Beautiful Bone Marrows
making sense of all things myeloid

BLPG, Bristol, May 2014

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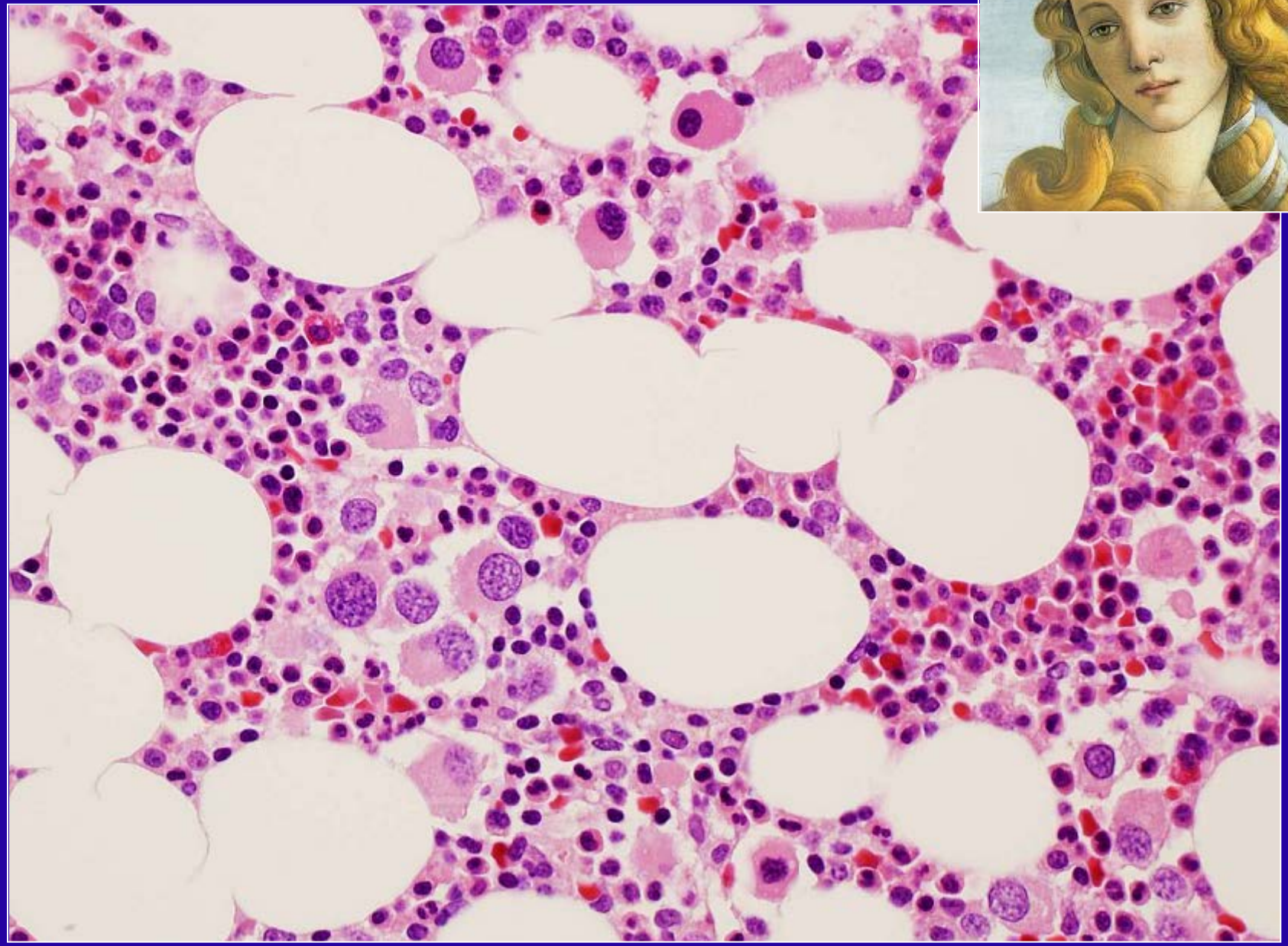
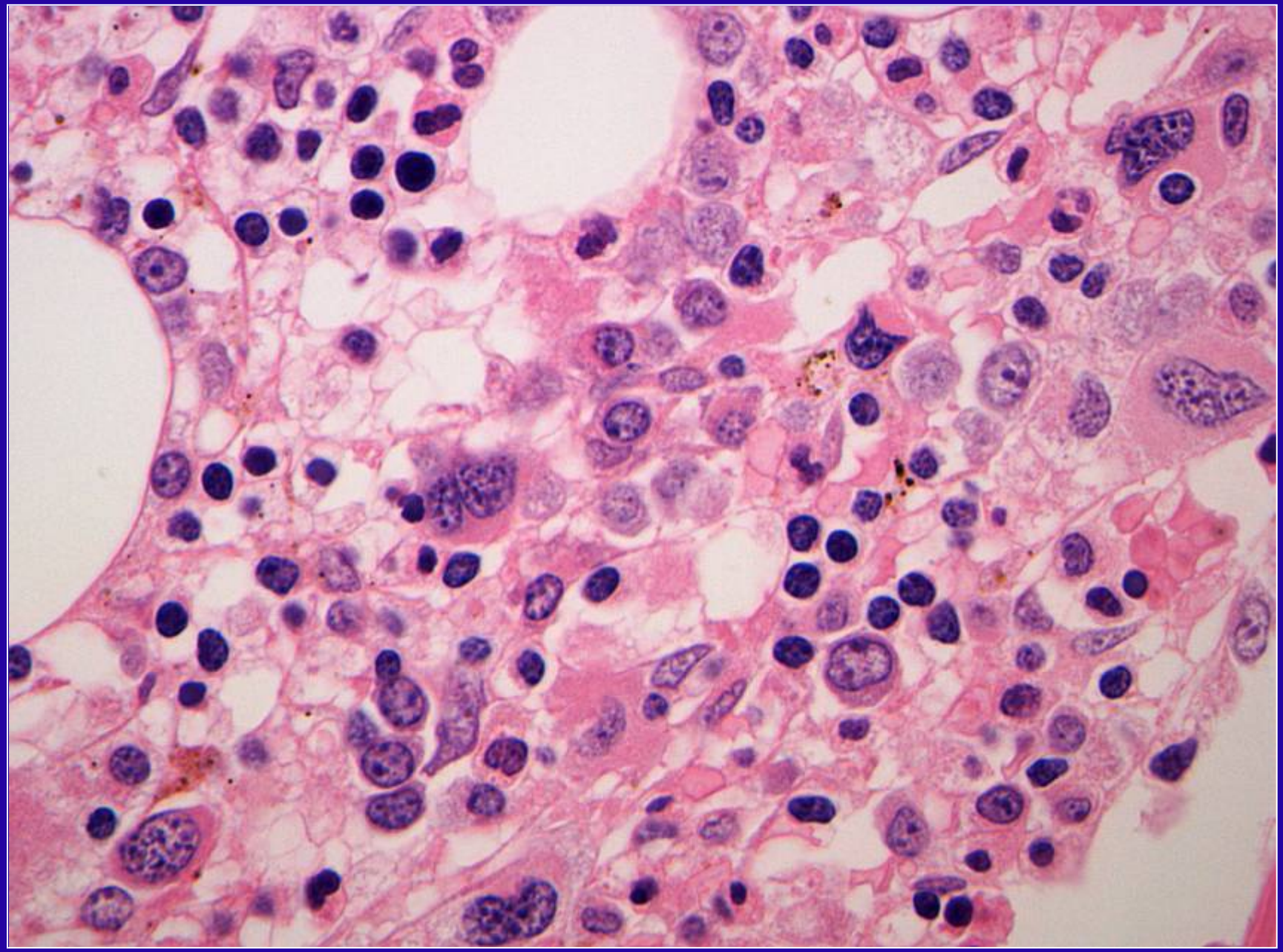
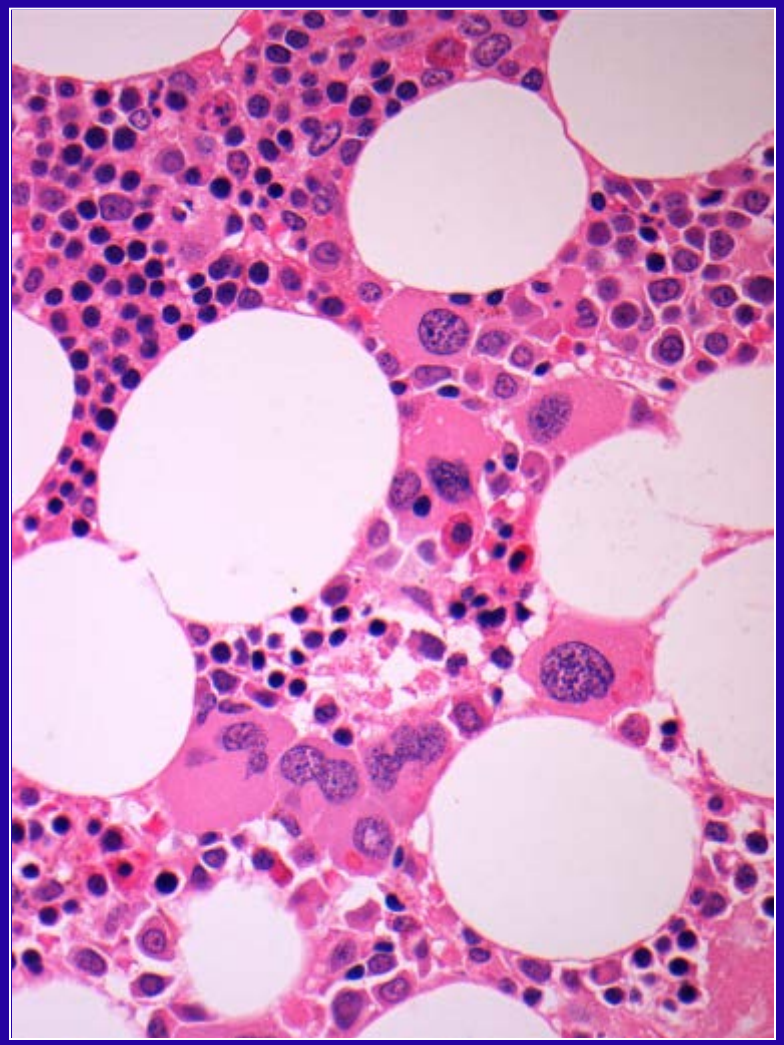
aesthetically pleasing marrows...

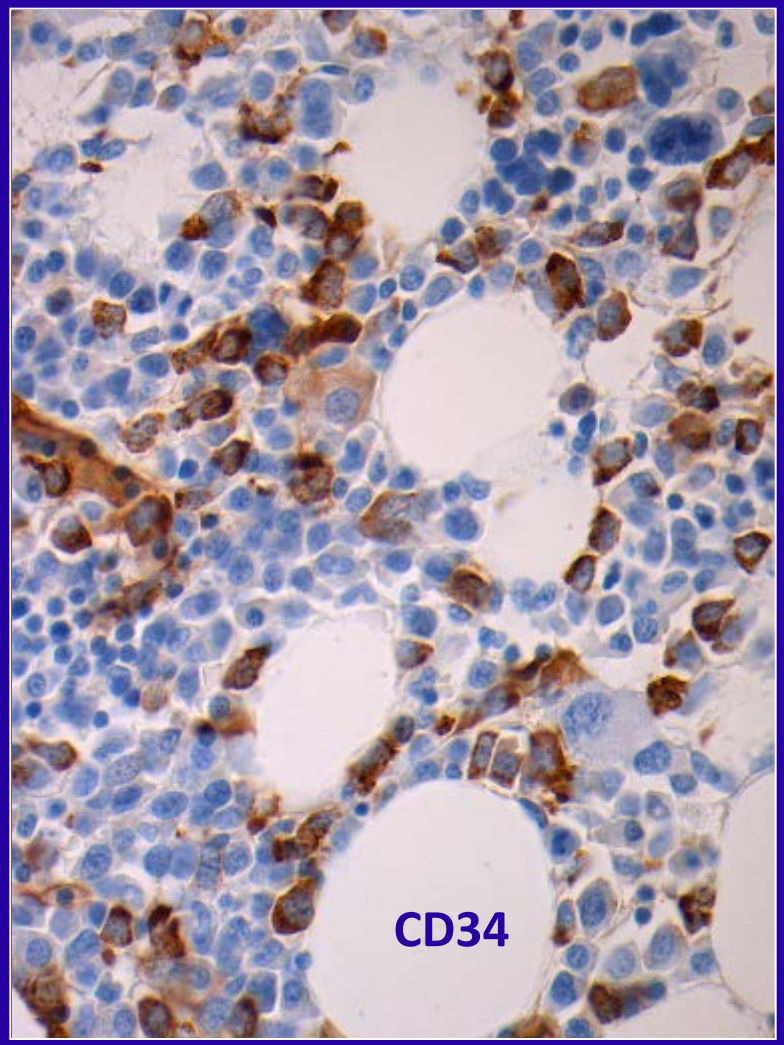


not all isolated 5q- cases have the classical megakaryocytic morphology



not everything which looks like 5q- syndrome is 5q- syndrome:





complex karyotype, including 5q-

> 10% of blasts

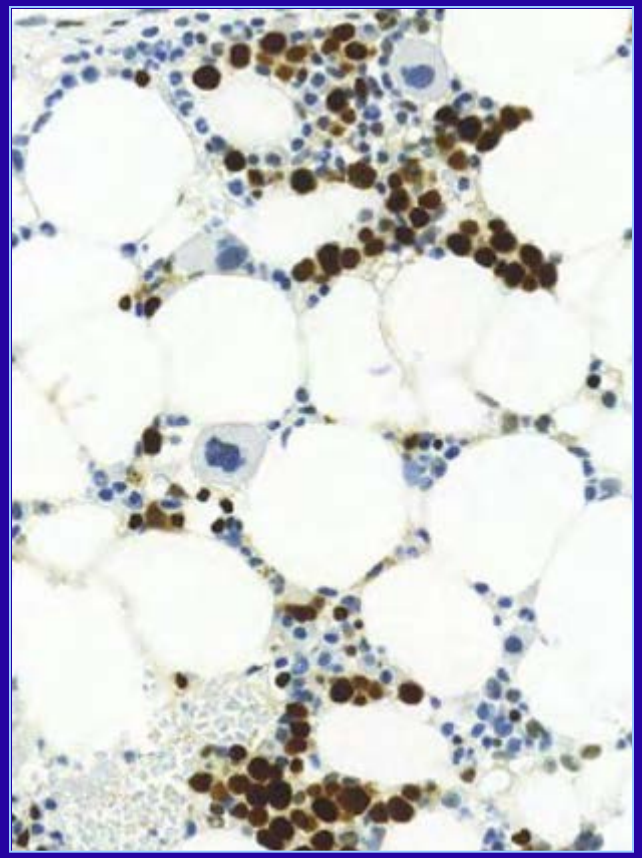
RAEB2

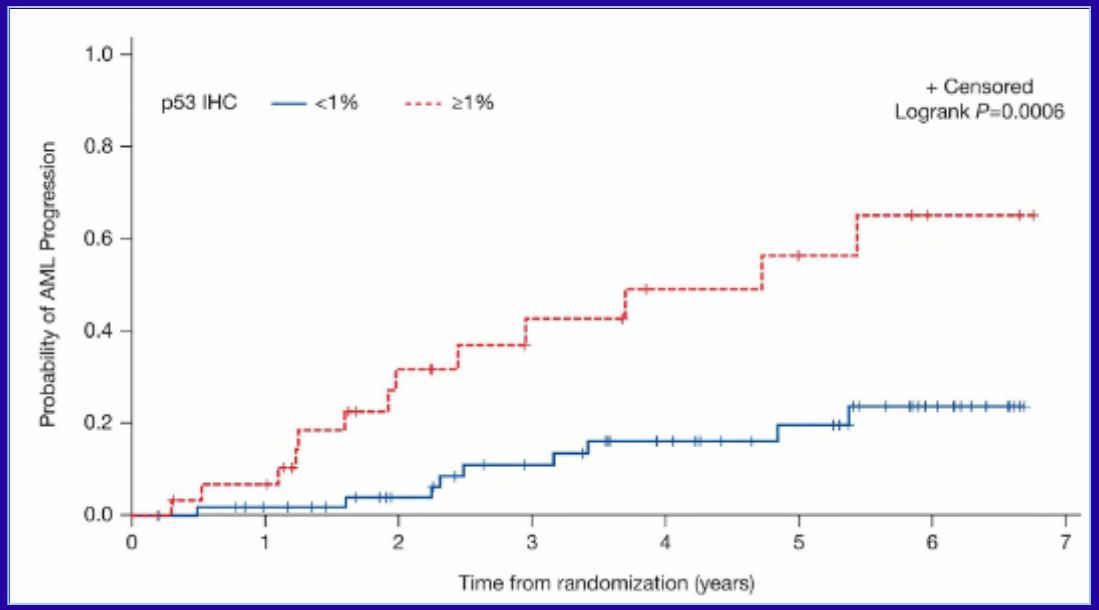
digression:

simple immunohistochemistry and 5q- prognosis

strong nuclear p53

35% of cases (n=85)



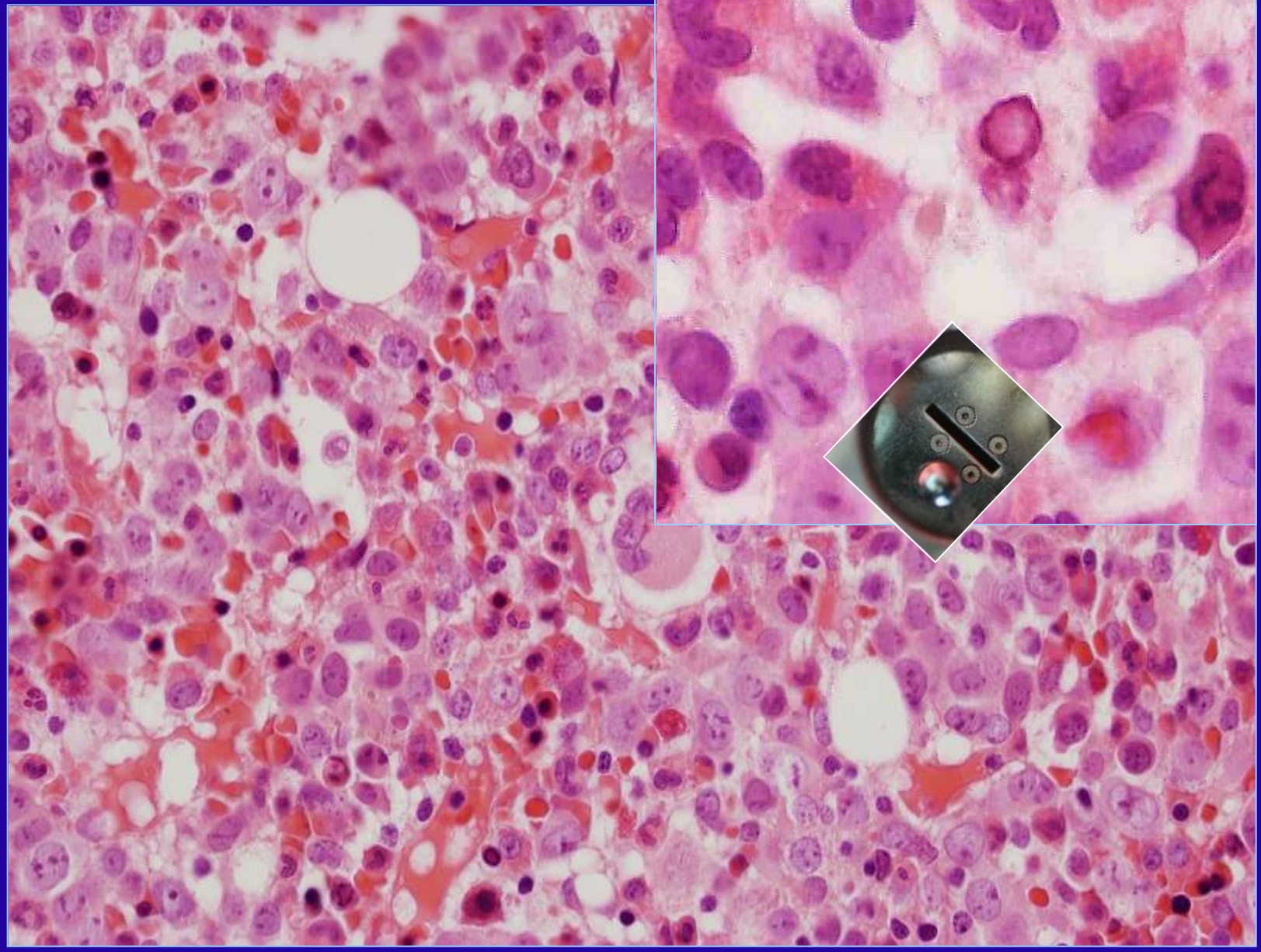


Saft L et al. Haematologica 2014, ahead of print

Mimics of MDS and AML

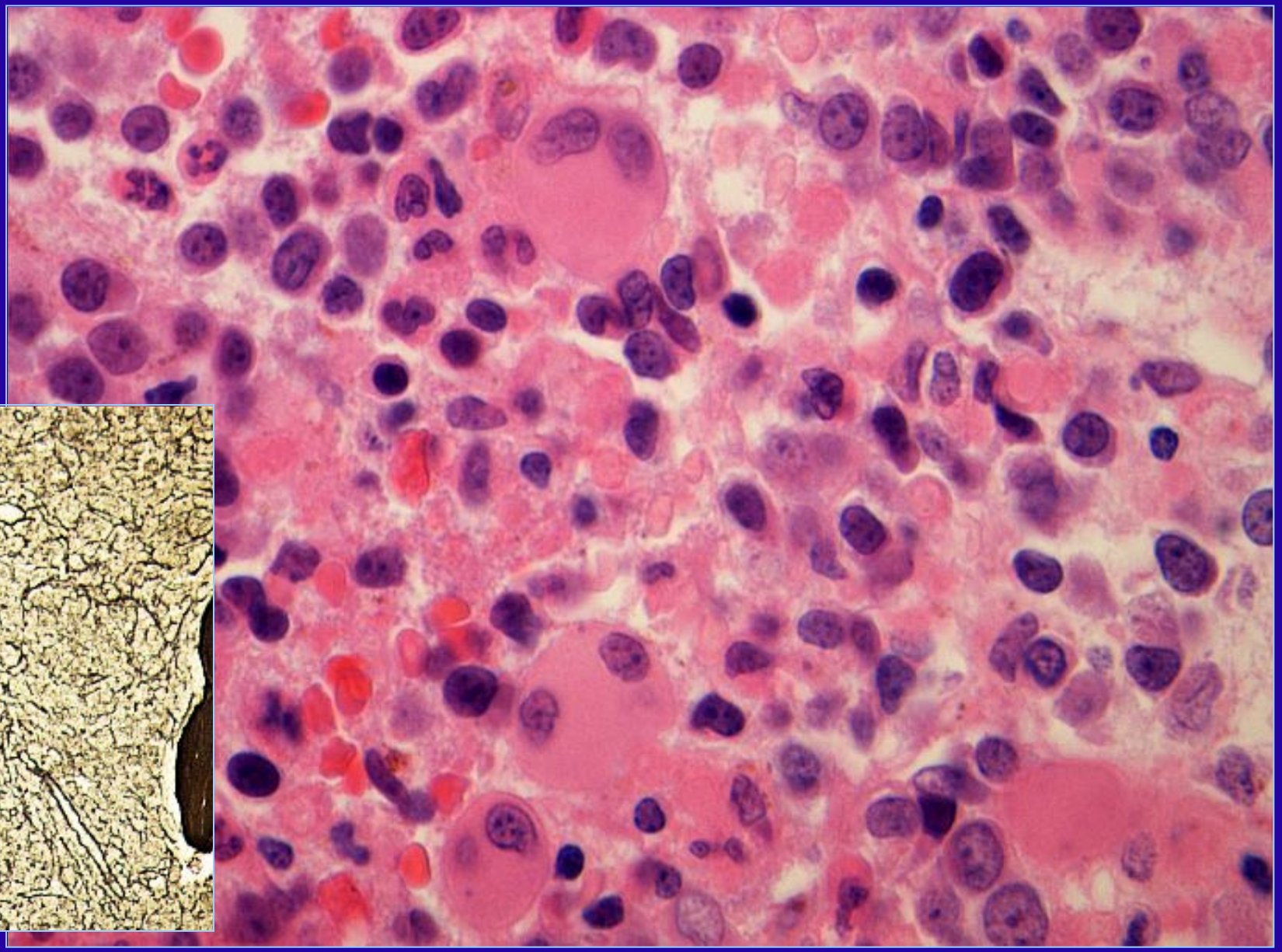
Polish, wz. 1993 under heavily French influence, as usually

