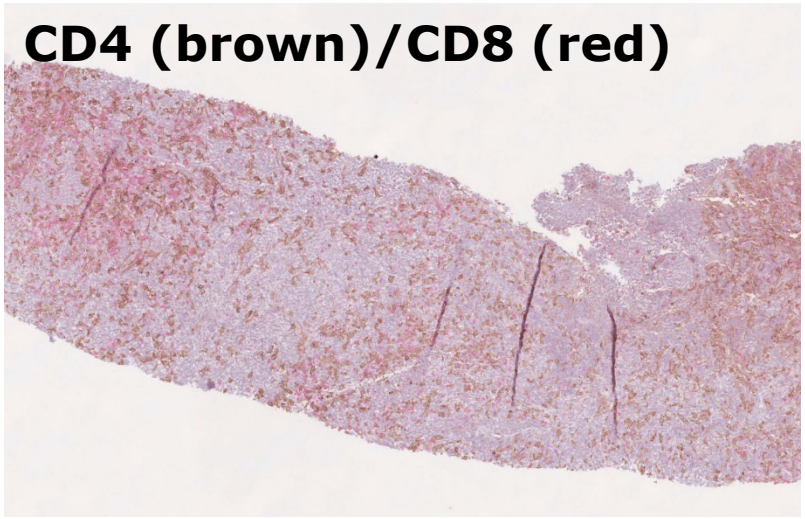
(X20)

Histology









Histology

- Other IHCs:
  - Positive: TIA1 and CD30 (subset)
  - Negative: TdT, CD56, Pax5, CCR4 and GATA3

Summary

- Infiltration of abnormal mature lymphoid cells in H&E
- Negativity of Pax5

  ≠ B cell lymphoma
- Positivity of CD2 and TIA-1
- Double negative (CD4-/CD8-) immunophenotype
- Negativity of TdT and CD56

  ≠ Lymphoblastic lymphoma

  ≠ NK Lymphoma

Molecular Pathology

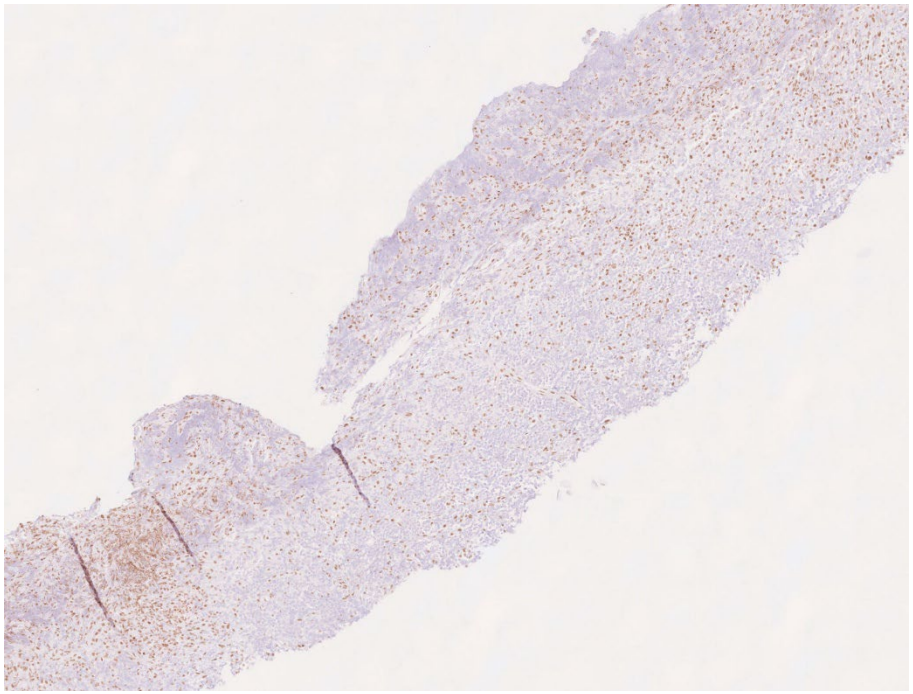
- Next Generation Sequencing

  (TruSight Oncology 500 Gene Panel):

  - SMARCB1 loss.

