INTERESTING CASE PRESENTATION

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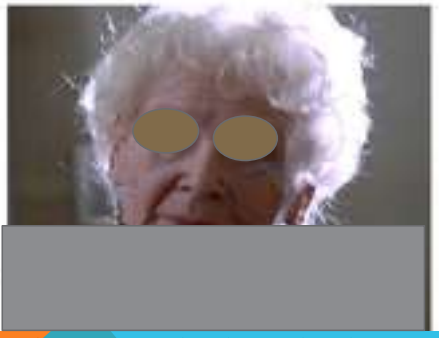
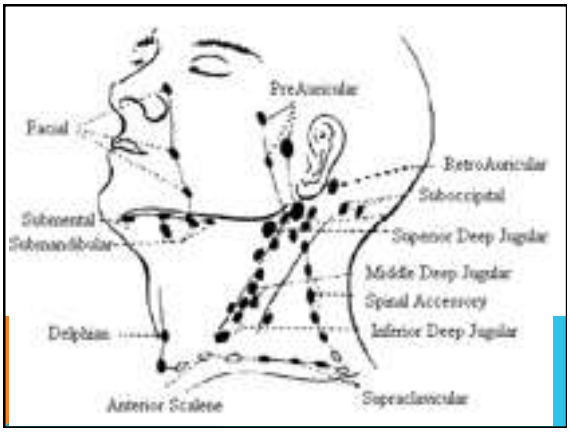
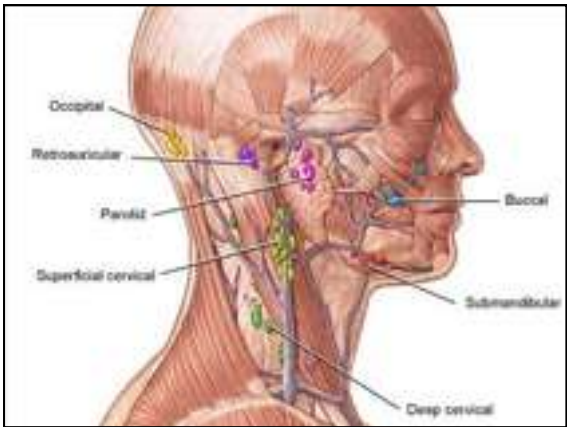
95 FEMALE WITH OVER 10 YEARS OF HISTORY OF ASYMPTOMATIC CLL PRESENTED WITH A PROGRESSIVELY GROWING PAINLESS LT MALAR MASS

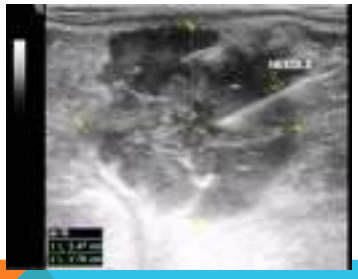


IS IT A LYMPH NODE OR TUMOR NODULE?