Megaloblastic anaemia (B12)



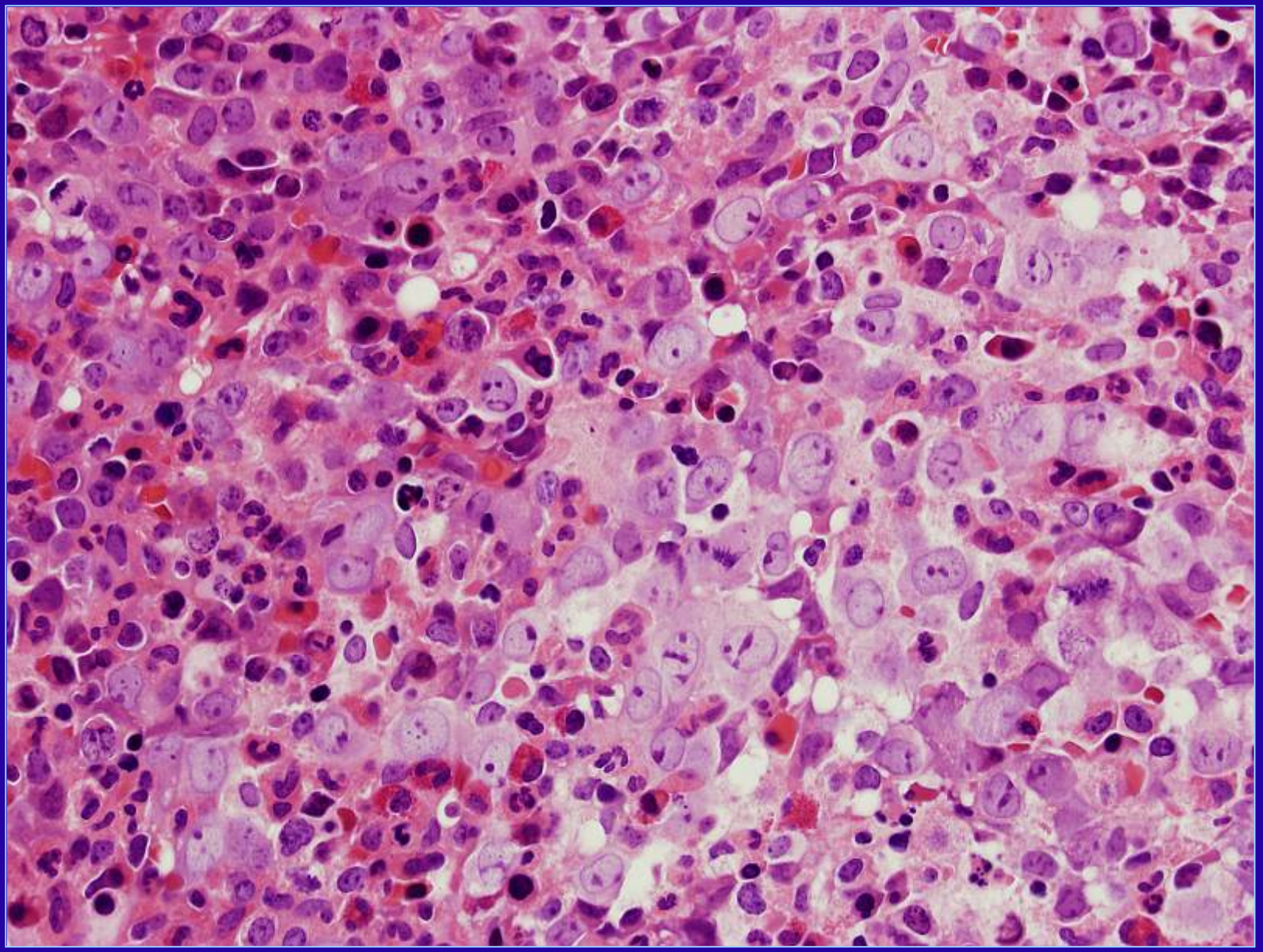
note
'dysplastic'
Mgk!

Megaloblastic anaemia – folate deficiency

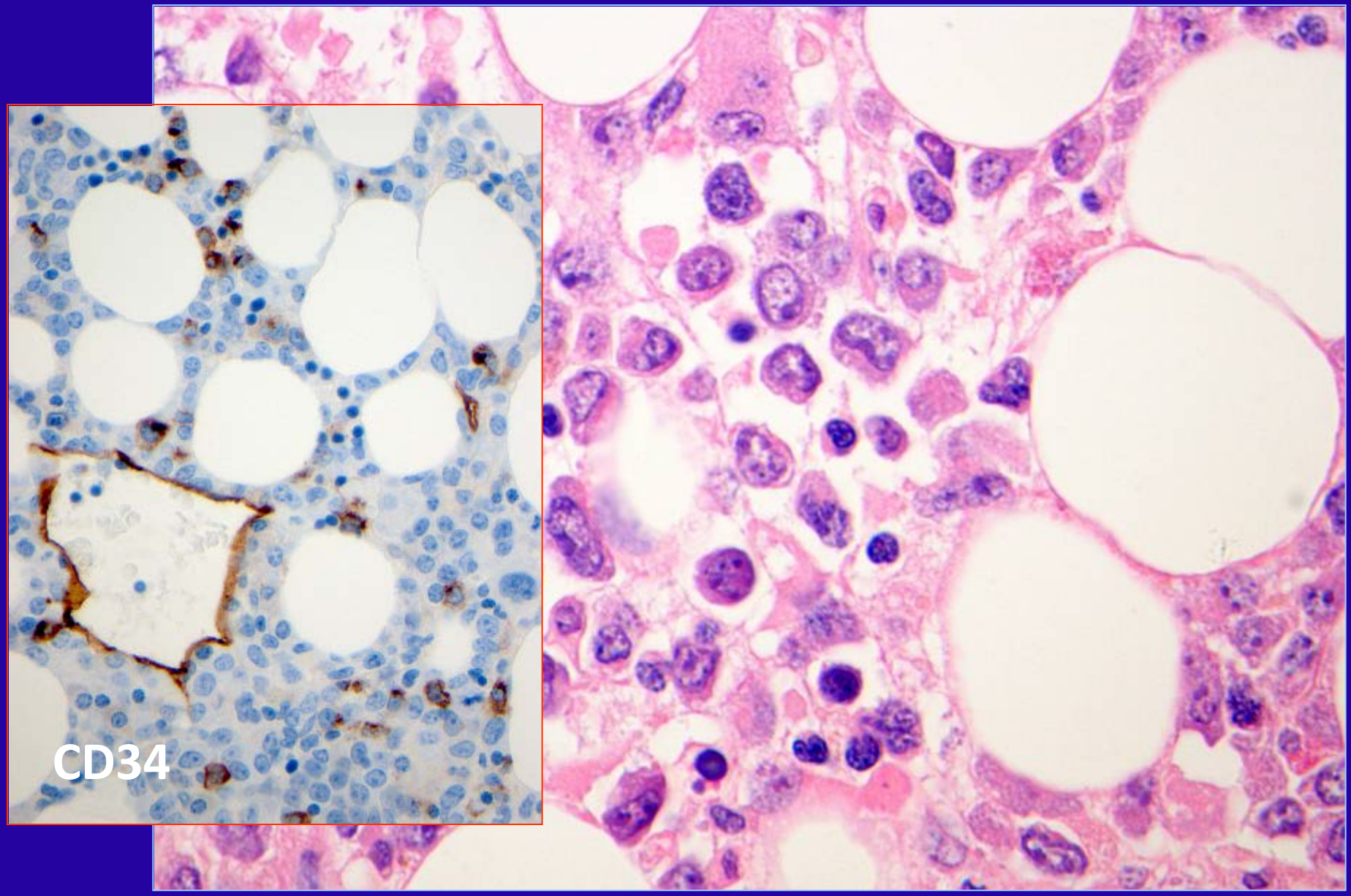


MCV = 87

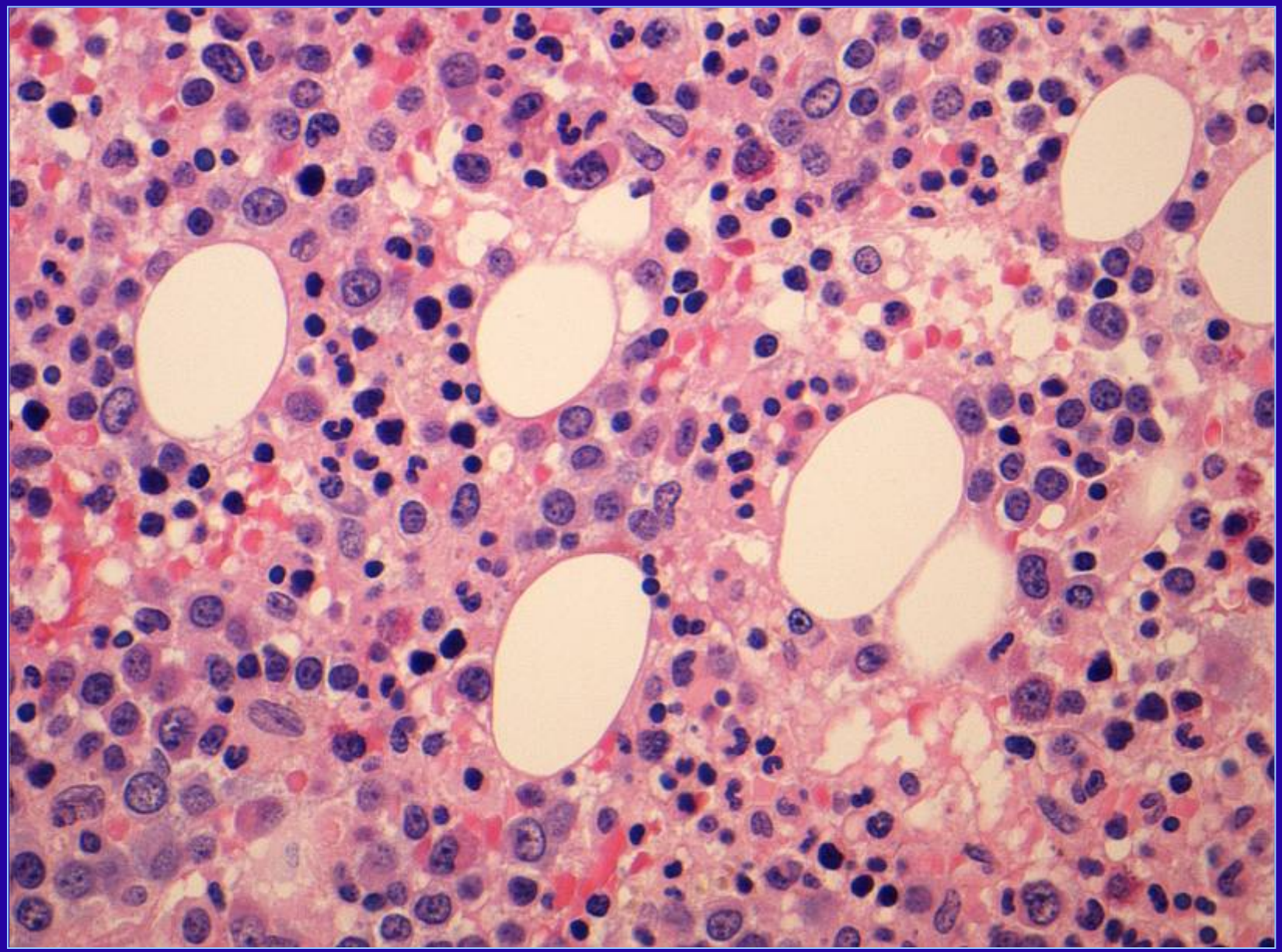
Vit B12 deficiency & Fe deficiency



Toxic myeloid maturation arrest



M 40’ HIV+, new fever, anaemia and lymphadenopathy



Total white cell count	*	3.72
Haemoglobin estimation	*	11.2
Platelet count		155
Red blood cell (RBC) count	*	3.81
Mean corpuscular volume (MCV)		83.4
Mean corpusc. haemoglobin(MCH)		29.5
Haematocrit	*	0.32
RBC Distribution Width	*	16.6
% Hypochromic RBC's		1.3
Neutrophil count (Absolute)		3.54
Lymphocyte count (Absolute)	*	0.12
Monocyte count (Absolute)	*	0.03
Eosinophil count (Absolute)	*	0.01
Basophil count (Absolute)		0.00

...HIV “Myelopathy”

Had Hodgkin’s lymphoma at that time

Total white cell count		6.44
Red blood cell (RBC) count		5.17
Haemoglobin estimation		153
Haematocrit		0.461
Mean corpuscular volume (MCV)		89.2
Mean corpusc. haemoglobin(MCH)		29.6
Mean corpusc. Hb. conc. (MCHC)		332
RBC Distribution Width		12.4
Platelet count		204
Platelet distribution width		11.3
Neutrophil count (Absolute)		4.33
Lymphocyte count (Absolute)	*	1.18
Monocyte count (Absolute)		0.69
Eosinophil count (Absolute)		0.20
Basophil count (Absolute)		0.04
Nucleated RBC		0.00

2014

HIV: don't get fooled by a mimic of a mimic

British Journal of Haematology, 2001, **112**, 900–908

Acute myeloid leukaemia in human immunodeficiency virus-infected adults: epidemiology, treatment feasibility and outcome

Laurent Sutton,[1] Pascal Guénel,[2] Marie-Laure Tanguy,[3] Bernard Rio,[4] Nathalie Dhedin,[5] Philippe Casassus[6] and Olivier Lortholary[6] for the French Study Group on Acute Myeloid Leukaemia in HIV-infected Patients [1]*Service d'Hématologie, Hôpital Pitié-Salpétrière, Paris,* [2]*INSERM U 88, Hôpital National, Saint-Maurice,* [3]*Département de Statistiques Médicales, Société Française de Greffe de Moelle, Hôpital Pitié-Salpêtrière, Paris,* [4]*Département d'Hématologie, Hôpital de l'Hotel Dieu, Paris,* [5]*Département d'Hématologie, Hôpital Henri Mondor, Creteil, and* [6]*Service de Médecine Interne, CHU Avicenne, Bobigny, France*

Received 15 August 2000; accepted for publication 24 November 2000

Summary. The epidemiology and clinical outcome of acute myeloid leukaemia in human immunodeficiency virus (HIV)-infected adults is poorly documented. We retrospectively surveyed all French haematology centres for adult acute myeloid leukaemia (AML) cases diagnosed between January 1990 and July 1996 who were found to be HIV-seropositive before or at the time of AML diagnosis. Medical charts were reviewed to determine the stage of HIV infection, the characteristics of AML and the response of AML to chemotherapy. Sixteen cases of AML (13 men, three women) were reported by 12 haematology units. Based on assumptions on the size, age and sex distribution of the HIV-infected population in France, the estimated risk of AML in 1990 to 1996 among HIV-infected adults was twice that of the general population (standardized incidence ratio = 2·05; 95% confidence interval, 1·17–3·34). Two other cases occurring before 1990 were spontaneously notified to the authors and were included in the clinical analysis. At AML diagnosis, the median $CD4^+$ cell count was 275×10^6/l and nine patients had acquired immune deficiency syndrome (AIDS). Fifteen patients were scheduled for remission-induction therapy of AML. No deaths were related to AML treatment. Complete remission was obtained in 11 out of 15 patients. Three patients were long-term survivors: two remain alive in complete remission at 8 years and 9 years, respectively, and the third died of AIDS at 8 years. A $CD4^+$ cell count above 200×10^6/l at AML diagnosis was predictive of longer survival (log-rank test: $P = 0{\cdot}004$). Like many other malignancies, the incidence of AML appears to be increased in HIV-infected patients. Our results show a twofold higher incidence, although this needs to be confirmed in a specifically designed prospective epidemiological study. Such patients, especially those with $CD4^+$ cell counts above 200×10^6/l at AML diagnosis, should receive remission-induction therapy, which can confer long-term survival.

Keywords: acute myeloid leukaemia, HIV infection, chemotherapy.

(only 2/18 possibly had t-AML)

Clinical and cytogenetic characteristics of myelodysplastic syndrome in patients with HIV infection

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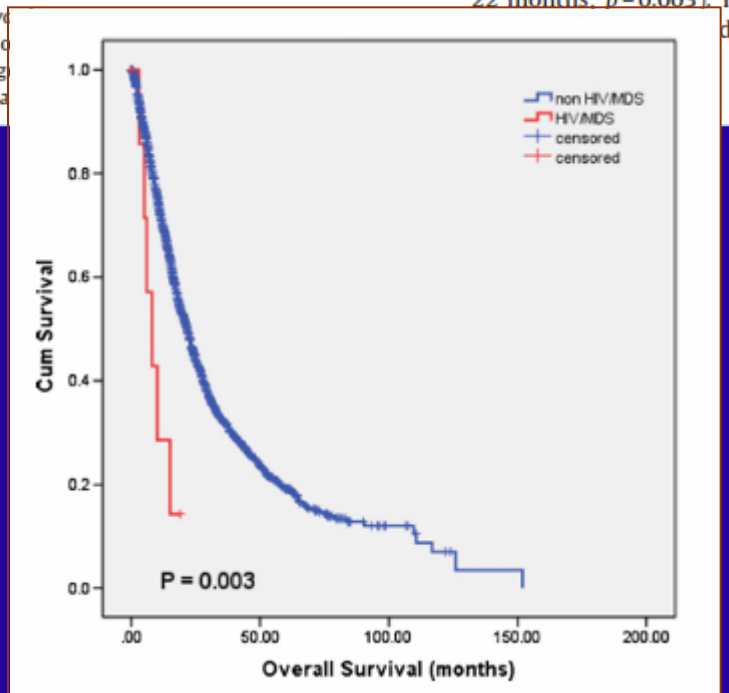
Keyw
Myelo
Cytog
Huma

ABSTRACT

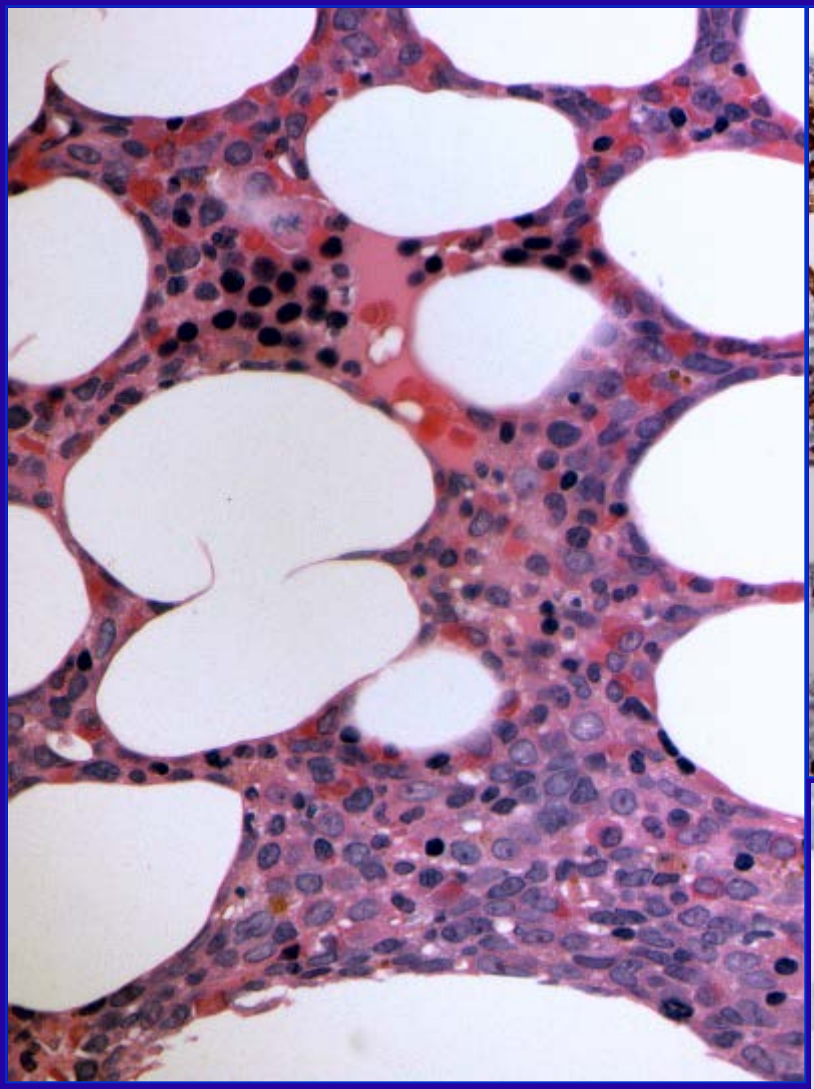
We report eight patients of myelodysplastic syndrome (MDS) with HIV infection. Compared to a historical cohort of HIV-uninfected MDS patients, HIV/MDS were younger ($p = 0.019$), had more complex cytogenetics ($p = 0.015$), and more often had 7q deletion or monosomy 7 ($p = 0.011$). In five patients, HIV/MDS transformed to acute myeloid leukemia, with a median time to transformation of 7 months. Also, the median overall survival was shorter in the HIV/MDS than in their HIV-uninfected counterparts (8 vs. 22 months; $p = 0.003$). These results suggest that HIV/MDS is a high-risk MDS necessitating thorough d follow-up.