Histology

INI1



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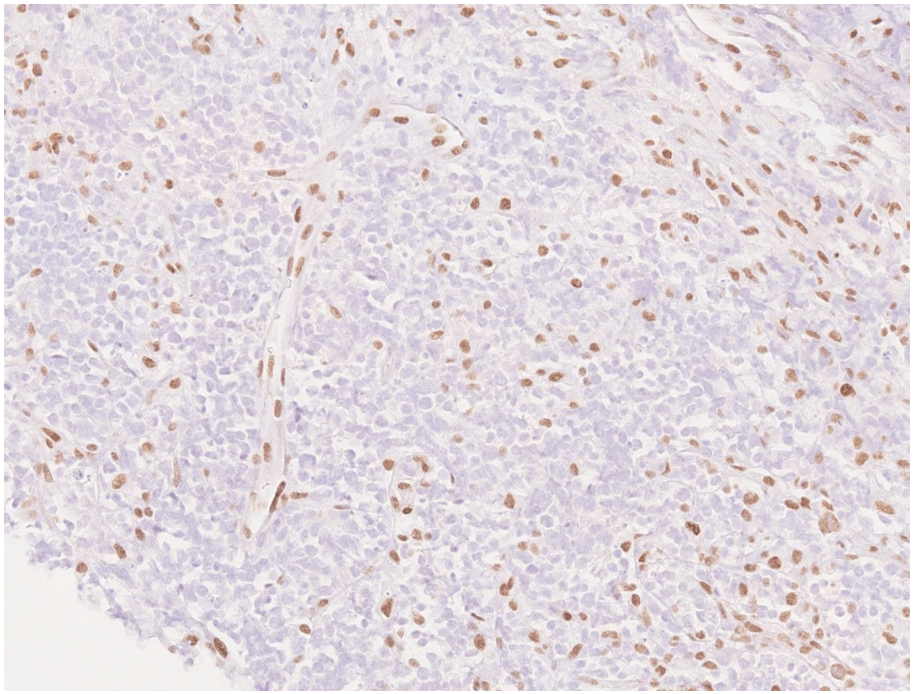

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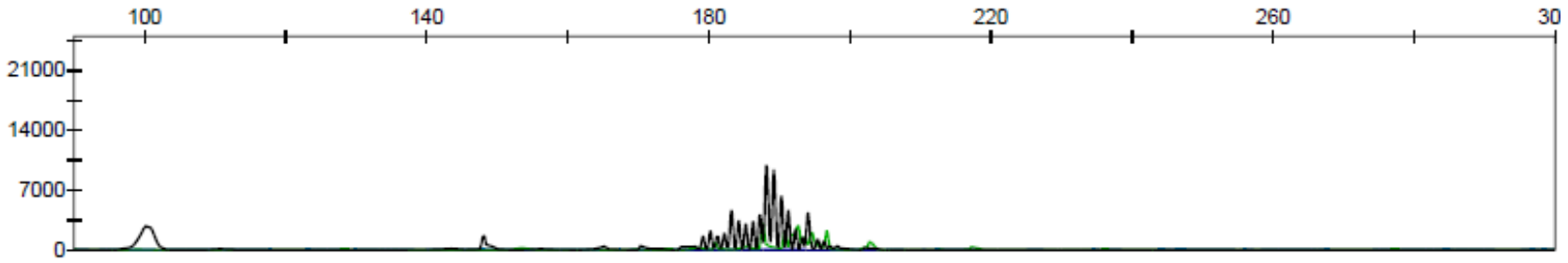
Molecular Pathology

- PCR for T cell receptor gamma rearrangement:
  - Irregular polyclonal rearrangement pattern detected.

