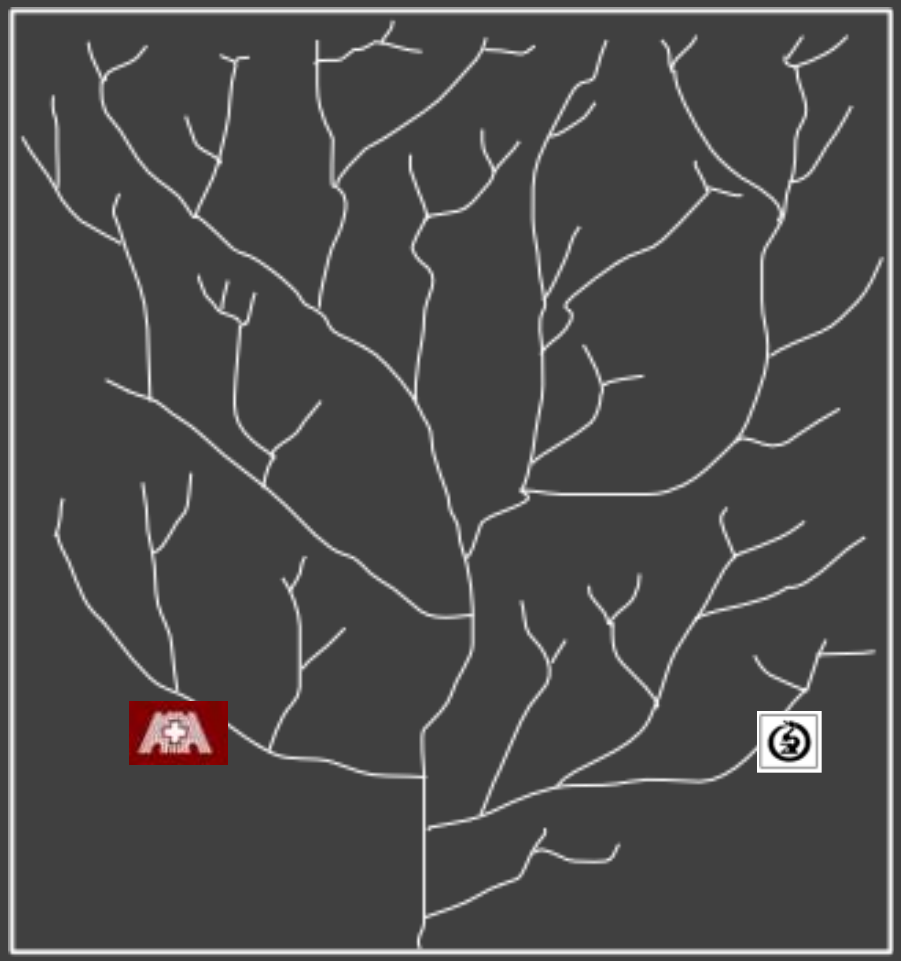


Dendritic and histiocytic cell tumors

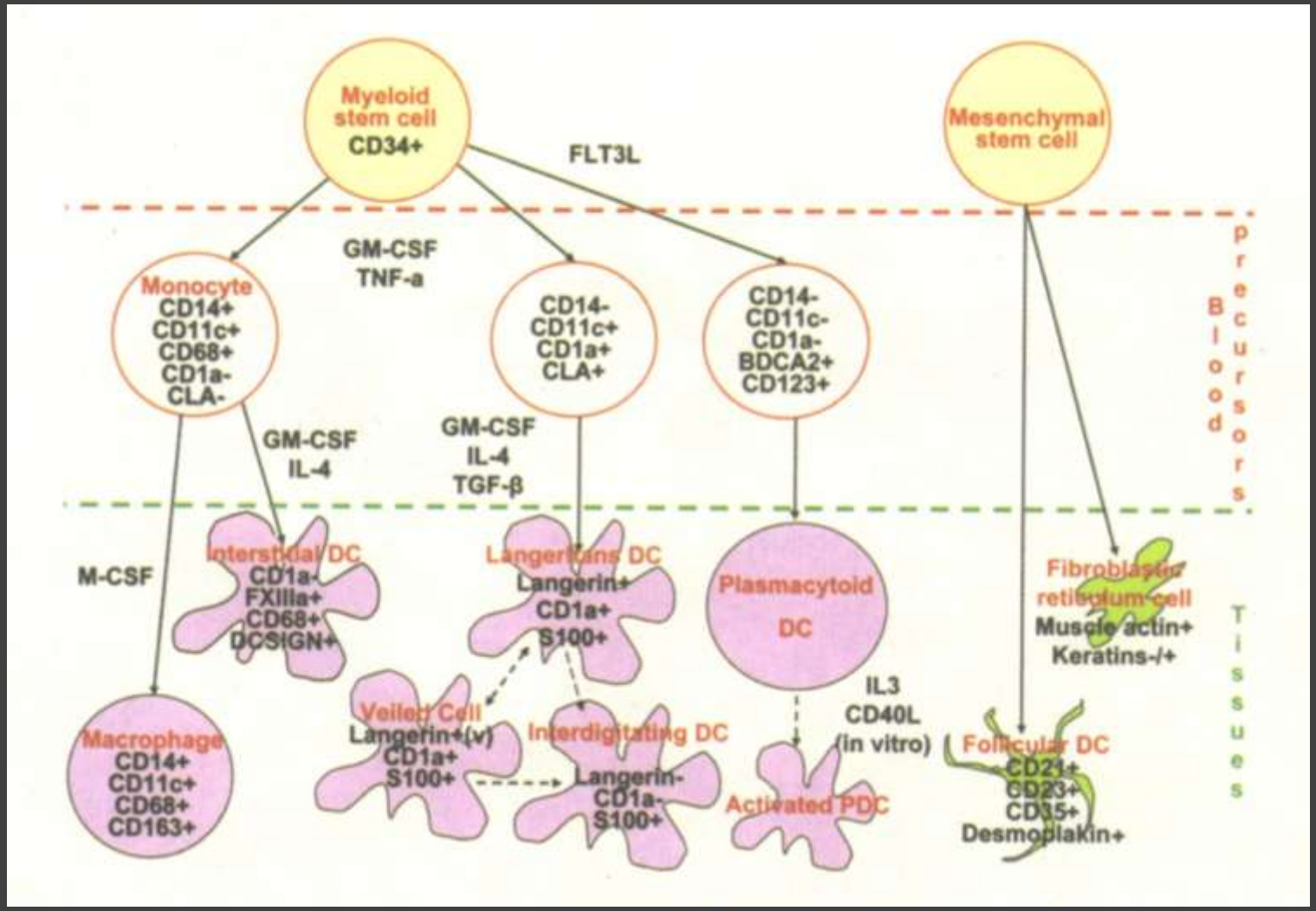
in hemato (patho) logy LT

K. Andrekutė, U. Mickys, 2010

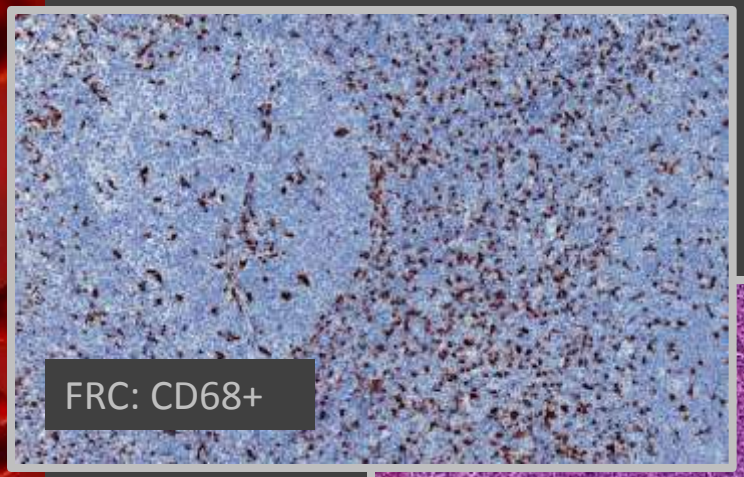
“We are not talking about the facts, but interpretations and interpretations of interpretations only...”

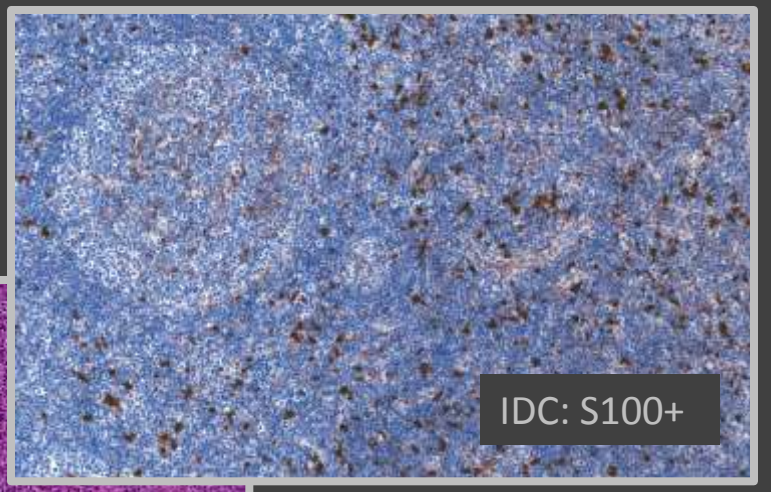
F. Skårderud

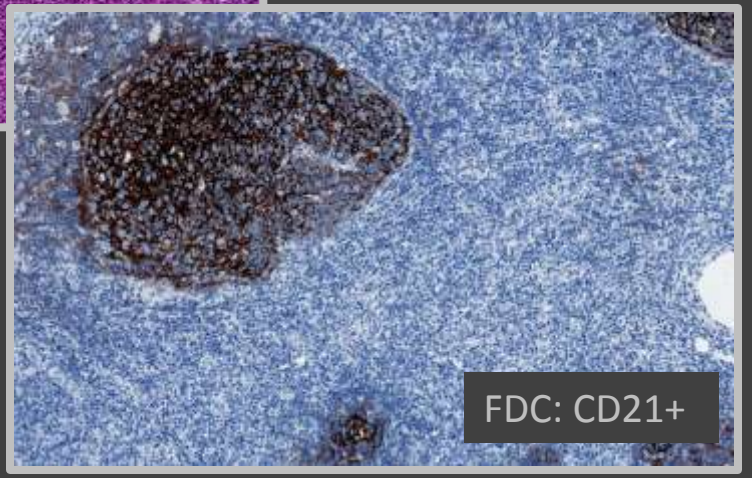
D/H cells and related tumors (WHO 2008)



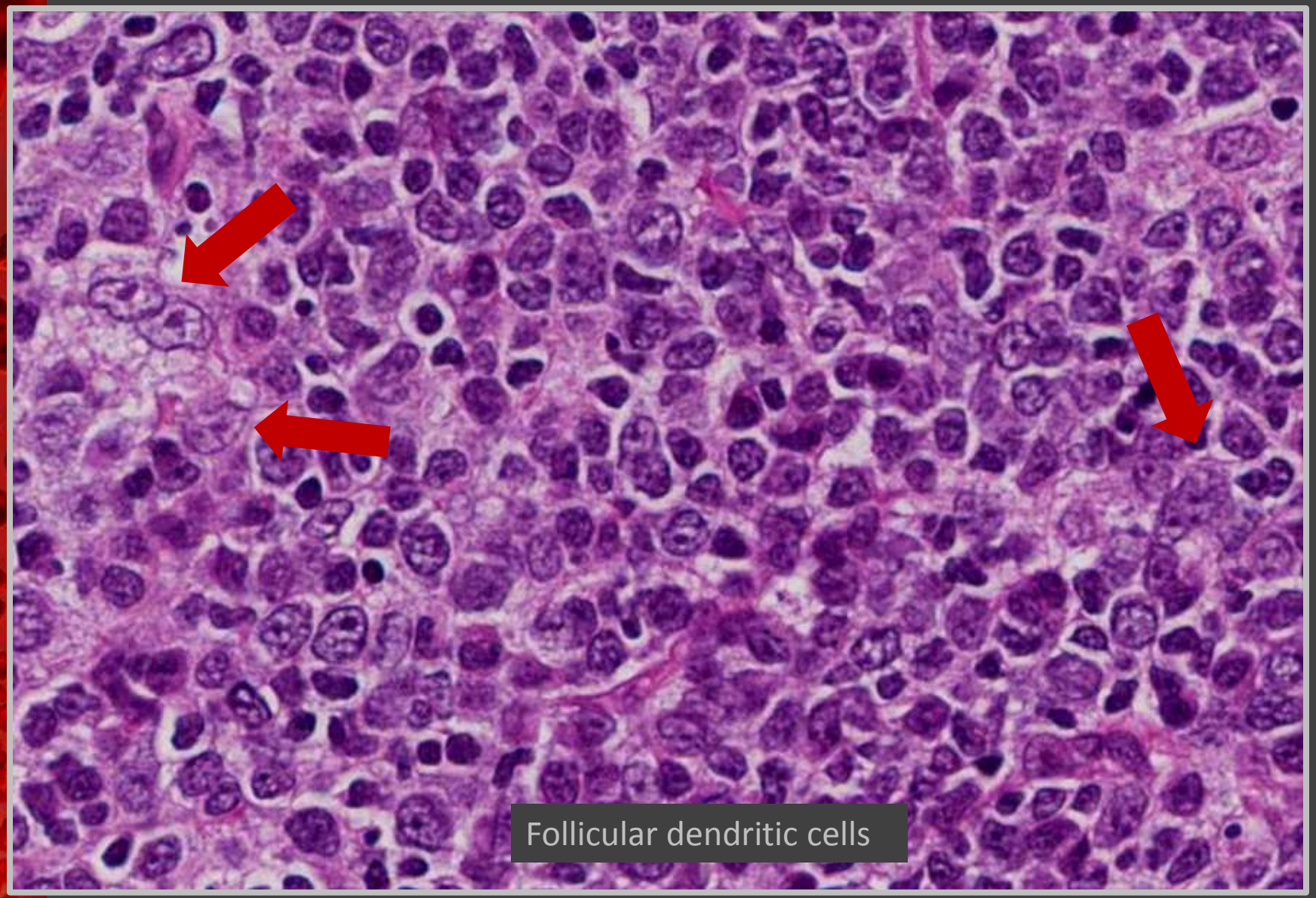
Reactive lymphadenopathy

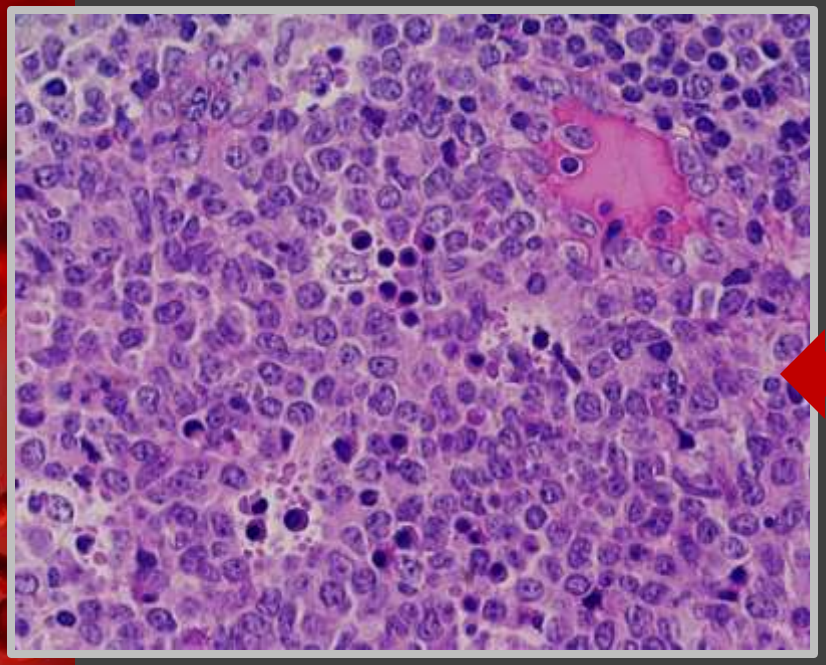


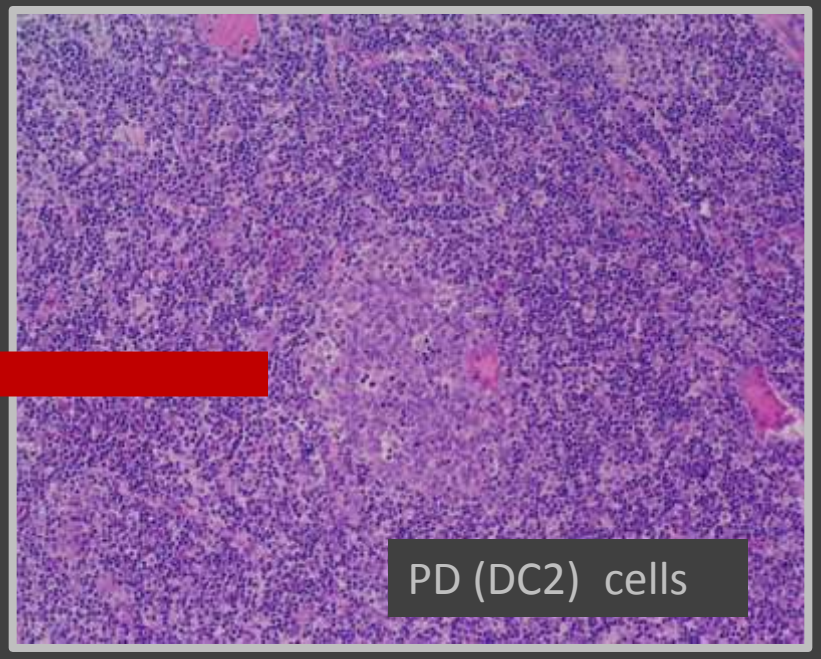


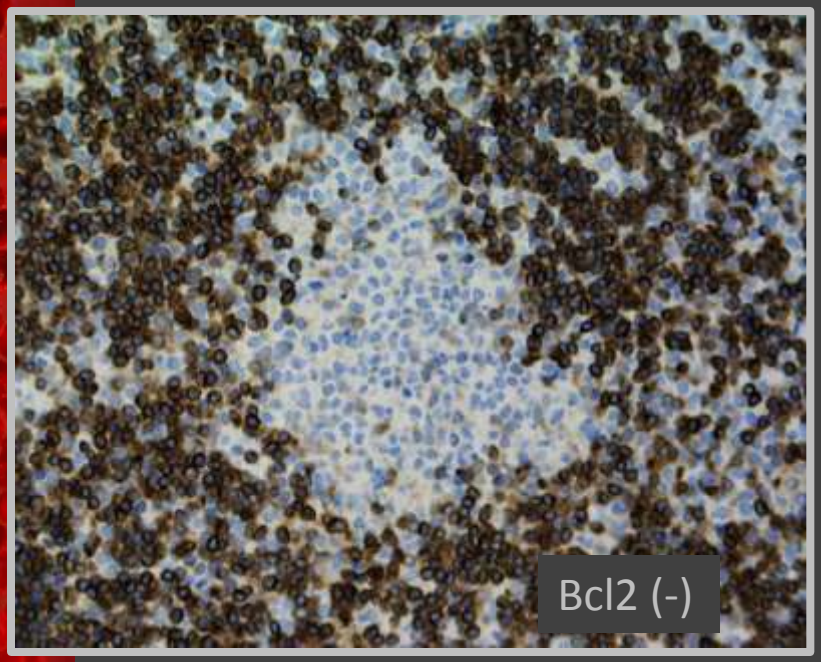


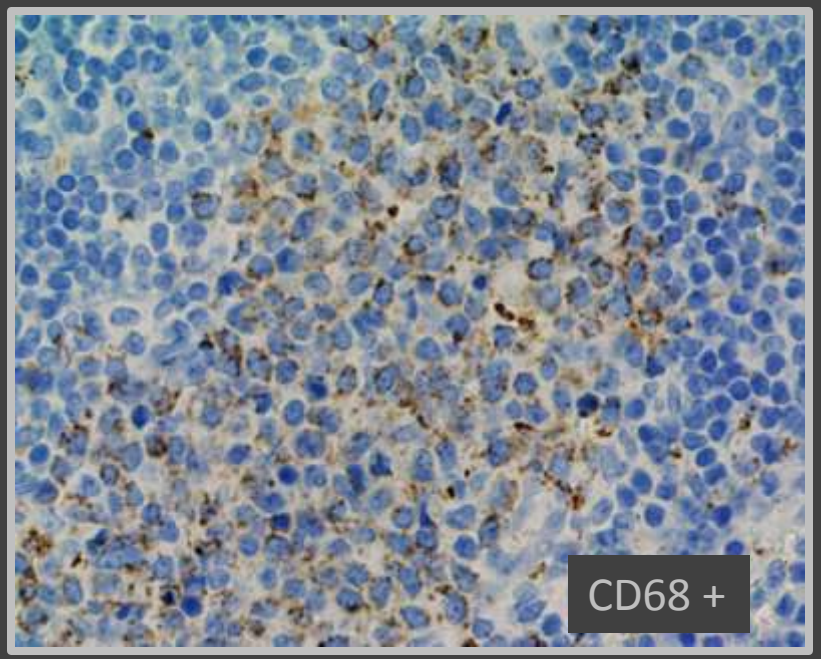
Center of lymphoid follicle






PD (DC2) cells


Bcl2 (-)


CD68 +

D/H cells and related tumors: IH

IH	LC	IDC	FDC	PDC	Ma	DIDC	FRC
CD1a	++						
CD4	+			+	+	+/-	
CD21			++				
CD23			++				
CD35			++				
CD68	+/-	+/-		++	++	+	
CD123				++			
S100	++	++	+/-		+/-	+/-	
Fascin		++	+/++		-/+	+	
Langerin	++						
Lysozyme	+/-				+		
TCL1				+			
PanCK							+
Asm Actin							+

Histiocytic and dendritic cell tumors (WHO 2008)

- Histiocytic sarcoma
- Langerhans cell... :
  - histiocytosis
  - sarcoma
- Interdigitating cell sarcoma
- Follicular dendritic cell sarcoma
- Other:
  - Fibroblastic reticulum cell tumor
  - Indetermined cell dendritic cell tumor (skin)
  - Rosai- Dorfman disease
- Disseminated juvenilie xantogranuloma (JXG)

Case #2

Heterogeneity in "GIST"

Case #2 was presented in Hemato- Onco- Pathology meeting "GIST and GIST like tumors" in Vilnius, 2009

#2

Case #2

60-year-old women first presented with abdominal pain in 2003.