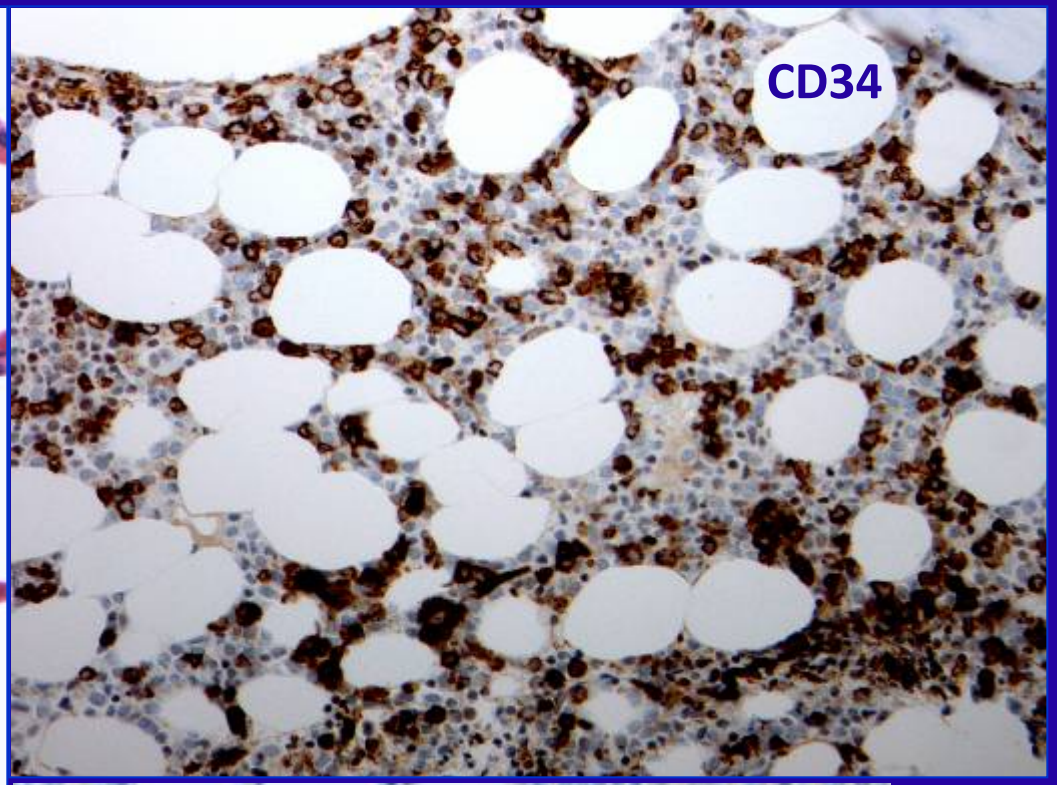


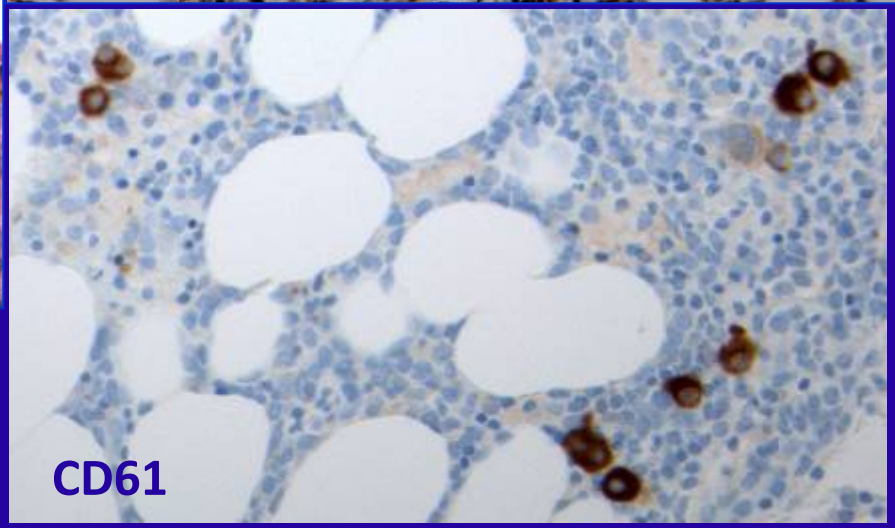
median survival 8 vs. 22 months

M40

long history of HIV infection (currently negligible viral load)







2003: B-ALL

2013: sudden pancytopenia

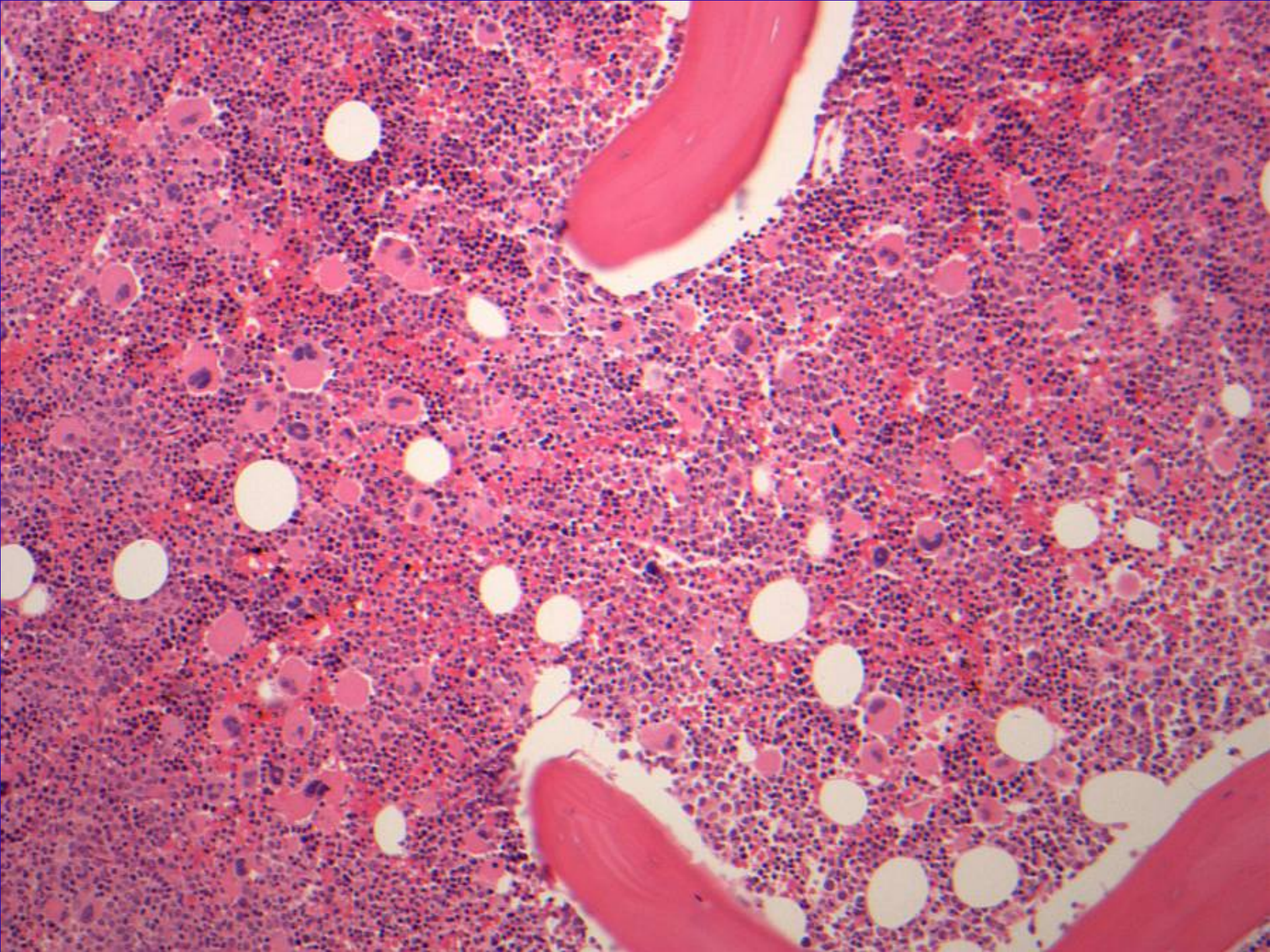
M82

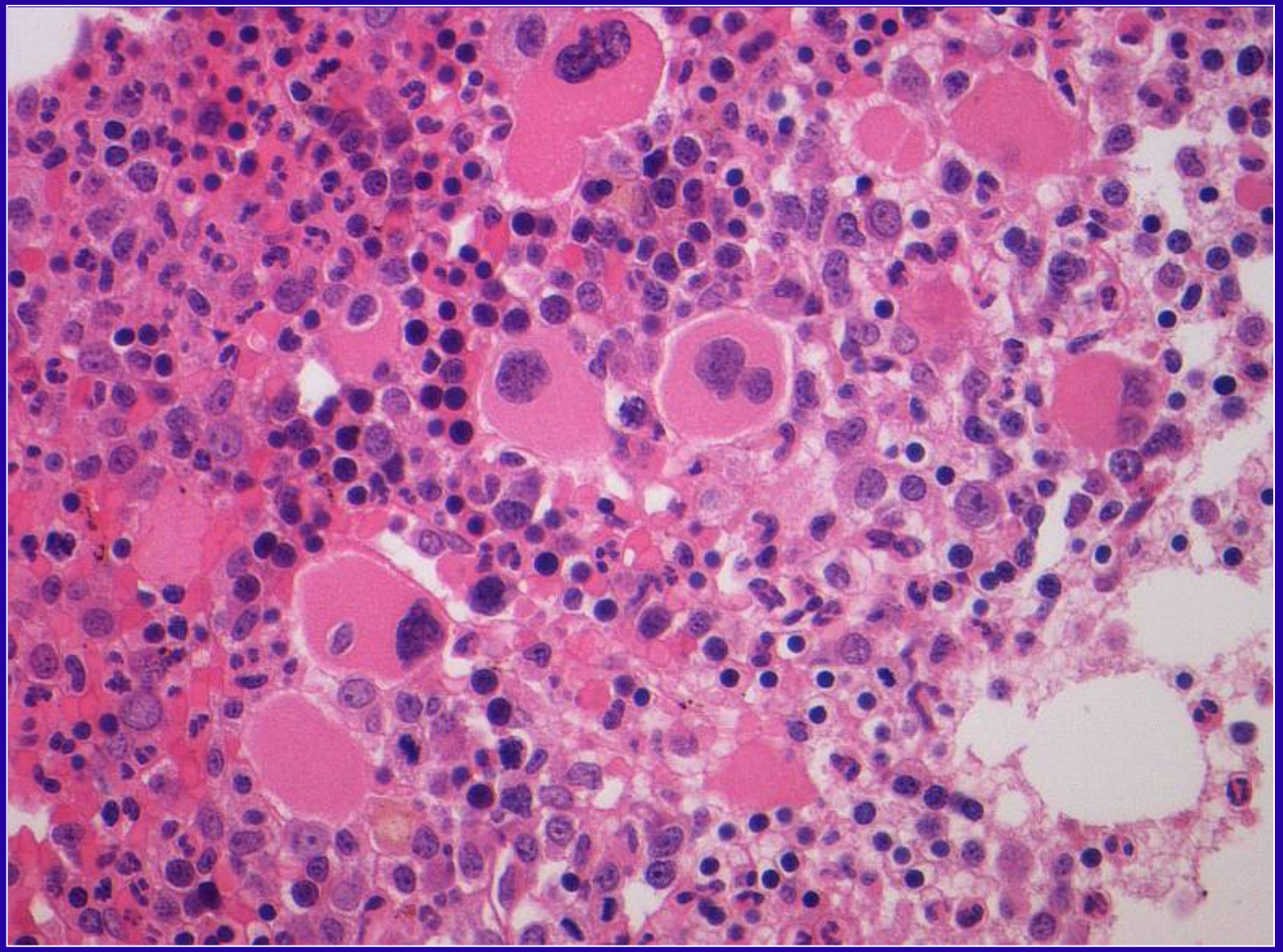
Pancytopenia
Transfusion-dependent
Excessive alcohol consumption

Hb	9	g/dL
plt	60	x 10^9/L
N	0.7	x 10^9/L
Ly	0.7	x 10^9/L

no significant increase in blasts on BM aspirate and flow cytometry

no dysplasia on BM aspirate
normal karyotype





?MDS
?MDS/MPN

...but remains asymptomatic & stable for last 6 years

Association between alcohol drinking and MDS – published studies.

Author	Year	Country	Cases		Controls		OR	95% CI	Type of controls
			Drinkers	Non-drinkers	Drinkers	Non-drinkers			
Pekmezovic T	2006	Serbia Montenegro	37	43	36	124	2.96	1.67–5.27	Hospital
Strom SS	2005	US, Texas	172	73	218	70	0.76	0.51–1.11	Hospital
Dalamaga M	2002	Greece	83	1	82	2	2.02	0.18–22.76	Hospital
Nagata C	1999	Japan	55	55	411	410	1	0.67–1.49	Population
Ido M	1996	Japan	56	60	42	64	1.42	0.84–2.42	Hospital
Summary estimate							1.31	0.79–2.18	

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Leukemia Research

journal homepage: www.elsevier.com/locate/leukres

Review

Smoking and alcohol intake as risk factors for myelodysplastic syndromes (MDS)

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Myelodysplastic syndromes (MDS)
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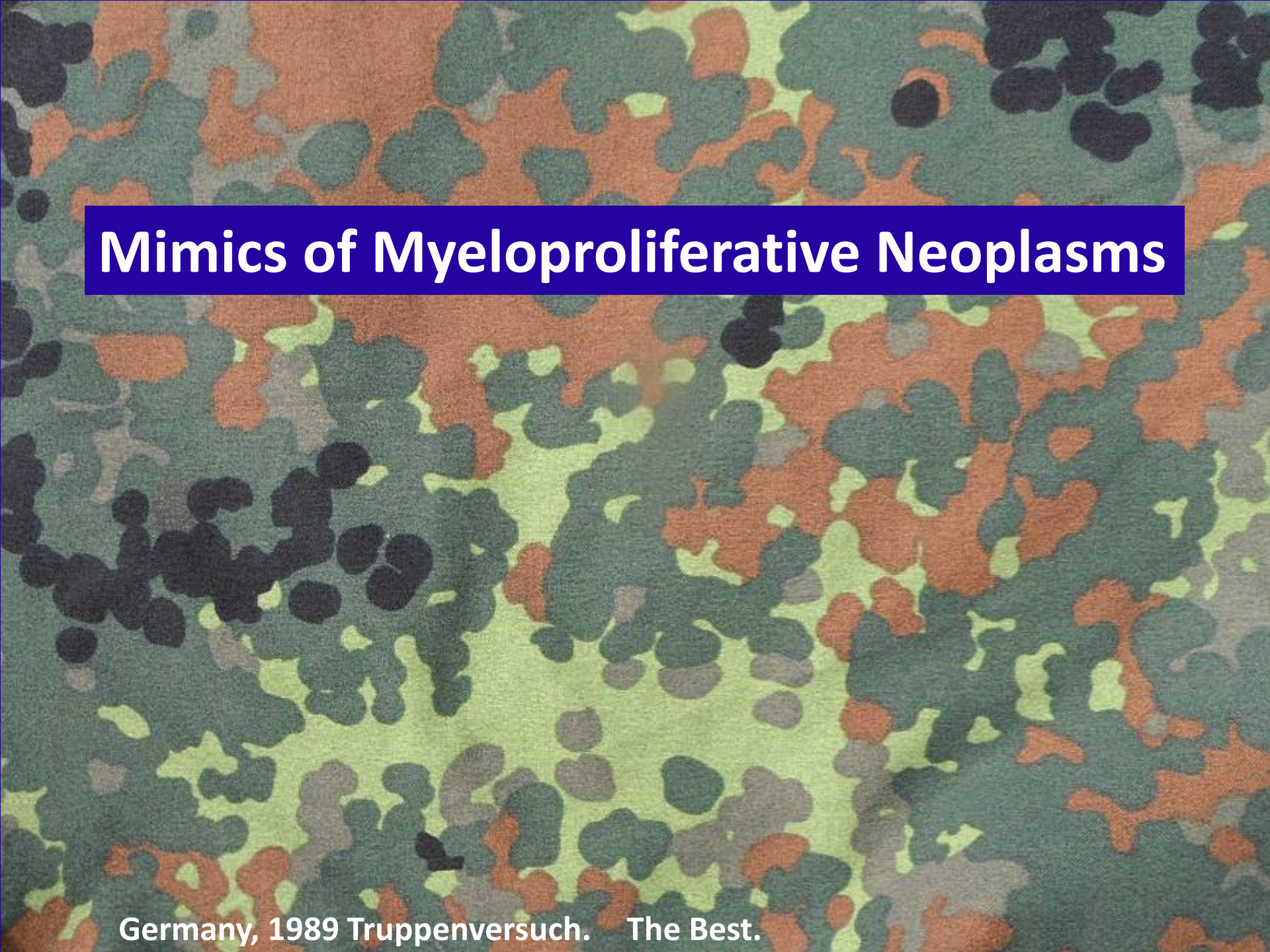
Risk factors

ABSTRACT

The term myelodysplastic syndromes (MDS) include a diverse group of diseases in which the bone marrow production of blood cells is disrupted. In spite of the wealth of information on therapeutic options, little is known about the epidemiology of MDS, including population variations and risk factors. A narrative review of published literature and meta-analyses were conducted, identifying and summarizing key reports that describe the association between smoking, alcohol and MDS. There were 10 case–control studies that looked at the association between smoking and MDS, for a total of 1839 cases and 2831 controls. The meta-estimate for the association between ever smoking and MDS was 1.45 (95% CI: 1.21–1.74), with heterogeneity among studies ($p = 0.05$), but no evidence of publication bias. The relationship between alcohol consumption and MDS has been examined in five studies, including 745 cases and 1642 controls. The overall association was 1.31 (95% CI: 0.79–2.18), with significant heterogeneity ($p = 0.003$) and no evidence of publication bias. This re-analysis of published data strongly suggests that smoking is significantly associated with MDS, while alcohol does not seem to play a major role in MDS etiology. Large epidemiological studies incorporating biomarkers of exposure, along with pooled analysis are needed to better address the contribution of lifestyle factors to the development of MDS.

Mimics of Myeloproliferative Neoplasms



F53

Summer 2012: liver failure of unclear aetiology

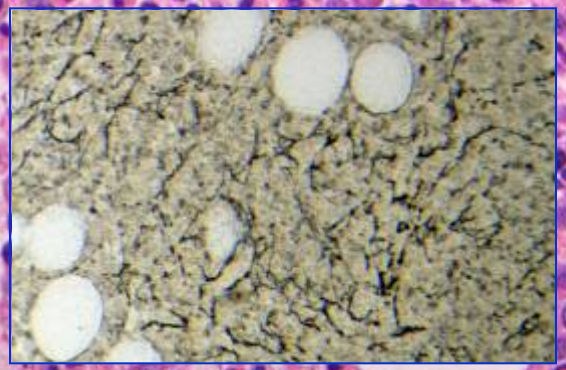
Total white cell count	*	42.46	Dec 2012	10^9/l
Red blood cell (RBC) count	*	3.26		10^{12}/l
Haemoglobin estimation	*	10.0		g/dl
Haematocrit	*	0.333		l/l
Mean corpuscular volume (MCV)	*	102.1		fl
Mean corpusc. haemoglobin(MCH)		30.7		pg
Mean corpusc. Hb. conc. (MCHC)		30.0		g/dl
RBC Distribution Width		14.6		%
Platelet count	*	483		10^9/l
Platelet distribution width		11.0		
Neutrophil count (Absolute)	*	37.24*		x10^9/l
Lymphocyte count (Absolute)		1.80		x10^9/l
Monocyte count (Absolute)	*	1.49		x10^9/l
Eosinophil count (Absolute)	*	1.64		x10^9/l
Basophil count (Absolute)	*	0.29		x10^9/l
Nucleated RBC		0.00		x10^9/l

BCR/ABL (-)
JAK2 WT
karyotype normal

no dysplastic features on aspirate/film
no excess of blasts

***ANC ~37-40 Sept. 2012 – Feb 2013**

denies excessive alcohol consumption **(statement supported by the patient's husband)**



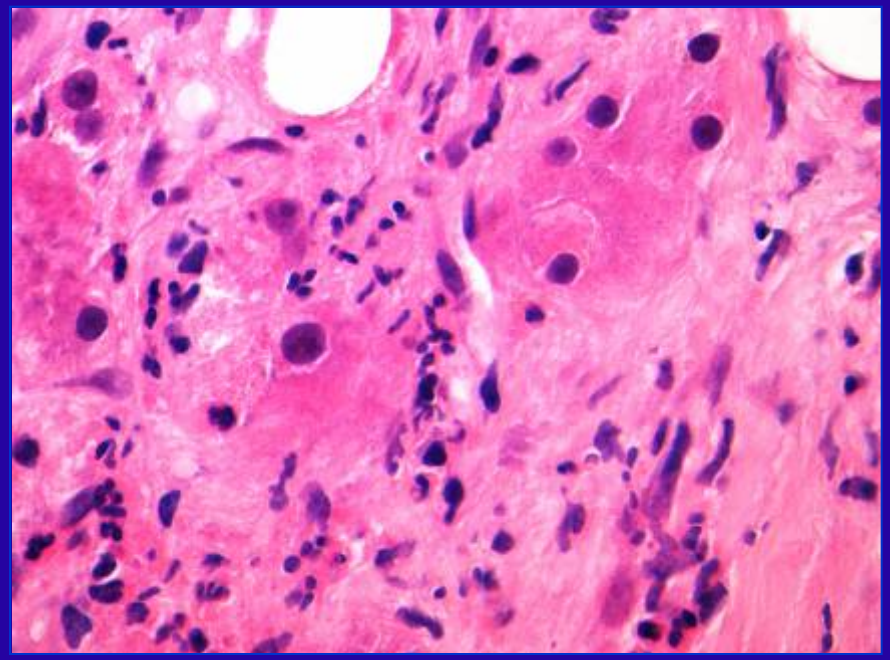
CONCLUSION

TREPHINE BONE MARROW BIOPSY:

- UNRESOLVED DIFFERENTIAL DIAGNOSIS BETWEEN CHRONIC MYELOMONOCYTIC LEUKAEMIA (CMML-1) AND FLORID REACTIVE CHANGES OF UNKNOWN ORIGIN (possibly secondary to the liver disease).

2nd opinion:

Suspicious but not diagnostic of myeloproliferative or overlap myelodysplastic/ myeloproliferative process although not classifiable and reaction cannot be excluded.



liver biopsy

alcoholic hepatitis

(diagnosis: Dr G Langman)

a bottle of wine per day

(in the morning)

1: Morales AM, Hashimoto LA, Mokhtee D. Alcoholic hepatitis with leukemoid reaction after surgery. J Gastrointest Surg. 2006 Jan;10(1):83-5.

2: Argüelles-Grande C, Leon F, Matilla J, Domínguez J, Montero J. Steroidal management and serum cytokine profile of a case of alcoholic hepatitis with leukemoid reaction. Scand J Gastroenterol. 2002 Sep;37(9):1111-3.

3: Juturi JV, Hopkins T, Farhangi M. Severe leukocytosis with neutrophilia (leukemoid reaction) in alcoholic steatohepatitis. Am J Gastroenterol. 1998 Jun;93(6):1013.

4: Larvol L, Colardelle P, Callard P, Levecq H. [Acute alcoholic hepatitis and leukemoid reaction]. Gastroenterol Clin Biol. 1993;17(12):972-3.

5: Mitchell RG, Michael M 3rd, Sandidge D. High mortality among patients with the leukemoid reaction and alcoholic hepatitis. South Med J. 1991 Feb;84(2):281-2.

6: Petracca E, Ramazzina E, Zennaro R. [Leukemoid reaction in acute alcoholic hepatitis]. Clin Ter. 1988 Aug 31;126(4):249-53.

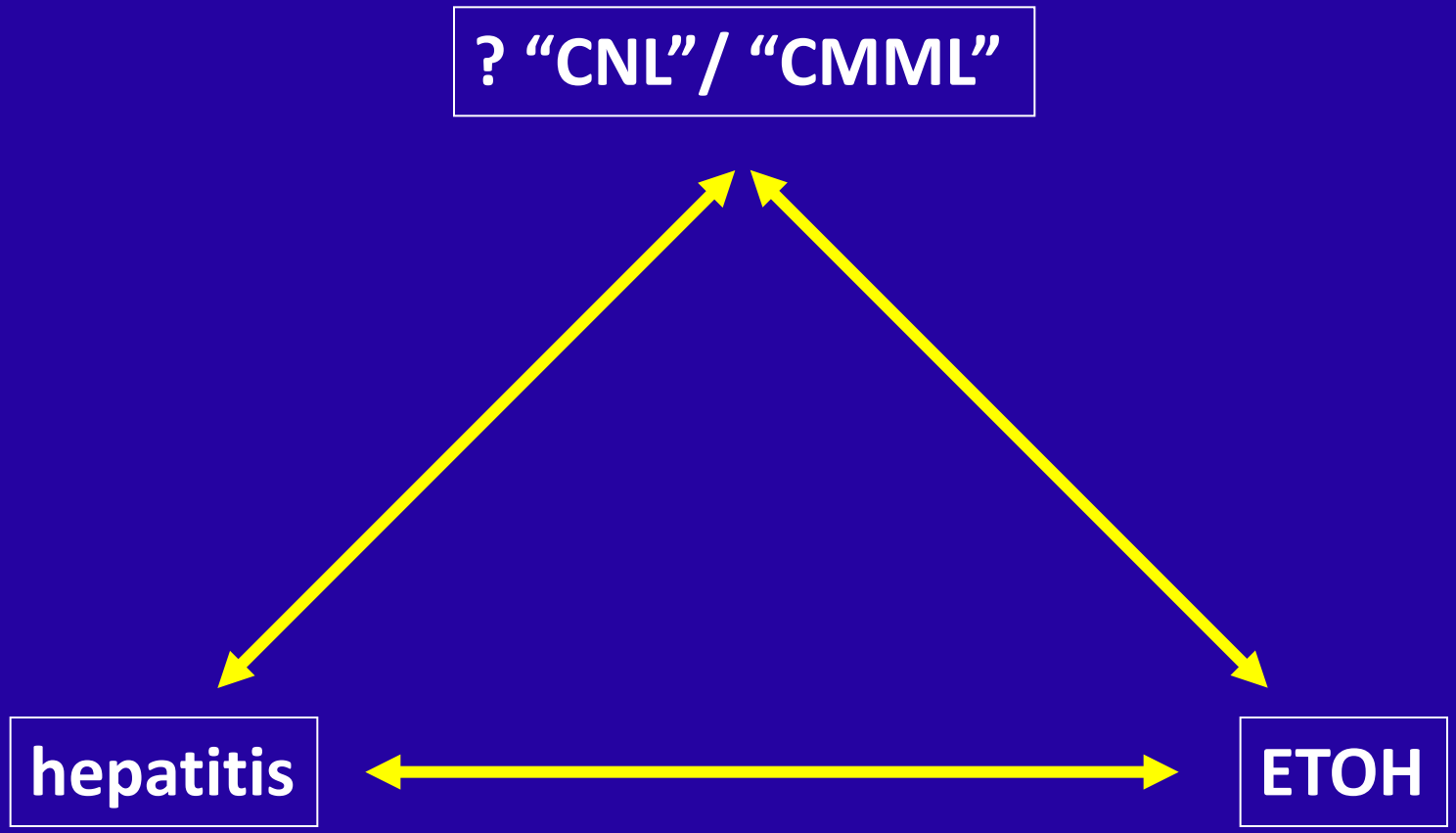
7: Natali G, Trotta A, Colantonio D, Cascone F, Di Lauro G, Ruggieri M, Di Pietro M. [Leukemoid reaction in a case of severe acute alcoholic hepatitis]. Minerva Med. 1982 May 19;73(21):1497-501.

8: Dao C, Forrestier F, Malvy JL, Boisson J, Bousser J. [Letter: Leukemoid reaction during acute alcoholic hepatitis]. Nouv Presse Med. 1976 May 22;5(21):1363-4.

