Diagnostic Slide Session
Case 2015-2

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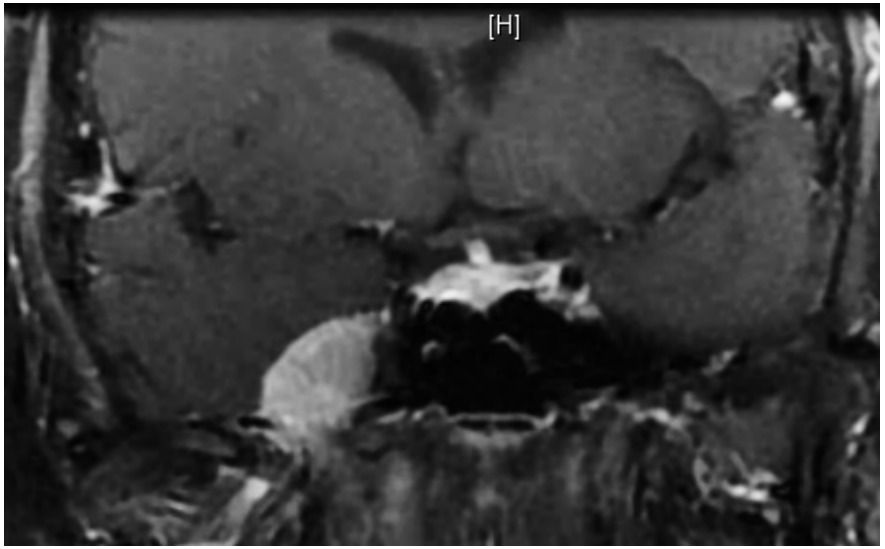
Clinical History:

18 year old woman with right facial pain and hyperalgesia

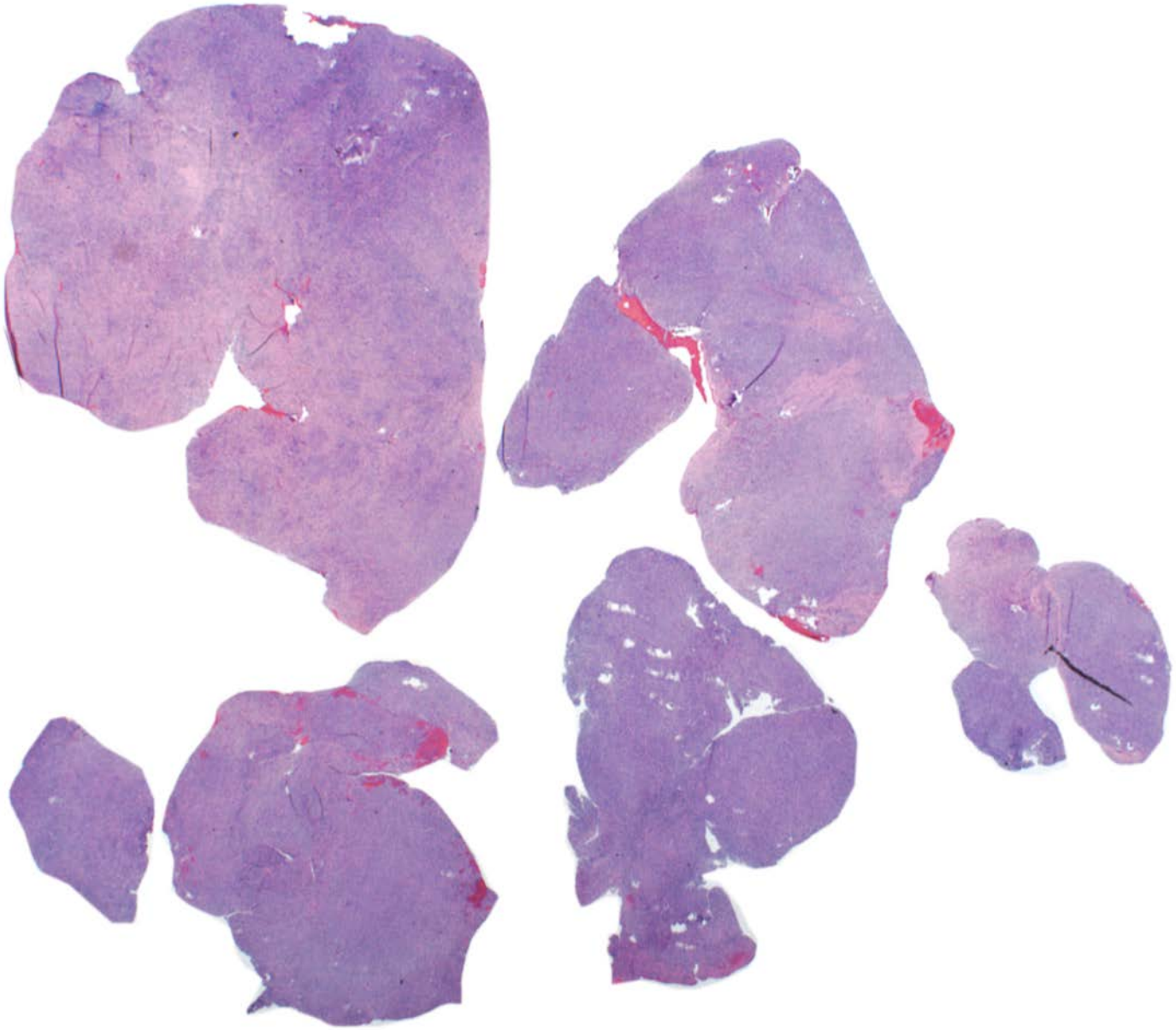
Past Medical History:

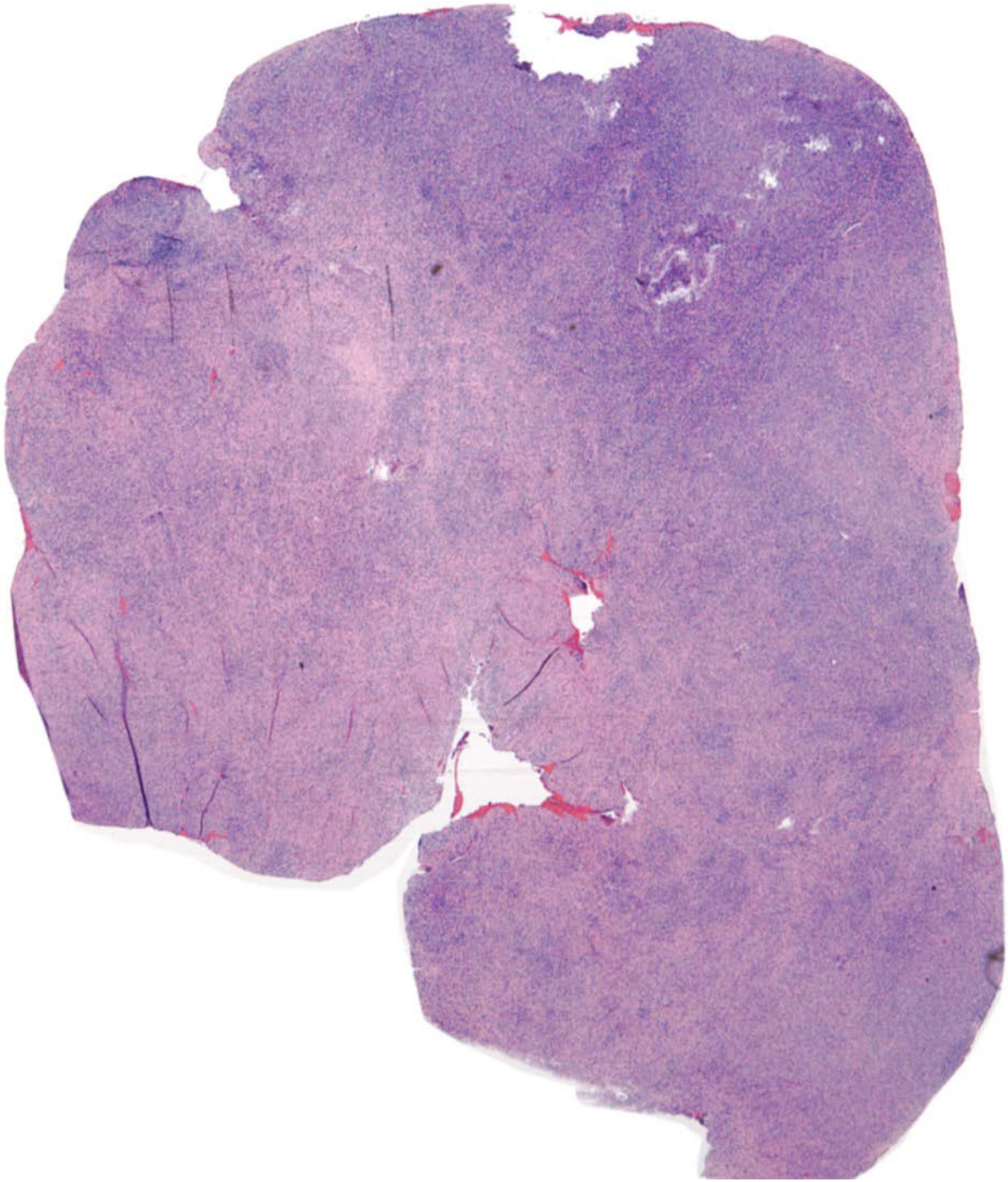
- dilated cardiomyopathy
- pulmonary hypertension
- moderate bilateral hearing loss
- orthotopic heart transplant at 17 years of age complicated by renal insufficiency, DRESS syndrome, pulmonary nocardiosis

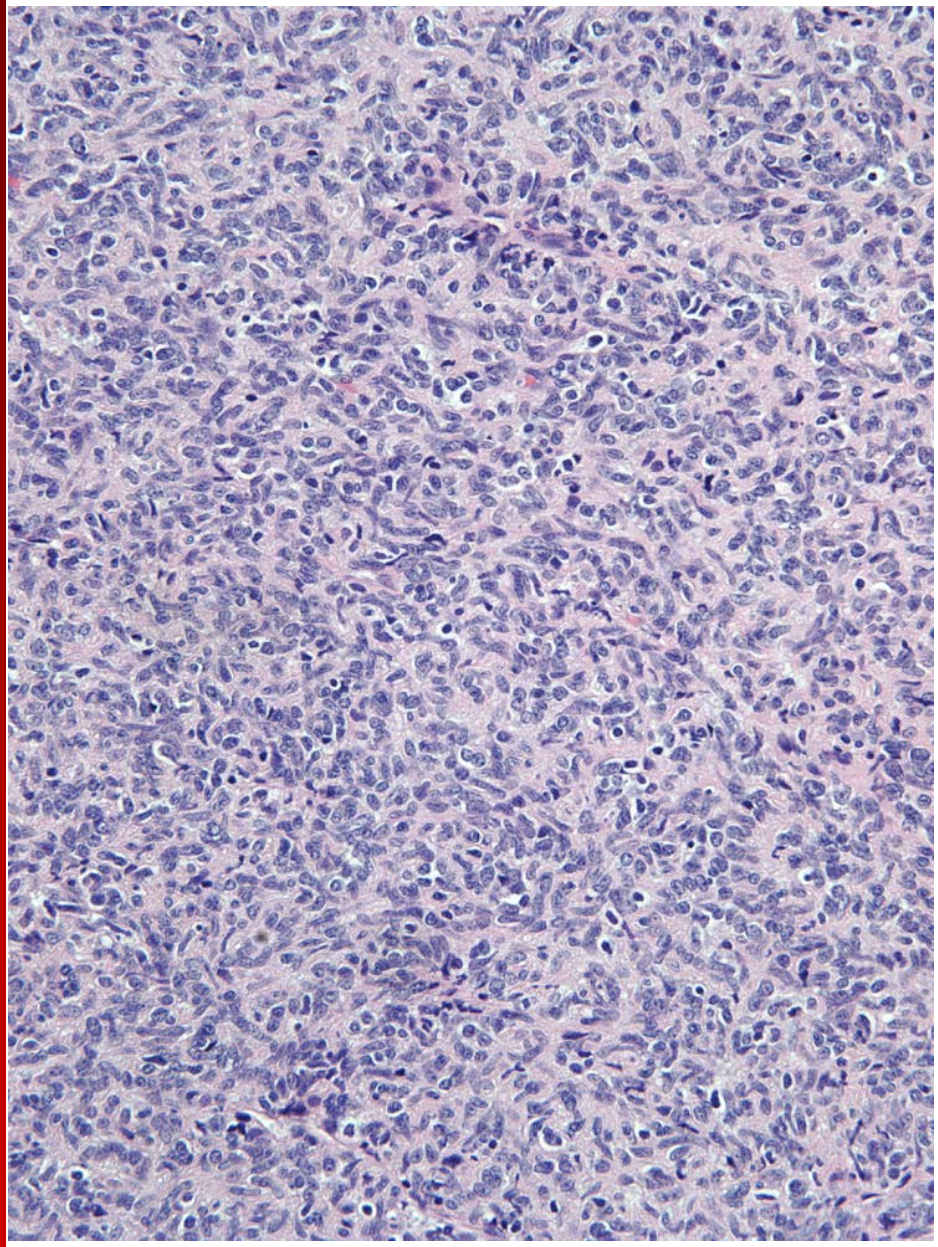
MRI revealed an enhancing, extra-axial, 20mm mass lesion in Meckel's cave. The mass abutted the trigeminal nerve and extended through the foramen ovale.