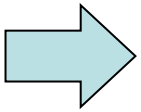


Diagnosis

Peripheral T-cell lymphoma (PTCL) with *SMARCB1* loss

Diagnosis

- From our experience, cases with PTCL-*SMARCB1* loss often show:
  - Double negative T cell immunophenotype
  - Aberrant expression of myeloid markers
  - Polyclonal TCR rearrangement

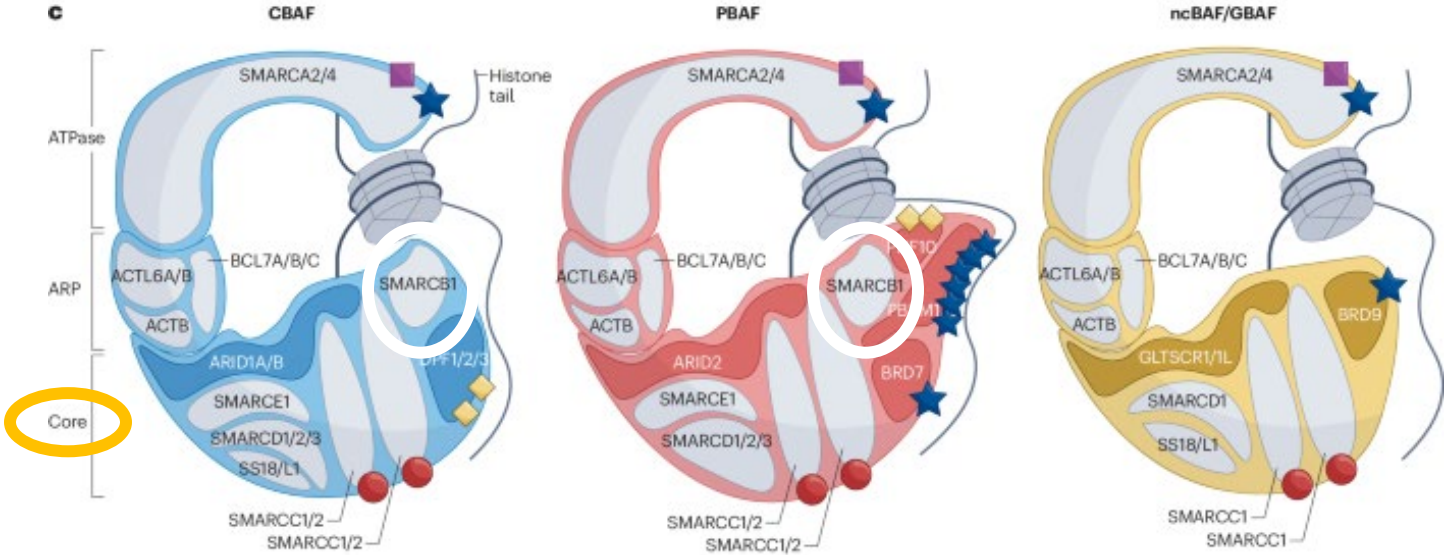


If we see these features, we check INI1 expression.

SMARCB1 is a Core Subunit of SWI/SNF chromatin remodeling complex.

- SMARCB1: SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily B, Member 1.