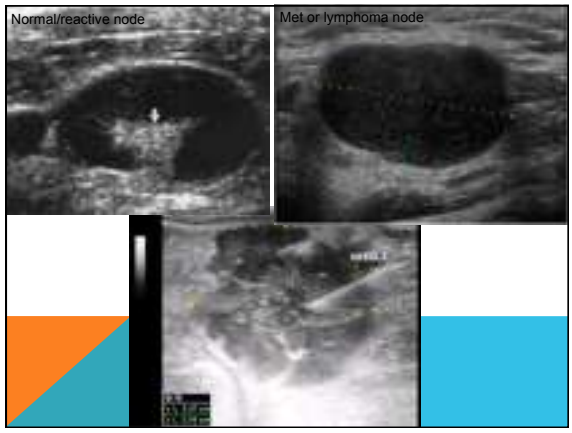


ULTRASOUND GUIDED FNA BIOPSY

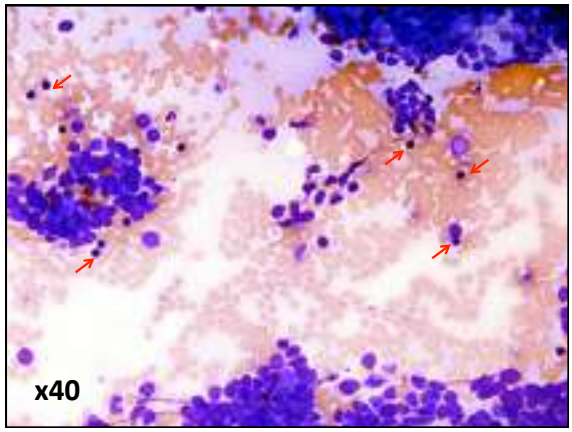


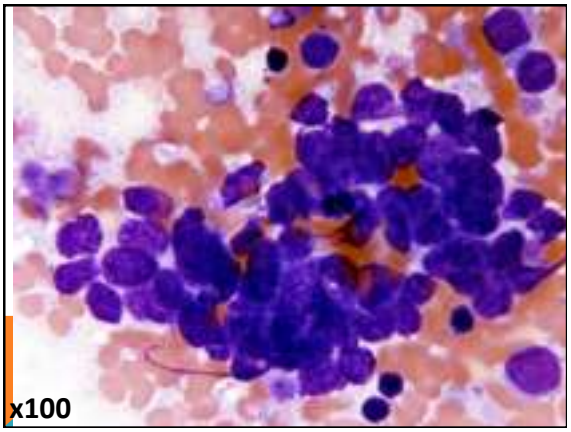
left malar mass

(GE LogIQ e US machine)



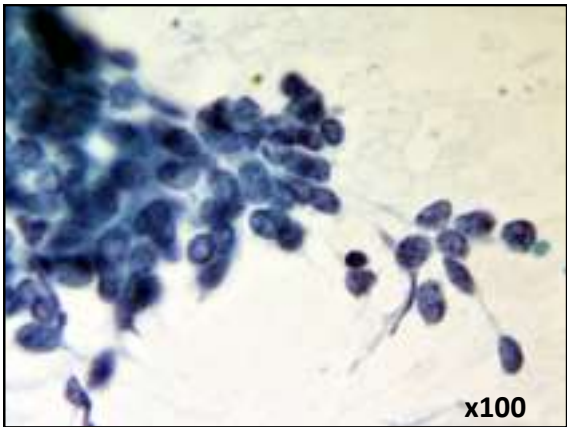
LESS LIKELY TO BE LYMPH NODE

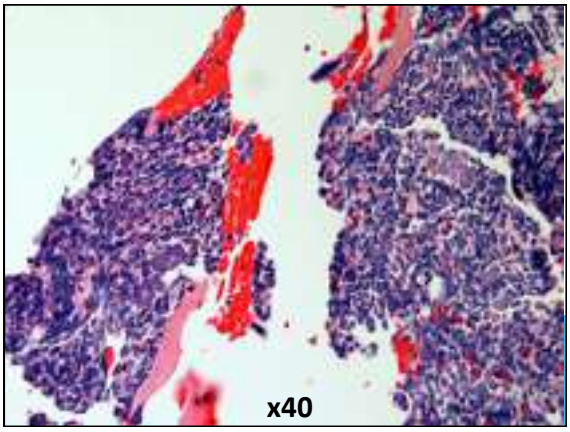


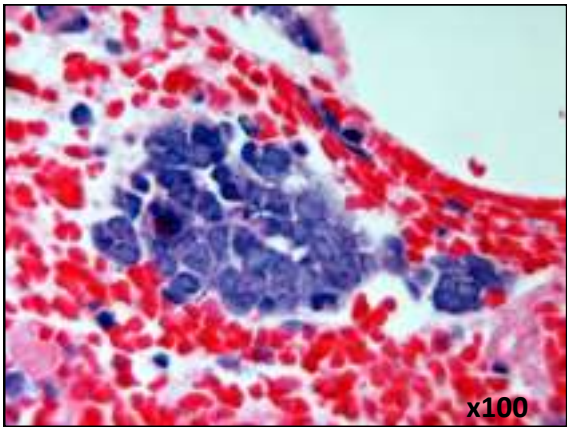


Onsite Decision Making Process

1. Preliminary diagnosis
   - Small round blue cell tumor
2. Differential diagnoses
   - Metastatic small cell carcinoma
   - Lymphoma
   - Merkel cell carcinoma
   - Amelanotic melanoma
   - Other small round blue cell tumors
3. What type of ancillary studies?
   - Immunostains
   - Flow cytometry
4. Enough material for ancillary studies?
   - RPMI medium (Cell Block + Flow)