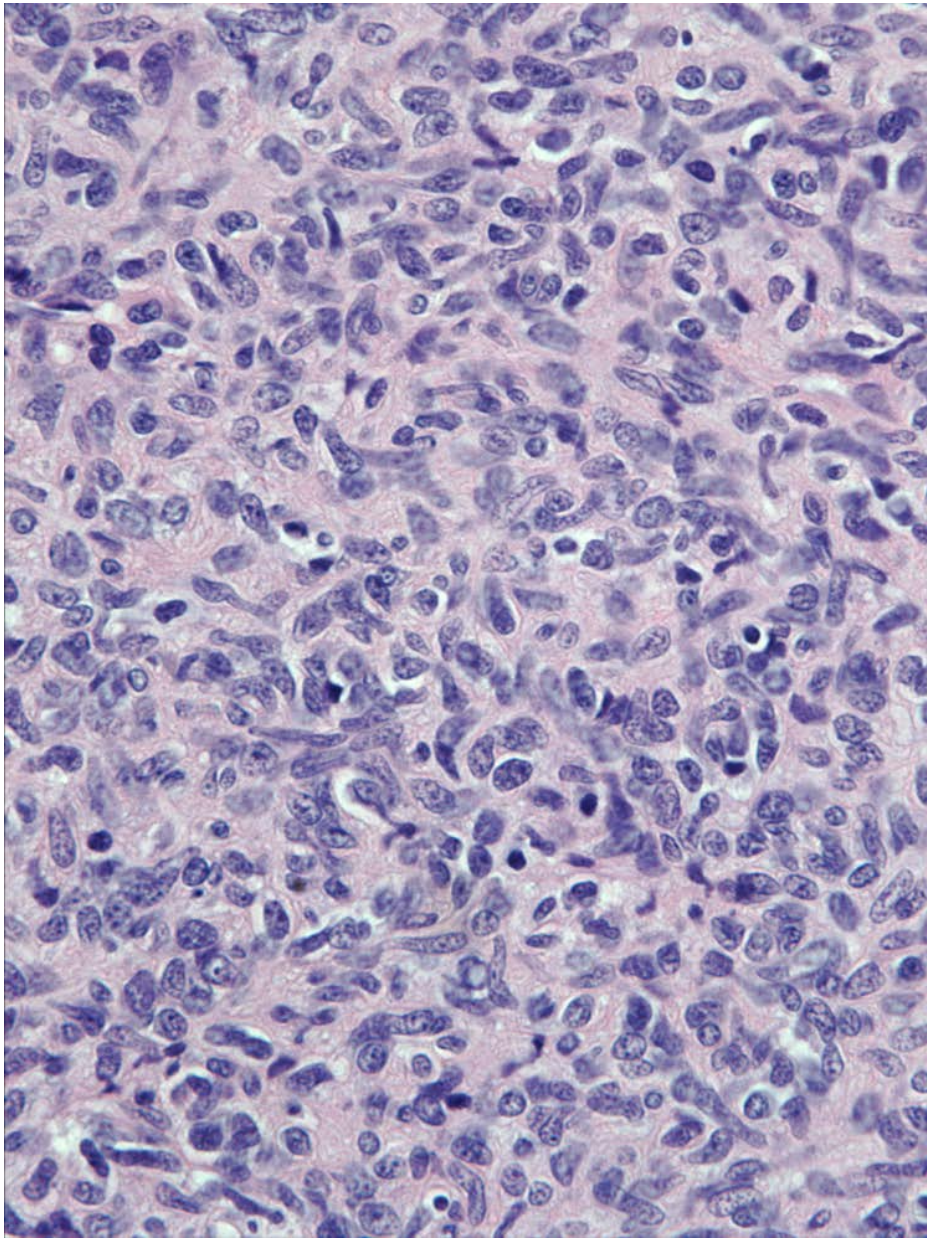


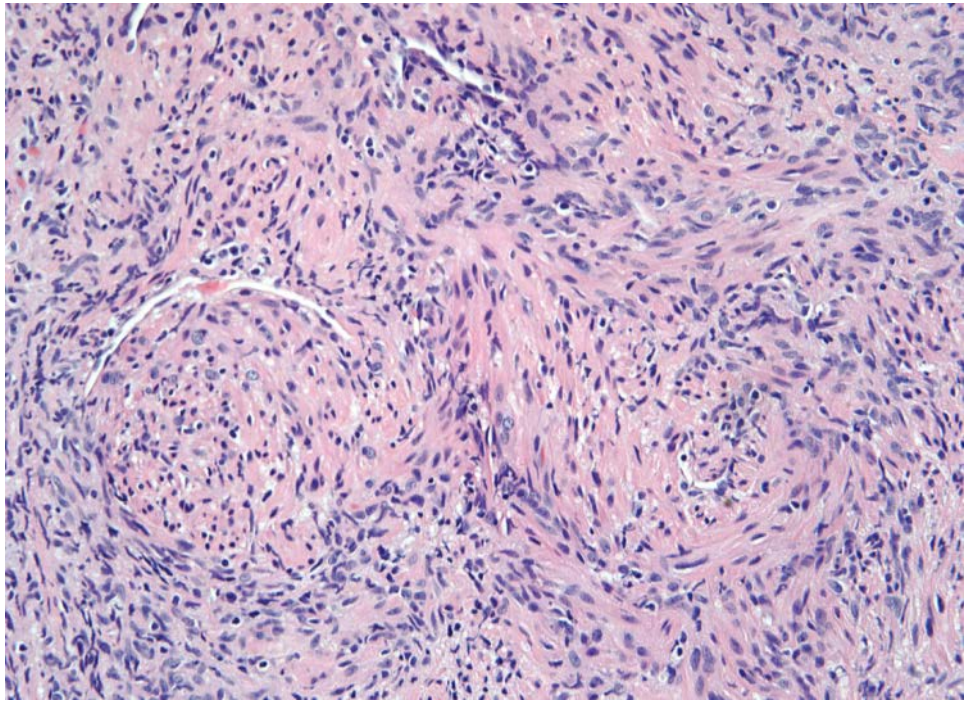
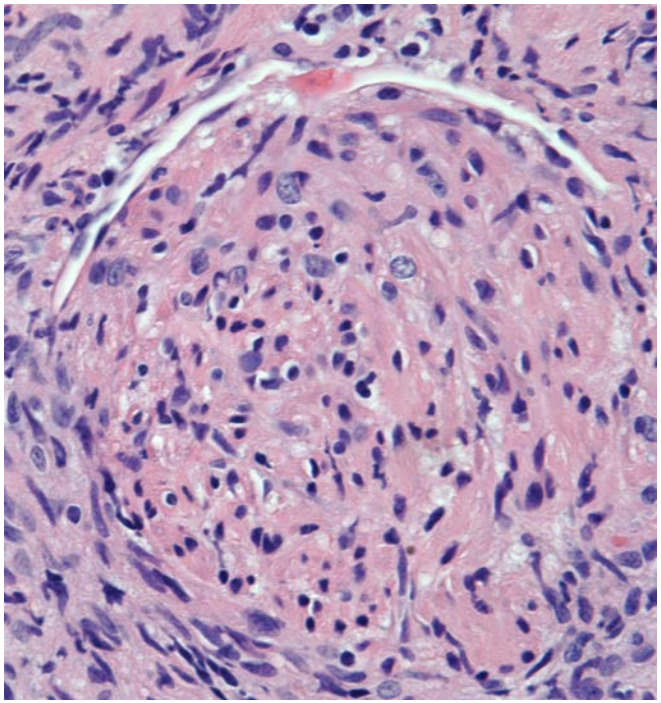
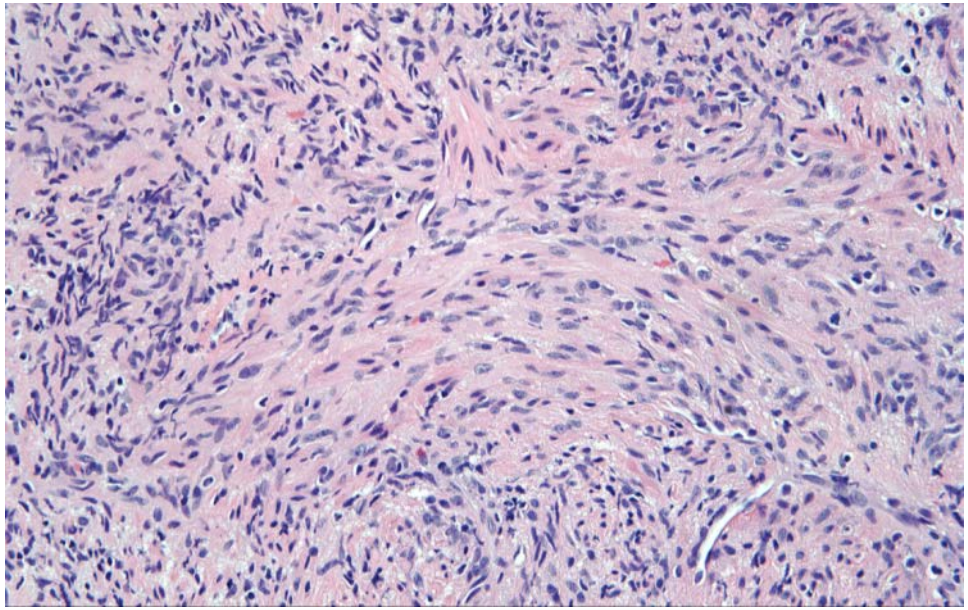
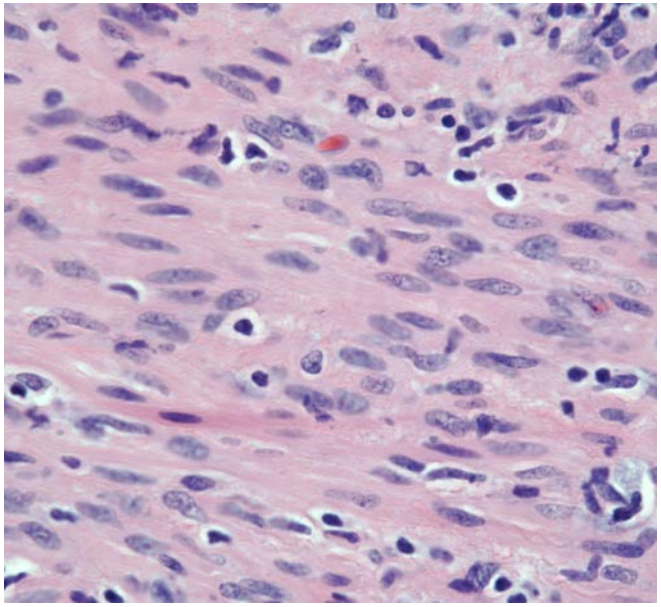
Subtotal Excision