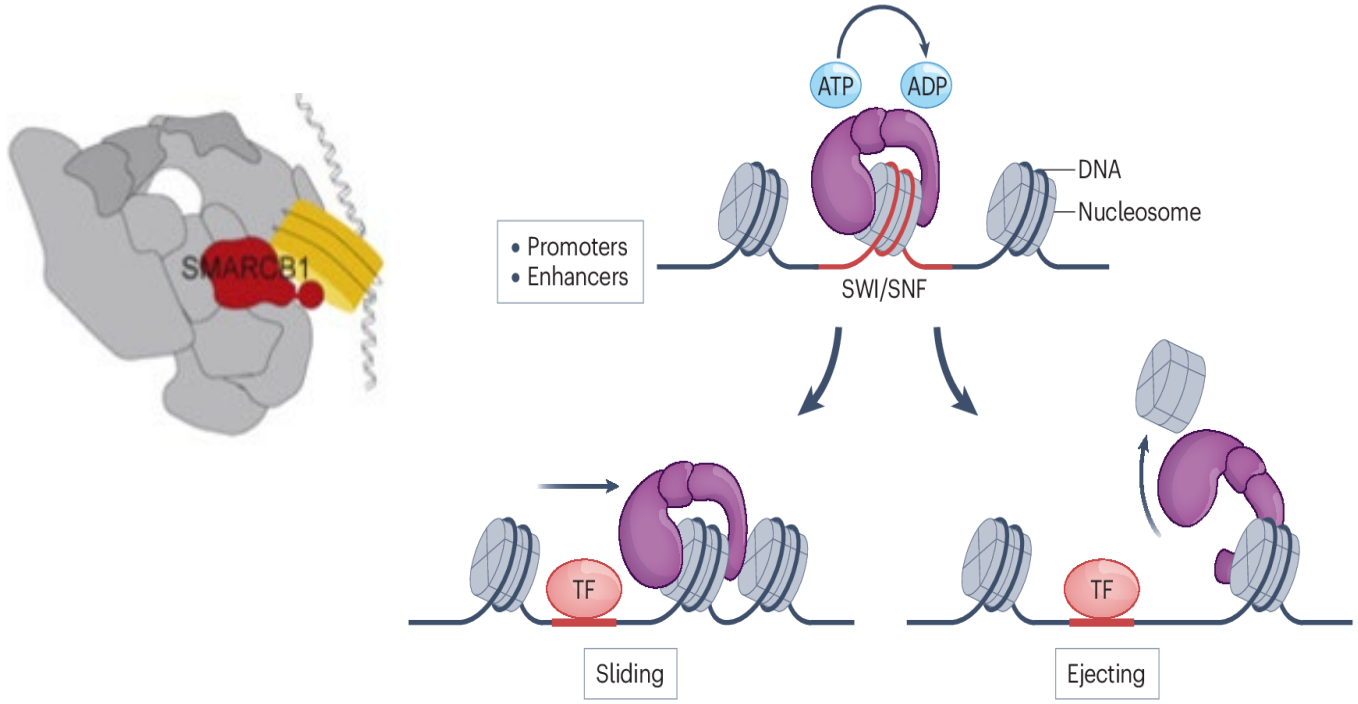
- 3 main subtypes of SWI/SNF chromatin remodeling complex in humans.



- SMARCB1 encodes INI1 (Integrase Interactor1) which is ubiquitously expressed in the nuclei of all normal human cells.

Hollmann TJ. *Am J Surg Pathol* . (2011) and Review from Malone HA. *Nature reviews drug discovery.* (2024).

SWI/SNF Complex is Involved in Mobilizing the histone–DNA, Causing Nucleosome Sliding, Dissociation, or Replacement.

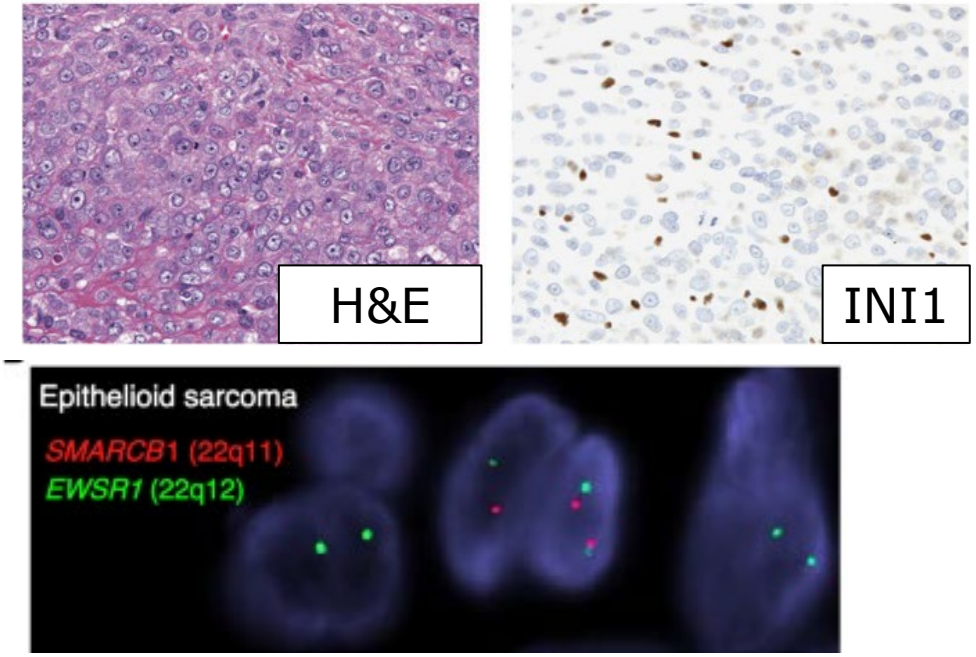


Valencia AM. *Cell.* (2019) and Review from Mittal P. *Nature Reviews Clinical Oncology* (2020)

SMARCB1 Inactivation is Found in a Wide Range of Malignancies.