9: Wallach H, Jacobs J. Alcoholic hepatitis with leukemoid reaction. South Med J. 1975 Oct;68(10):1266-70.

10: Baur HR, Pierach CA, Dhar GJ, Gülmen G. Alcoholic hepatitis with leukemoid reaction and thrombocytosis. Minn Med. 1975 Sep;58(9):668-70.

11: COLMAN RW, SHEIN HM. Leukemoid reaction, hyperuricemia and severehyperpyrexia complicating a fatal case of acute fatty liver of the alcoholic. Ann Intern Med. 1962 Jul;57:110-5.


? “CNL”/ “CMML”
hepatitis
ETOH

Recent appointment

Total white cell count		5.44	10^9/l
Red blood cell (RBC) count		4.20	10^{12}/l
Haemoglobin estimation		144	g/L
Haematocrit		0.424	l/l
Mean corpuscular volume (MCV)	*	101.0	fl
Mean corpusc. haemoglobin(MCH)	*	34.3	pg
Mean corpusc. Hb. conc. (MCHC)		340	g/L
RBC Distribution Width		12.4	%
Platelet count		215	10^9/l
Platelet distribution width		11.1	
Neutrophil count (Absolute)		2.92	x10^9/l
Lymphocyte count (Absolute)		1.56	x10^9/l
Monocyte count (Absolute)		0.58	x10^9/l
Eosinophil count (Absolute)		0.36	x10^9/l
Basophil count (Absolute)		0.02	x10^9/l
Nucleated RBC		0.00	x10^9/l

...I was pleased to see you looking quite well in yourself, having put on a lot of weight and also pleased to report that your blood tests are also normalising.

I think this has all been achieved following rigorous abstention from alcohol consumption ...

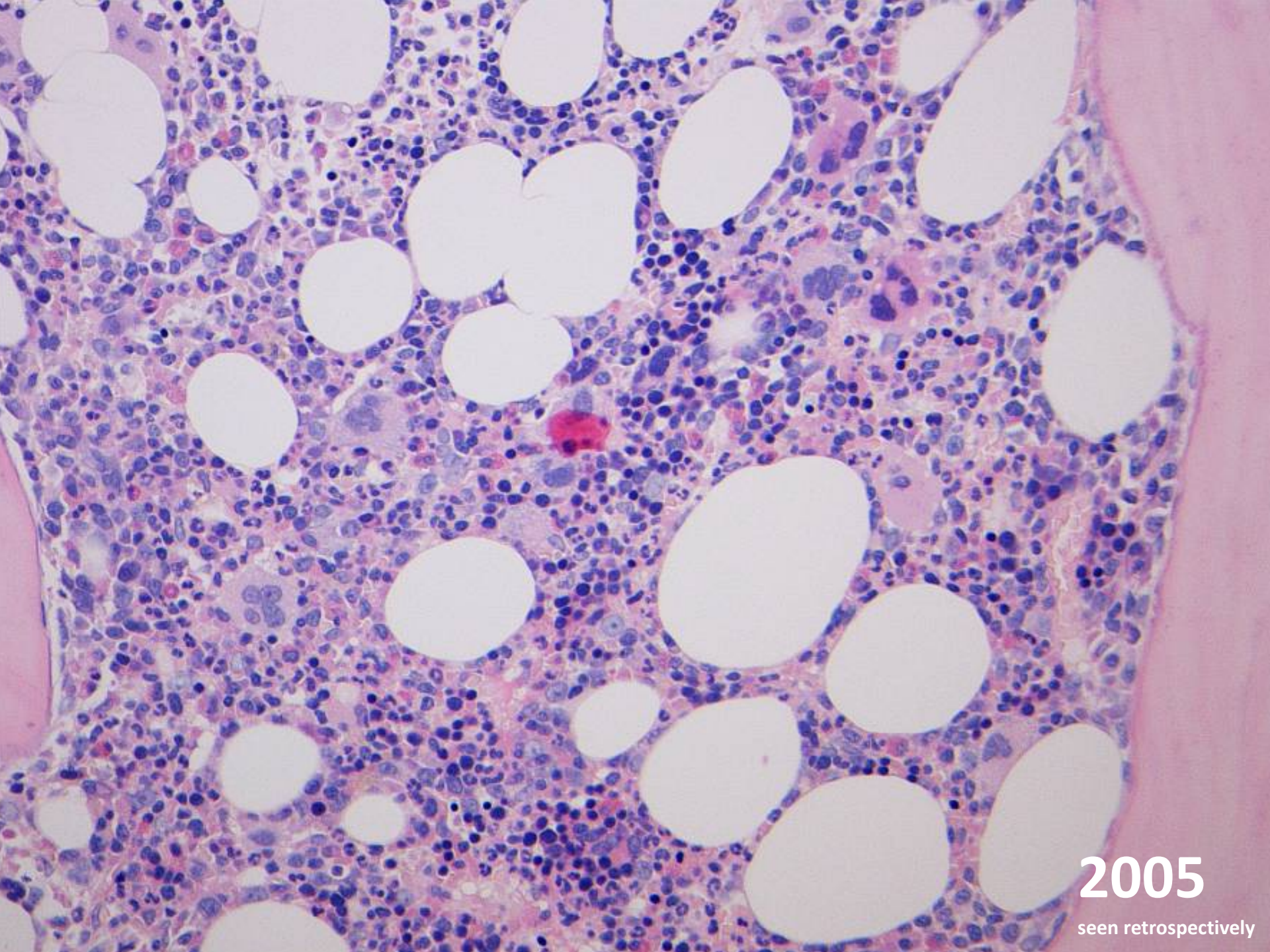
M, late 40’

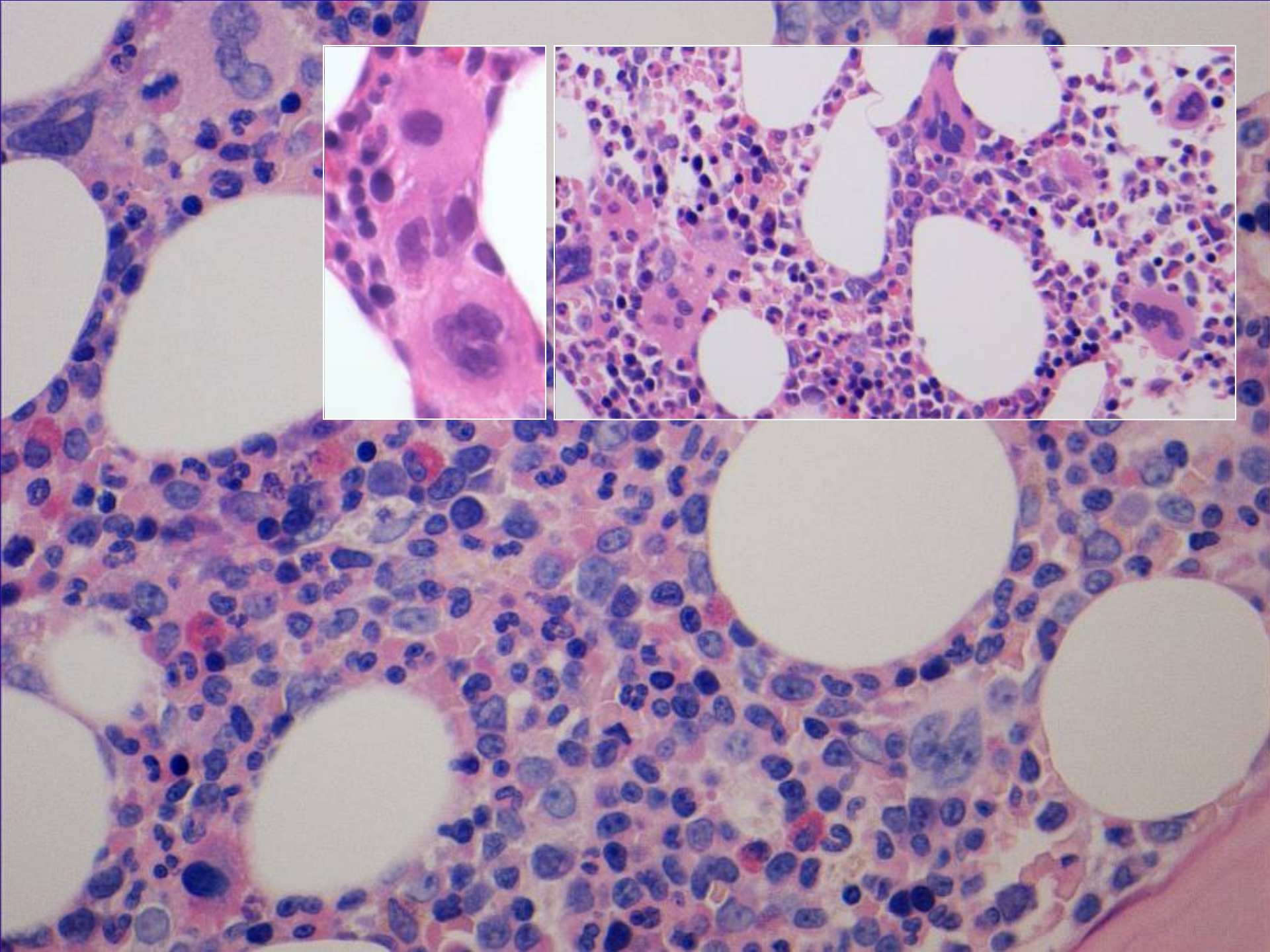
history of thrombocytosis and polycythaemia
splenomegaly at presentation (2005)
JAK2-negative

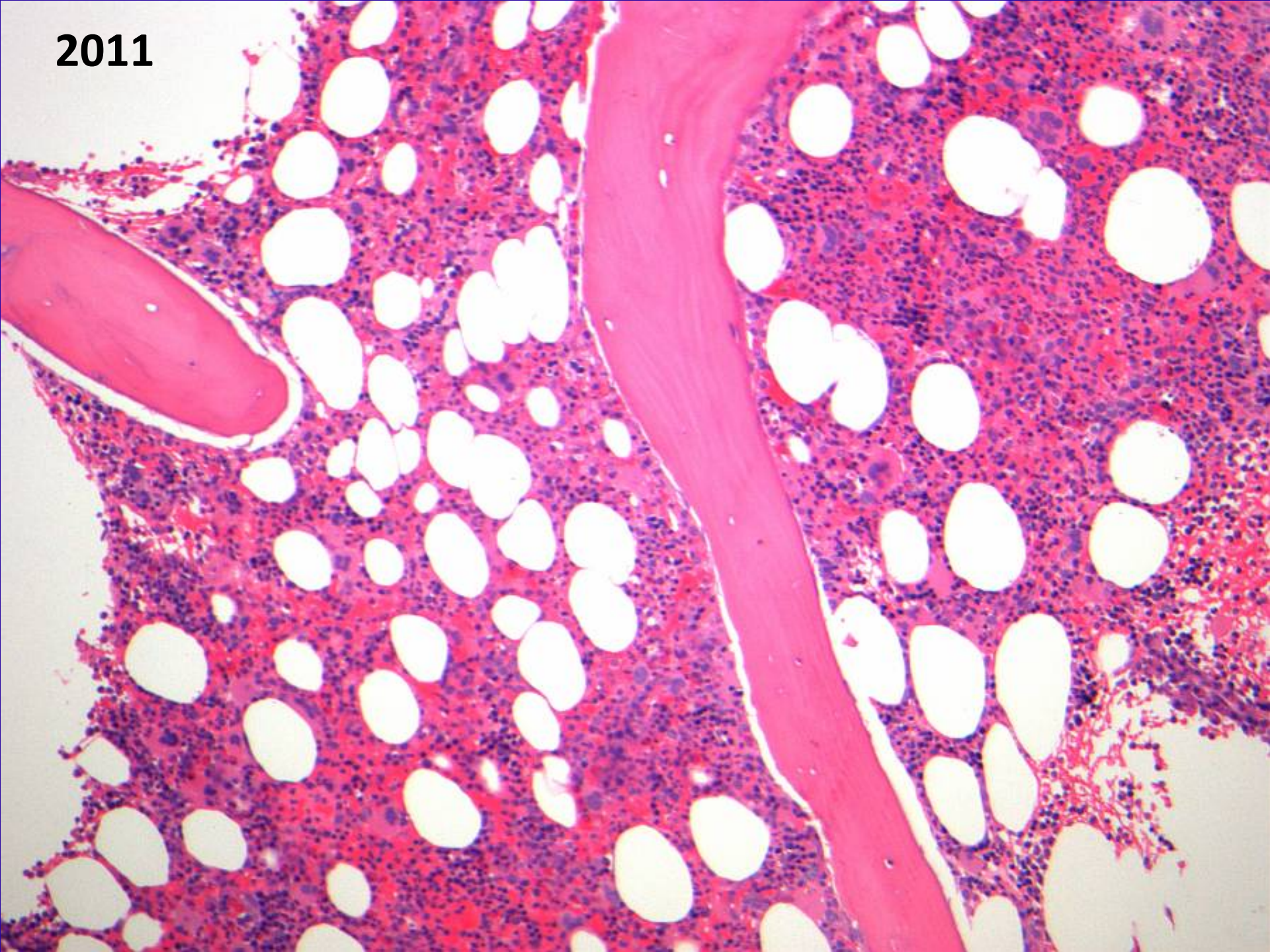
diagnosis of myeloproliferative disorder in outside institution

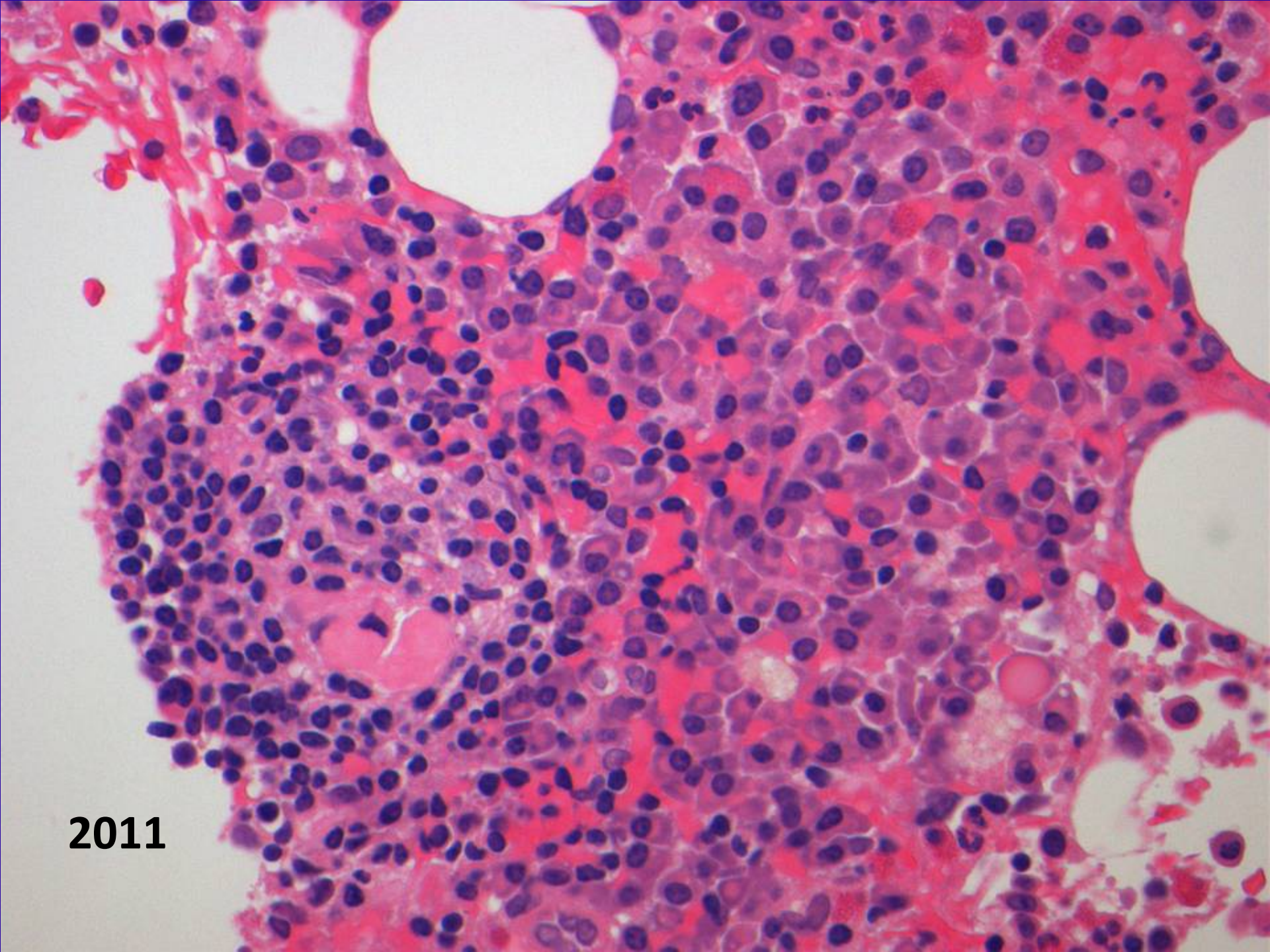
put on Hydroxycarbamide, later discontinued - cytopenias

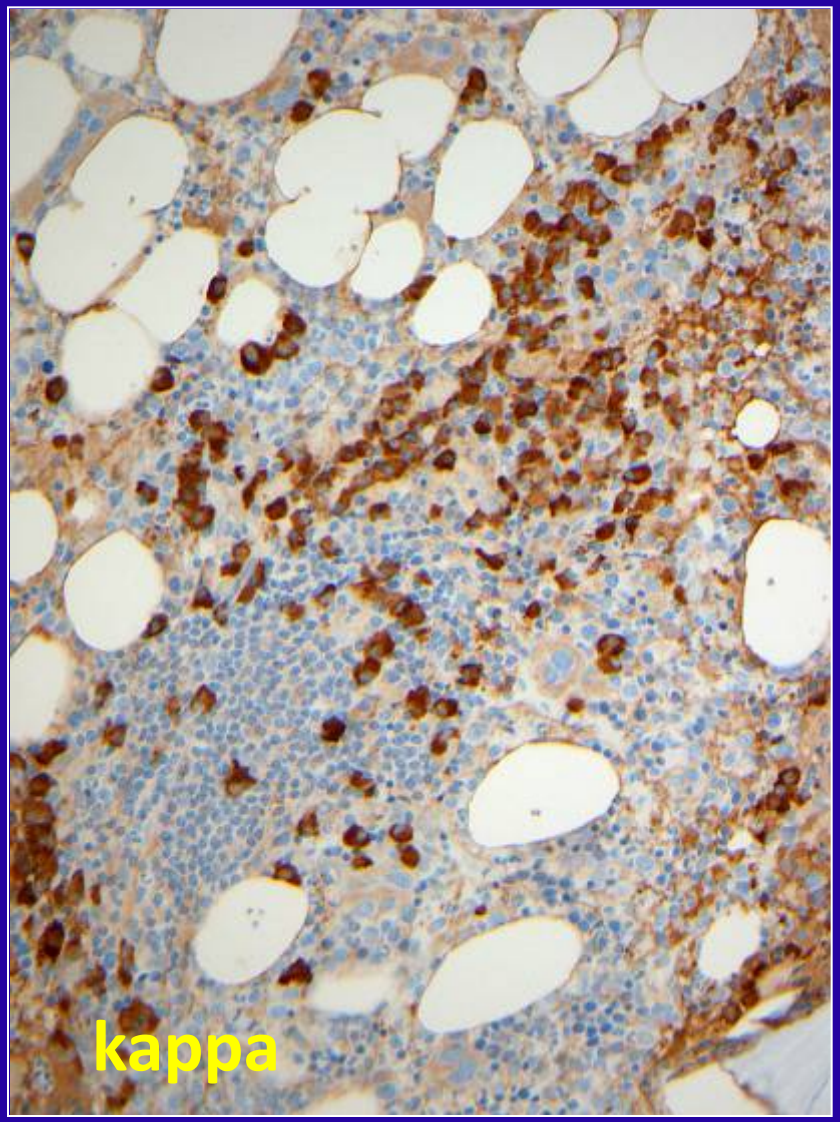
no evidence of paraproteinaemia

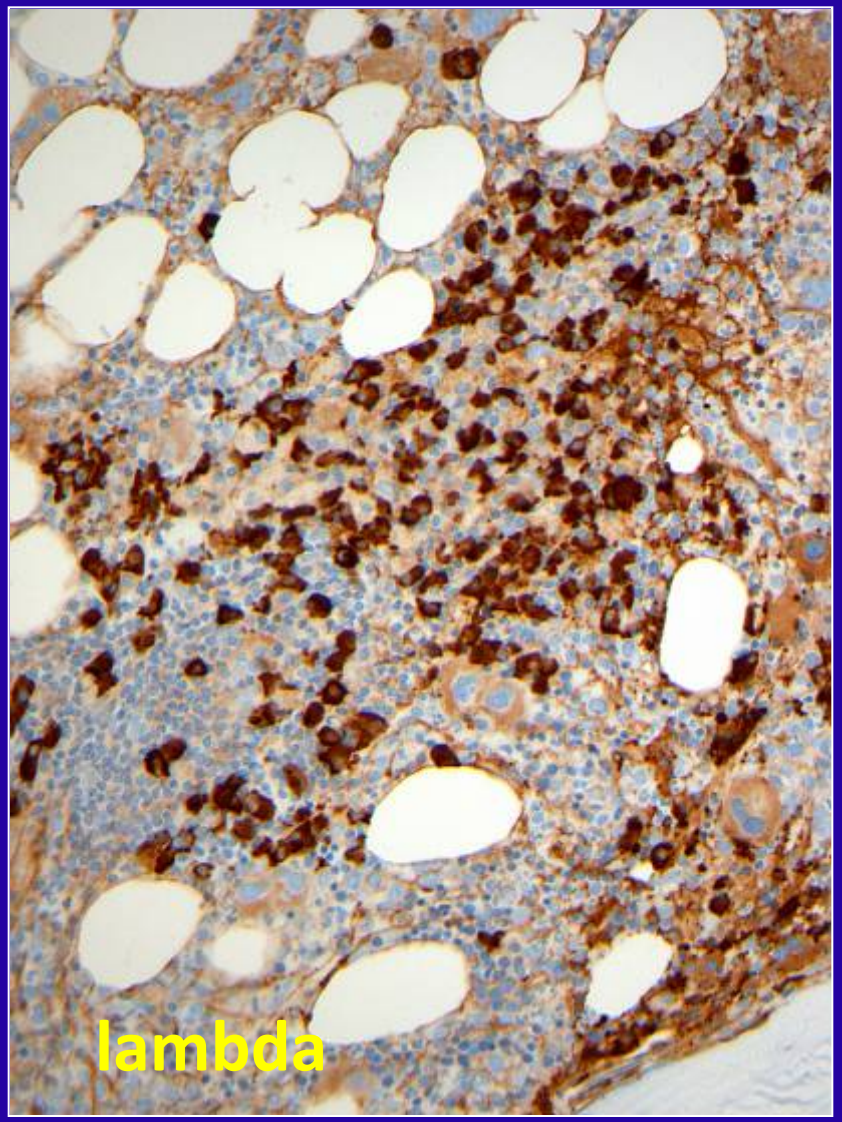

2005
seen retrospectively




2011


2011


kappa


lambda

A lot of confusion
I have suspected a lymphoma...

POEMS syndrome strongly suggested by a Dermatologist

Skin Manifestations and Vascular Endothelial Growth Factor Levels in POEMS Syndrome

Impact of Autologous Hematopoietic Stem Cell Transplantation

Stéphane Barete, MD; Roger Mouawad, PhD; Sylvain Choquet, MD; Karine Viala, MD; Véronique Leblond, MD, PhD; Lucile Musset, MD; Zahir Amoura, MD, PhD; David Khayat, MD, PhD; Camille Francès, MD

Objectives: To investigate skin manifestations of the polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (POEMS) syndrome and their correlation with serum vascular endothelial growth factor (s-VEGF-A) levels and to describe the impact of autologous peripheral blood stem cell transplantation (aPBSCT) on these manifestations and the correlation with s-VEGF-A levels.

Design: Case series from January 1993 through June 2007.

Setting: Hospitalized care in Assistance Publique-Hôpitaux de Paris in Pitié-Salpêtrière and Tenon hospitals.

Patients: Twenty-three patients with POEMS syndrome, 10 of whom were clinically followed up after aPBSCT.

Main Outcome Measures: Description and distribution of clinical lesions at POEMS syndrome diagnosis, skin evaluation after aPBSCT, and s-VEGF-A levels measured at POEMS syndrome diagnosis and after aPBSCT.