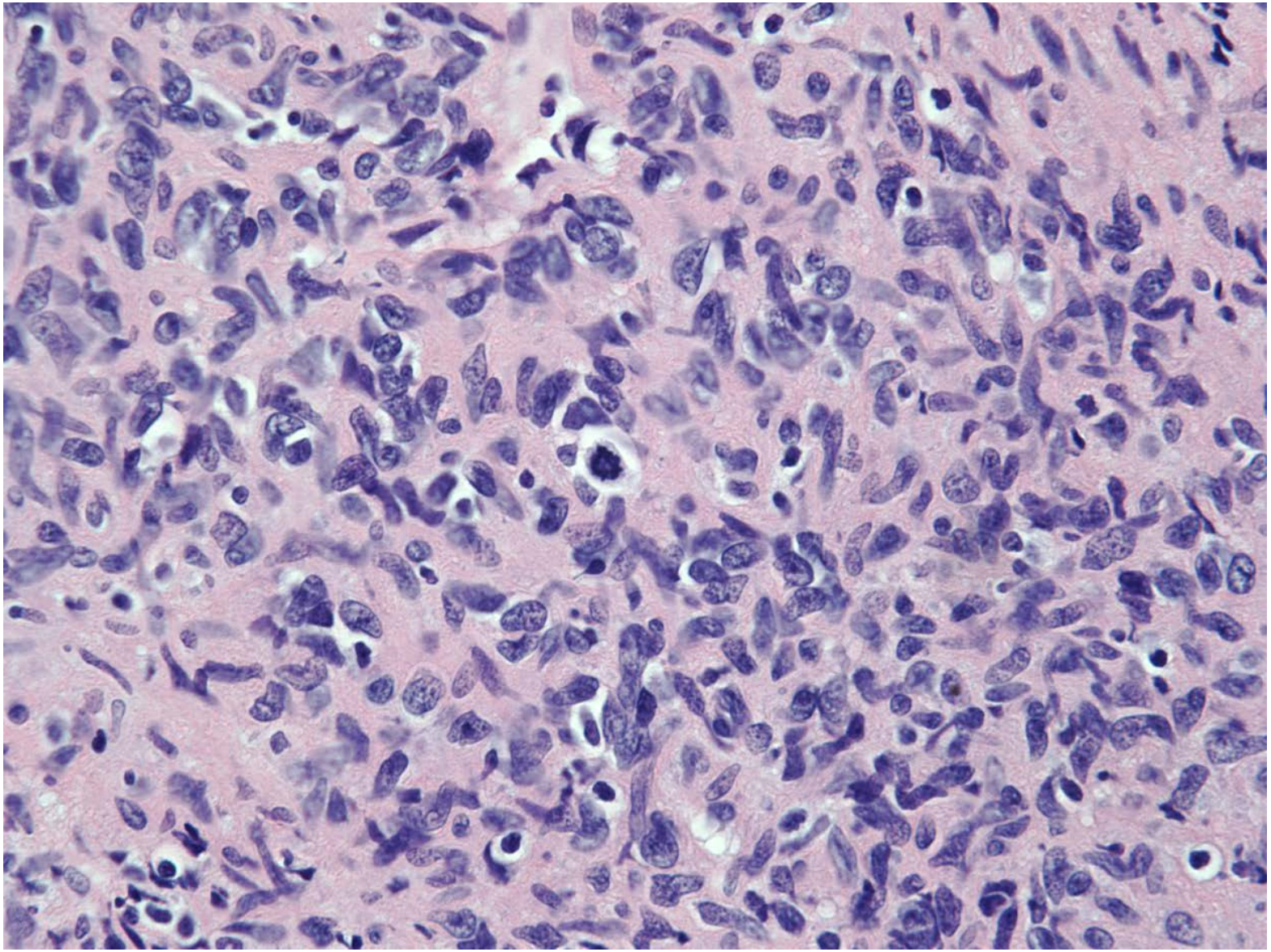






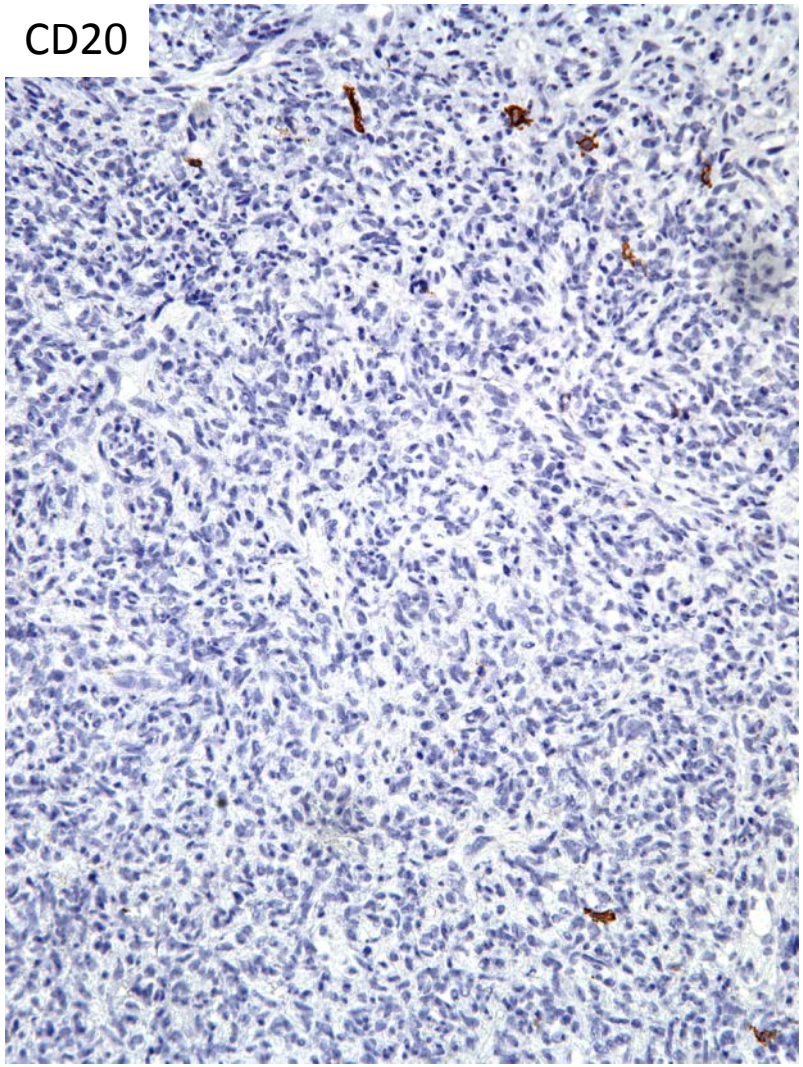





Rare Mitotic Figures

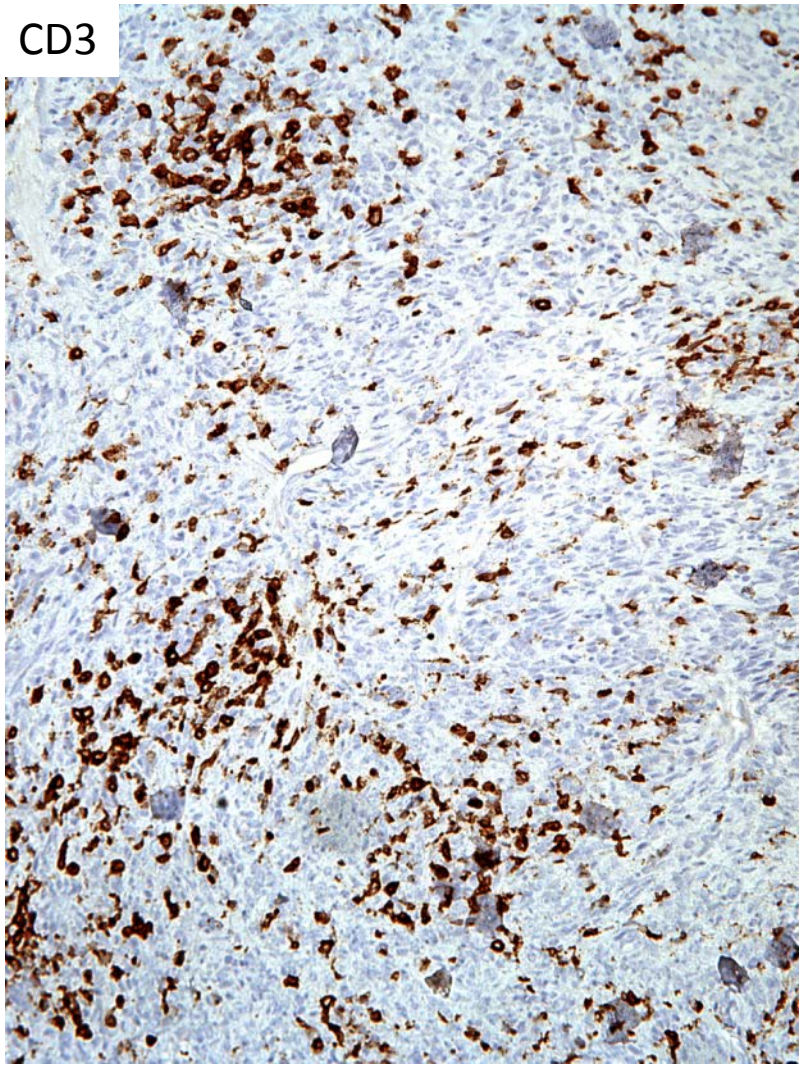


Differential Diagnosis?