3 years later an abdominal CT scan: the tumor of jejunum: the patient refuses the treatment.

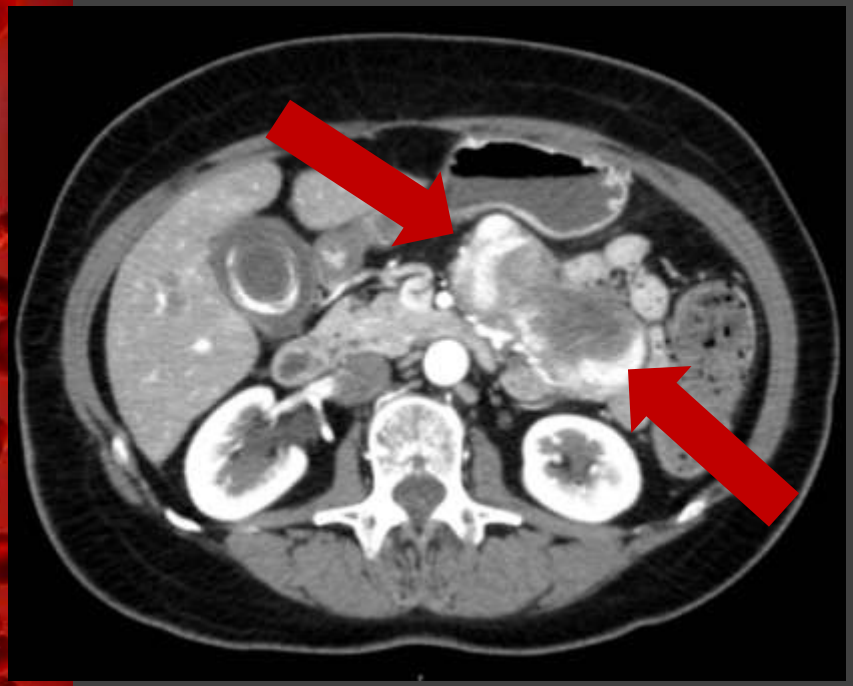
In April of 2009 the pain increased and the weight loss appeared. Abdominal CT scan: the tumor increased in size and mesenterial lymphadenopathy.

Soon after the jejunal tumor was resected.

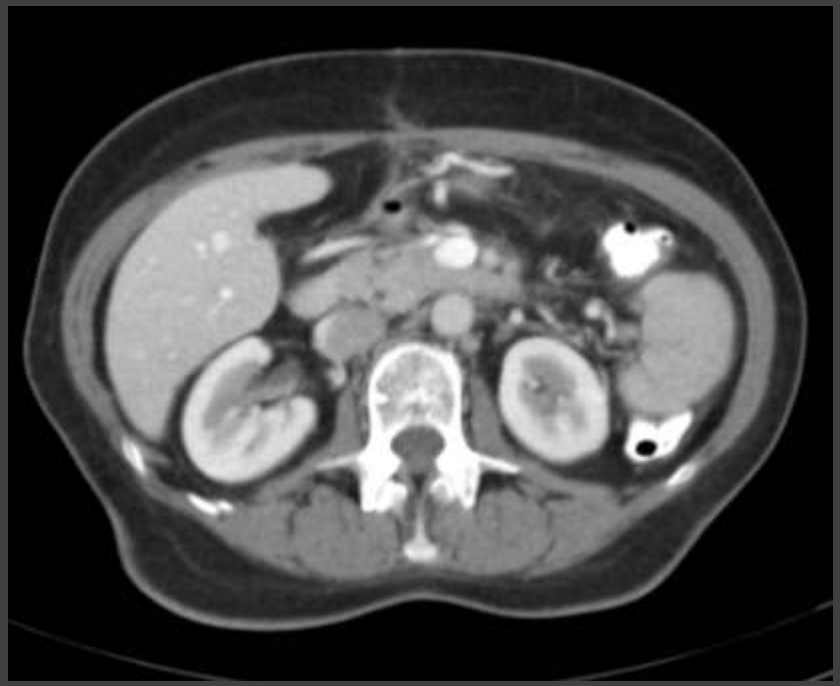
Macro: the 6,5x3x6 cm lobated bright brown tumor in the muscularis propria.

The primary pathologic diagnosis: “high risk GIST CD117(-)”.