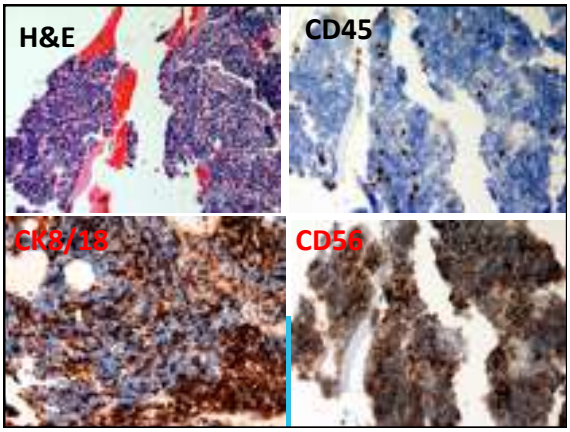


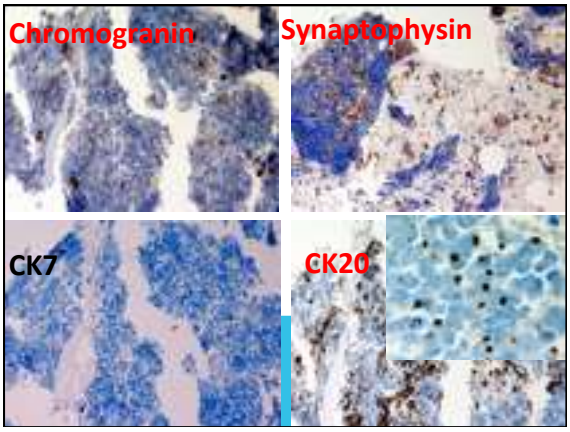


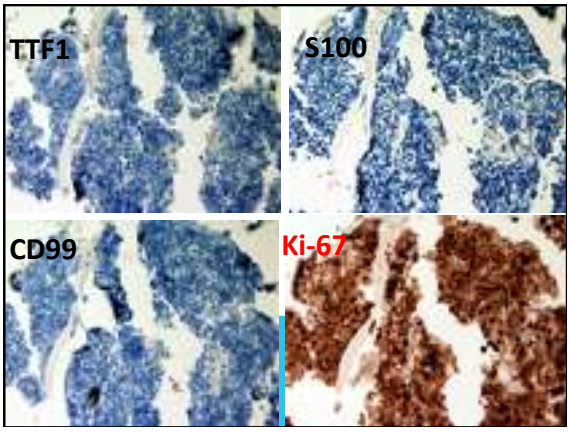
IHC Characteristics of small round blue cell tumor

Tumor	CAM5.2 or AE1/AE3	CK20	Neuroendocrine Markers	CK7 or TTF-1	LCA (CD45)	S100
MCC	+	+	+	-	-	-
SCLC	+	-	+	+	-	-
Lymphoma	-	-	-	-	+	-
Melanoma	-	-	+	-	-	+
Neuroblastoma	-	-	+			
ES/PNET CD99+						
Rhabdomyosarcoma	desmin+, myoglobin+, muscle specific actin+					

MCC=Merkel cell carcinoma; SCLC = small cell lung cancer, ES/PNET: Ewing's sarcoma / primitive neuroectodermal tumor



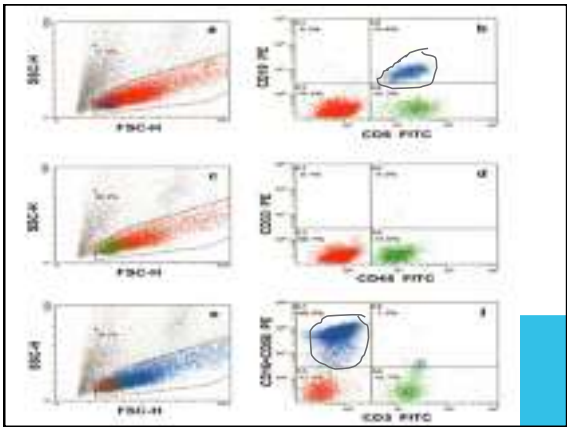




Summary of cytological and immunocytochemistry studies

Immunostains	Cohesive small to intermediate round blue cells	Dispersed small round blue cells
Neuroendocirne markers		
CD56	+	-
Chromogranin	+	-
Synaptophysin	+	-
Cytokeratins		
CK8/18	+(diffuse)	-
CK20	+(dot like cytoplasmic pattern)	-
Ki-67	~80-90%	20-30%
Others		
CK7		-
TTF-1		-
CD45(LCA)	-	+
S100	-	-
CD99	-	-

Merkel cell Carcinoma(MCC)