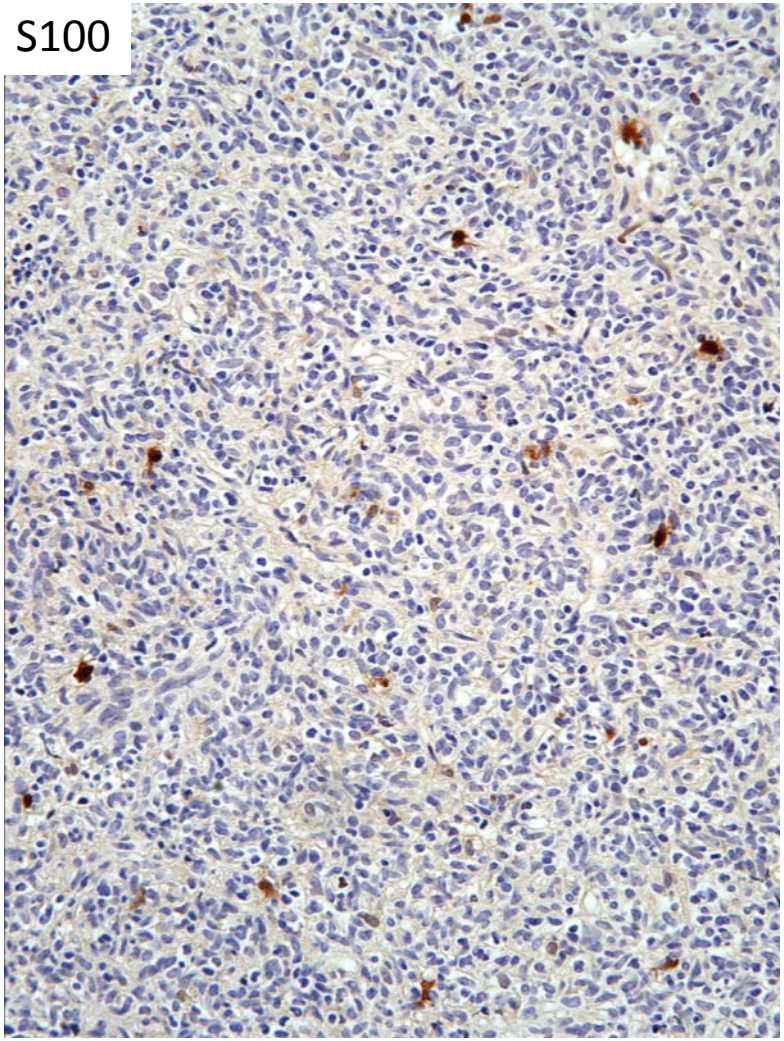
CD20



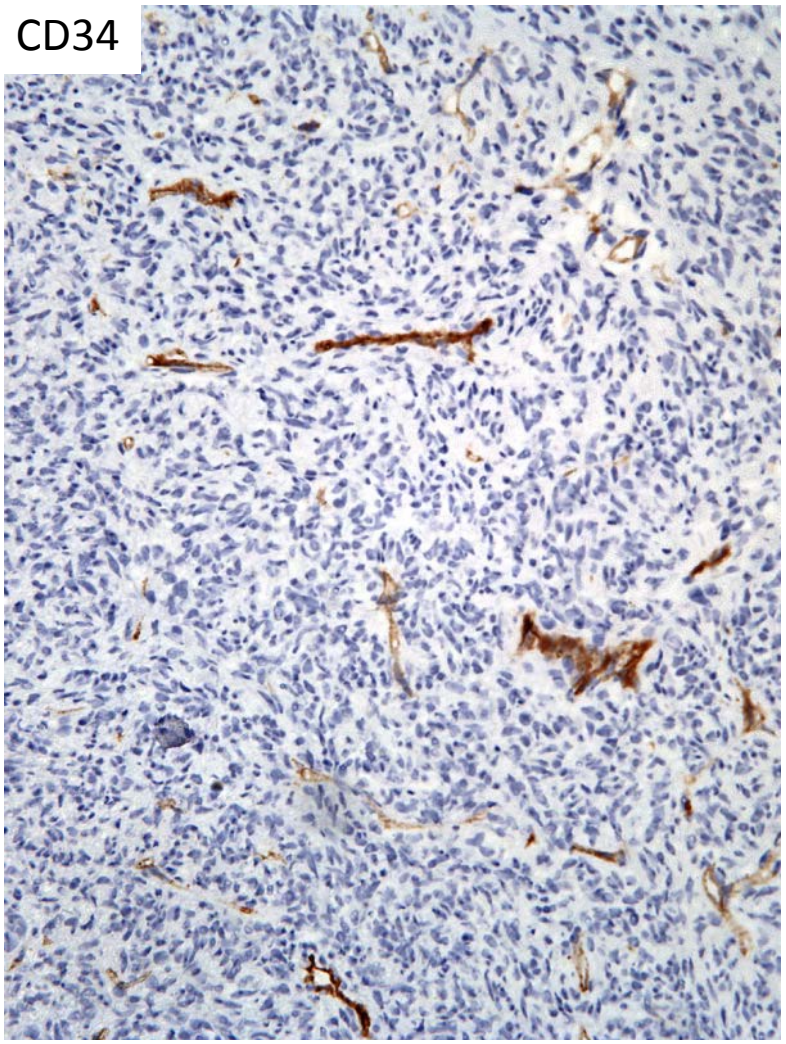
CD3



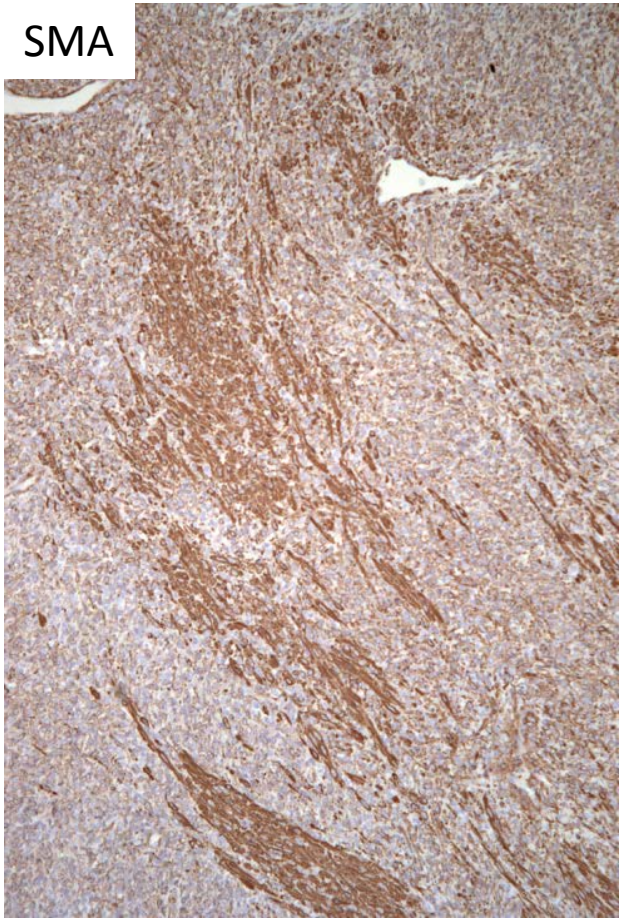
S100



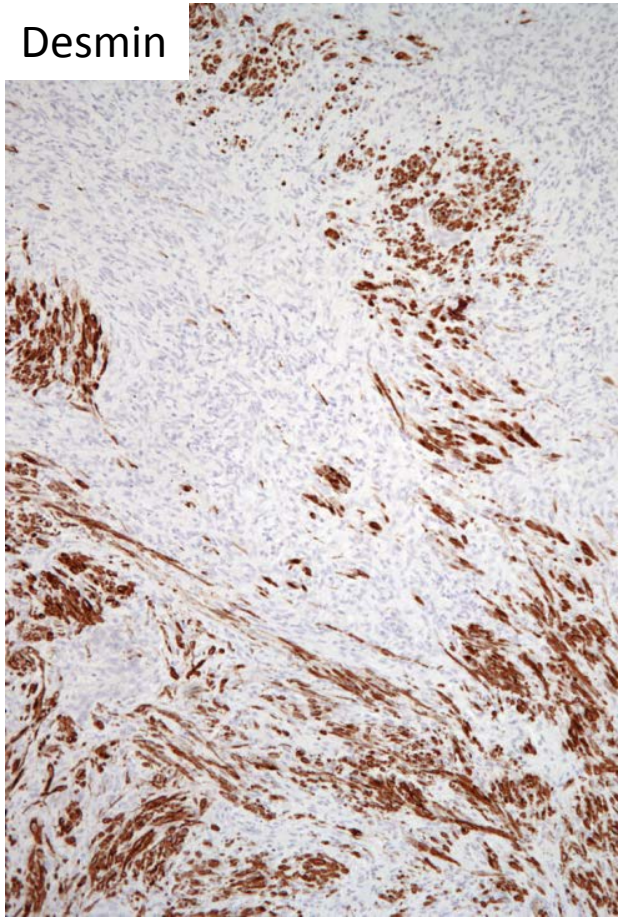
CD34



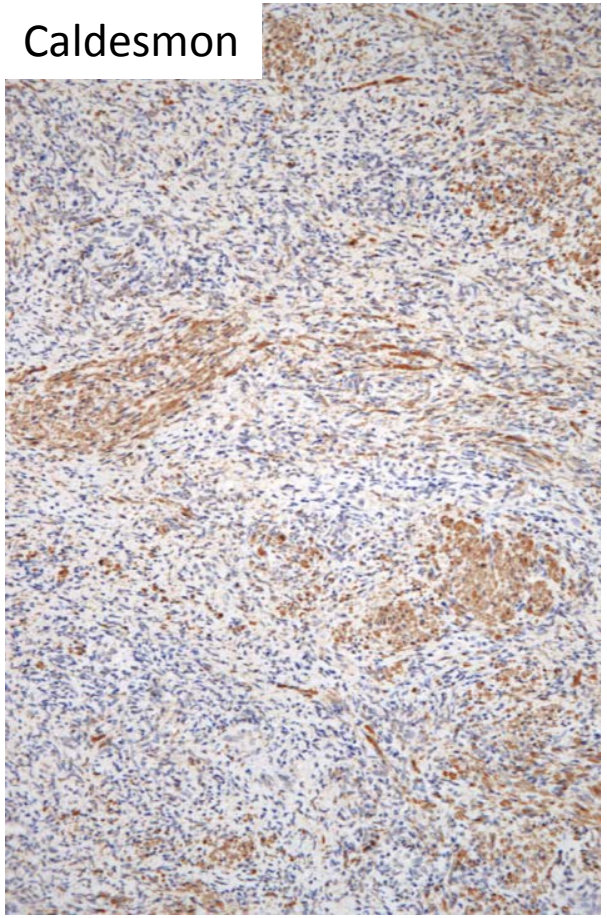
SMA



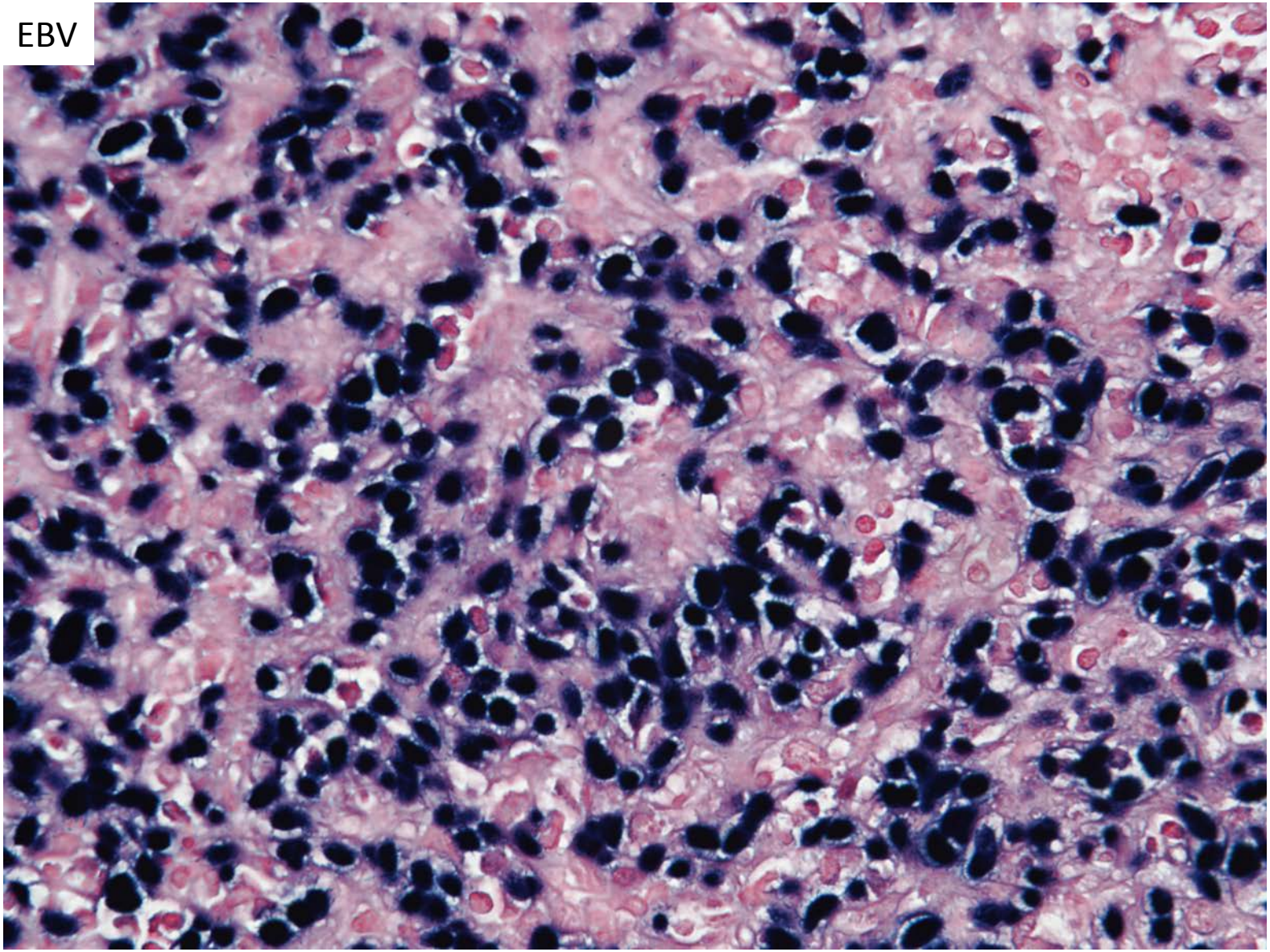
Desmin



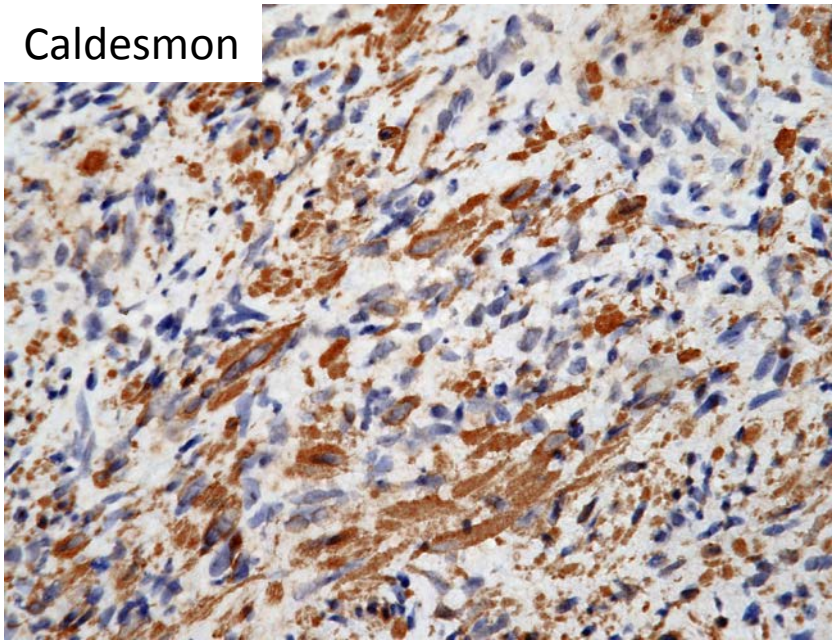
Caldesmon

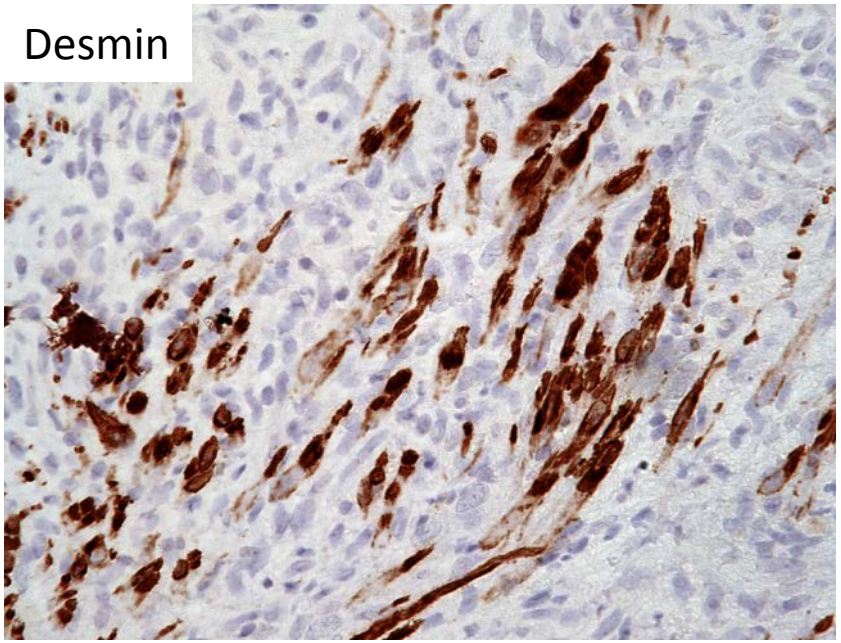


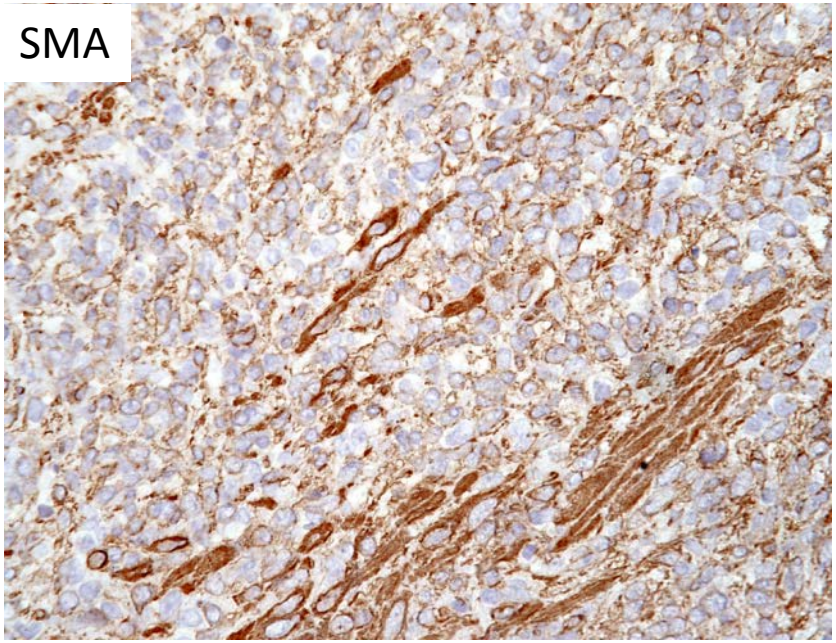
EBV

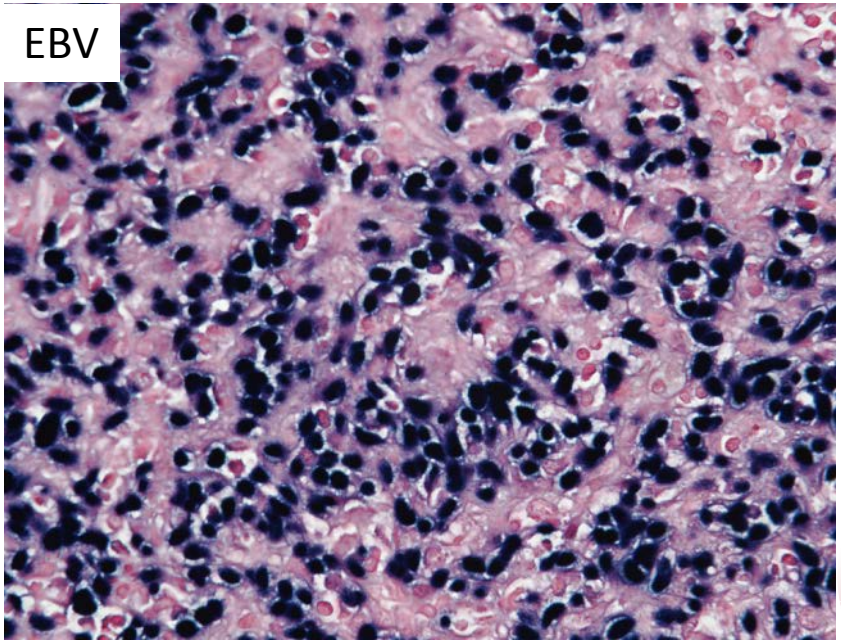


EBV-Associated Smooth Muscle Tumor









Discussion: Clinical and diagnostic features

EBV associated neoplasms:
Burkitt lymphoma, Hodgkin lymphoma, extranodal NK/T cell lymphoma, post-transplant lymphoproliferative disorder, nasopharyngeal carcinoma, gastric carcinoma, and mesenchymal (smooth muscle) tumor.

Historical:
1st recognition of a smooth muscle tumor arising in an immunocompromised patient: 1970
Causative link between EBV and smooth muscle tumors recognized in 1995.

Clinical setting:
Immunosuppression most commonly due to AIDS or transplantation (typically 30-161 months post transplant)