Case #2

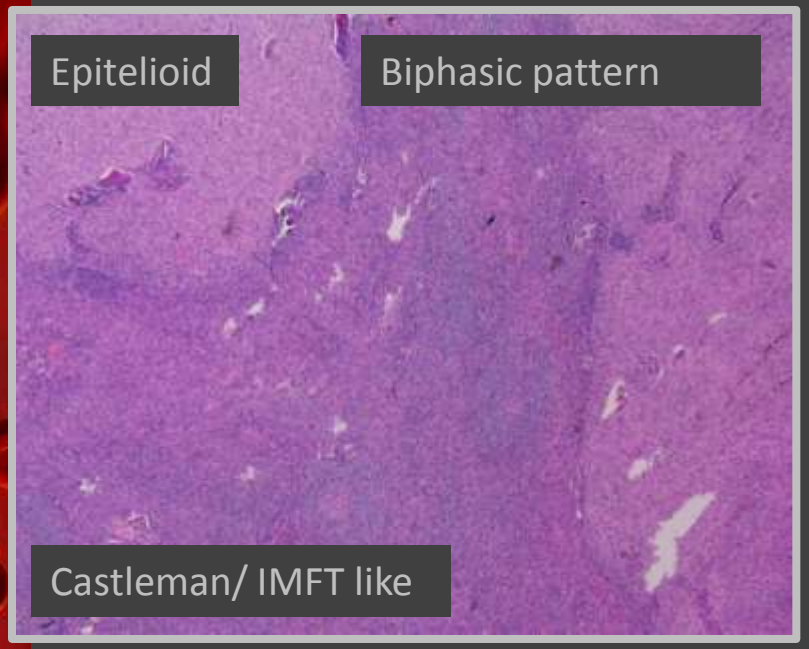


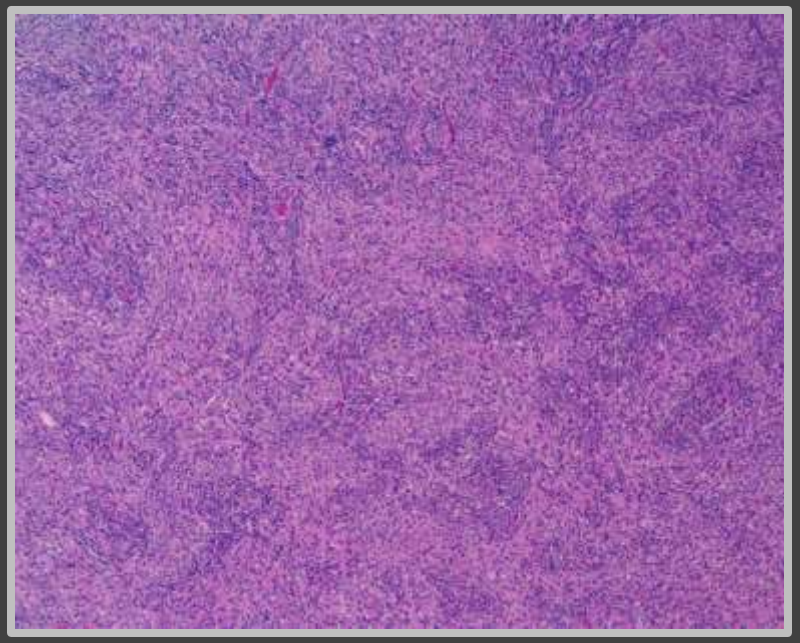
Before



After

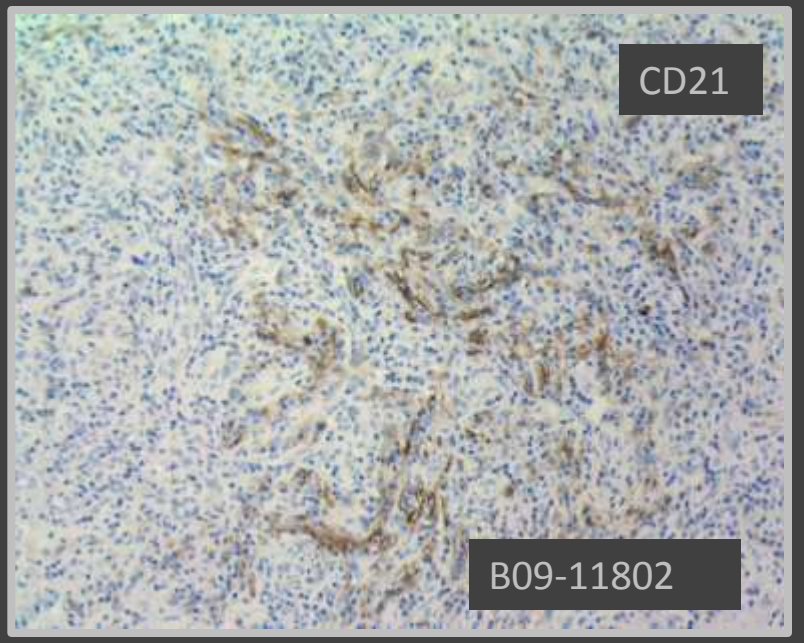
#2

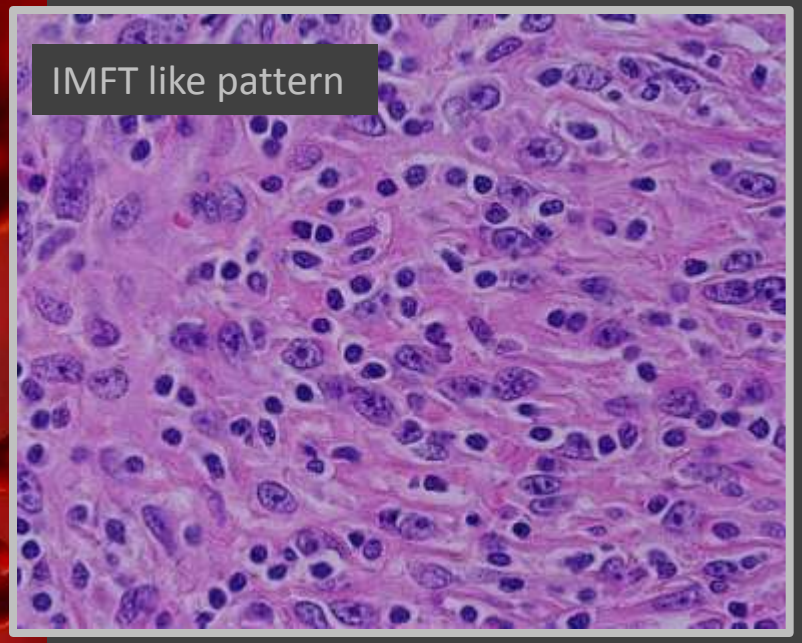

Epitelioid
Biphasic pattern
Castleman/ IMFT like

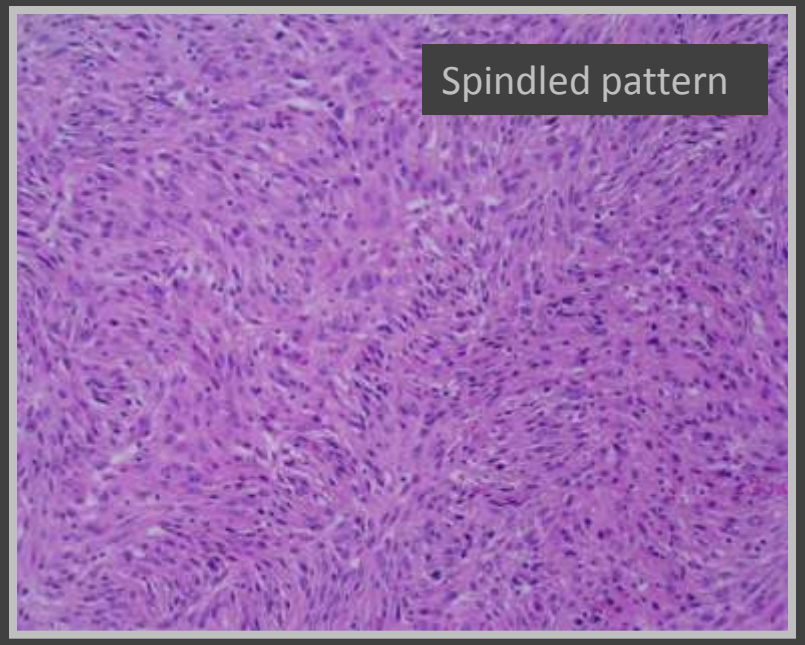


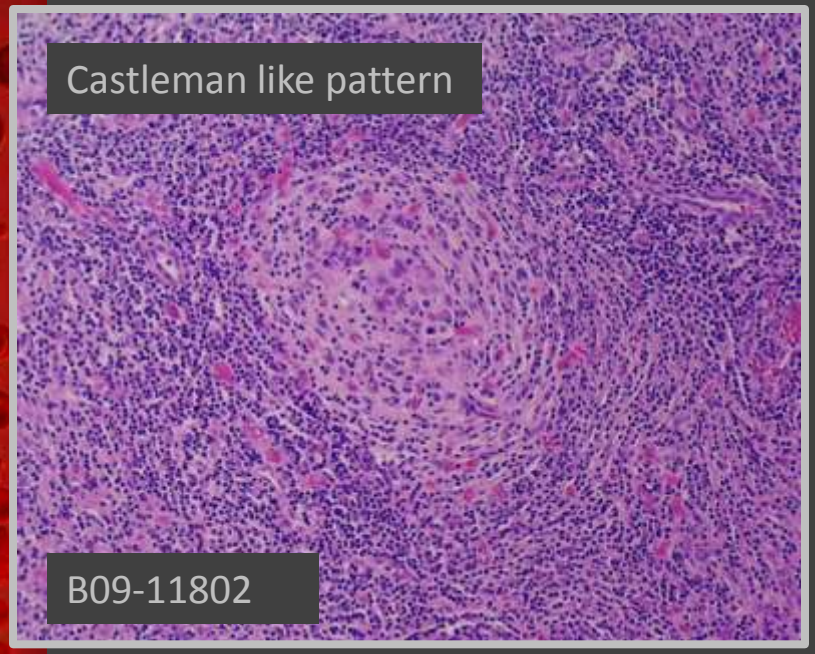

Sclerosis

#2

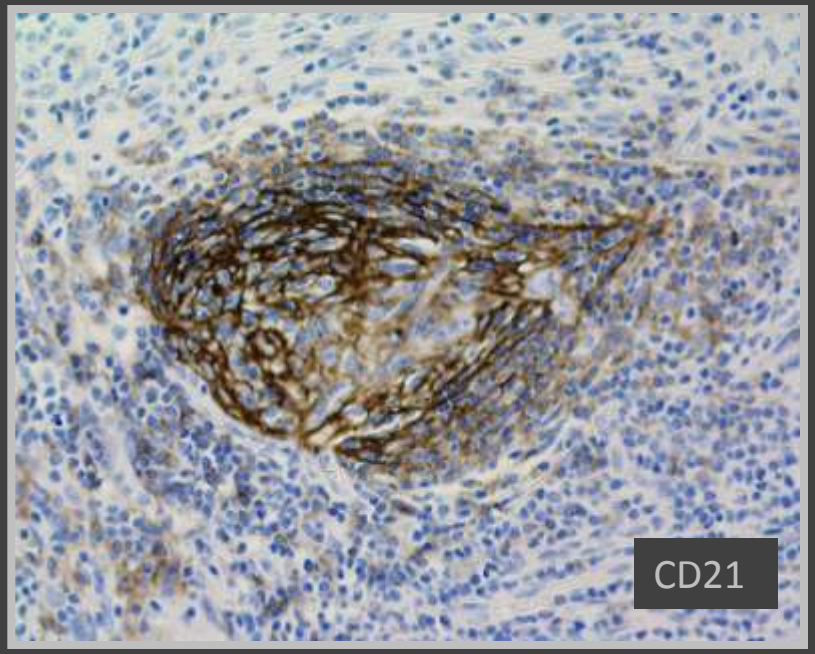

CD21
B09-11802

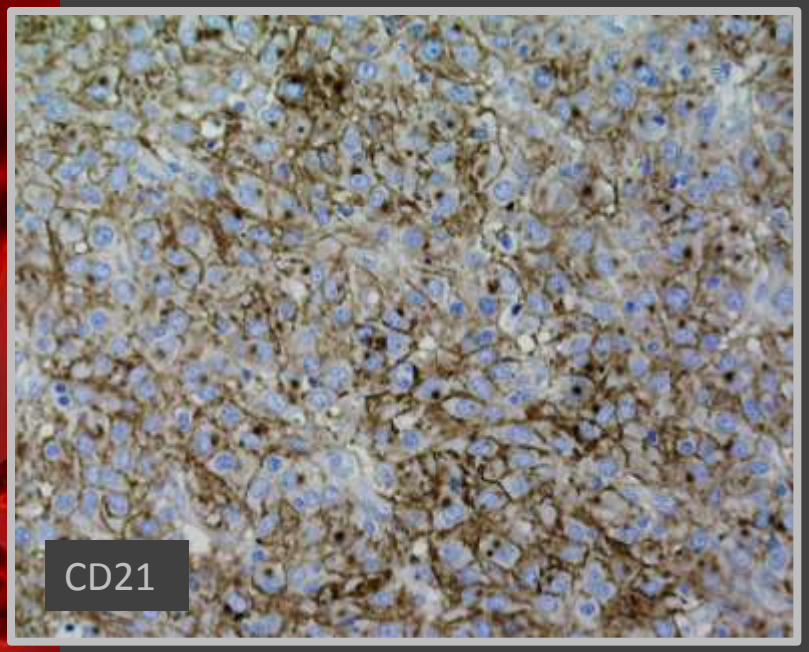

IMFT like pattern

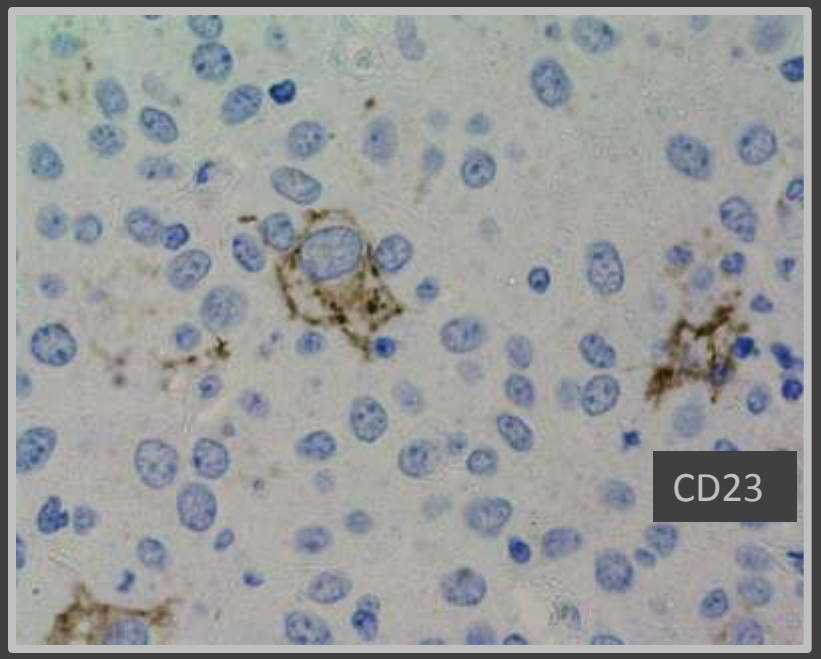

Spindled pattern

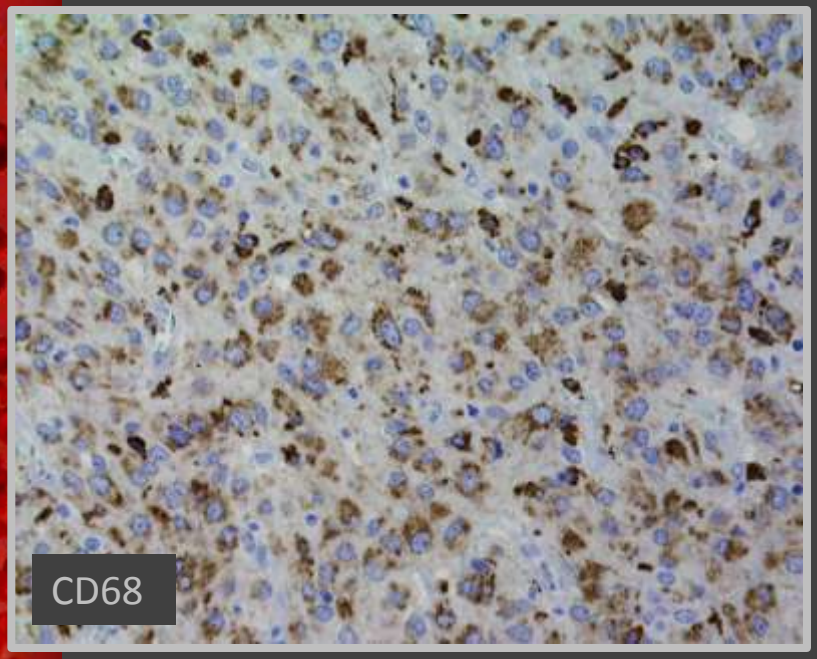

Castleman like pattern
B09-11802

#2

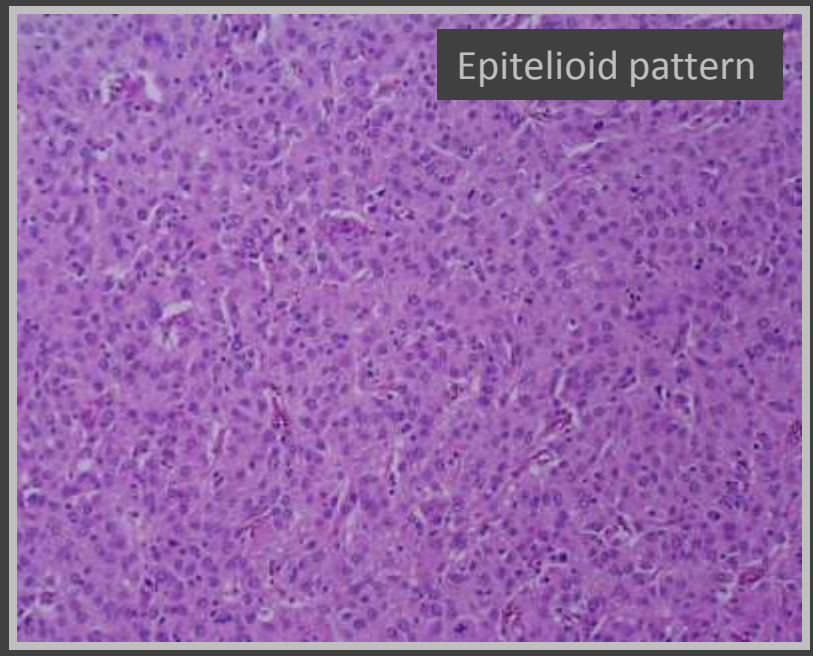

CD21







#2



Case #2

IH 1 (Vilnius): CD21, CD68 (epithelioid pattern), Vimentin positive; CD23 single cells positive (epithelioid pattern); CyclinD1, EMA positive, CD117, CD34, Asm Actin, Desmin, S100, Pan CK, ALK1, CD20, CD3, EBV LMP1, LCA, Bcl2, CD5, CD1a negative. Ki67 proliferative index was high up to 40% (epithelioid pattern). Mitoses ~ 25/ 10HPF.

The patient didn`t receive any adjuvant treatment and is on follow up for 11 months with no evidence of disease progression.

IH 2 (Basel) : DOG1(-), CD43(-)

Case was discussed in telepathology group: INCTR Hematopathology Forum: https://www.ipath-network.com/ipath/object/view/11610

and consulted by dr.A.Tzankov, dr.S.Dirnhofer (Basel Uni, Swiss)

Case #2

Differential diagnosis:

1. GIST CD117(-);
2. Inflammatory myofibroblastic tumor (ALK1(-); age)
3. Other?

D/H cells and related tumors: IH

IH	LC	IDC	FDC	PDC	Ma	DIDC	FRC
CD1a	++						
CD4	+			+	+	+/-	
CD21			++				
CD23			++				
CD35			++				
CD68	+/-	+/-		++	++	+	
CD123				++			
S100	++	++	+/-		+/-	+/-	
Fascin		++	+/++		-/+	+	
Langerin	++						
Lysozyme	+/-				+		
TCL1				+			
PanCK							+
Asm Actin							+

FDC sarcoma

- Median age 44 yrs.
- F/M ~1/ 1 (F > IMFT like variant)
- Rarely associated with Castleman limfadenopathy (hialine- vascular type usually): simultaneously or in background
- Not associated with EBV (IMFT like variant associated?)
- Size (average): ~ 5 cm
- Nodes, tonsils, gastrointestinal tract, soft tissue, skin, mediastinum, liver, spleen
- Mts: nodes and liver
- Indolent (sometimes aggressive) course: slowly growing mass, abdominal pain, sometimes systemic disease (IMFT like variant), paraneoplastic pemphigus
- HISTO: “meningeoma like whorls”, spindled or epitelioid pattern, oncocytic/ clear cells, myxoid stroma, cystic change, fibrovascular septation, multinuclear giant cells, sometimes CASTLE/thymoma or cHL imitating patterns. IMFT like variant is described in liver and spleen; Mitoses 1-5/ 10 HPF
- IH: 1 or more FDC markers: CD21/CD23/CD35+; EMA/S100/CD68+/-; Ki67 various: 1-25%
- Therapy: surgery +/- radio/chemo. Recurrences >50%. Fatal 10-20%, especially “high grade”, with high Ki67 index, necrosis, > 6 cm or intraabdominal

“Think about FDC sarcoma, if you see a meningeoma/ thymoma/ GIST in the wrong place... But it can mimic also the neoplasms typical for this site…”

F. Facchetti

Case #2

Diagnosis:

Jejunal (nodal?) follicular dendritic cell (FDC) sarcoma

Case #3

Reminescence
or
“Anonymous sarcoma”

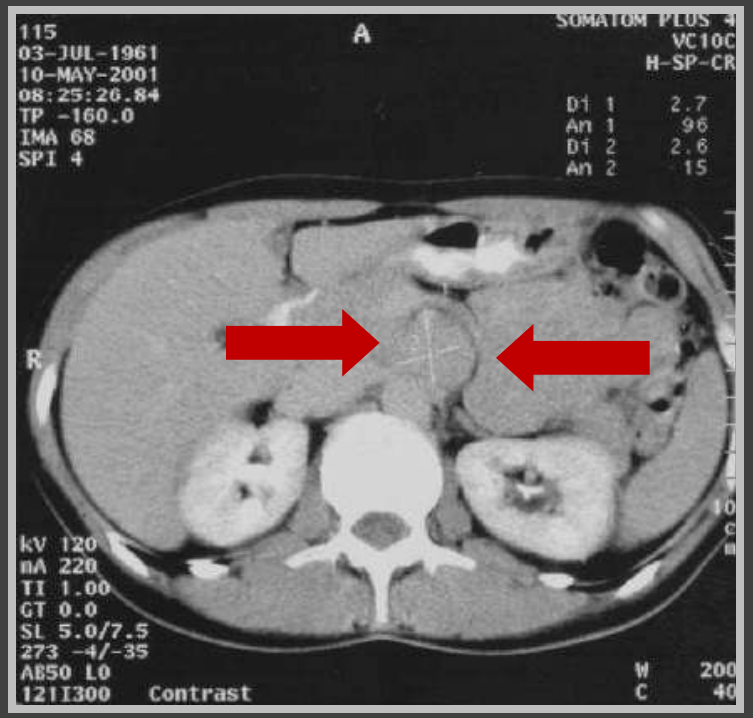
Case #3 was presented in Belgium-Lithuanian
GI pathology seminar in Vilnius, 2003 and in Hemato- Onco-Pathology meeting “GIST and GIST like tumors” in Vilnius, 2009

#3

Case #3

A previously healthy 42-year-old woman was admitted due to abdominal pain, nausea, anorexia, fulness feeling after meal and subfebrile fever in May of 2001. Abdominal sonoscopy and CT scan revealed 2.8x2.9 cm parapancreatic mass, localised below body of the pancreas in close contact with a.mesenterica superior.

The core biopsy: “chronic inflammation and fibrosis”.

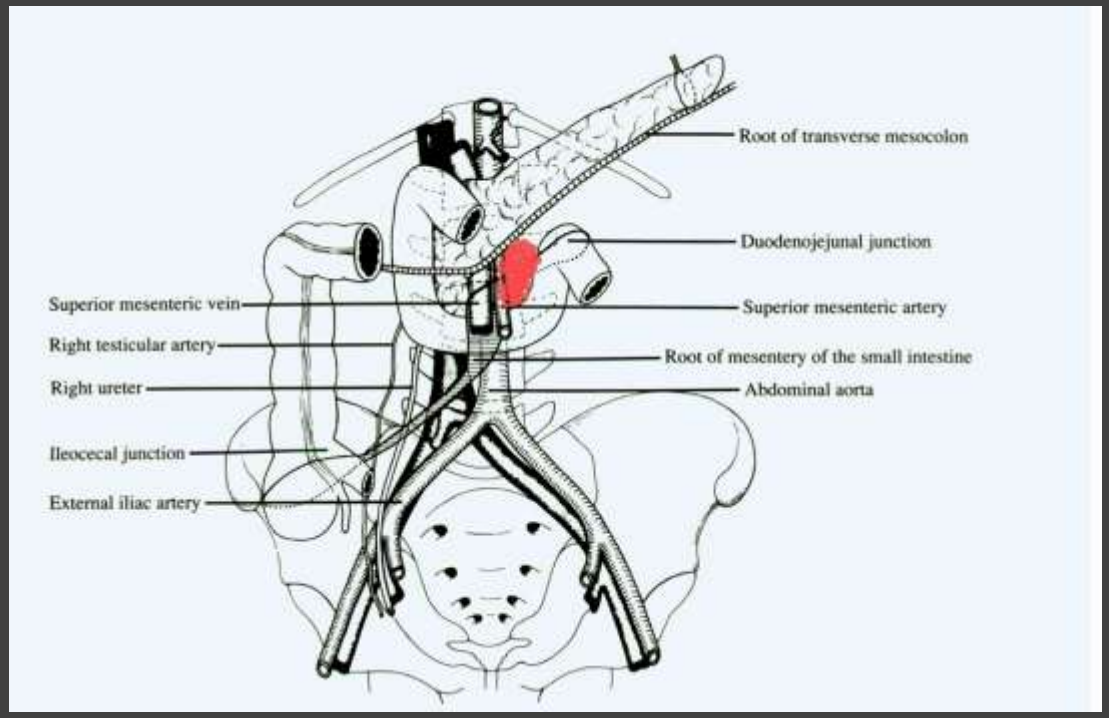


#3

Case #3

3 months later the patient underwent tumor resection (upper middle laparotomy) . Macro: nodular mass 4.7x4.5x2.5 dirty yellow with 2.7 cm irregular brown focus.

Primary diagnosis:"inflammatory myofibroblastic tumor with uncertain biologic behavior".



#3

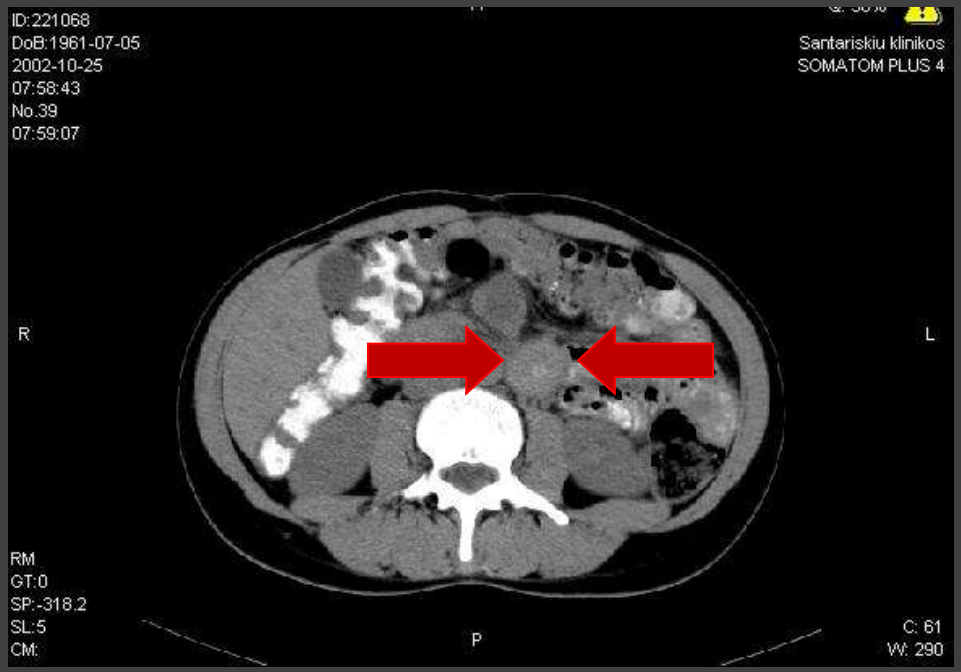
Case #3

After 17 months (in October of 2002) the patient was hospitalized due to abdominal pain around umbillicus, nausea, fullness feeling after meal and mild diarhoea.

2.5x2.2 cm recurrent tumor in the same location, more laterally (closed to superior mesenteric artery, below body of the pancreas) was resected.

Macro: Fat tissue and 2 cm fleshy brown colored tissue.

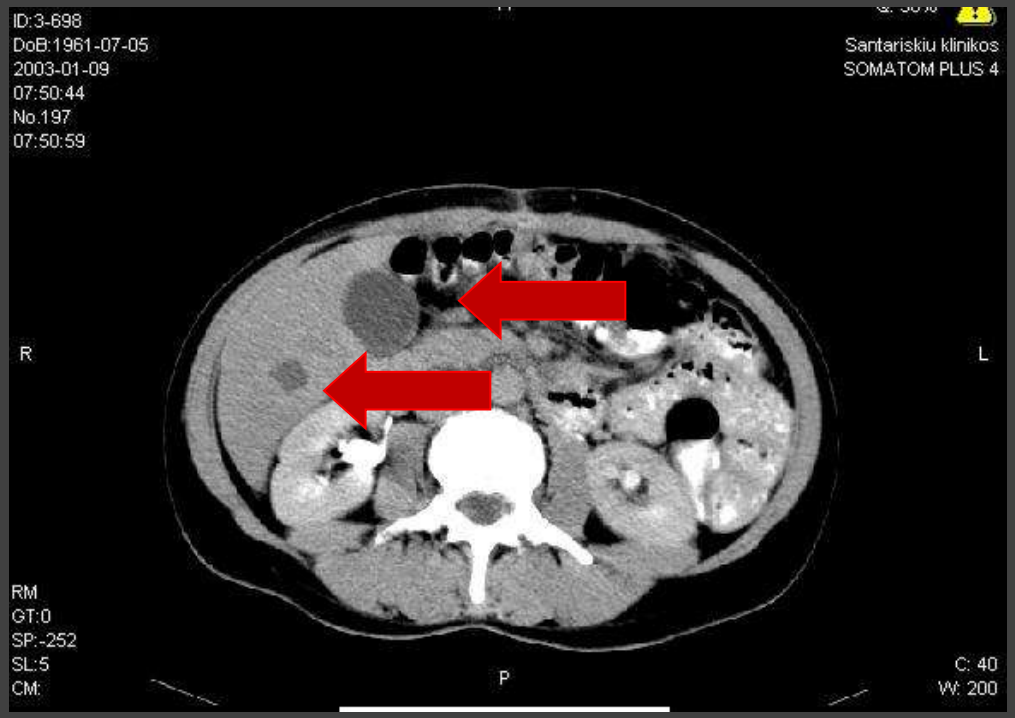
Primary diagnosis: "low grade stromal sarcoma, probable GIST"



#3

Case #3

In January of 2003 (after 20 months) the patient was admitted due to operational wound infection, CT scan was applied, core biopsy from liver was taken and multiple tumor metastases with the same histology were found.