Summary of flow cytometry studies

Markers	small to intermediate cells/higher granularity (69%)	Small cells/low granularity (group1, 17%)	Small cells/low granularity (group 2, 14%)
CD33	-	-	-
CD45	-	+	+
CD16/56	+	-	-
CD3	-	-	+
CD7	-	-	-
CD4	-	-	+(partial)
CD8	-	-	+(partial)
CD19	-	+	-
CD20	-	+(dim)	-
CD5	-	+	-
CD10	-	-	-
CD23	-	+	-
Kappa	-	-	-
Lambda	-	+	-
FMC	-	-	-
CD22	-	-	-
CD25	-	-	-
CD38	-	-	-
CD103	-	-	

Neuroendocrine differentiation

CLL/SLL

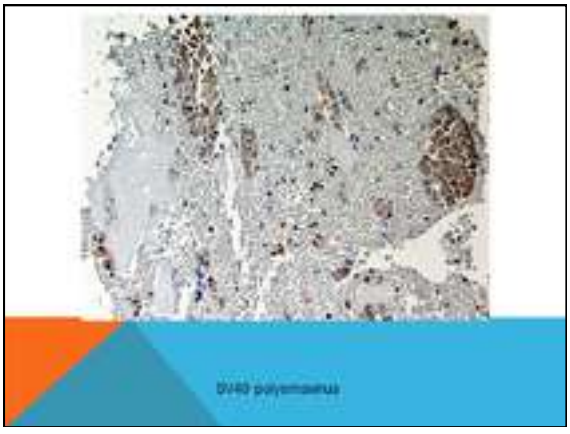
Mixed T lymphocytes

CLL collision to MCC or Peripheral blood contamination?

1. CLL x 10 years, asymptomatic, without treatment, WBC (6 months ago): 20.6 x10^9/L with lymphocytes 54% (blast 0%)

2. FNA sample was grayish white non-bloody

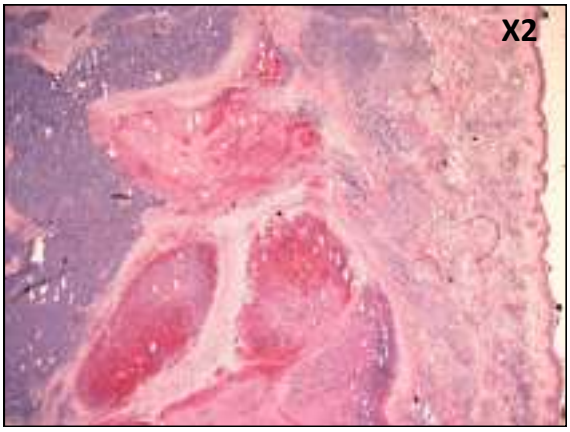
NOT BLOOD CONTAMINATION !

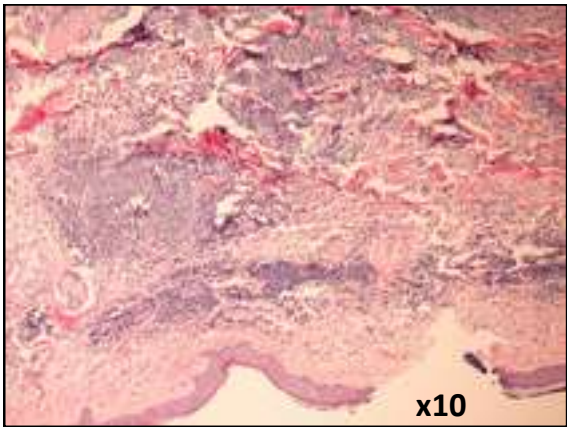


Final Cytological Diagnosis

Collision Tumor comprised of Merkel Cell Carcinoma (MCC) and Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)

Collision tumor: a rare condition in which two neoplasms, both growing in the same general area, collide with the tumor elements and become intermingled.