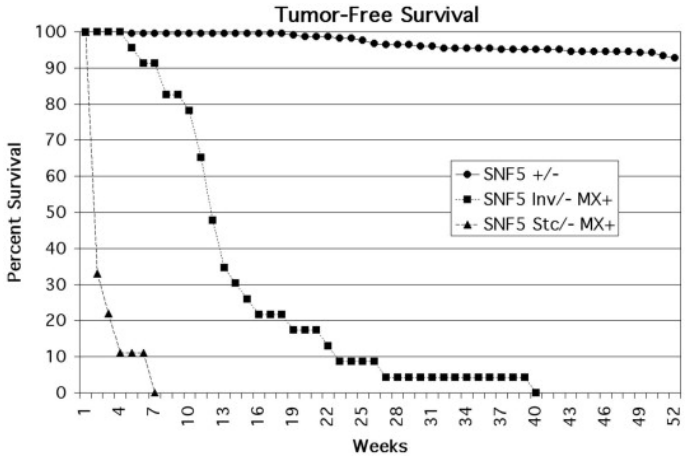
- *SMARCB1* deficiency is seen in various human malignancies, mainly in rhabdoid tumor, epithelioid sarcoma and epithelioid MPNST.
- In bone-soft tissue tumor, 80% of SMARCB1-deficient cases harbor biallelic *SMARCB1* loss, mostly displaying INI1 loss in immunohistochemistry.

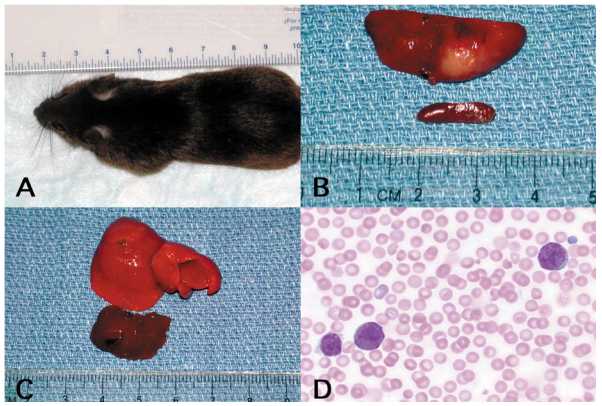
Epithelioid sarcoma



Sullivan LM. *Modern Pathology* (2013) and Dermawan JK. (2022) *Modern Pathology*.

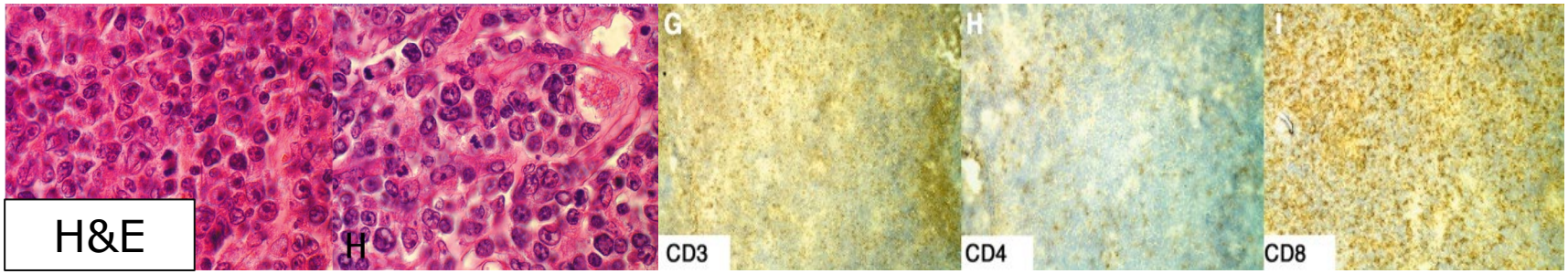
Conditional KO Mice with *Smarcb1* Inactivation Develop CD8+ PTCL





100% of the mice developed tumors with a median onset of 11 weeks.