#3

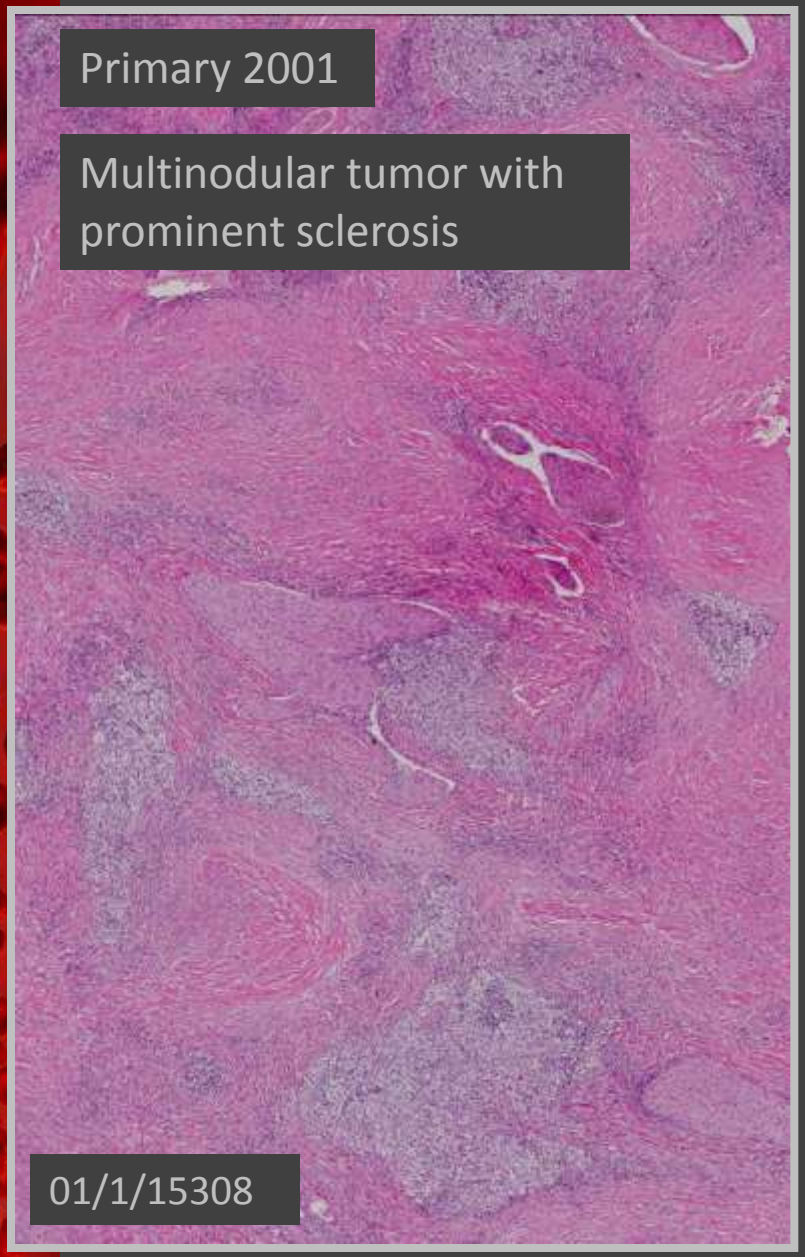
Case #3

Pathology records:

Biopsy:	"chronic inflammation and fibrosis"
Resection 1:	"inflammatory myofibroblastic tumor with uncertain biologic behavior".
Resection 2:	"low grade stromal sarcoma, probable GIST"
Liver biopsy:	metastasis of sarcoma

Primary 2001

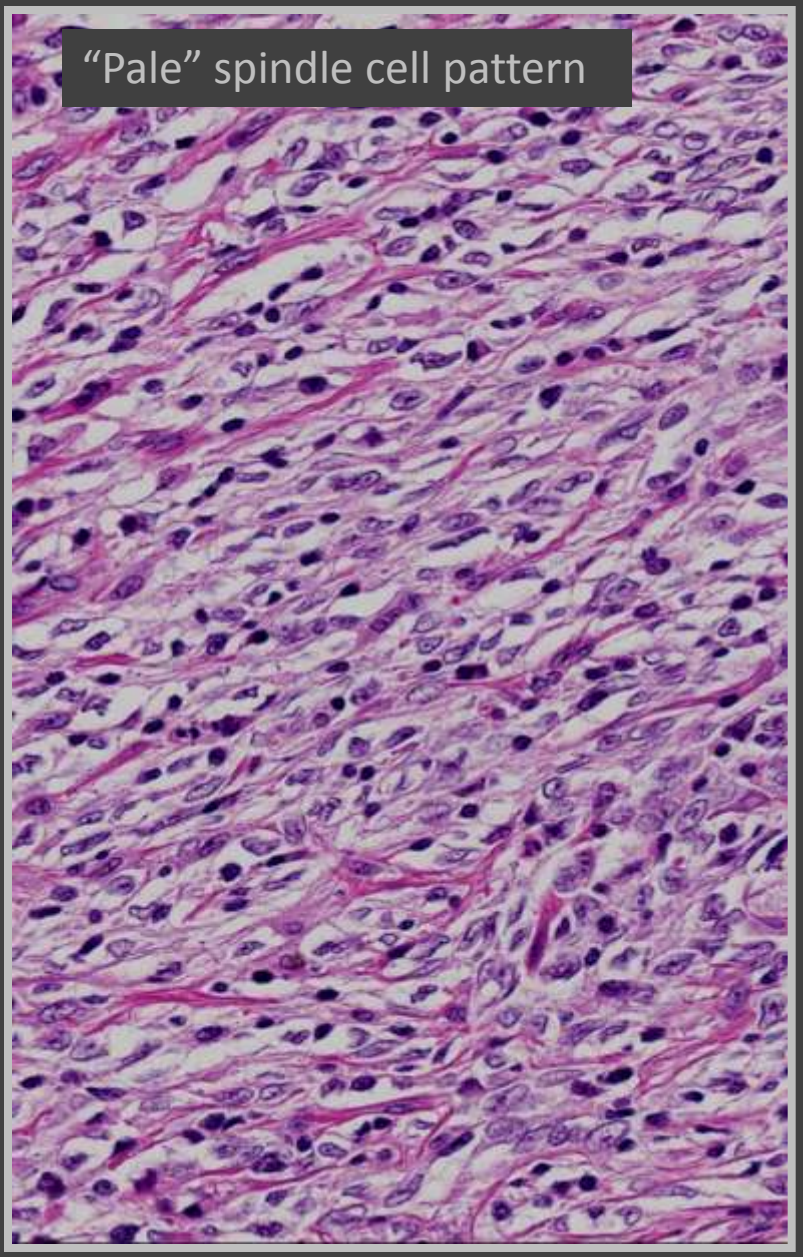
Multinodular tumor with prominent sclerosis



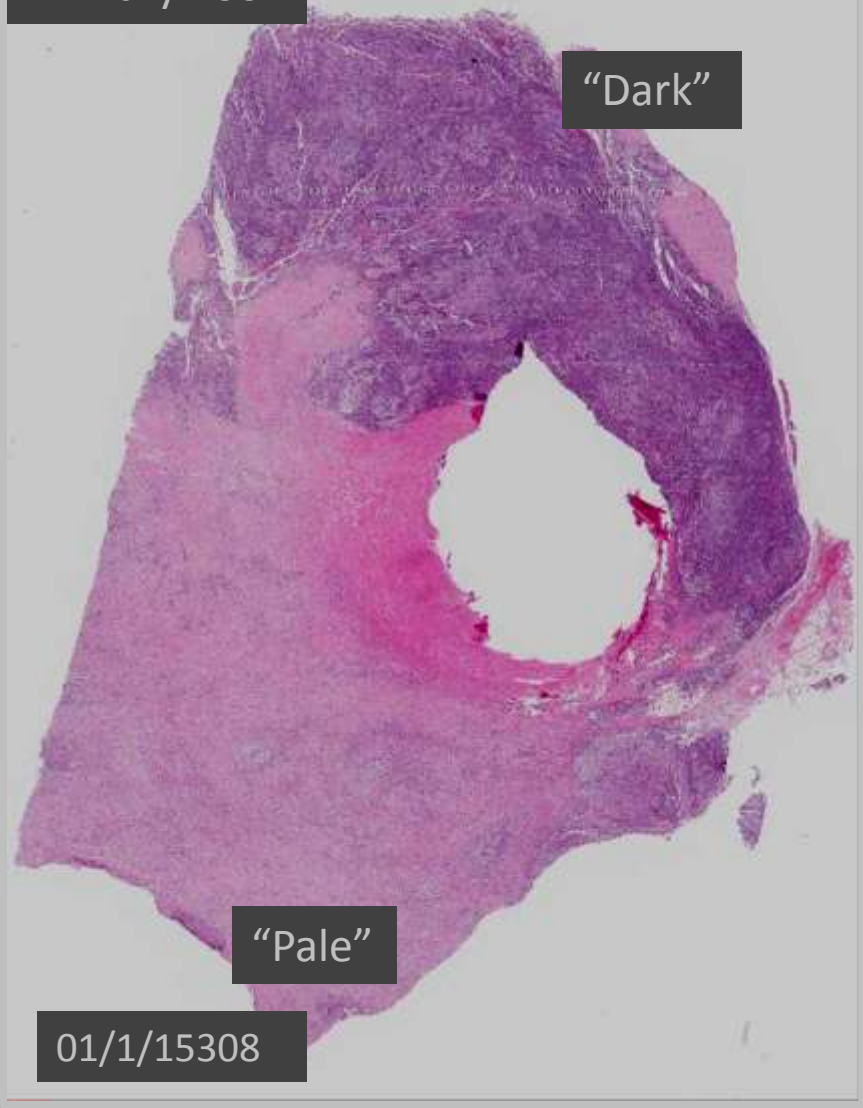
01/1/15308

#3

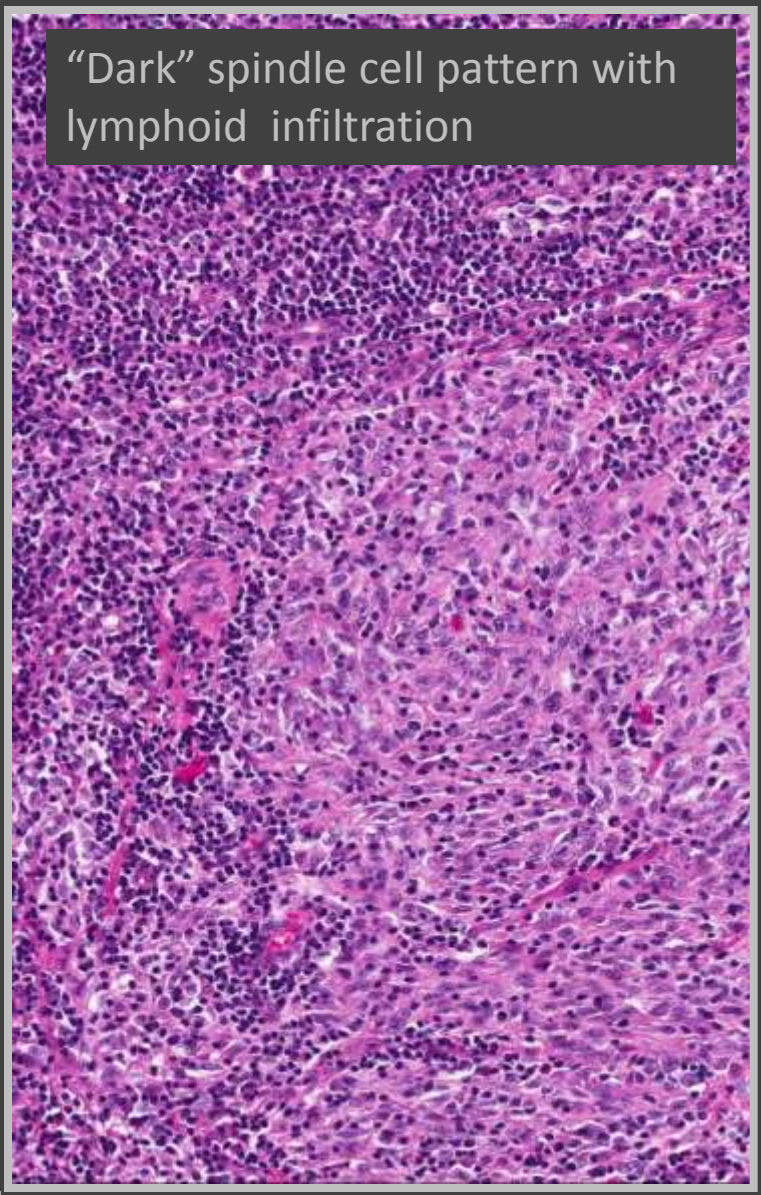
“Pale” spindle cell pattern



Primary 2001



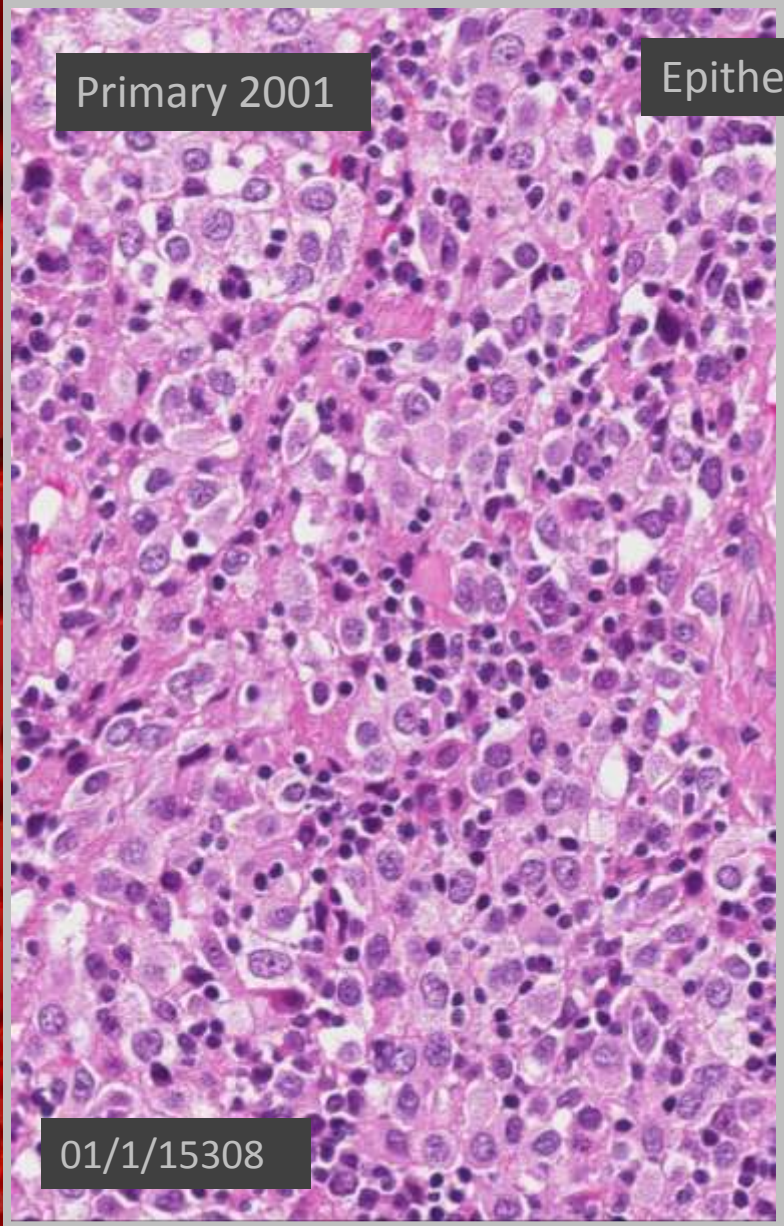
"Dark" spindle cell pattern with lymphoid infiltration