Results: In 21 patients with skin manifestations at POEMS syndrome diagnosis, the most common skin manifestations were hemangiomas (18 patients [86%]), hyperpigmentation (16 [76%]), skin thickening (12 [57%]), acrocyanosis (12 [57%]), hypertrichosis (11 [52%]), acquired facial lipoatrophy (11 [52%]), and white nails (8 [38%]). The median s-VEGF-A level was not different between patients with and without skin manifestations except in those with hypertrichosis ($P=.04$). After aPBSCT, no significant correlation was observed between s-VEGF-A level decreases and response of skin manifestations, again except for hypertrichosis ($P=.007$).

Conclusions: Acquired facial lipoatrophy and livedo should be added to the skin manifestations of POEMS syndrome. Despite a role of s-VEGF-A in various skin manifestations, the impact of s-VEGF-A level decreases on skin outcomes is weak after aPBSCT, mostly resulting in clinical stabilization.

Arch Dermatol. 2010;146(6):615-623

Bone marrow histopathology in POEMS syndrome: a distinctive combination of plasma cell, lymphoid, and myeloid findings in 87 patients

Linda N. Dao,[1] Curtis A. Hanson,[1] Angela Dispenzieri,[1,2] William G. Morice,[1] Paul J. Kurtin,[1] and James D. Hoyer[1]

[1]Department of Laboratory Medicine and Pathology and [2]Department of Hematology, Mayo Clinic, Rochester, MN

POEMS is an uncommon syndromic disorder characterized by *p*olyneuropathy, *o*rganomegaly, *e*ndocrinopathy, *m*onoclonal protein, and *s*kin changes. There are few descriptions of the bone marrow pathology of POEMS; therefore, peripheral blood smears and bone marrow aspirates and biopsies from 87 patients (143 total, bridization. Monotypic plasma cells were detected in 44 pretreatment cases (66%); the majority of plasma cells expressed λ light chain (91%). The monotypic plasma cells typically were present in a background of increased polytypic plasma cells. Lymphoid aggregates were found in 33 (49%) pretreatment cases and in tested had the *JAK2*^{V617F} mutation. In summary, we have identified a novel constellation of features that should strongly suggest POEMS syndrome as part of the differential diagnosis. The constellation of λ-restricted monoclonal gammopathy, plasma cell rimming around lymphoid aggregates, and megakaryocytic hyperplasia in a bone marrow is highly suggestive of this diagnosis, especially in the context of a peripheral neuropathy. (*Blood*. 2011;117(24):6438-6444)

Table 1. Summary of clinical findings of patients with POEMS syndrome

	Total patients, n = 87
Age, y (range, median)	(20-74, 49)
Sex	
Male	57
Female	30
CBC	
Hemoglobin, g/dL (range, median)	(7.8-17.7, 13.7)
White blood cells, $\times 10^9$/L (range, median)	(0.3-18.8, 6.4)
Platelets, $\times 10^9$/L (range, median)	(21-1281, 371)
Serum protein studies	
IgA λ	39
IgG λ	32
IgM λ	1
IgA λ and IgG λ	2
IgG κ and IgA λ	5
IgG κ and IgG λ	1
IgG κ	2
IgA κ and IgGκ	1
None detected	4

'MPN-like' PB counts possible

Blood 2011;117:6436-6444

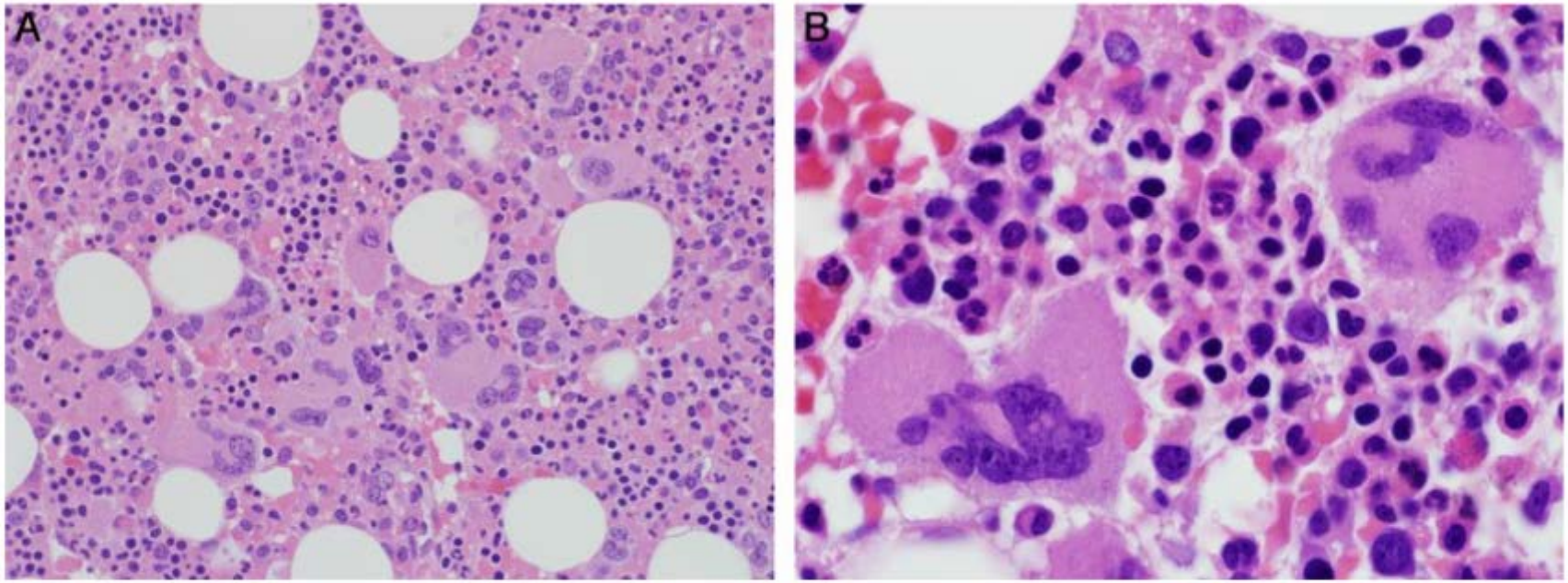


Figure 4. Megakaryocyte clusters and atypical morphology. (Left) Megakaryocyte clusters were a common finding, original magnification ×400. (Right) Cytologically atypical megakaryocytes with abnormal nuclear segmentation and visible nucleoli. Photomicrographic images were obtained with an Olympus BX51 microscope equipped with an Olympus DP71 camera and software. Original magnifications: left panel, 40×/1.30 oil UPlanFL N lens; right panel, 100×/1.40 oil UPlanS Apo lens.

28% - megakaryocytic atypia

35% - excess of megakaryocytes

78% - clusters of megakaryocytes

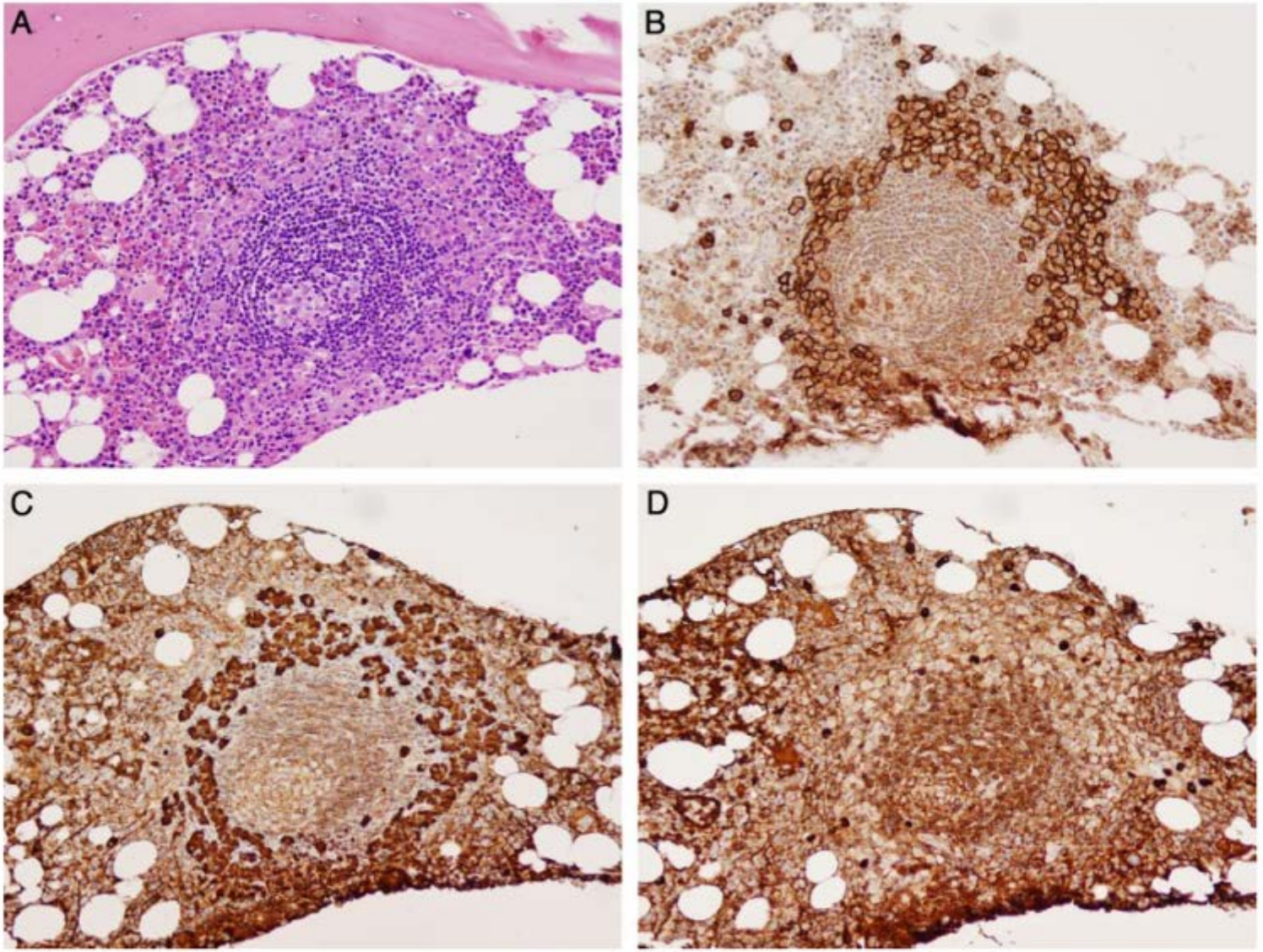
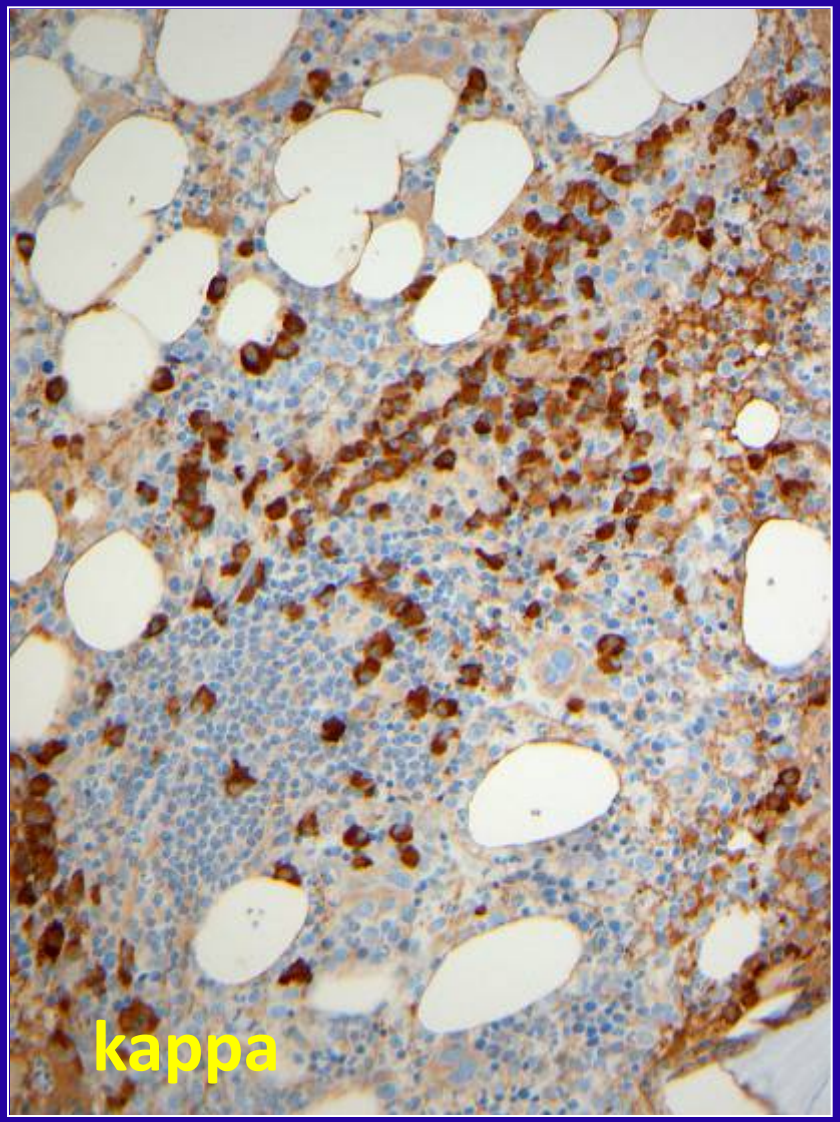
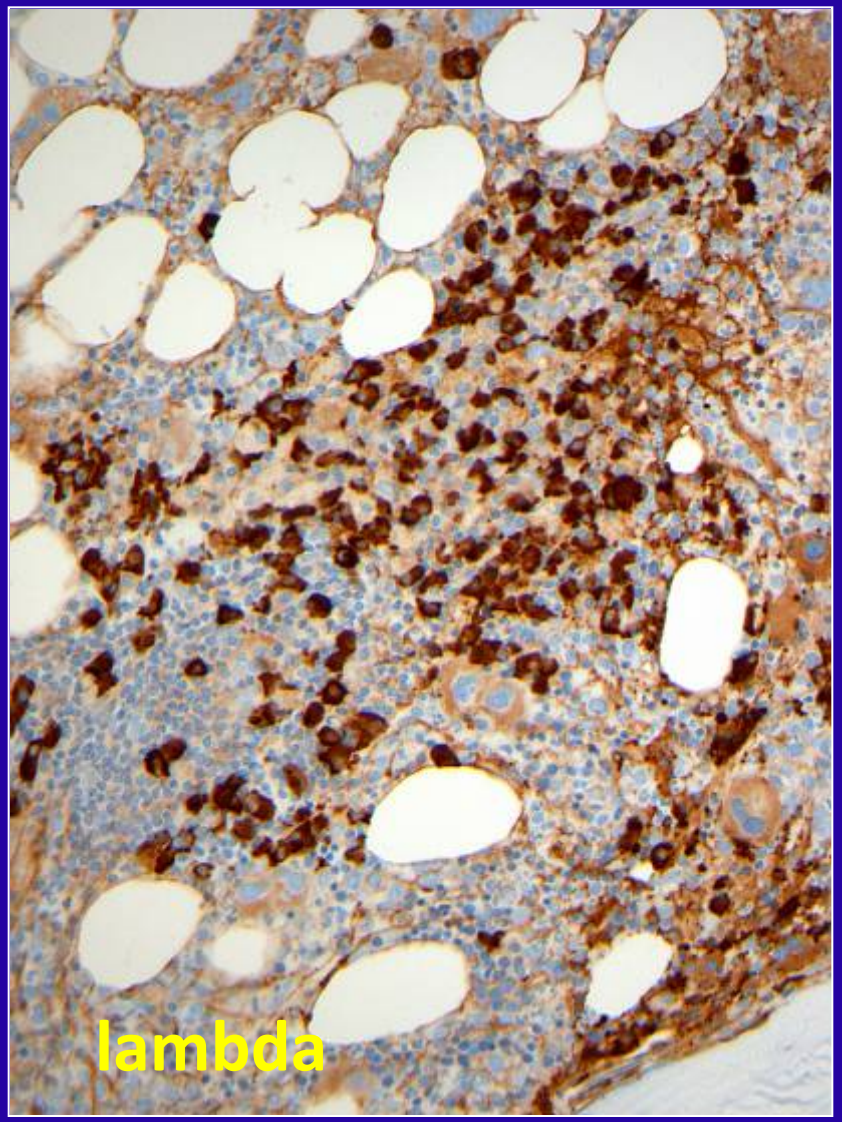


Figure 3. Bone marrow biopsy of lymphoid aggregate rimmed by PCs. (A) The lymphoid aggregate has a regressed germinal center that is Castleman-like (H&E). (B) CD138 positive PCs form a distinctive rim around the lymphoid aggregate. (C) The PCs are monotypic for λ immunoglobulin light chains (D) and negative for κ immunoglobulin light chains by IHC. Photomicrographic images were obtained with an Olympus BX51 microscope equipped with an Olympus DP71 camera and software. Original magnification 20×/0.50 UPlanFL N lens for all panels.

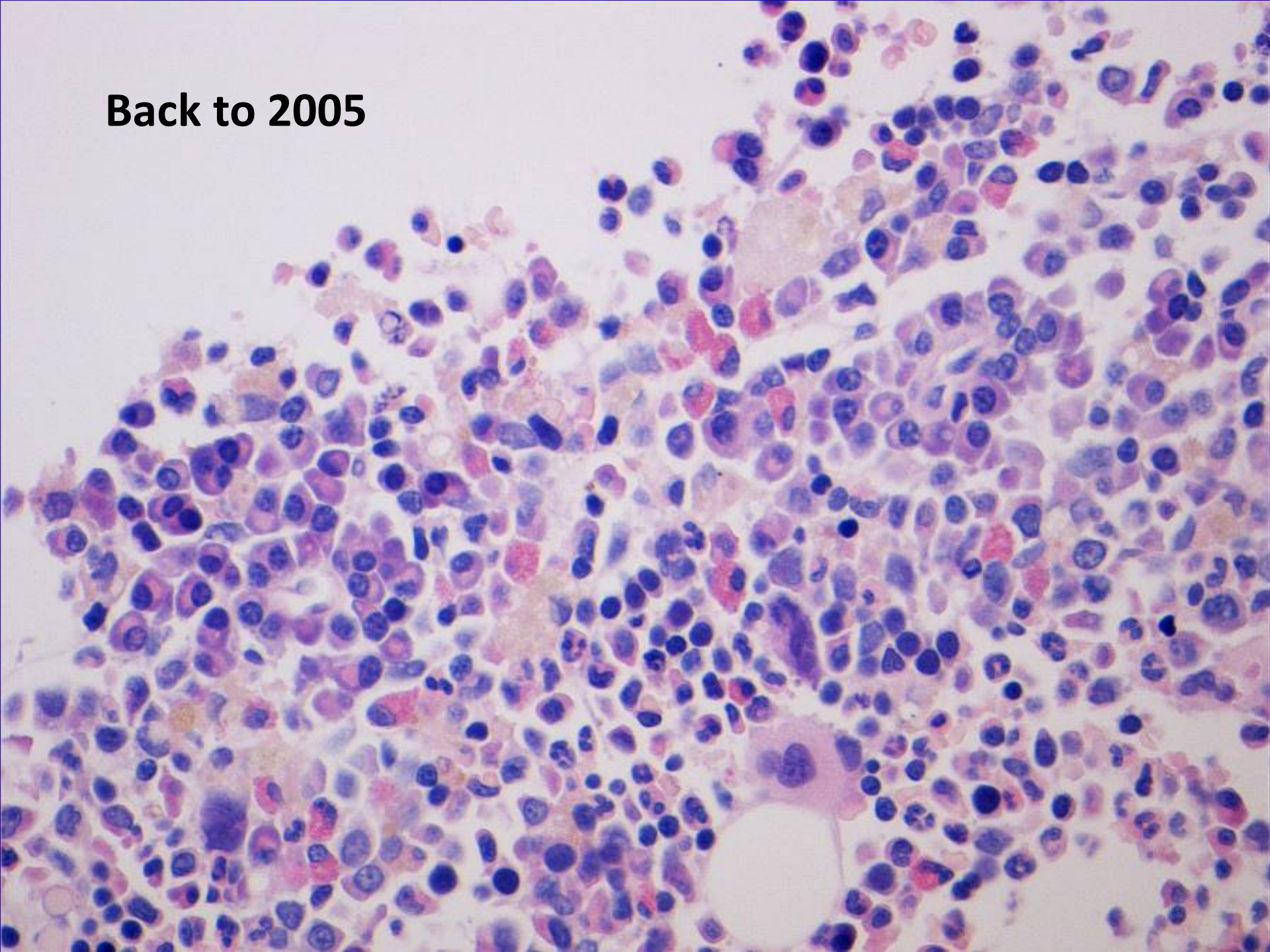




25 cases with PCs rimming lymphoid aggregates:

24	kappa+ PCs
1	lambda+ PCs
7	polytypic PCs

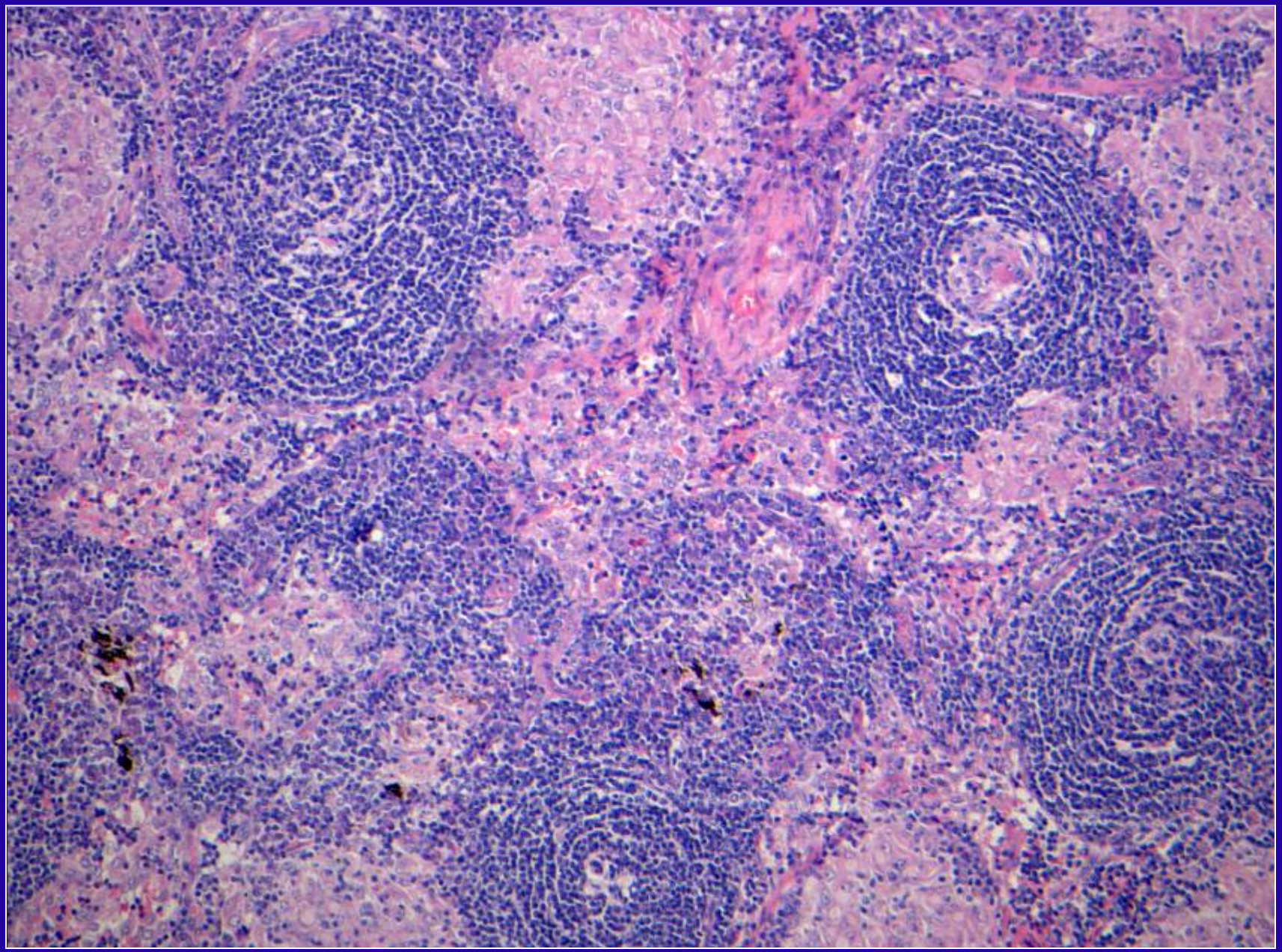
Blood 2011;117:6436-6444


Back to 2005

Mediastinal LNs

2007

(over 30 papers on Castleman-type lymphadenopathy in POEMS, only 1 on sarcoid-like granulomas)