X2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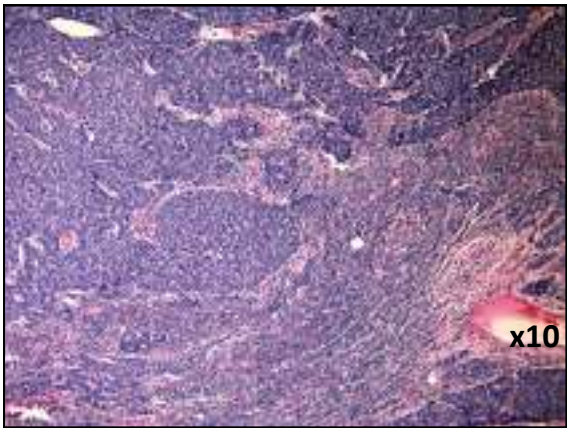
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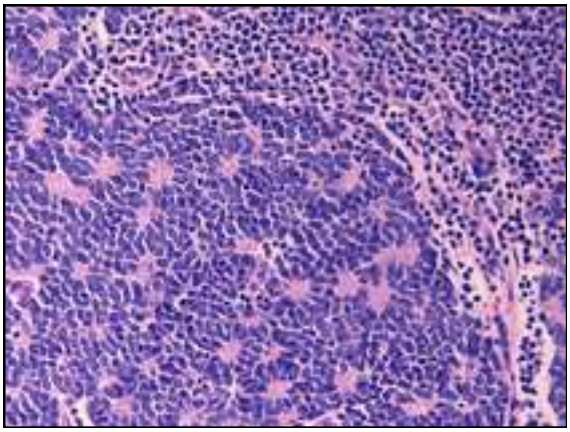

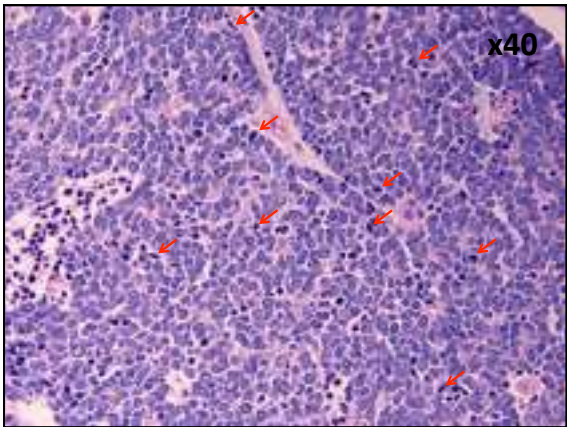
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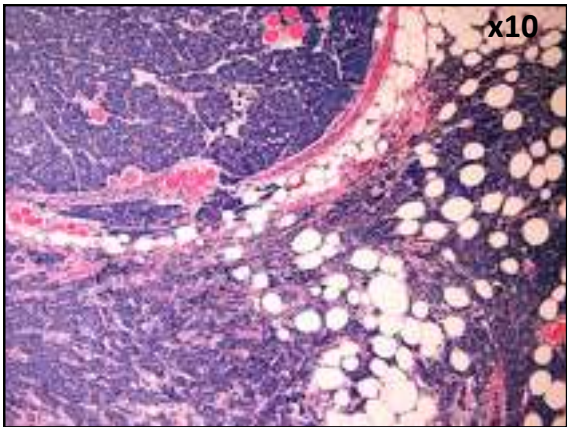
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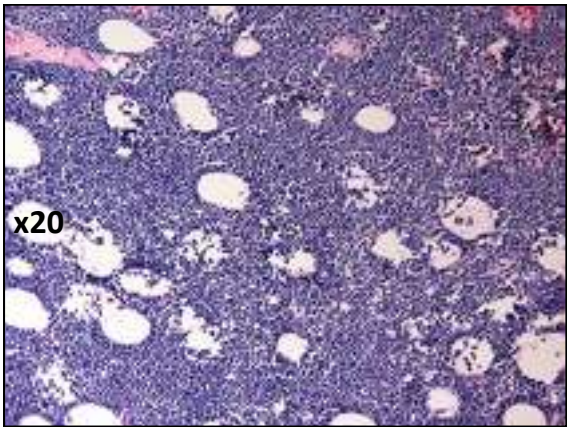