#3

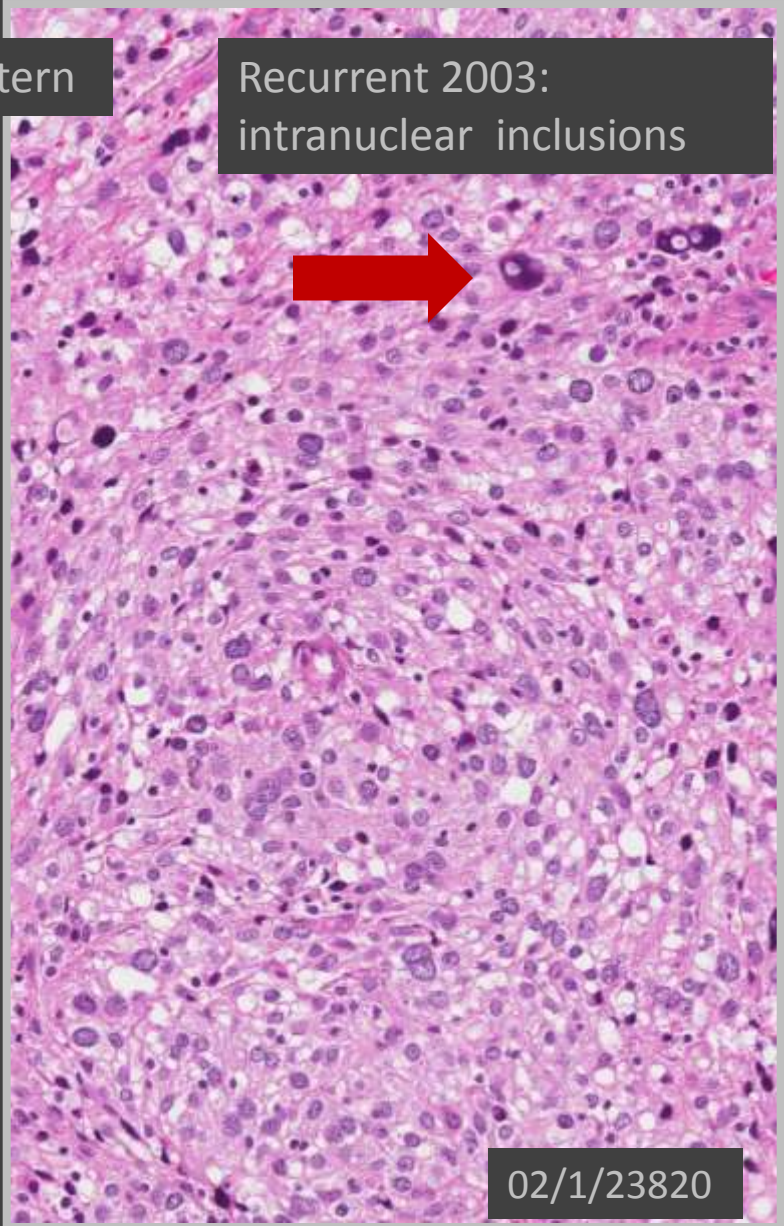
Primary 2001

Epithelioid pattern



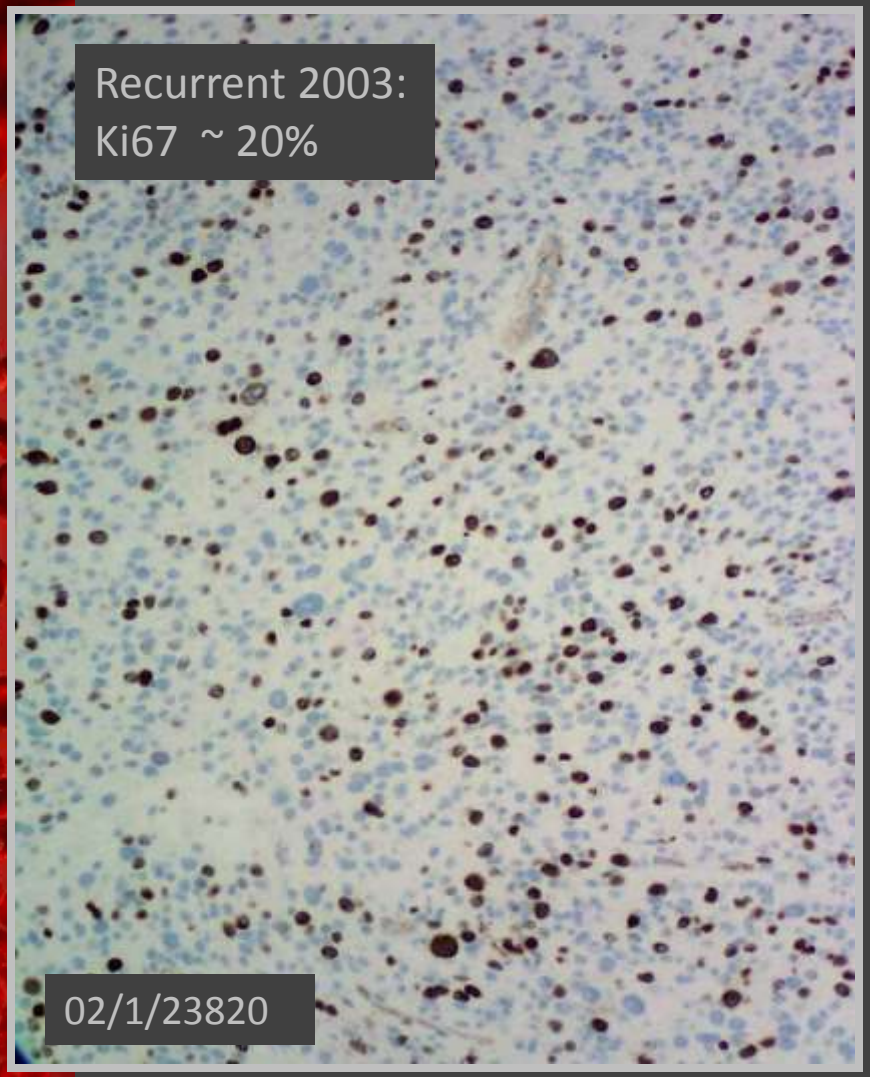
01/1/15308

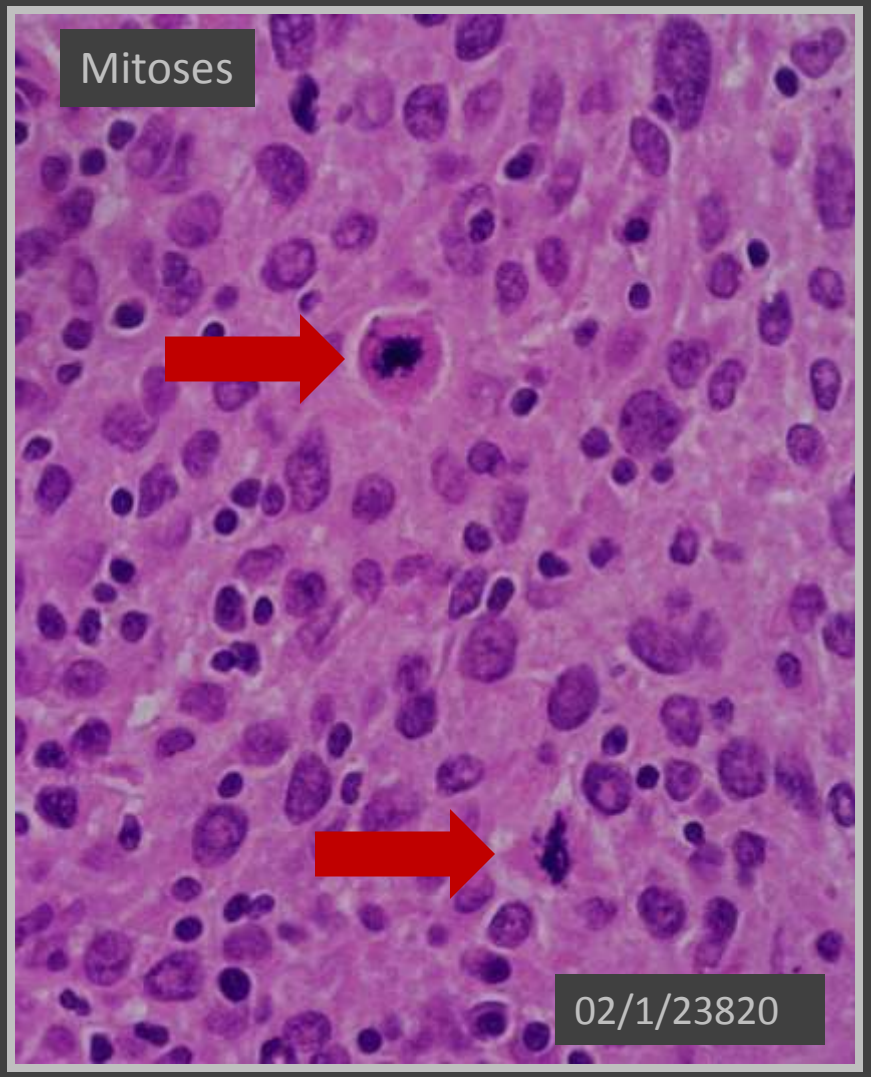
Recurrent 2003:
intranuclear inclusions

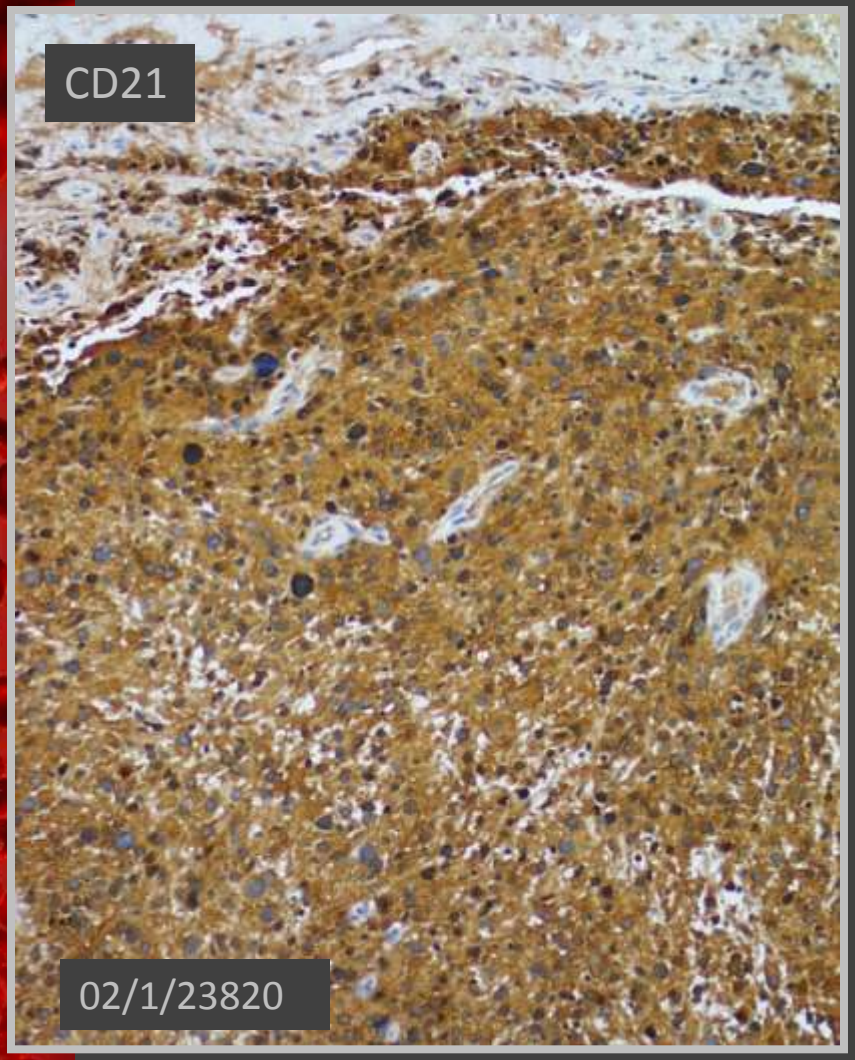


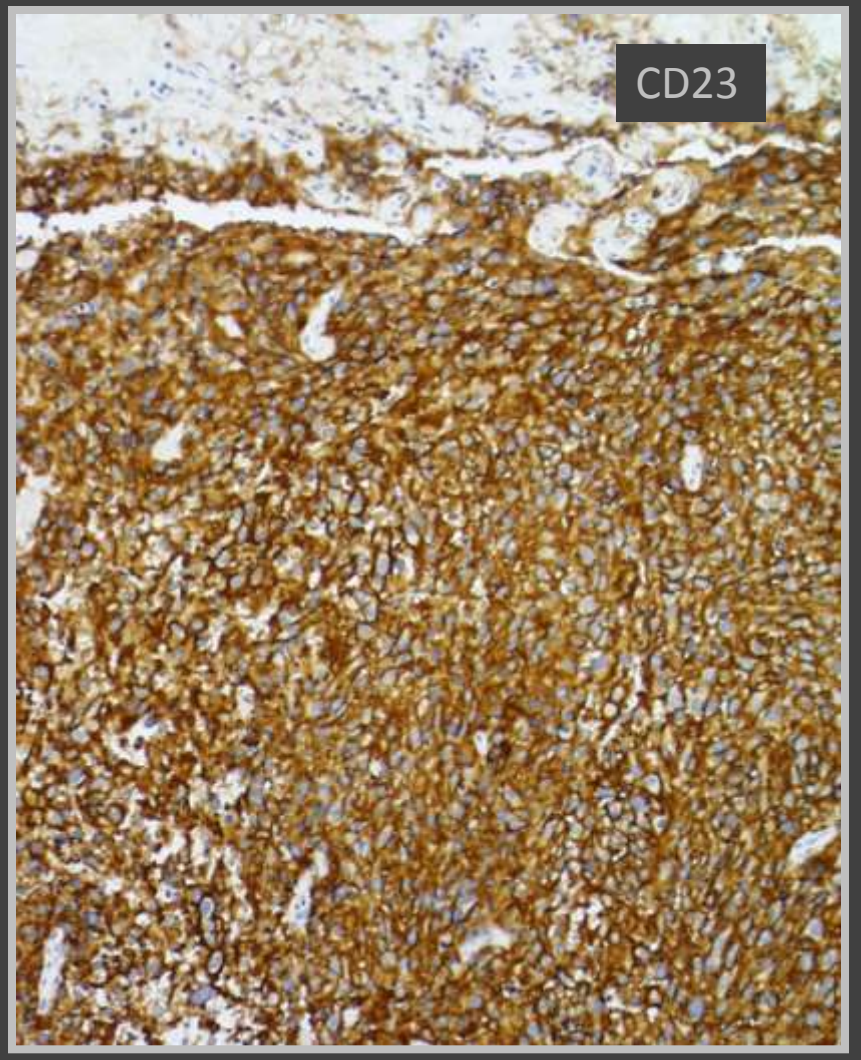
02/1/23820

#3


Recurrent 2003:
Ki67 ~ 20%
02/1/23820


Mitoses
02/1/23820





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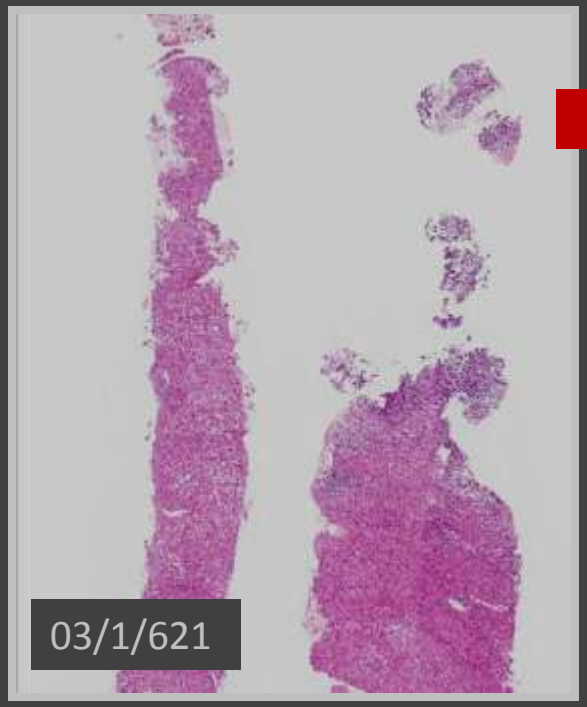
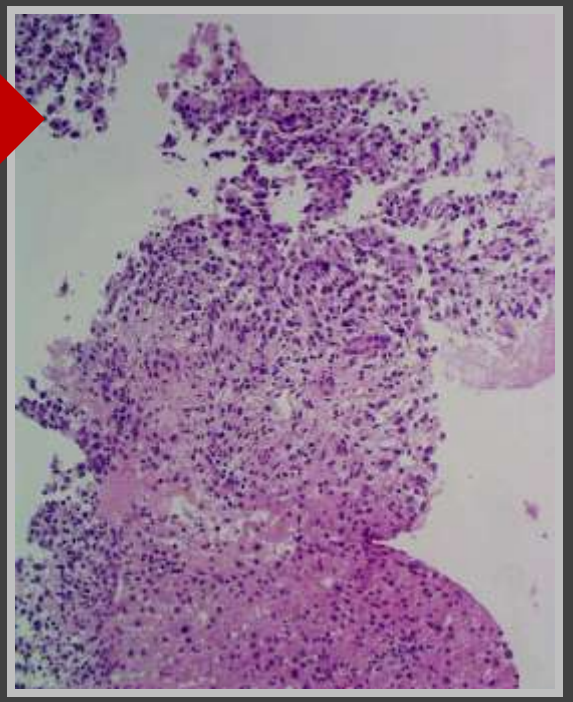
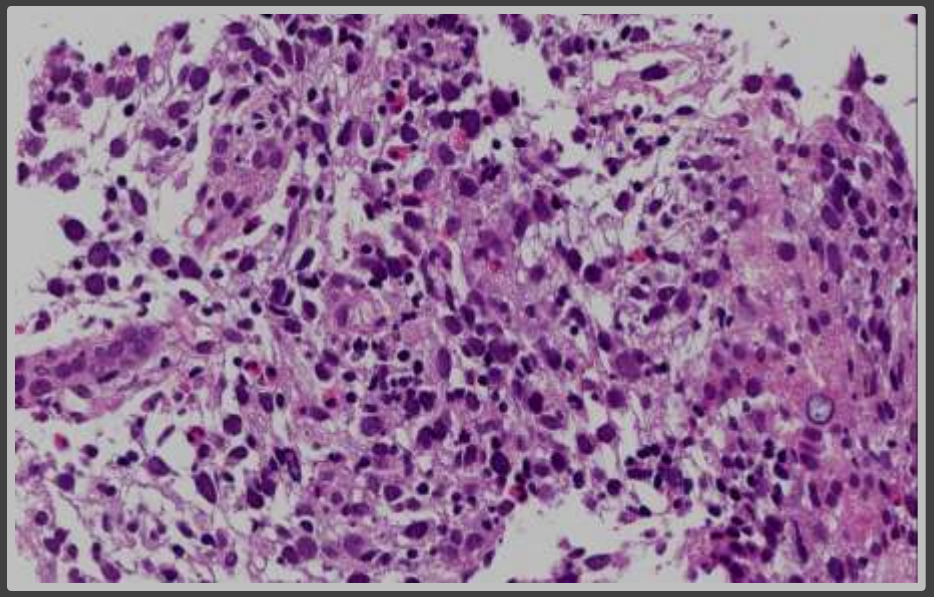


2003: liver biopsy: tumor metastasis





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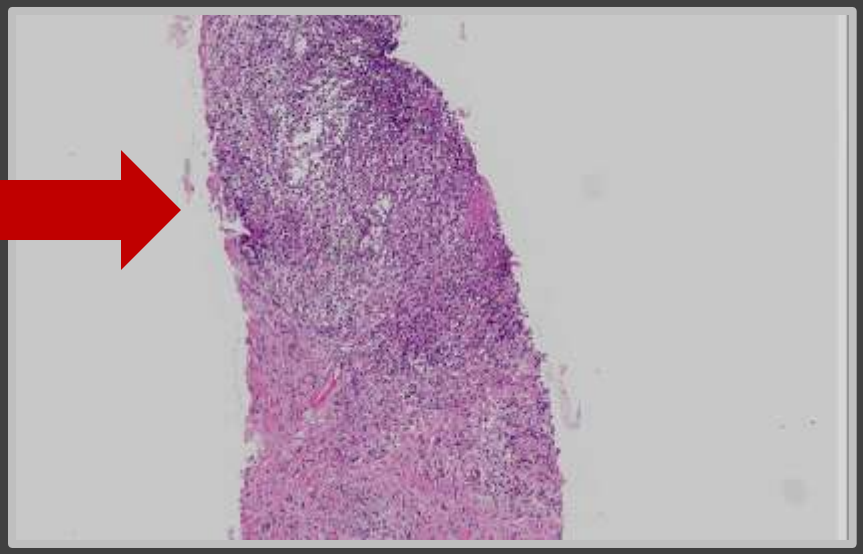
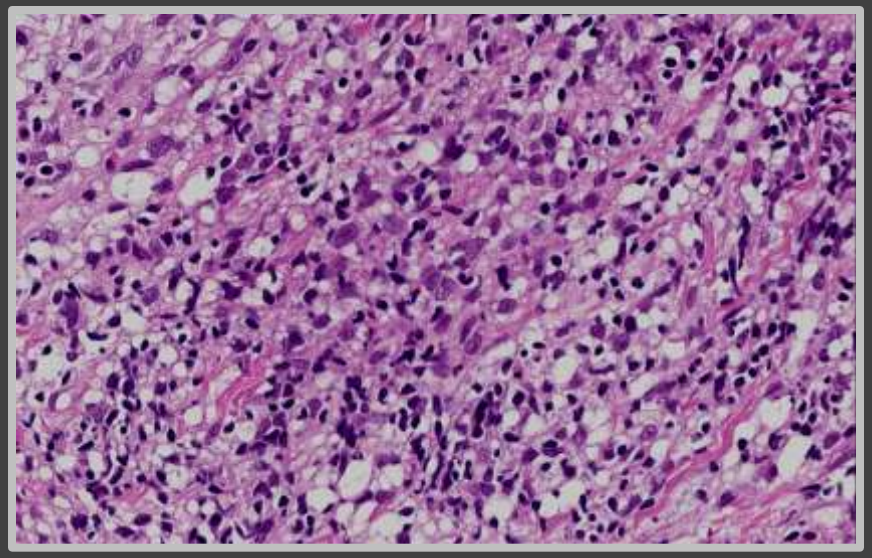




2001: retro biopsy: the scattered tumor spindle cells

Case #3

Retrospectively the case was additionally evaluated for FDC markers (CD23 and CD21) in Leuven University, Belgium (R.Sciott) in 2003.

Final IH:

CD21/ CD23/ Vimentin positive; NSE positive; Desmin positive (focal, weak, <10%); Asm Actin, CK8, CD34, S100, GFAP, EMA, GFAP, Synaptophysin, CD68, Calretinin, Pan CK, LCA, CD30, HMB45 negative. Ki67 proliferative index was high ~ 20%.

Additionally IH in Aalborg, Denmark (2003): Myogenin, Myf4, Slow Myosin, neurofilament protein, Inhibin A, Melan A, CD117 negative, p53 positive (10%).

Mitoses ~10/ 10 HPF.

Any adjuvant therapy was applied.

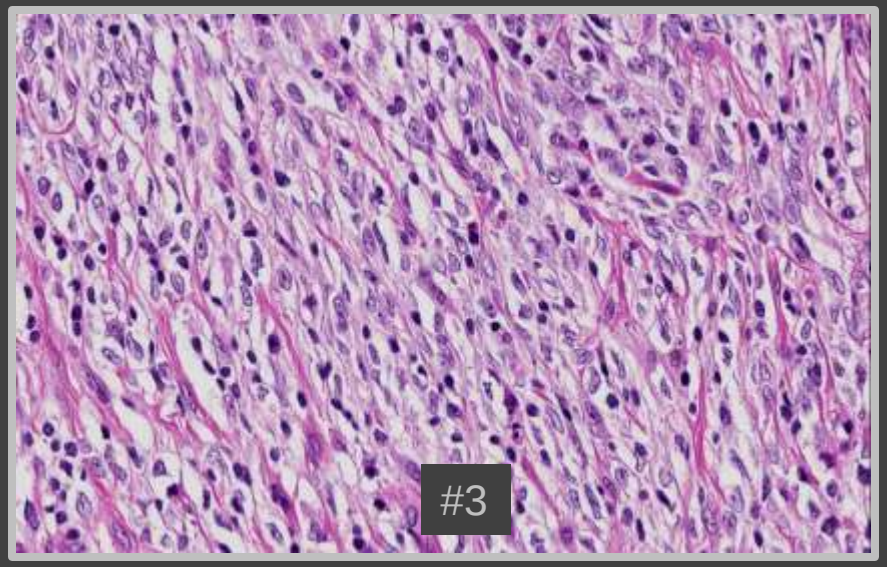
The patient was lost for follow up and died in 48 months after the diagnosis due to unknown reasons.

Case #3

Differential diagnosis:

1. Inflammatory myofibroblastic tumor (ALK1?);
2. GIST CD117(-);
3. Dedifferentiated liposarcoma;
4. Low grade sarcoma NOS.