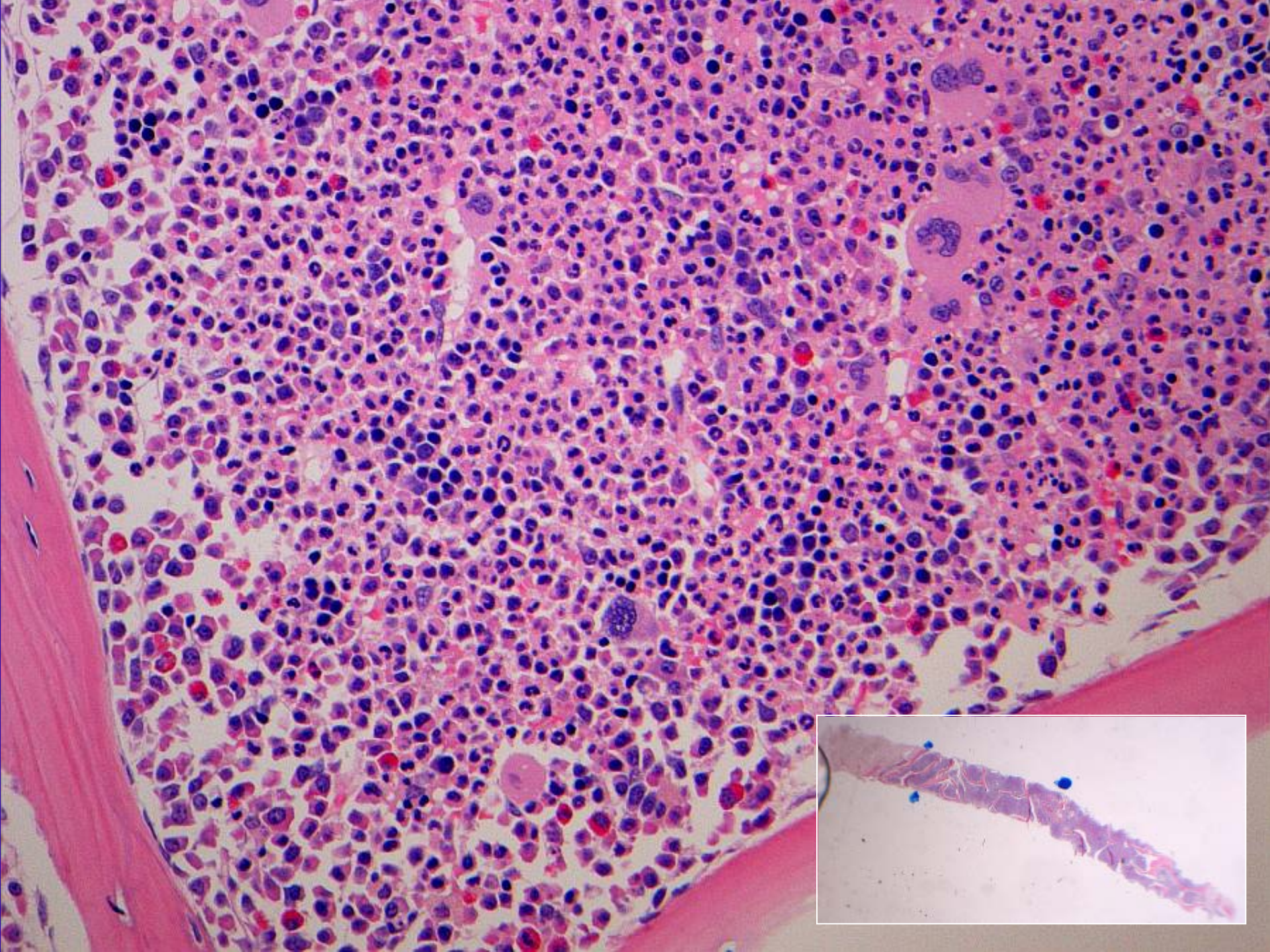
M51

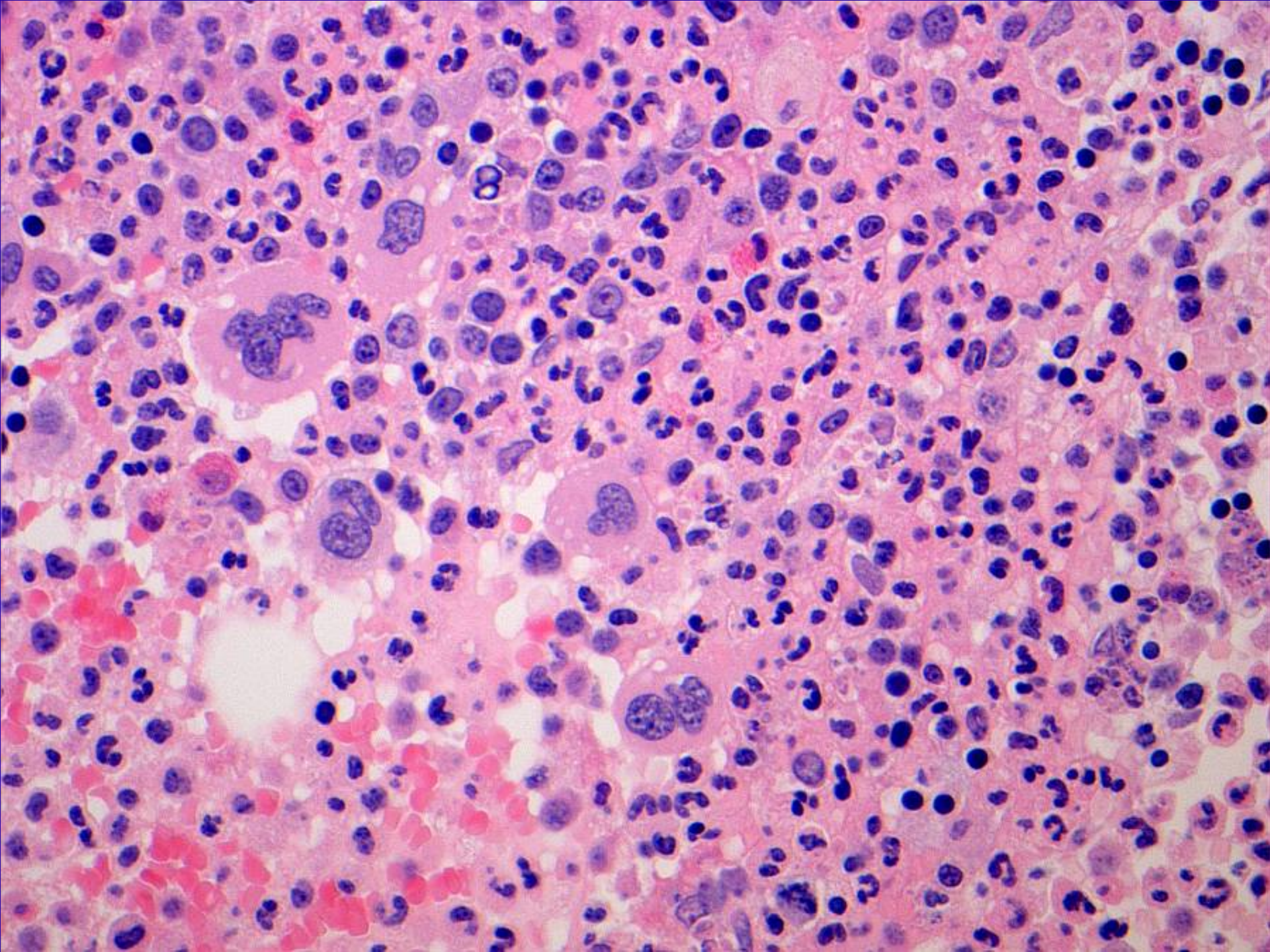
regular blood donor
20cm spleen found

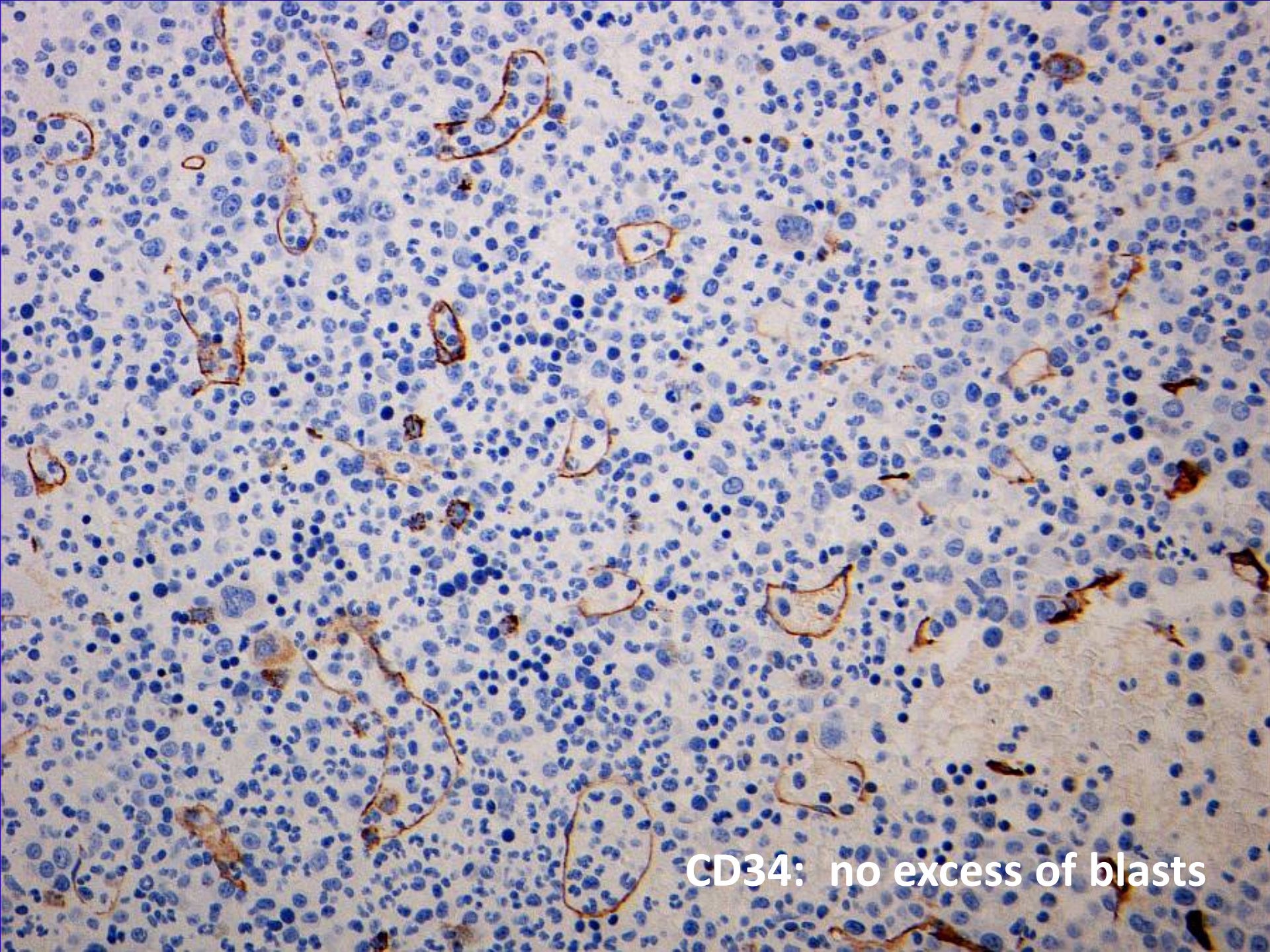
FBC				
	Total white cell count	*	18.50	10^9/l
	Haemoglobin estimation	*	12.5	g/dl
	Platelet count		153	10^9/l
	Red blood cell (RBC) count		4.87	10^{12}/l
	Mean corpuscular volume (MCV)		80.7	fl
	Mean corpusc. haemoglobin(MCH)	*	25.6	pg
	Haematocrit	*	0.39	l/l
	RBC Distribution Width		14.0	%
	% Hypochromic RBC's		1.2	%
	Neutrophil count (Absolute)	*	16.41	x10^9/l
	Lymphocyte count (Absolute)	*	1.44	x10^9/l
	Monocyte count (Absolute)		0.40	x10^9/l
	Eosinophil count (Absolute)		0.14	x10^9/l
	Basophil count (Absolute)		0.03	x10^9/l

NEUTROPHILIA

N 23 x 10^9/L already 5 years earlier!

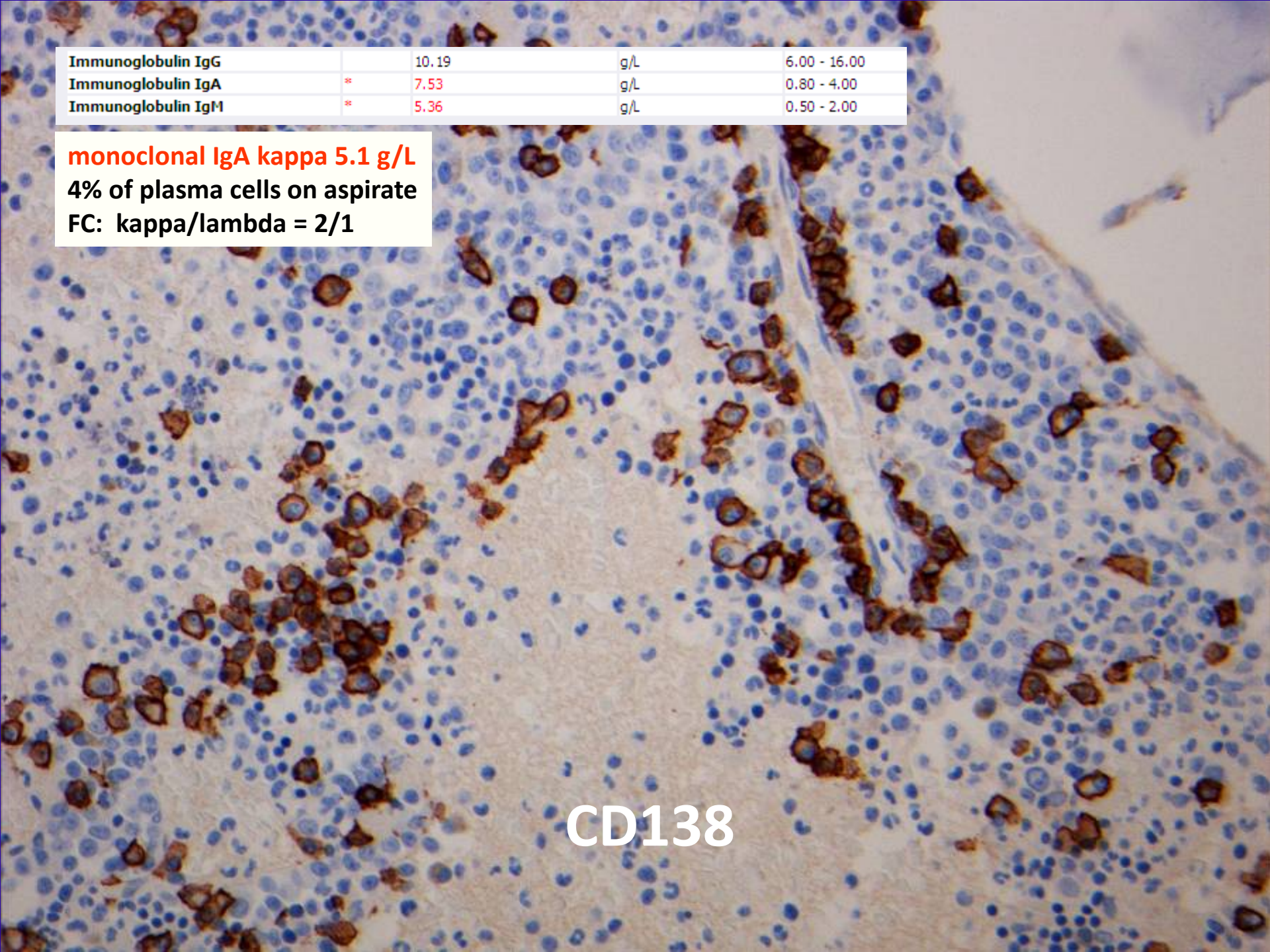


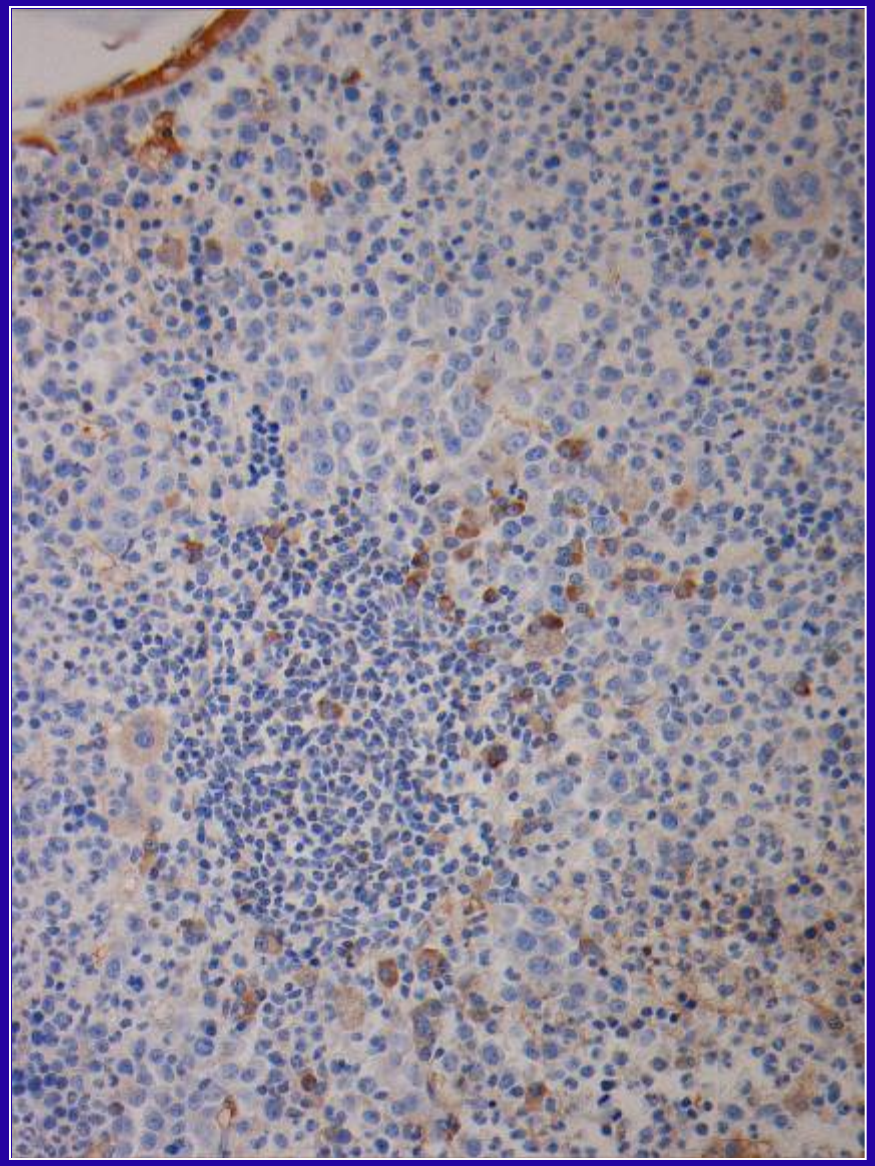



CD34: no excess of blasts

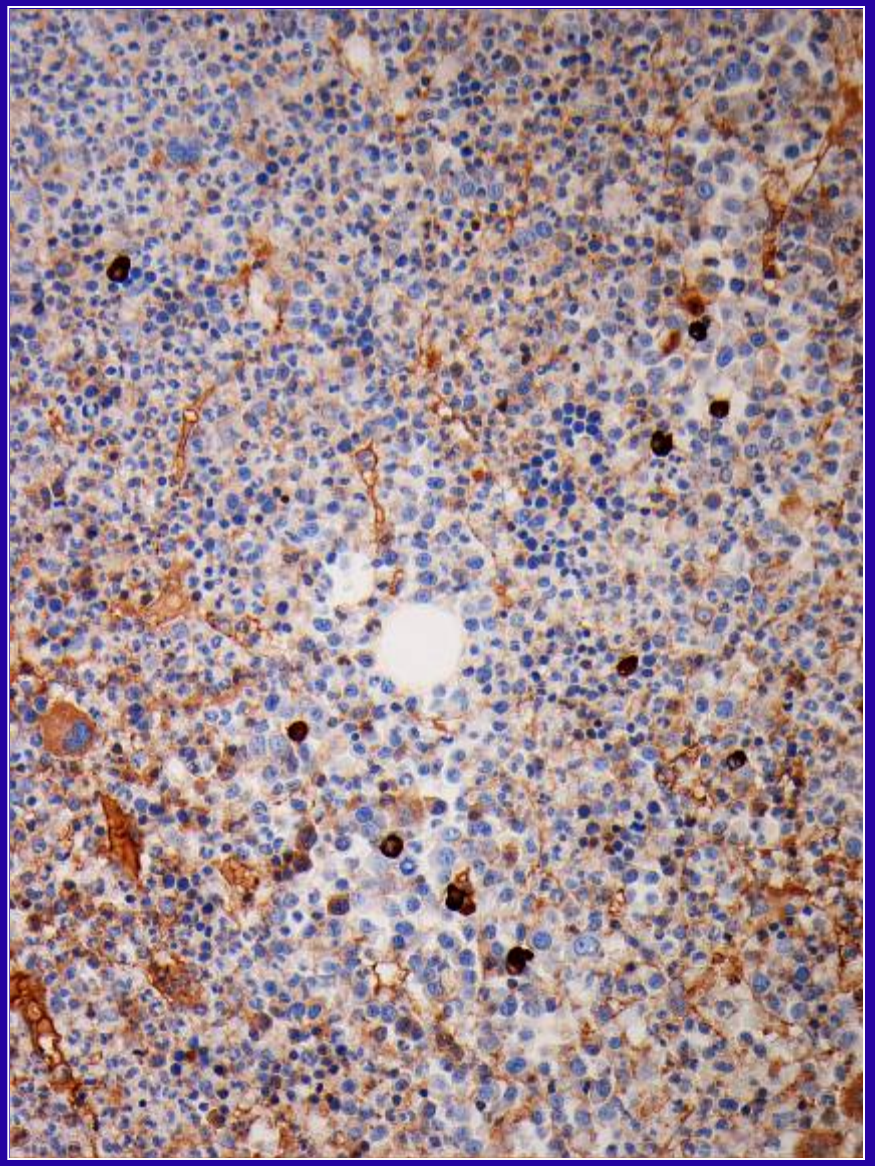
Immunoglobulin IgG		10.19	g/L	6.00 - 16.00
Immunoglobulin IgA	*	7.53	g/L	0.80 - 4.00
Immunoglobulin IgM	*	5.36	g/L	0.50 - 2.00

monoclonal IgA kappa 5.1 g/L
4% of plasma cells on aspirate
FC: kappa/lambda = 2/1

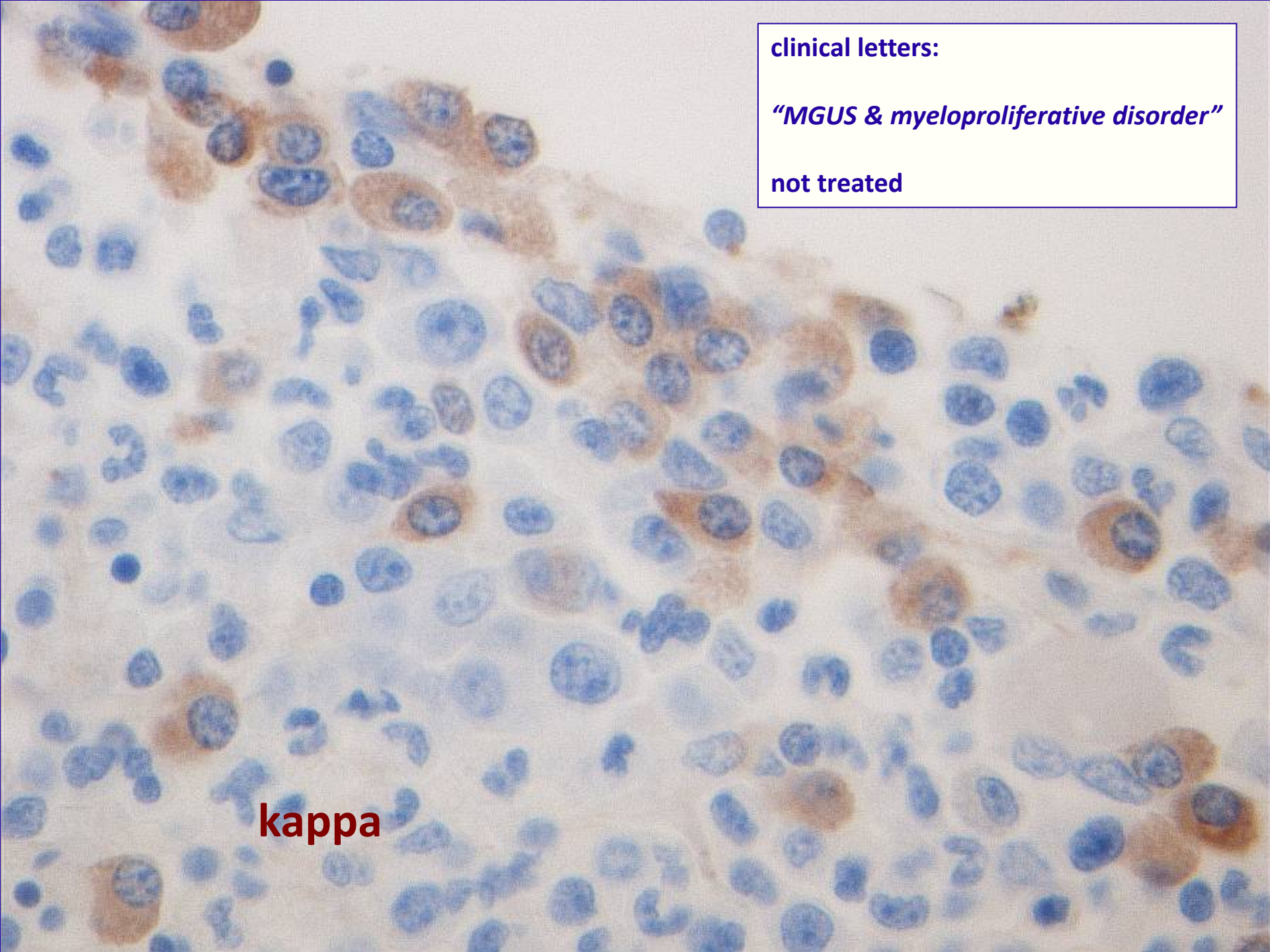




kappa



lambda


clinical letters:
"MGUS & myeloproliferative disorder"
not treated
kappa

Clonality of chronic neutrophilic leukaemia associated with myeloma: Analysis using the X-linked probe M27β

G R Standen, F J Steers, L Jones

Abstract

***Aims*—To determine whether myeloid proliferation was monoclonal or polyclonal in a woman with chronic neutrophilic leukaemia and myeloma.**

***Methods*—The X-linked probe, M27β was used to determine the clonality of the neutrophil population by analysis of restriction fragment length polymorphisms and X inactivation pattern.**

***Results*—A polyclonal pattern of X inactivation was obtained for the neutrophil population in this patient.**

***Conclusion*—The myeloid expansion in chronic neutrophilic leukaemia associated with myeloma represents a polyclonal reactive response to the plasma cell clone rather than a co-existent myeloproliferative disorder.**

(*J Clin Pathol* 1993;46:297–298)

recently been reviewed and a
drawn to the disproportionate
light chain restriction in thi
patients.[4] It remains unclea
whether the chronic neutrophil
myeloid hyperplasia seen in these
sents a distinct clonal haemopat
clonal reactive response to the
population.