Tumor Biopsy



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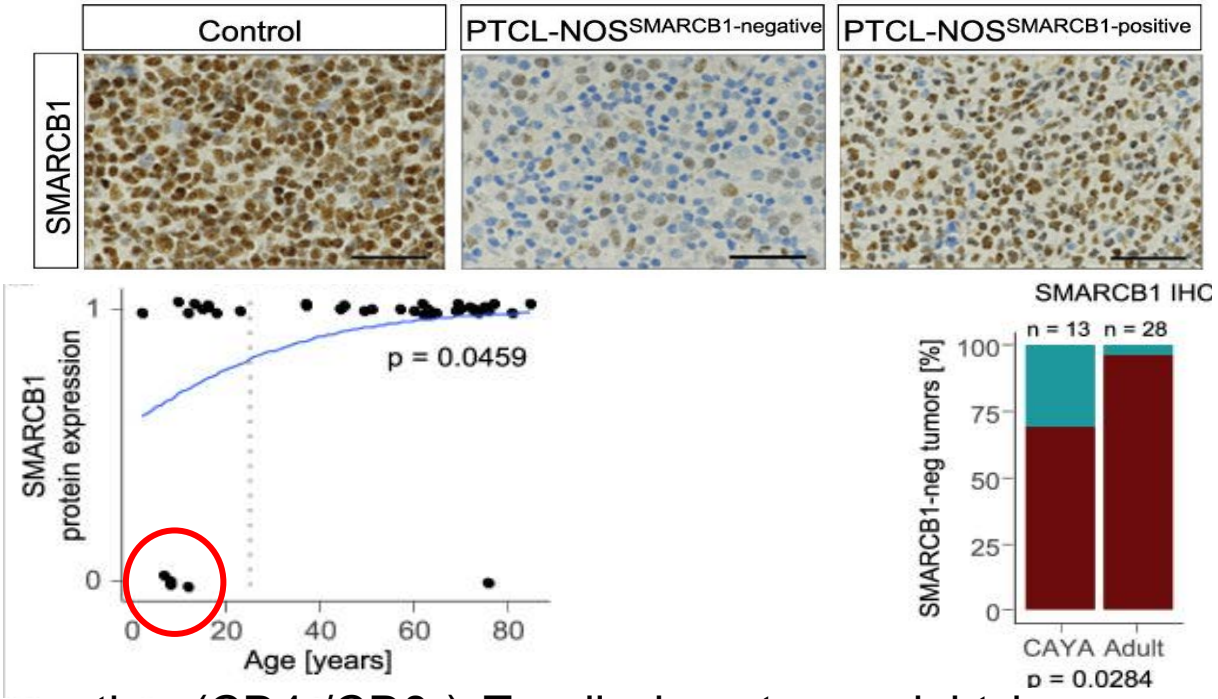
Roberts CWM. (2002) *Cancer Cell.*

PTCL with SMARCB1 loss is Identified Predominantly in Young Individuals.

- PTCL with *SMARCB1* loss by IHC have been reported, mainly in young individuals. A subset of PTCL cases from old individuals showed SMARCB1 loss.



- Double negative (CD4-/CD8-) T cell phenotype might be a common in *SMARCB1* in PTCL cases.

Fischer A. (2024) *Nat. Commun.*

Follow-up

- Patient underwent EPOCH.

  (Etoposide, Prednisolone, Oncovin, Cyclophosphamide and Hydroxydaunorubicin)

- Achieved complete response after 3 cycles.

- After completion of 6 cycles of EPOCH, PET/CT revealed near-complete resolution of all previously seen abnormalities. No new sites of lymphoma throughout the body.

- CNS prophylaxis with Methotrexate is on-going.