P.S. CD117 was implemented in 2002, CD21/CD23- in 2003 .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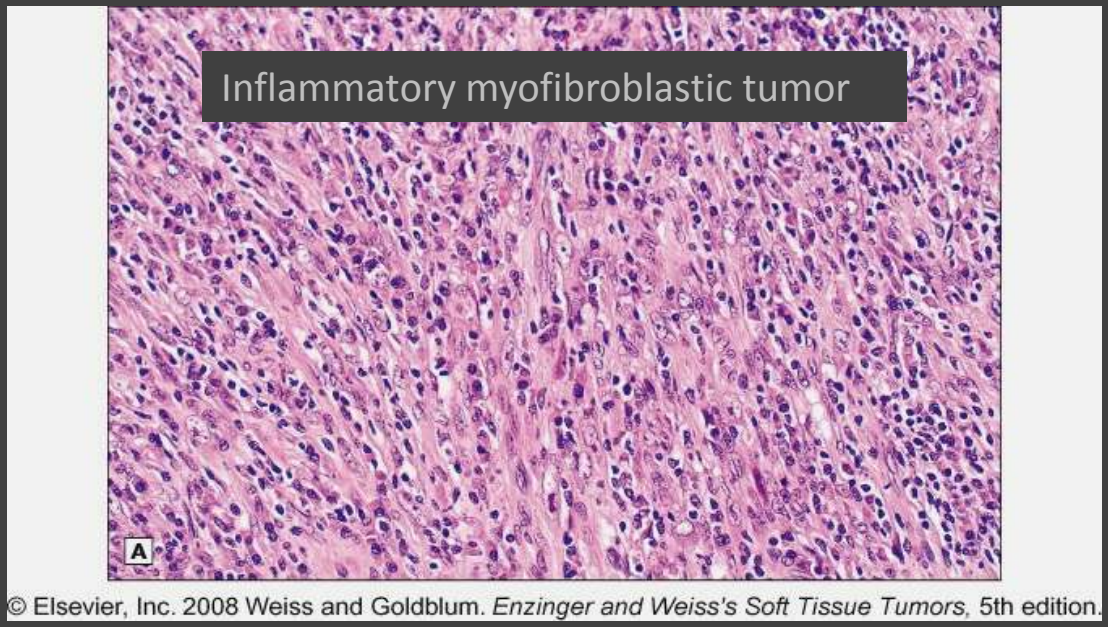

Inflammatory myofibroblastic tumor
A
© Elsevier, Inc. 2008 Weiss and Goldblum. *Enzinger and Weiss's Soft Tissue Tumors*, 5th edition.

#3

Case #3

Diagnosis:

Retroperitoneal (nodal?) follicular dendritic cell (FDC) sarcoma (biphasic) with multiple metastases to liver

Case #3

"The eyes see only what the mind is prepared to comprehend."

R.W.Davies (1913-1995)

Case #1

Classics
or
“GIST” biopsy

Case #1, was presented in Hemato- Onco- Pathology meeting “GIST and GIST like tumors” in Vilnius, 2009

#1

Case #1

79-year-old a woman was previously diagnosed with mandibular diffuse B cell lymphoma in 2005. IH: CD20+; Bcl6+; MUM 1-/+; BCL 2-/+; CD10(-); CD30+.

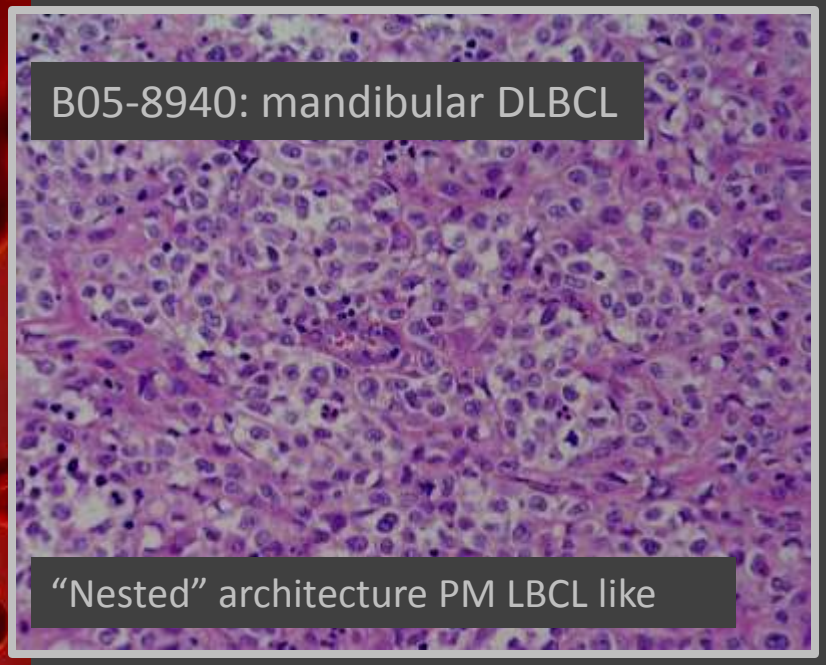
It was successfully treated with combined chemotherapy and radiotherapy.

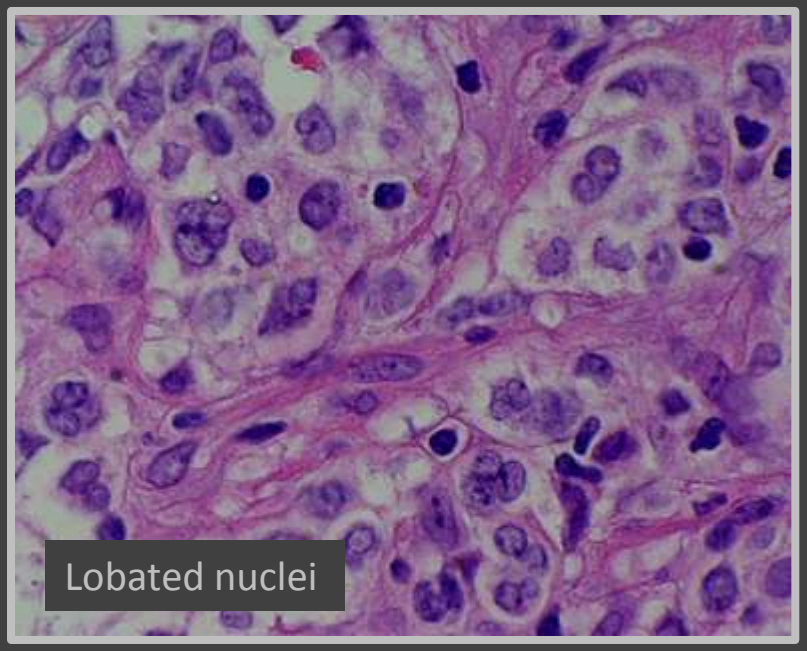
After 3 years the patient presented with a 6-month history of abdominal pain.

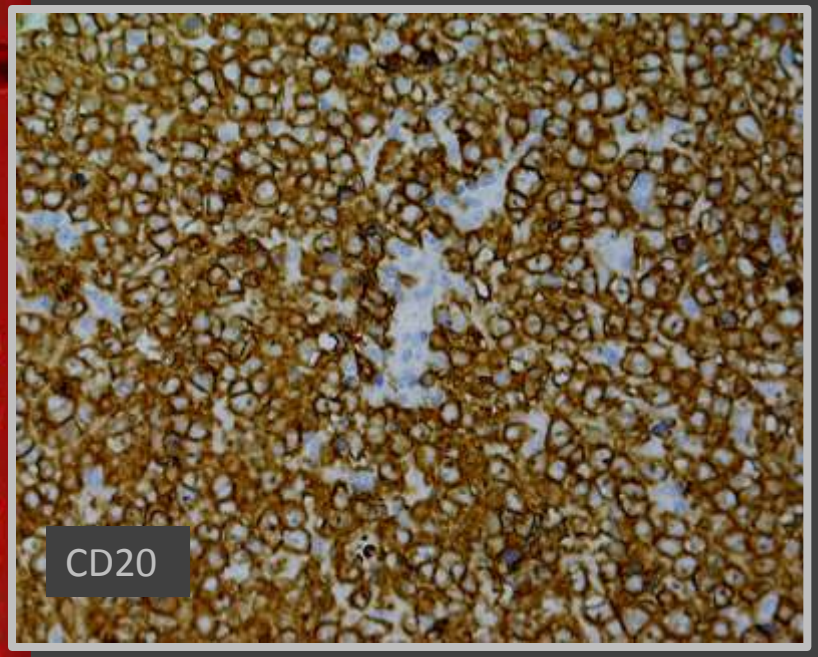
CT scan: a retroperitoneal mass of 12 cm.

Th core biopsy was taken from ~12 cm (sonoscopically) tumor in between of right kidney, liver, v. cava infwerior (adrenal tumor?).

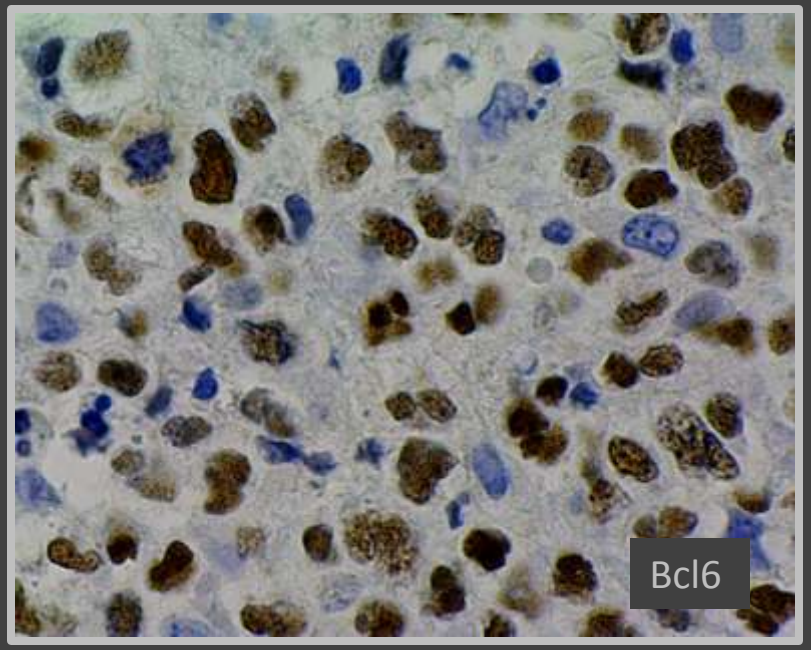
Primary diagnosis: “mesenchymal tumor, most probably high risk gastrointestinal stromal tumor (GIST)”.