We used the X-linked probe
Southern analysis[5] to study the
the neutrophil population in a
senting with IgG λ myeloma who
ly developed chronic neutrophilic

Case report

The patient studied was a 67 ye
whose clinical features have
described in detail.[4] She preser
with an orbital plasmacytoma a
to have an IgG λ paraproteinaem

1. Coexistence of chronic neutrophilic leukemia with multiple myeloma.
Dinçol G, Nalçaci M, Doğan O, Aktan M, Küçükkaya R, Ağan M, Dinçol K.
Leuk Lymphoma. 2002 Mar;43(3):649-51. Review.
PMID: 12002774 [PubMed - indexed for MEDLINE]

2. [Association of chronic neutrophilic leukemia and myeloma with fibrillar inclusions in granulocytes]
Mori H, Takahashi N, Tada J, Maeda T, Higuchi T, Shimizu T, Harada H, Miyoshi Y, Okada S, Niikura H, et al.
Rinsho Ketsueki. 1995 Feb;36(2):121-7. Review. Japanese.
PMID: 7715083 [PubMed - indexed for MEDLINE]

3. Coexistence of chronic neutrophilic leukemia with light chain myeloma.
Cehreli C, Undar B, Akkoc N, Onvural B, Altungoz O.
Acta Haematol. 1994;91(1):32-4. Review.
PMID: 8171934 [PubMed - indexed for MEDLINE]

4. Clonality of chronic neutrophilic leukaemia associated with myeloma: analysis using the X-linked probe M27 beta.
Standen GR, Steers FJ, Jones L.
J Clin Pathol. 1993 Apr;46(4):297-8.
PMID: 8098719 [PubMed - indexed for MEDLINE] Free PMC Article Free text

5. [Chronic neutrophilic leukemia associated with myeloma. Simultaneous presentation]
Diéguez JC, Fernández Jurado A, Amián A, Rodríguez JN, Martino ML, Cañavate M, Prados D.
Sangre (Barc). 1992 Oct;37(5):403-6. Review. Spanish.
PMID: 1293783 [PubMed - indexed for MEDLINE]

6. [Neutrophilic leukemia and multiple myeloma. 2 cases]
Troussard X, Lebrun E, Macro M, Galateau F, Reman O, Leporrier M.
Ann Med Interne (Paris). 1992;143(2):136-9. Review. French. No abstract available.
PMID: 1530222 [PubMed - indexed for MEDLINE]

7. Chronic neutrophilic leukemia and multiple myeloma. An association with lambda light chain expression.
Standen GR, Jasani B, Wagstaff M, Wardrop CA.
Cancer. 1990 Jul 1;66(1):162-6. Review.
PMID: 2112978 [PubMed - indexed for MEDLINE]

8. Chronic neutrophilic leukaemia preceding for seven years the development of multiple myeloma.
Rovira M, Cervantes F, Nomdedeu B, Rozman C.
Acta Haematol. 1990;83(2):94-5. No abstract available.
PMID: 2106202 [PubMed - indexed for MEDLINE]

9. Kappa light chain myeloma developing in a patient with chronic neutrophilic leukaemia.
Zoumbos NC, Chrysanthopoulos C, Starakis J, Kapatais-Zoumbos K.
Br J Haematol. 1987 Apr;65(4):504-5. No abstract available.
PMID: 3472591 [PubMed - indexed for MEDLINE]

10. An association between chronic neutrophilic leukaemia and multiple myeloma with a study of cobalamin-binding proteins.
Lewis MJ, Oelbaum MH, Coleman M, Allen S.
Br J Haematol. 1986 May;63(1):173-80.
PMID: 3458500 [PubMed - indexed for MEDLINE]

11. Chronic neutrophilic leukemia and myeloma. Report on long survival.
Franchi F, Seminara P, Giunchi G.

J Clin Pathol 1996;**49**:858–860

Granulocyte-colony stimulating factor concentrations in a patient with plasma cell dyscrasia and clinical features of chronic neutrophilic leukaemia

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M Fujita
J Takahara

Department of Internal Medicine, Zentsuji National Hospital
S Oda
M Iwamoto
K Marumoto

Correspondence to:
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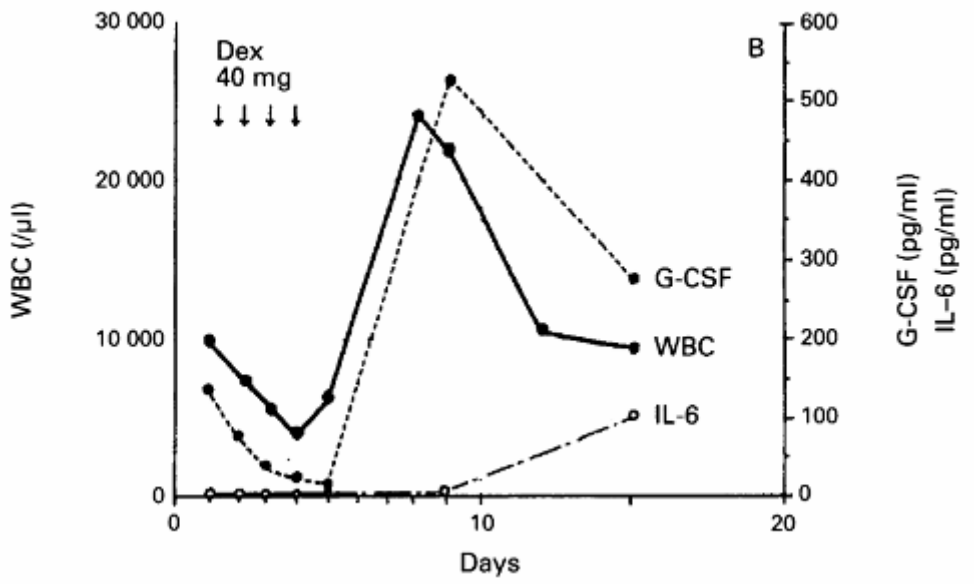
M Nagai, S Oda, M Iwamoto, K Marumoto, M Fujita, J Takahara

Abstract
In order to study the pathogenesis of plasma cell dyscrasias with associated clinical features of chronic neutrophilic leukaemia, the concentration of granulocyte-colony stimulating factor (G-CSF) was measured in a patient, a 73 year old man, who underwent steroid pulse
rations and
atment de-
on of dex-
bsequently.
primary
cultures of bone marrow cells, but large amounts of interleukin-6 were found in the culture supernatant. These observations suggest that the neutrophilia observed in the patient represented a reactive response to G-CSF secreted from abnormal plasma cells or stromal cells rather than the existence of a genuine myeloproliferative disorder.
(*J Clin Pathol* 1996;**49**:858–860)

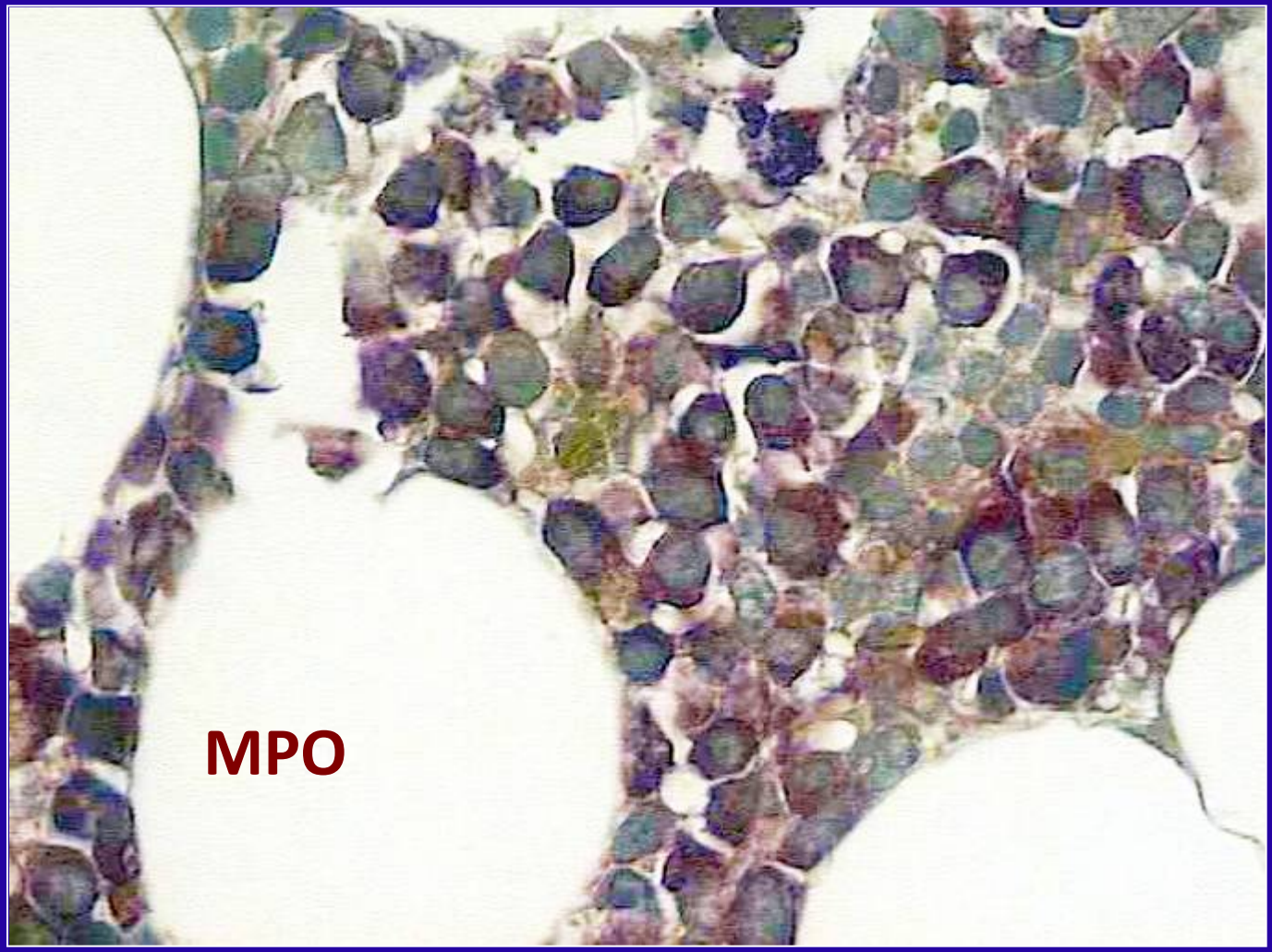
Keywords: chronic neutrophilic leukaemia, myeloma, G-CSF, steroid, regulation.



Talking about G-CSF...

Sweden, M90
Good on long distance, poor on short distance
may reflect contemporary Swedish military doctrine

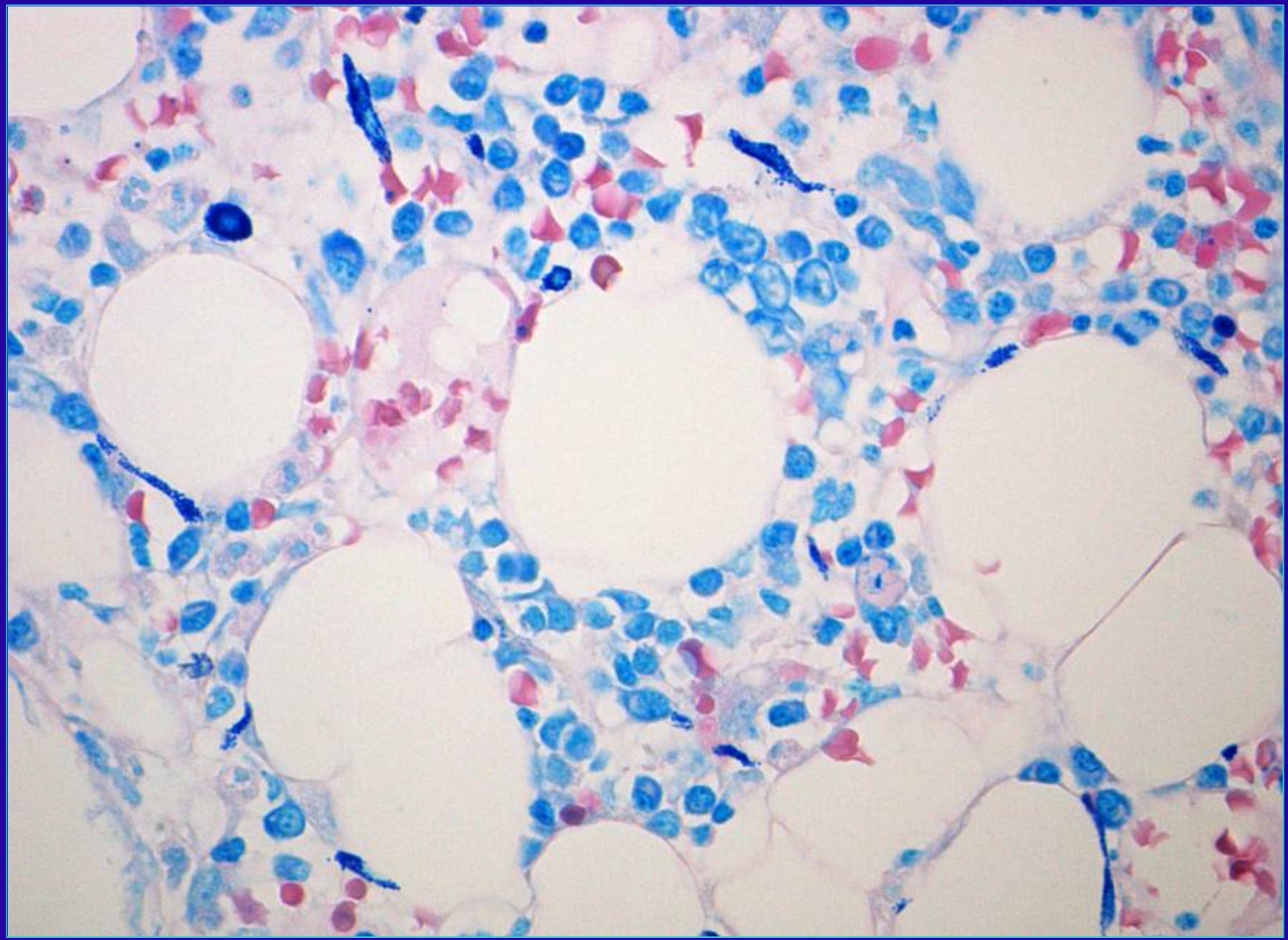
M 60, *"gastric cancer, chemotherapy, anaemia"*

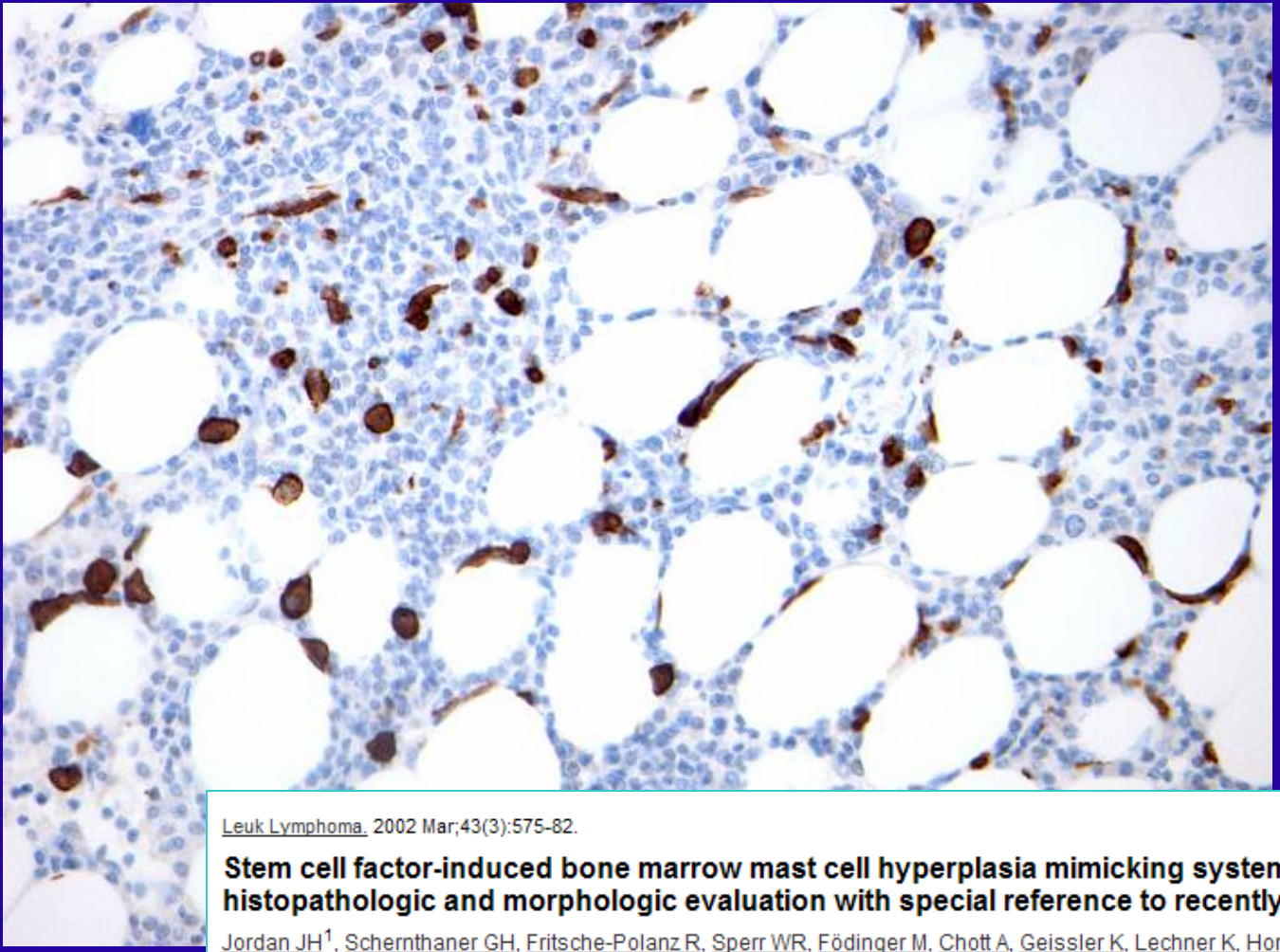


Less known G-CSF effects mimicking myeloid neoplasia

Denmark, M84 – a rarity; anybody heard about a Danish army?

Lymphoplasmacytic Lymphoma/WM on R-CVP, neutropenia





C-KIT

Leuk Lymphoma. 2002 Mar;43(3):575-82.

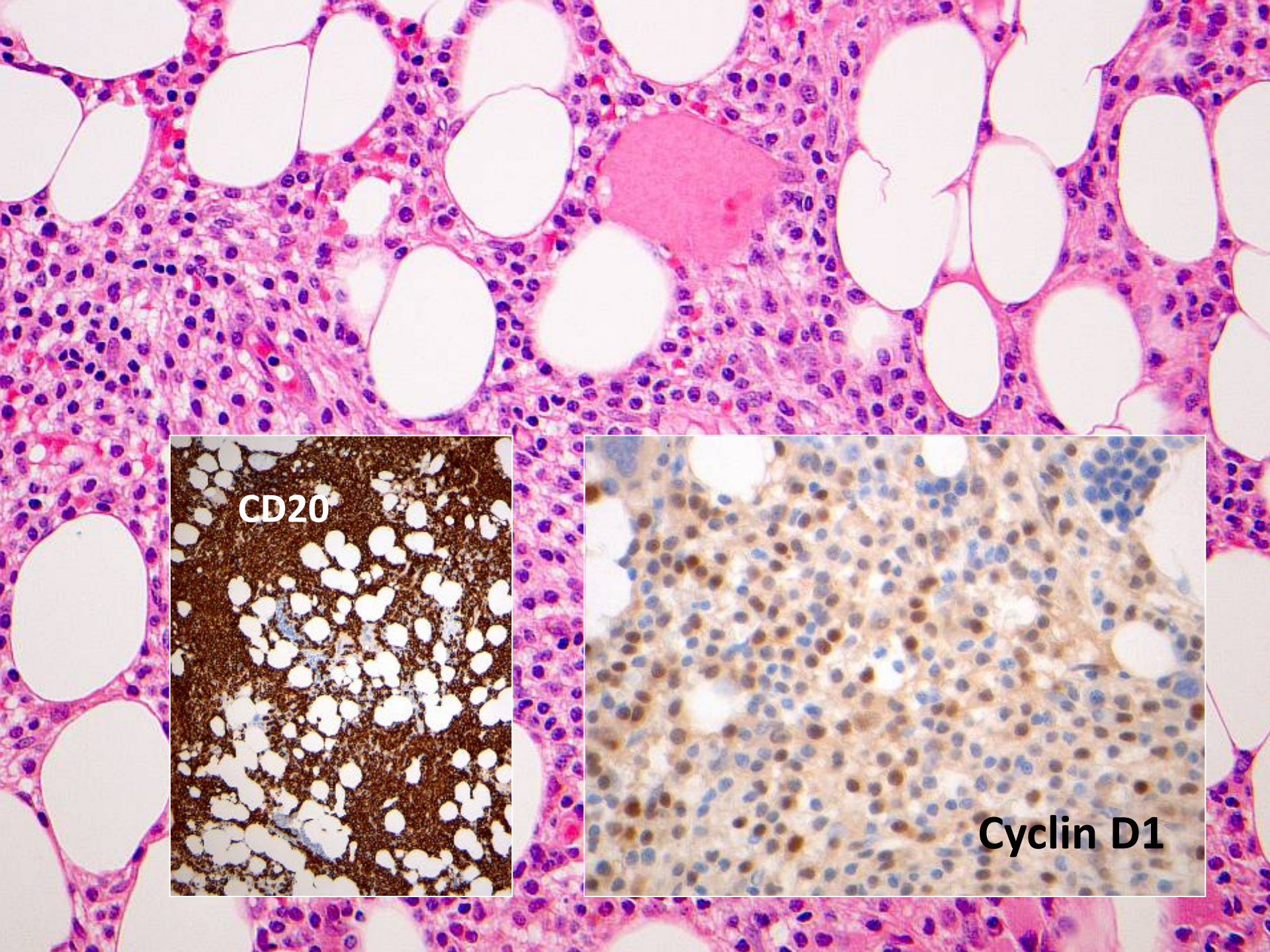
Stem cell factor-induced bone marrow mast cell hyperplasia mimicking systemic mastocytosis (SM): histopathologic and morphologic evaluation with special reference to recently established SM-criteria.