Sites of involvement: liver, kidney, heart, soft tissue, adrenal gland, lung, gall bladder, bone, bladder, spleen, thyroid, and brain

Pritzker KP, et al. Can Med Assoc J. 1970 Dec; 103 (13):1362-5.
Lee ES, et al. N Engl J Med. 1995 Jan;332(1):19-25.
Rogatsch H, et al. Am J Surg Pathol. 2000 Apr; 24(4):614-21.

Discussion: Clinical and diagnostic features

Histologic features:

- Dual population of spindle cells in fascicles and primitive round cells
- T cell infiltrate common
- Variable mitotic rate

Immunohistochemical profile:

- Smooth muscle actin strong and diffuse
- Caldesmon diffuse
- Desmin variable
- CD3 positive T lymphocytes common
- EBV extensive

Discussion: Prognostic features

Histologic features:

-Mitotic figures: Range 0-18 mitotic figures/10 hpfs (average <3/10hpf)
-Necrosis: present in a small subset
-Myxoid change: focally present in half of cases
-Nuclear pleomorphism: mild-moderate

TABLE 2. EBV Smooth Muscle Tumors: Histologic Features

Case No.	Site	Mitoses/10 HPF	Necrosis	Lymphocytes	Pleomorphism	Myxoid	Cell Shape	EBER	SMA	Desmin
1	Lung	1.8	No	Few	Mild	No	R/S	Positive	Positive	Negative