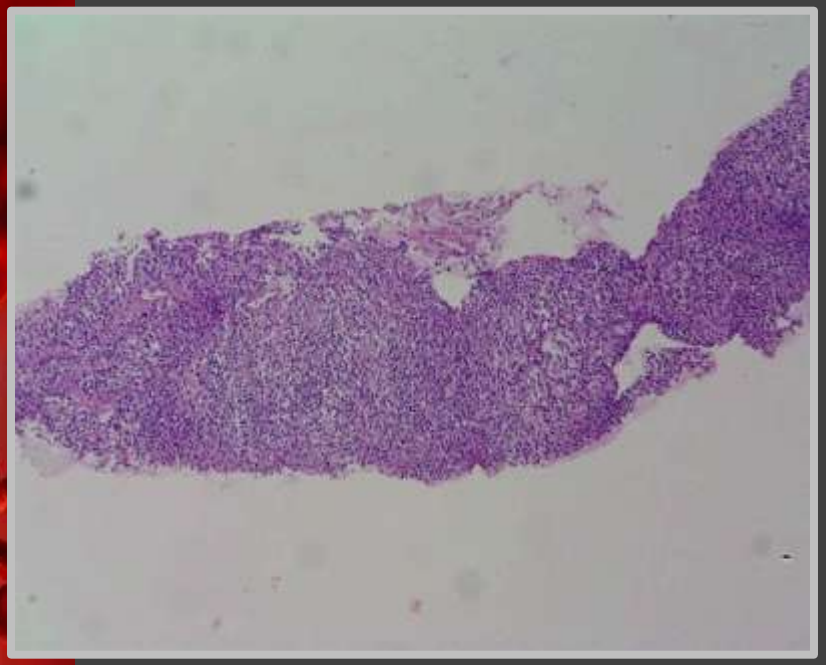

B05-8940: mandibular DLBCL
“Nested” architecture PM LBCL like

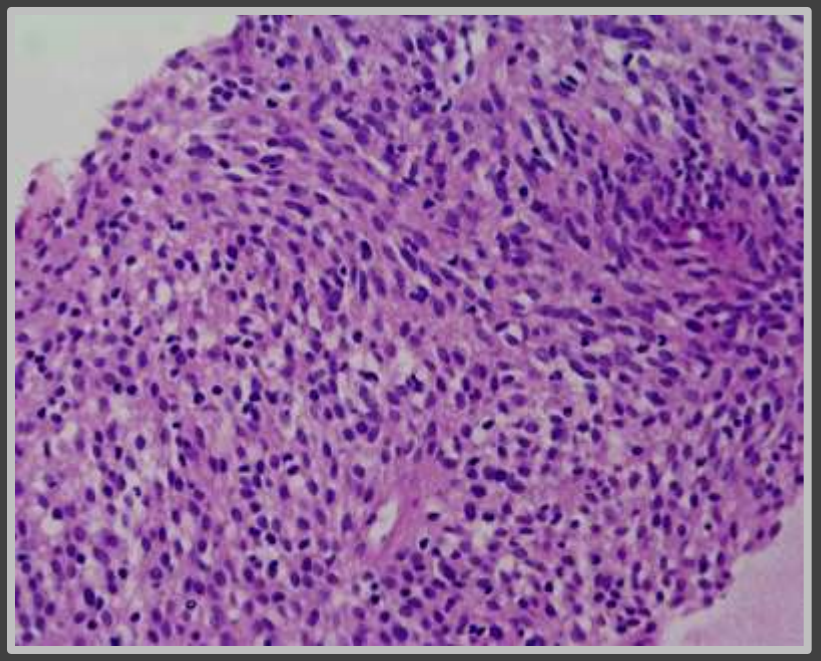

Lobated nuclei

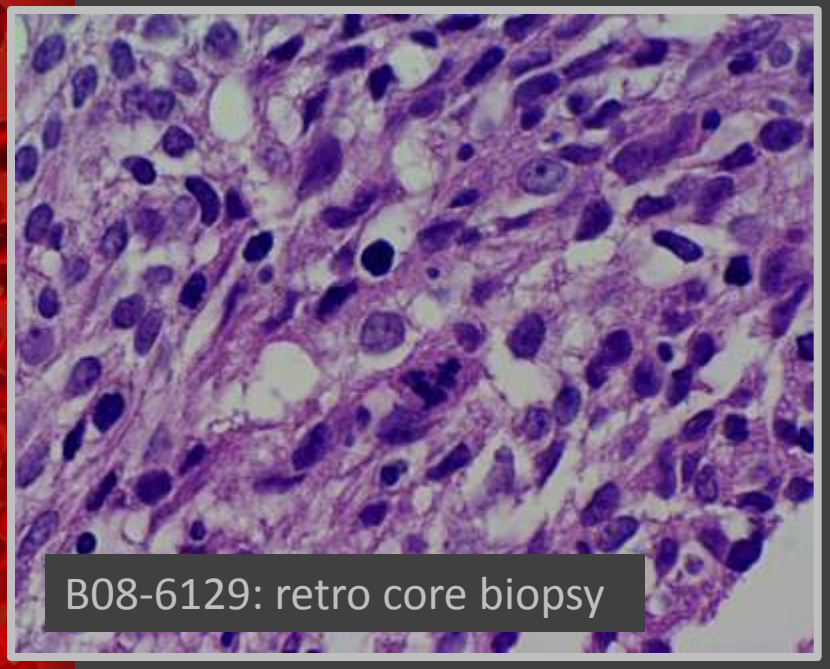

CD20

#1


Bcl6

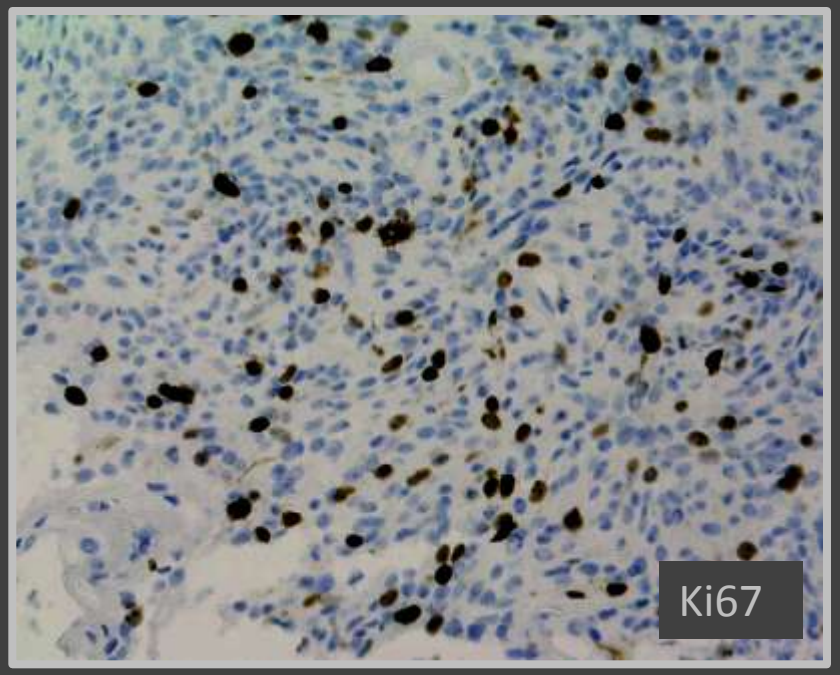




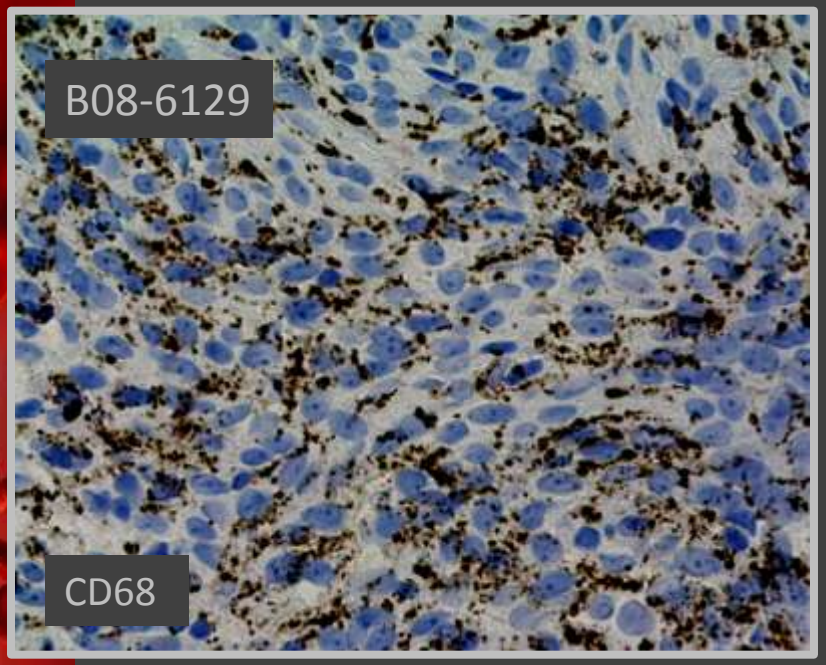


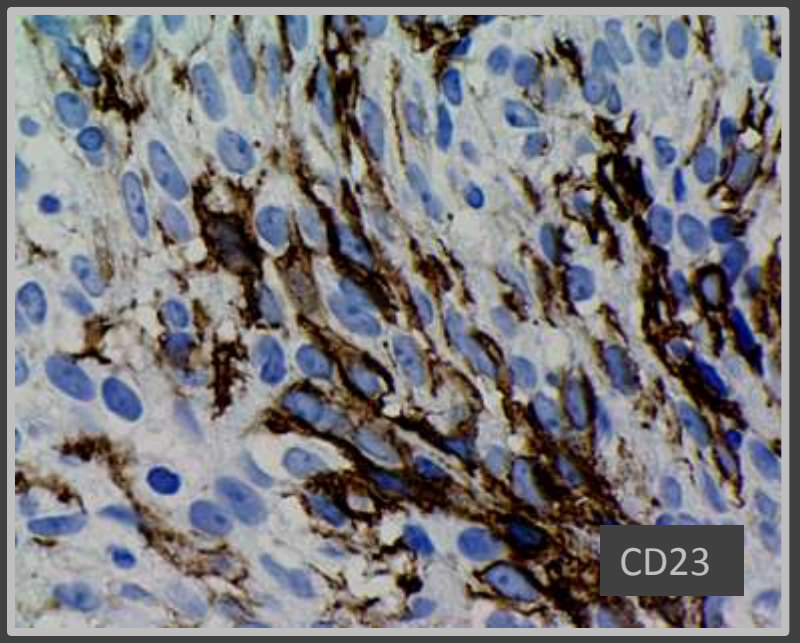
B08-6129: retro core biopsy

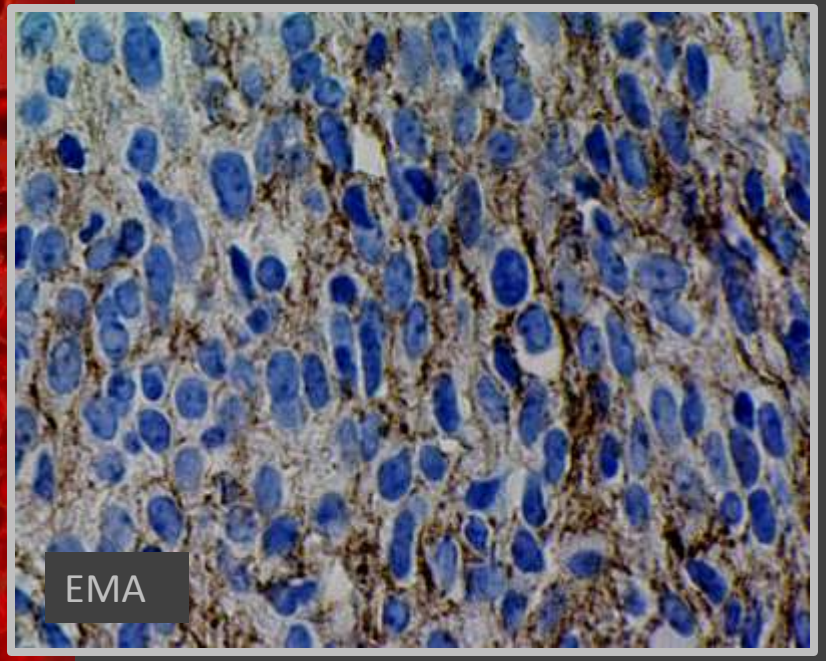
#1



Ki67







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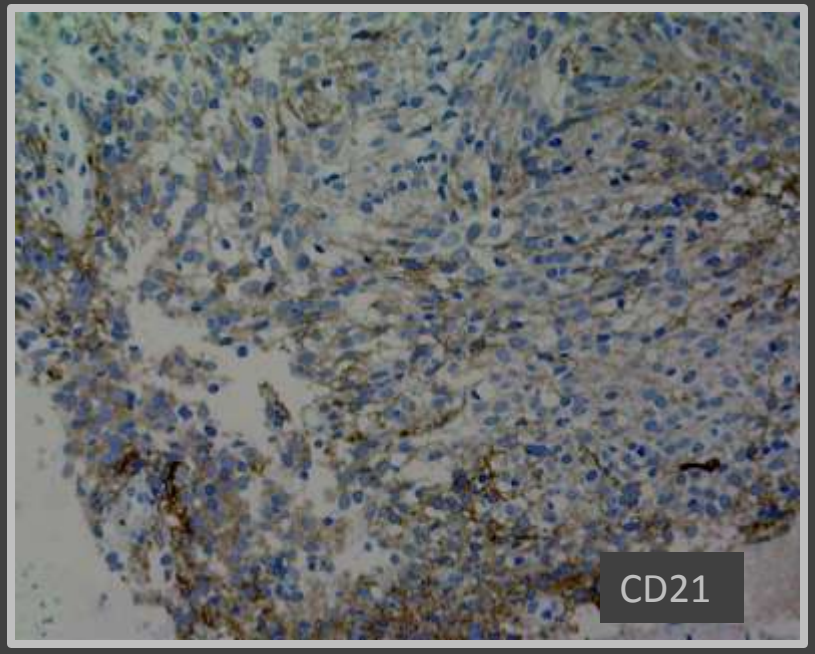


Case #1

IH: CD68, CD23, Vimentin and EMA positive; S100 and CD21 positive (weak, focal); CD117, CD34, AsmActin, Pan CK, CD1a, CD34, CD31, CD3, CD20, LCA, CD31, CD1a were negative. Ki67 proliferative index <5%.

No further surgical or adjuvant treatment were carried out at the time of last follow-up for 18 months after the initial diagnosis.

The case was discussed in telepathology group: INCTR Hematopathology
https://www.ipath-network.com/ipath/object/view/11609

Case #1

Diagnosis:

1. Mandibular diffuse large B cell lymphoma (2005)
2. Retroperitoneal (?) FDC sarcoma (2009)

Trans- or de- differentiation?

Non Hodgkin's lymphomas (FL/CLL) with histiocytic/dendritic cell tumors and the same IgH clonality:

Clonally related follicular lymphomas and histiocytic/dendritic cell sarcomas: evidence for transdifferentiation of the follicular lymphoma clone. Feldman AL, Arber DA, Pittaluga S, Martinez A, Burke JS, Raffeld M, Camos M, Warnke R, Jaffe ES. Blood. 2008 Jun 15;111(12):5433-9. Epub 2008 Feb 13.

IgH clonality in histiocytic/dendritic cell tumors :

High frequency of clonal immunoglobulin receptor gene rearrangements in sporadic histiocytic/dendritic cell sarcomas. Chen W, Lau SK, Fong D, Wang J, Wang E, Arber DA, Weiss LM, Huang Q. Am J Surg Pathol. 2009 Jun;33(6):863-73.

PCR IgH clonality testing in both tumors were unsuccessful (old parafin block and fragmented DNA; exhausted biopsy block)

Case #4

The Challenge in the inguinal region

Case #4 was presented in Hemato- Onco- Pathology meeting “GIST and GIST like tumors” in Vilnius, 2009

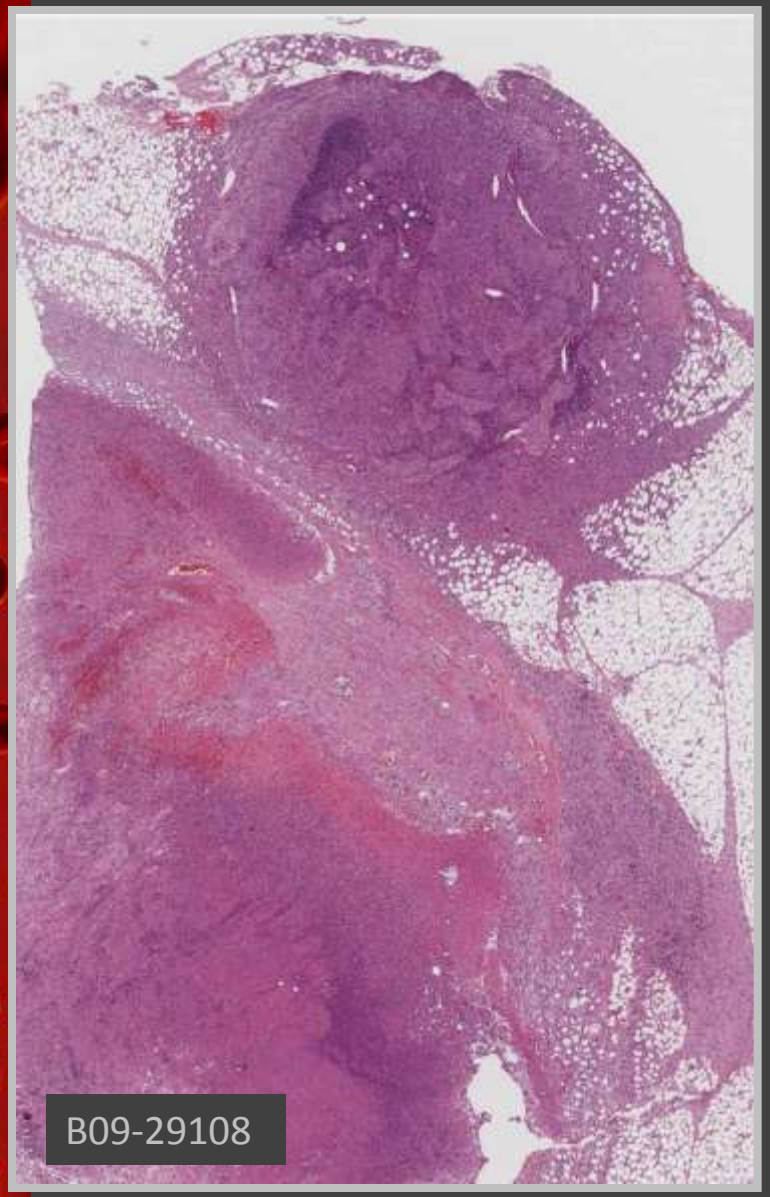
#4

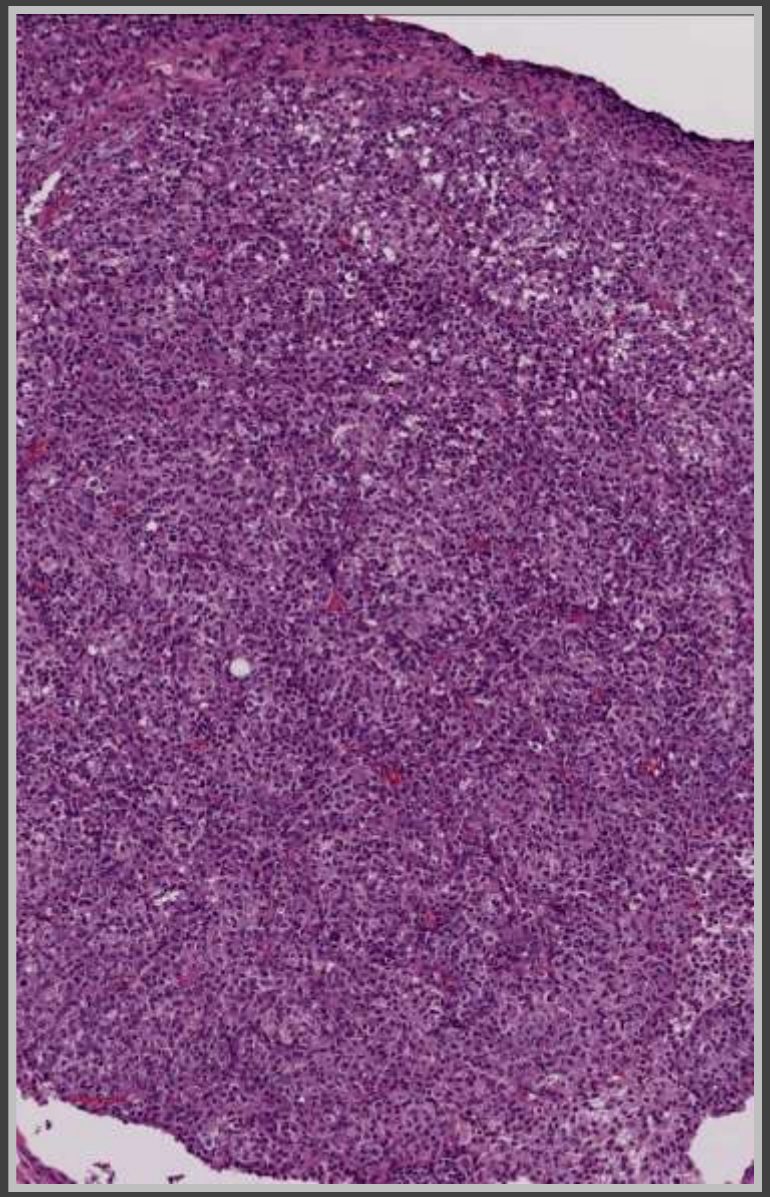
Case #4

77-year-old woman complained of abdominal discomfort for 8 months. Enlarged “suppurated” lymph node biopsy was taken.

Macro: 5 cm lymph node with central necrosis.

The patient died soon due to unrelated to the tumor cardiologic complications.





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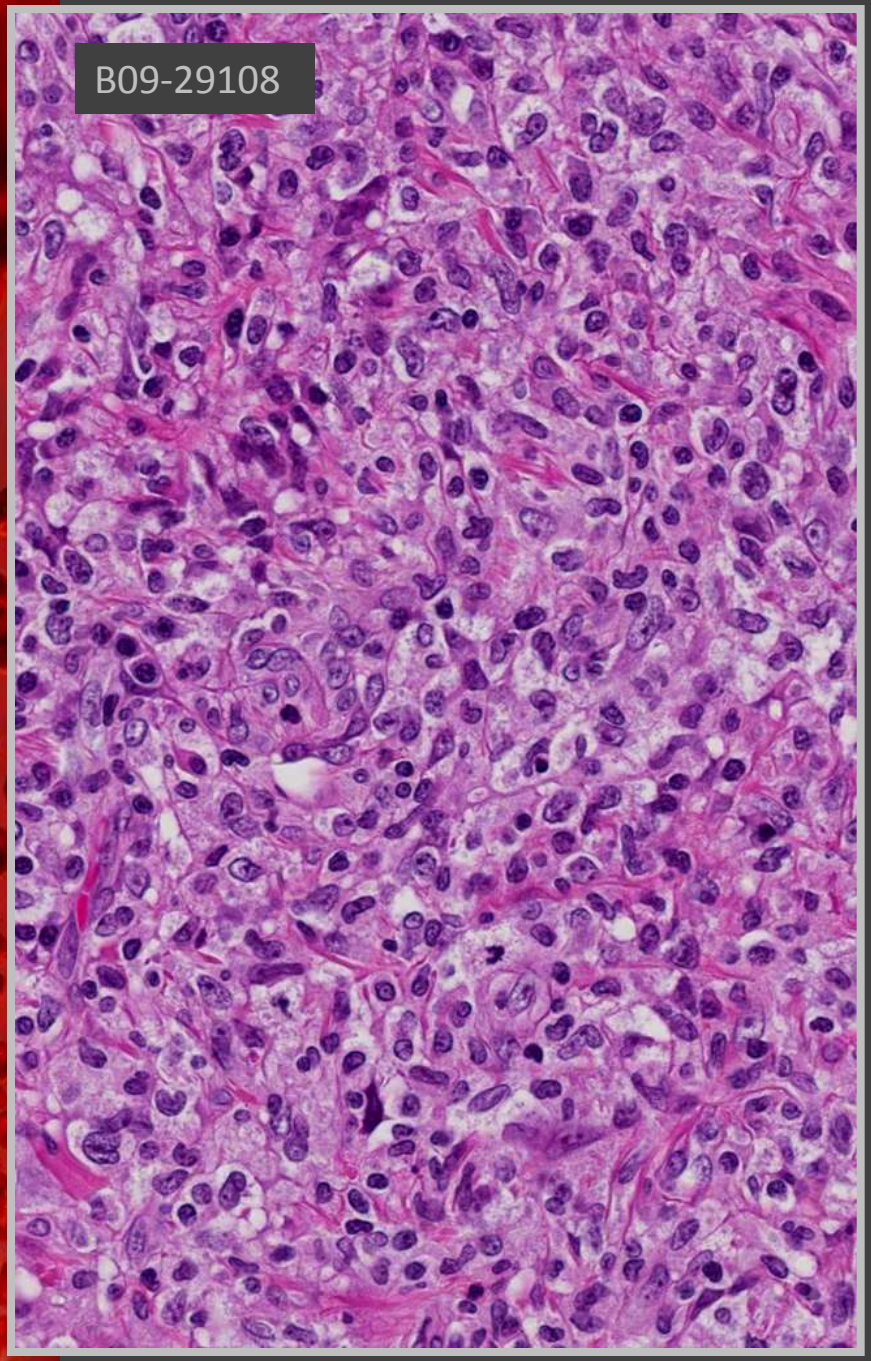

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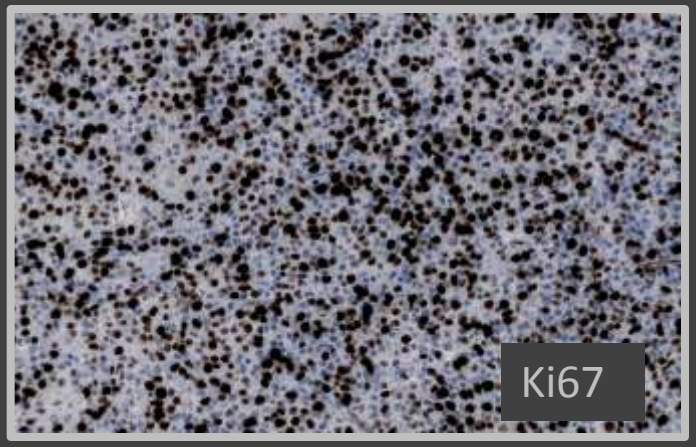