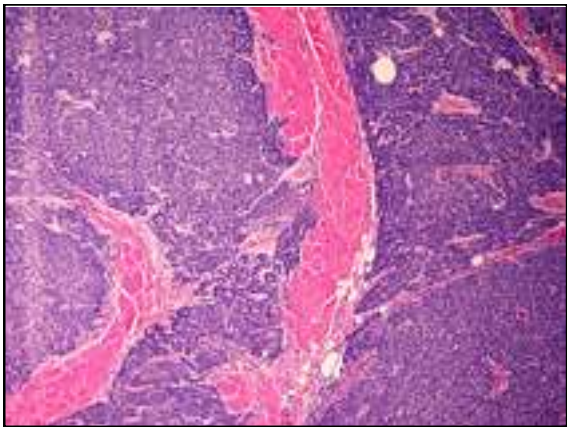

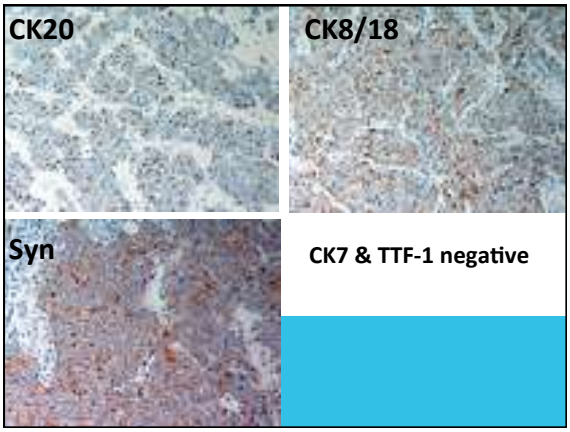

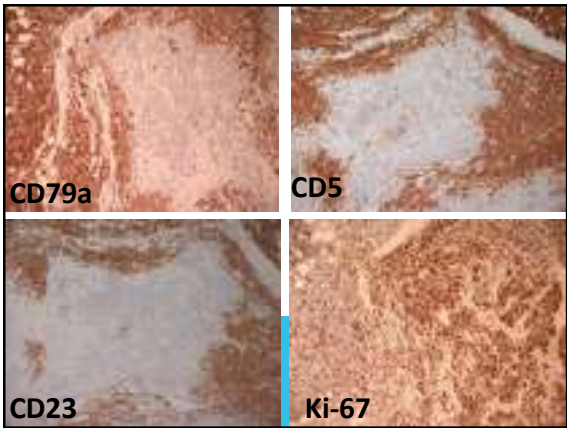

Surgical Pathological Diagnosis

Collision tumor between MCC and CLL/SLL.

- Superior, deep, and lateral margins are positive for Merkel cell carcinoma
- Lymph-vascular Invasion present

AJCC stage pT4 Nx Mx

Patient Fellow-up

1/17/2013	**US-FNA biopsy of malar mass**
1/18/2013	**MRI: No pathologic cervical lymphadenopathy**
2/01/2013	**Malar mass excision**
2/21/2013	**PET : multiple pulmonary subcentimeter nodules Suspicious for metastatic disease**
5/09/2013	**Surgical resection of left medial check: Malignant melanoma in situ**
3/13/2014	The patient is doing quite well considering she is 96-years of age.
5/05/2014	Patient was sent to ED after fell at home. She was awake and well oriented and stated "**there's nothing wrong with my head**."

Merkel Cell Carcinoma and CLL/SLL

1. **MCC** has been shown to be strongly associated with a number of **cutaneous and hematological malignancies.**

2. **CLL/SLL is the most frequent primary hematological malignancy r**eported in **association with MCC**. (172 MCC/4164 patients with CLL, SIR 15.7, CI 3.2-46.0).

3. The **complex interplay of immune dysregulation** in CLL patients and **Merkel cell polyomavirus** may explain in part the epidemiological association between B-cell malignancies and MCC

4. **Collision tumor of MCC and CLL/SLL is exceedingly rare**.
   - **Two collision tumors of recurrent or metastatic MCC and CLL/SLL** diagnosed by surgical pathology and cytology, respectively
   - **One collision tumor of primary MCC and CLL/SLL** diagnosed by surgical pathology

Take Home Messages

1. **MCC is a rare, aggressive, cutaneous , neuroendocrine cancer associated with Merkel cell polyomavirus (MCV or MCPyV).** **Five most common clinical features:**
   - older than 50 yo Caucasian
   - in sun exposed site
   - asymptomatic/lack of tenderness
   - rapidly growing nodule or mass
   - immunosuppressed

2. Diagnosis of MCC based on **morphology, immunostains and/or flow cytometry** is required to differentiate it from other SRBCTs.
   MCC is **positive for neuroendocrine markers and cytokeratins** (**CK20 perinuclear dot-like pattern is characteristic** for MCC)

3. **MCC** may present as a **second primary malignancy** associated with other malignancies **such as CLL/SLL, squamous cell carcinoma.**

4. Collision tumor of MCC and CLL/SLL is extremely rare.

5. **Being aware of the entity in a proper clinical context.** A correct diagnosis can be achieved by **application of appropriate ancillary studies**