	Vocal cord	11	No	Few	Mild	No	R	Positive	Positive	Negative
	Extradural	1.8	No	Few	Moderate	Focal	S	Positive	Positive	Positive

Deyrup AT, et al. Am J Surg Pathol. 2006 Jan;30(1):75-82.

Discussion: Prognostic features

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Features used to differentiate ordinary leiomyoma from leiomyosarcoma have not been shown to have prognostic significance.

Deyrup AT, et al. Am J Surg Pathol. 2006 Jan;30(1):75-82.

Discussion: Prognostic features

Multi-focality:
Greater than 50% of patients present with multiple EBV-SMT, originally interpreted as evidence for metastatic disease

EBV molecular studies to address address clonality
-relative number of Long Terminal Repeats
-EBV copy number

Discussion: Prognostic features

Multi-focality:
Greater than 50% of patients present with multiple EBV-SMT, originally interpreted as evidence for metastatic disease

EBV molecular studies have shown evidence for independent infection events

-relative number of Long Terminal Repeats

-EBV copy number

TABLE 3. EBV Smooth Muscle Tumors: Molecular Analysis

Case No.	Site	Relative No. of LTR	EBV Genomes/Cell
1	Extradural	1.99	2.94
	Lung	1	106.76
2	Bladder	ND	10.14
	Small bowel	ND	1.00
5	Nasopharynx	1	9.89
	Right tonsil	2.79	16.03
	Left tonsil	1.02	7.24
8	Liver	ND	3.30
9	Spinal cord	1	24.63
	Gallbladder	7.04	12.09

Deyrup AT, et al. Am J Surg Pathol. 2006 Jan;30(1):75-82.

Clinical follow-up

The EBV-SMT grew to fill in the resected space. Immunosuppression was decreased and follow-up cardiac biopsies demonstrated moderate acute cellular rejection. Immunosuppression was increased and therapy is now focused on pain control.

Conclusions

Consider EBV-SMT in immunosuppressed patients with spindle cell neoplasms.

EBV-SMT characterized by mixed round cell and spindle cell components, diffuse positive staining for SMA, variable desmin staining, and T cell infiltration.

Usual histologic features used to predict ordinary smooth muscle tumor prognosis do not apply to EBV-SMTs.

The presence of spatially segregated EBV-SMTs is correlated with separate infection events and does not indicate metastatic disease.

Thank You