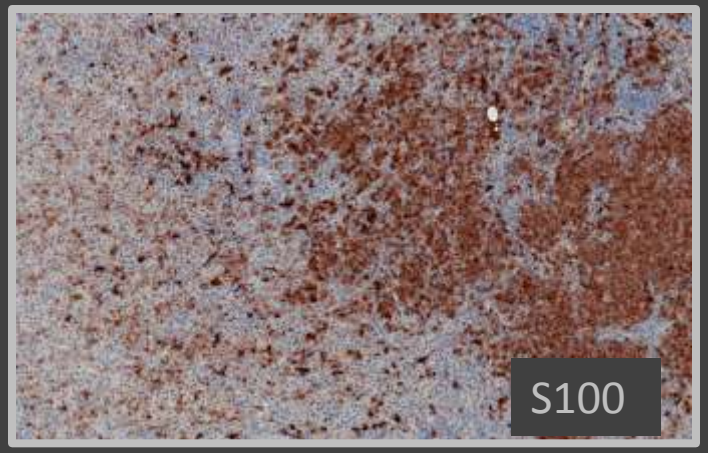

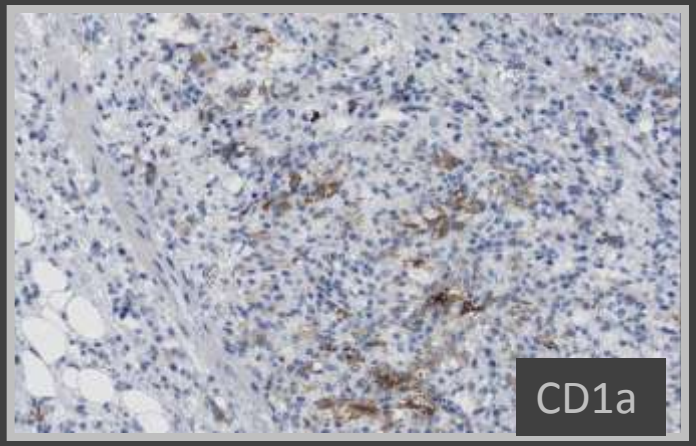

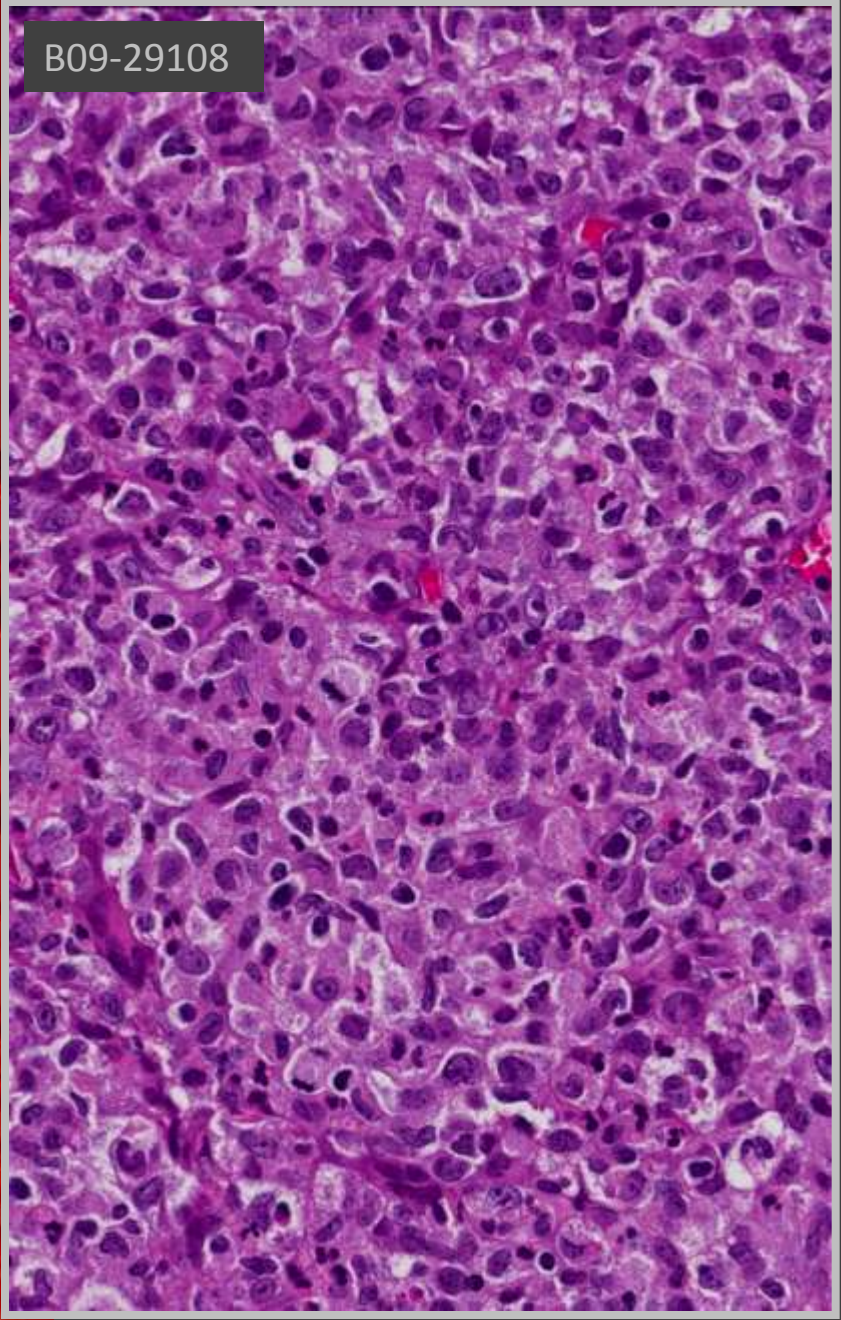
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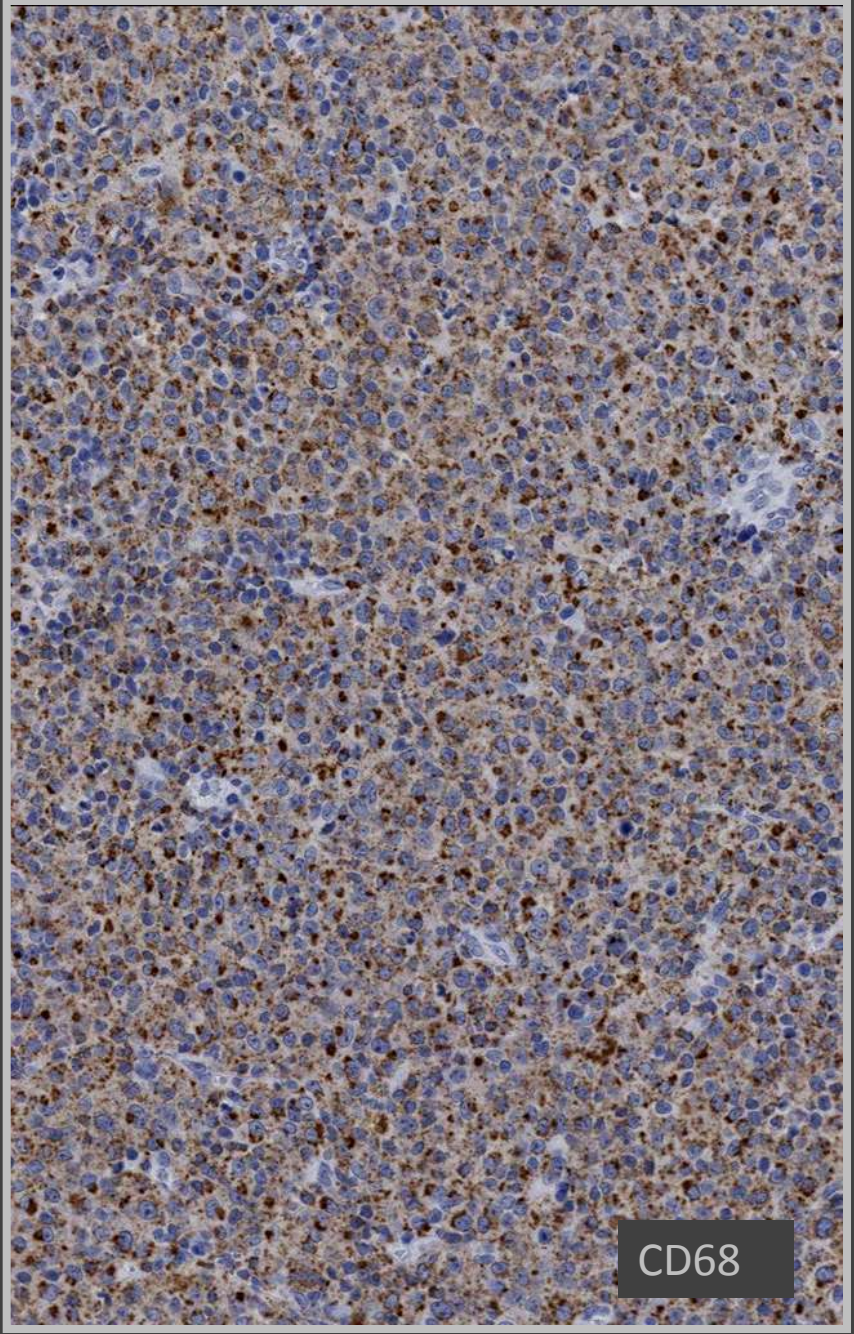

CD68

Case #4

Differential diagnosis:

1. Intergiditating cell sarcoma.
2. Histiocytic sarcoma.
3. Langerhans cell sarcoma.
4. Other?

Electron microscopy fails to demonstrate Birbeck's granules (differential diagnosis with Langerhans cell sarcoma) . Due to low quality (parafin block) cell junctions were broken and intercellular connections were not visualized.

The case was discussed in telepathology group: INCTR Hematopathology
https://www.ipath-network.com/inctr/object/view/10957

Interdigitating cell sarcoma (WHO 2008)

- Single cases or series
- Adult, rarely children
- V > M
- Asociated with B or T NHL
- Node or soft tissue or skin
- Asymtomatic, rarely symtomatic, splenomegaly/hepatomegaly
- HISTO: identical FDC sarcoma (spindled or epithelioid)
- IH: S100+, CD68+/-, Ki67 10-20%, EMA/CK(-), CD21/CD23(-), CD163/Lysozyme (-)
- Aggressive course, 50% fatal
- Visceral involvement/mts: liver, spleen, kidney, lung

D/H cells and related tumors: IH

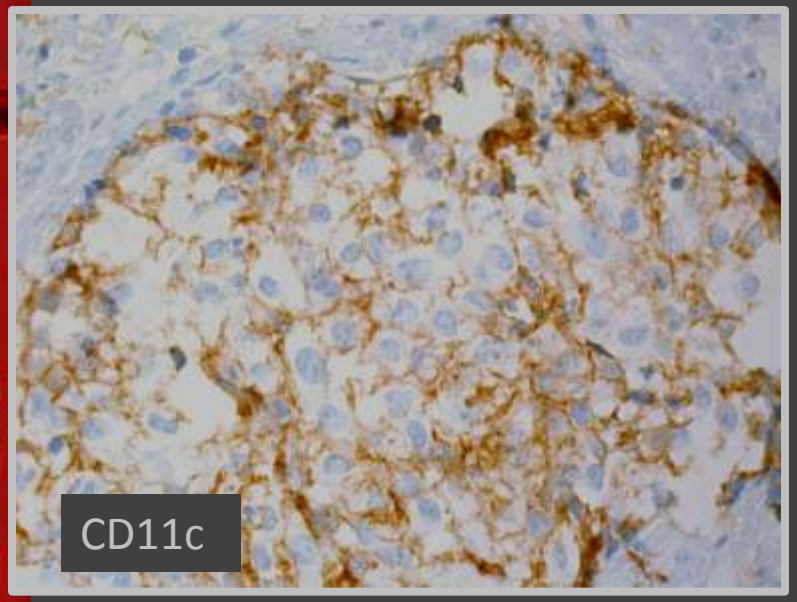
IH	LC	IDC	FDC	PDC	Ma	DIDC	FRC
CD1a	++						
CD4	+			+	+	+/-	
CD21			++				
CD23			++				
CD35			++				
CD68	+/-	+/-		++	++	+	
CD123				++			
S100	++	++	+/-		+/-	+/-	
Fascin		++	+/++		-/+	+	
Langerin	++						
Lysozyme	+/-				+		
TCL1				+			
PanCK							+
Asm Actin							+

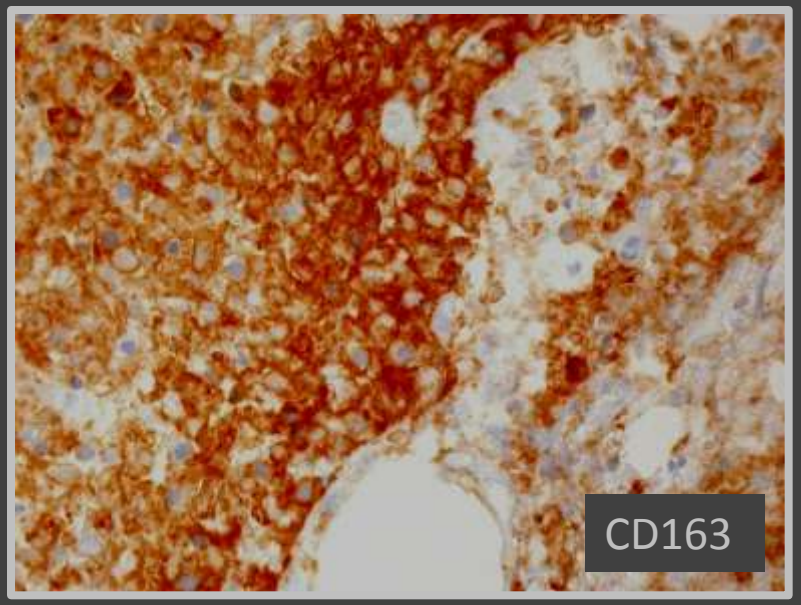
Case #4

IH 1 (Vilnius): LCA, CD68 (dotted), S100, CD4, Bcl6 positive, Pan Cytokeratin/ EMA/ CD20/ CD79a/CD30/ Pax5, CD3/ CD5/CD2/CD7/CD56/CD57/GranzymB, Ig kappa/lambda/ TdT/ CD34, CD117/ CD15/ MPO/Mum1/ CD21/ CD23, HMB45/MelanA/ CD117 negative. CD1a + single cells. Ki67 proliferative fraction ~ 60%.

IH 2 (Basel): CD11c, CD163, Lysozyme (weak) postive

Case was consulted by dr.A.Tzankov, dr.S.Dirnhofer (Basel Uni, Swiss)





Courtesy of A.Tzankov (Basel uni, Swiss)

Histiocytic sarcoma (WHO 2008)

- Small series and cases; aggressive (~80% fatal), usually high stage; relapses
- From infancy to elderly (mainly adults; median age 52 yrs)
- M ~ F (M > F?)
- Some associated with germ cell tumors (as component); some associated with lymphoma (CLL, FL, oth.), MDS, leukaemia
- Majority in extranodal sites: intestinal tract, skin, soft tissues; lymph nodes
- Rare systemic disease: “malignant histiocytosis”
- Solitary mass, relatively common fever and weight loss; skin: rash, solitary lesion or multiple tumors; intestinal obstruction; hepatosplenomegaly and pancytopenia may occur; lytic bone lesions
- HISTO: Large cells (mono- or pleomorphic) with sinusoid distribution: ovoid, sometimes spindled, usually vesiculated; abundant eosinophilic cytoplasm; haemophagocytosis sometimes; nuclei large, irregularly folded, eccentric, multinucleated cells; admixture of reactive cells (esp. pmn’s in CNS); Mitoses 10-30/10 HPF
- IH: CD163+; CD68+; Lysozyme+; S100+ (weak); CD1a/ Langerin(-), CD21/CD35/CD23(-), MPO(-); LCA / CD45RO, HLA-DR+; CD4+; B/T markers(-); Ki67 variable; HMB45(-)
- MOLECS: rarely (transdifferentiated cases) IgH clonal; 12p isochromosome (germ cell tumor asoc.)

Case #4

Diagnosis:

Nodal histiocytic sarcoma

The short summary: 4 cases

Gender	Age	Site	Mts	Procedure	DGN, yrs	Follow up
F	79	Retroperitoneum	(-)	Core biopsy	FDC sarcoma, 2008	AwD (18 months)
F	60	Jejunum	(-)	Resection	FDC sarcoma, 2009	AwoD (11 months)
F	40	Retroperitoneum	Mts liver	Core biopsy, 2 resections, mts core biopsy	FDC sarcoma, 2001	D, unknown, 48 months
F	77	Inguinal LN	(-)?	LN biopsy	Histiocytic sarcoma, 2009	D, other

The short summary: 4 cases

- Dendritic and histiocytic cell tumors are rare, but really existing categories with different genesis and definite immunophenotype:
  - FDC sarcoma: CD21/CD35/CD23 +
  - IDC sarcoma: S100+
  - Histiocytic sarcoma: CD68/CD163/ Lysozyme+
  - Fibrous DC sarcoma: PanCK+
  - Plasmacytoid DC tumor: CD123+
- Biological behavior: from indolent to aggressive
- Therapy: surgery+ no consensus (radio-; chemo-;)
- Please, keep it in mind, dealing with “low grade” like spindle cell or epithelioid proliferations in LN or extranodal sites

Acknowledgements

1. INCTR iPath hematopathology group (moderator N.Hurwitz)

2. Case #1: courtesy of R. Meškauskas (VPC)

Case #2: R. Sciott (Leuven, Belgium), E. Poškus (VULSK)

Case #3: courtesy of J. M. Mickienė (VPC); A.Tzankov, S. Dirnhofer (Basel uni, Swiss)

Case #4: A. Tzankov, S. Dirnhofer (Basel uni, Swiss)

3. Hematopathology team LT

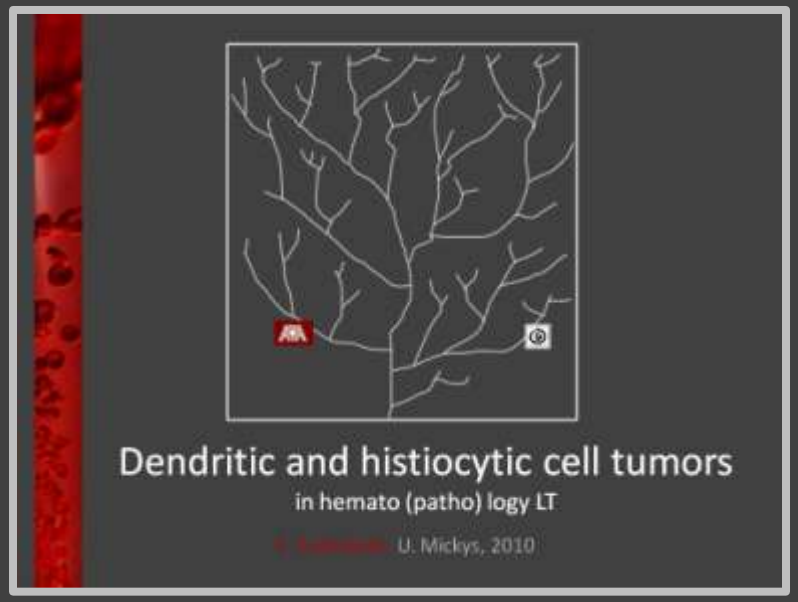
4. Hematopathology teams worldwide

5. Saints and Godfathers

Cornerstones and readings

1. S.H.Swerdlow, E.Campo, N.L. Harris et al. (eds). WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, IARC Press, 2008.
2. Pileri SA, Grogan TM, Harris NL et al. Tumours of histiocytes and accessory dendritic cells: an immunohistochemical approach to classification from the International Lymphoma Study Group based on 61 cases. Histopathology. 2002 Jul;41(1):1-29.
3. Chen W, Lau SK, Fong D, Wang J et al. High frequency of clonal immunoglobulin receptor gene rearrangements in sporadic histiocytic/dendritic cell sarcomas. Am J Surg Pathol. 2009 Jun;33(6):863-73.
4. Feldman AL, Arber DA, Pittaluga S et al. Clonally related follicular lymphomas and histiocytic/dendritic cell sarcomas: evidence for transdifferentiation of the follicular lymphoma clone. Blood. 2008 Jun 15;111(12):5433-9. Epub 2008 Feb 13.
5. Wang E, Hutchinson CB, Huang Q, et al. Histiocytic sarcoma arising in indolent small B-cell lymphoma: report of two cases with molecular/genetic evidence suggestive of a 'transdifferentiation' during the clonal evolution. Leuk Lymphoma. 2010 May;51(5):802-12.
6. …

Vilnius 2008

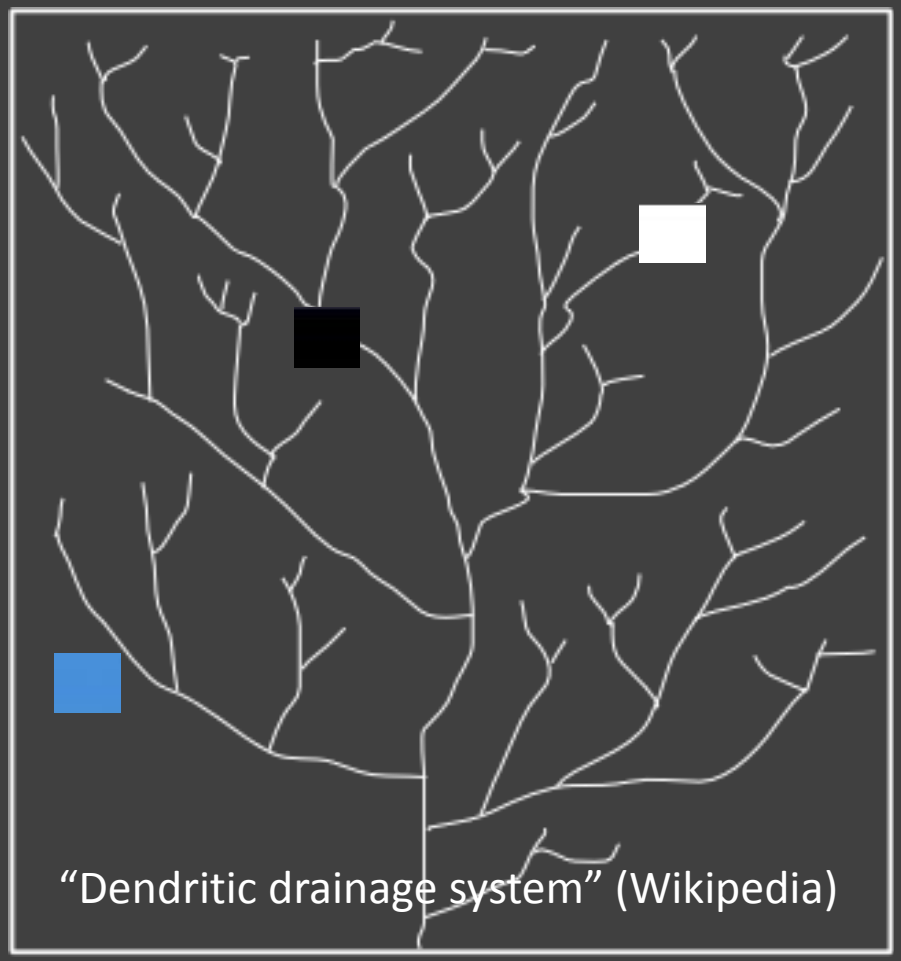


Tartu 2010

Riga 2012 ???

“This Life is Journey from shadow to shadow.”

Procol Harum (G.Brooker)



Dendritic and histiocytic cell tumors

in hemato (patho) logy LT

K. Andrekutė, U. Mickys, 2010