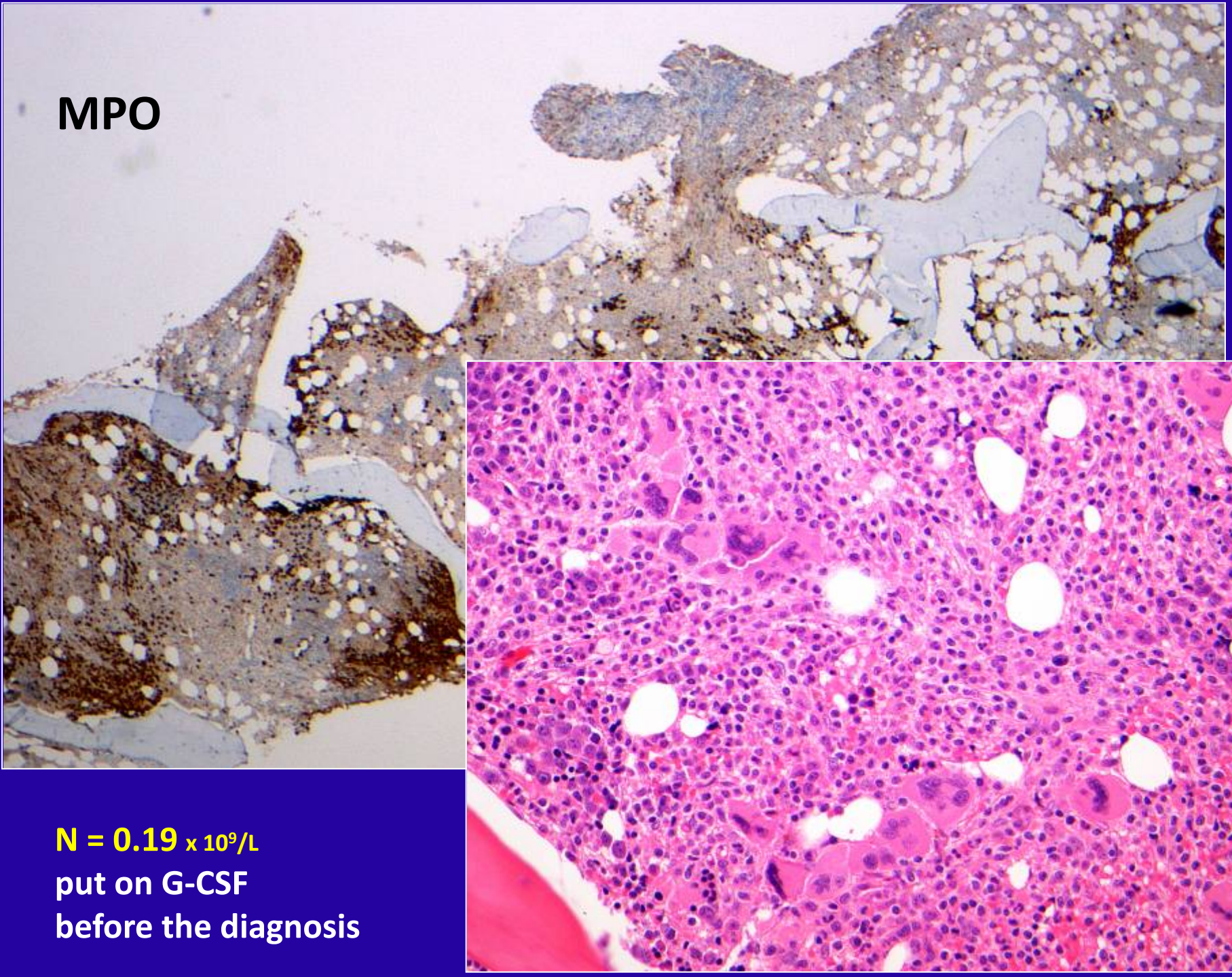
Jordan JH[1], Schernthaner GH, Fritsche-Polanz R, Sperr WR, Födinger M, Chott A, Geissler K, Lechner K, Horny HP, Valent P.

Author information

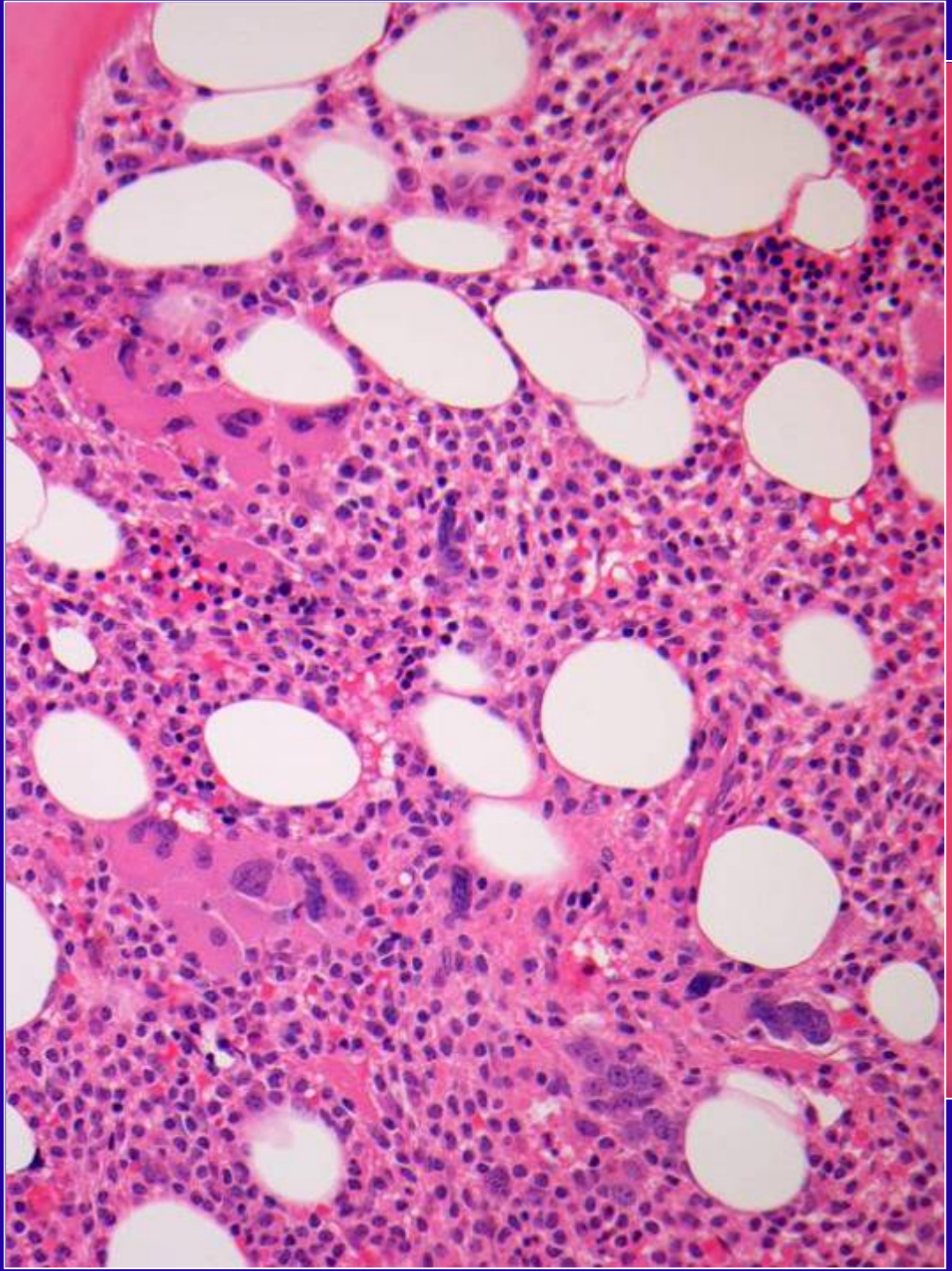
Abstract

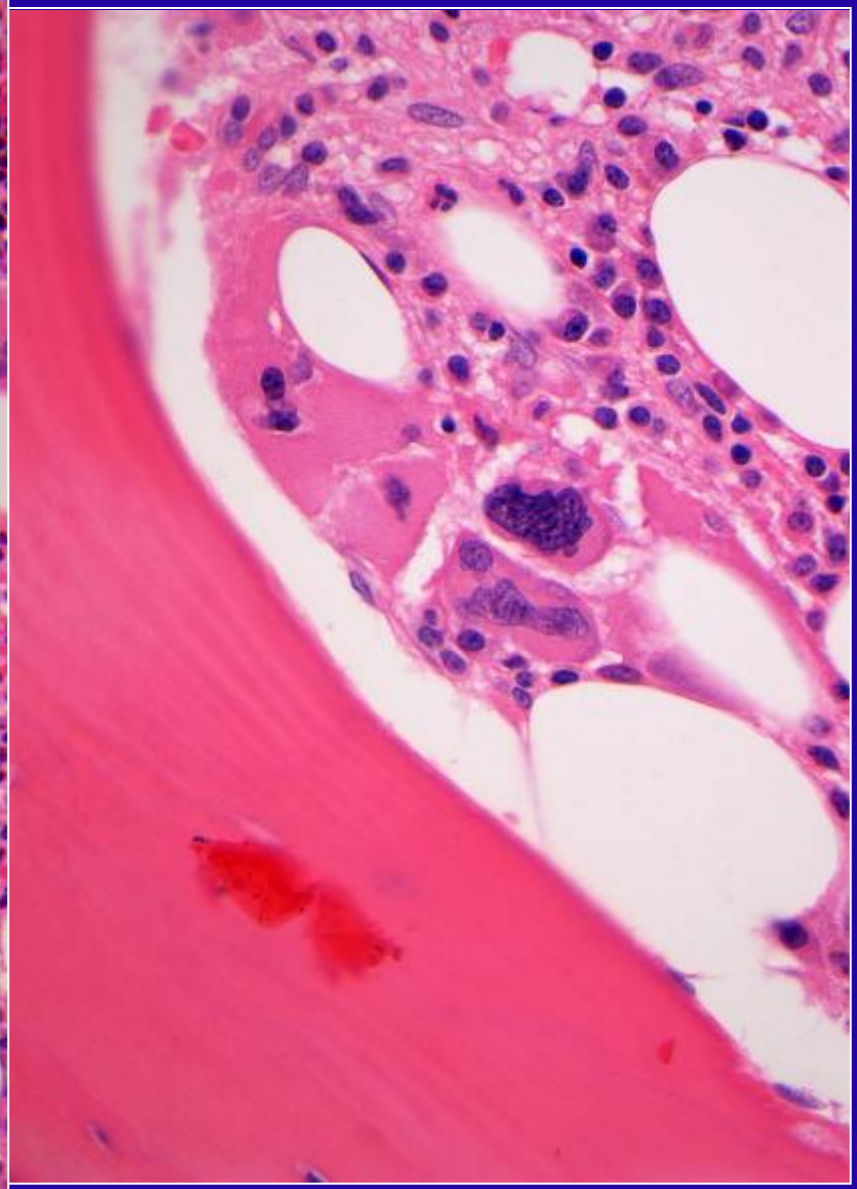
Although systemic mastocytosis (SM) is a well-defined hematologic neoplasm, it is sometimes difficult to discriminate between SM and a reactive mast cell (MC) hyperplasia. We describe a patient with aplastic anemia who was treated with recombinant stem cell factor (SCF). In response to SCF, the patient showed transient hematologic improvement and developed a marked increase in MC as well as a transient increase in serum tryptase. Histologic and immunohistochemical examination revealed a huge increase in MC in the bone marrow with focal infiltrates similar to SM. However, most of the SM-criteria were not met: First, MC showed normal cytomorphological characteristics without significant atypias (no cytoplasmic extensions, no oval nuclei, no hypogranulated cytoplasm). Furthermore, bone marrow MC were CD2- and CD25-negative and did not exhibit the C-KIT 2468 A-->T mutation (Asp-816-Val). After discontinuation of SCF the MC hyperplasia resolved confirming its reactive nature. Based on our case and similar cases mimicking mastocytosis, it seems of importance to apply recently established SM criteria in order to discriminate between reactive MC hyperplasia and true mastocytosis with certainty.


CD20
Cyclin D1



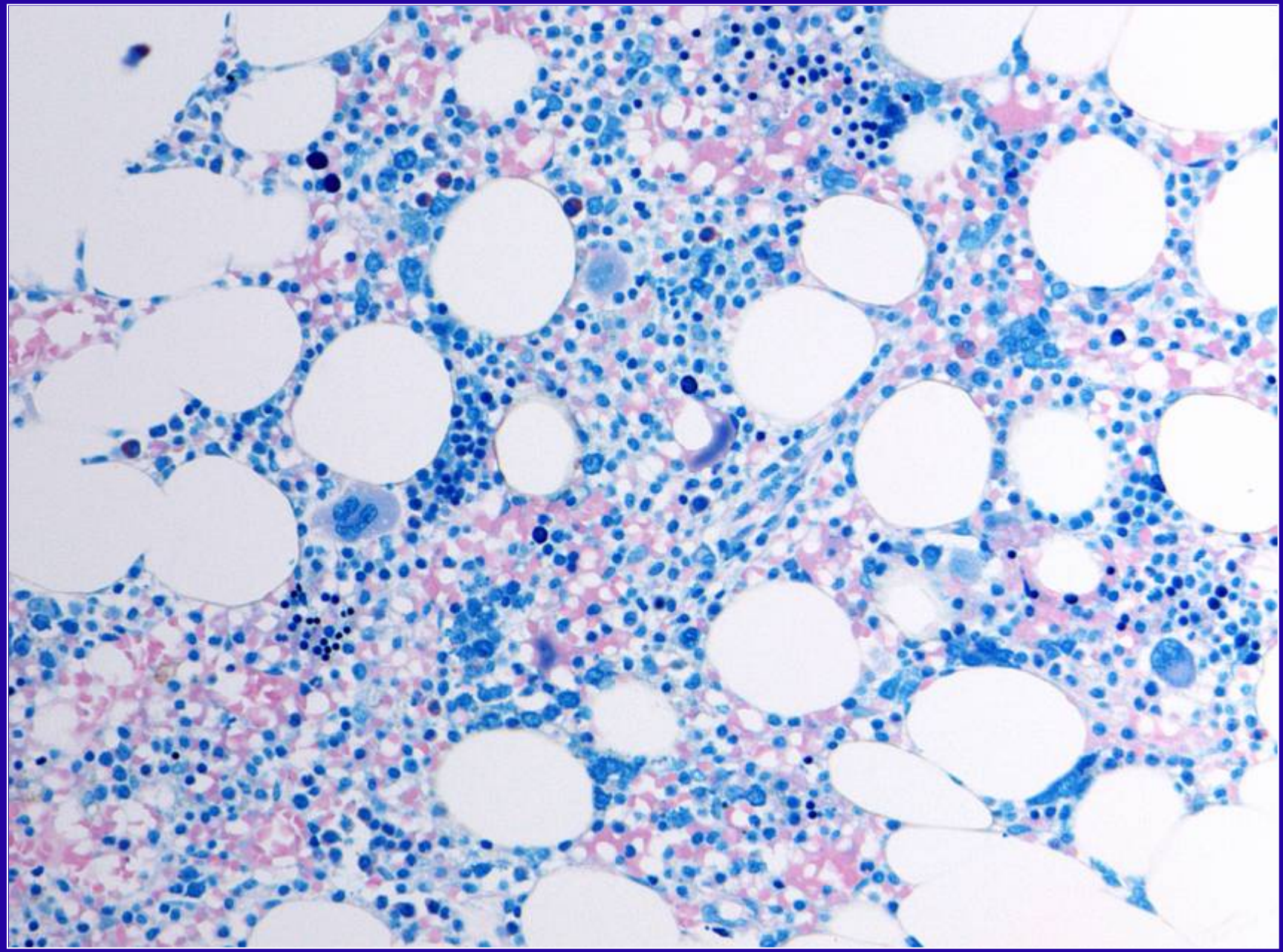
N = 0.19 x 10^9/L
put on G-CSF
before the diagnosis

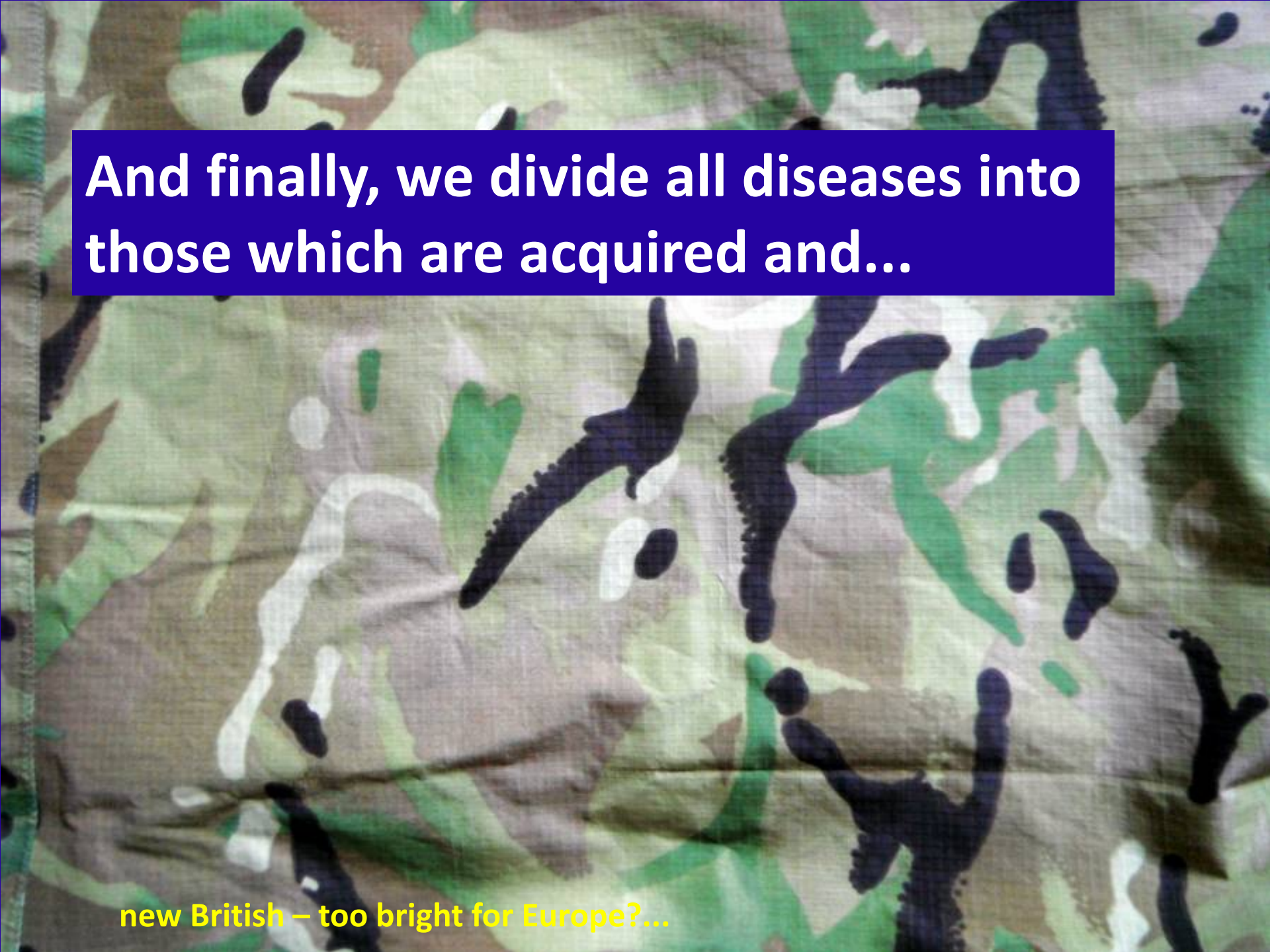




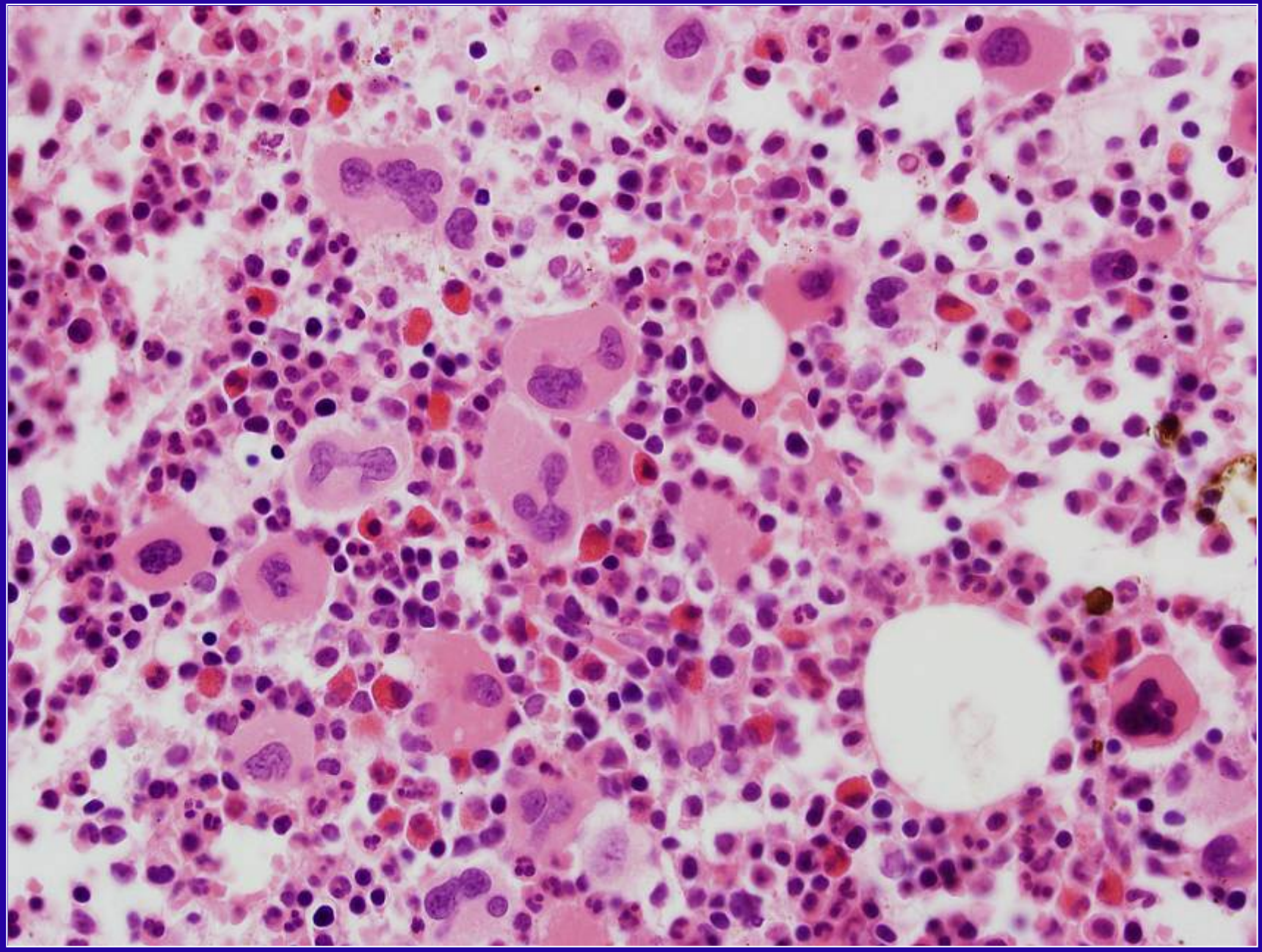
2 years later – relapse, this time no G-CSF

platelets were always normal or slightly low

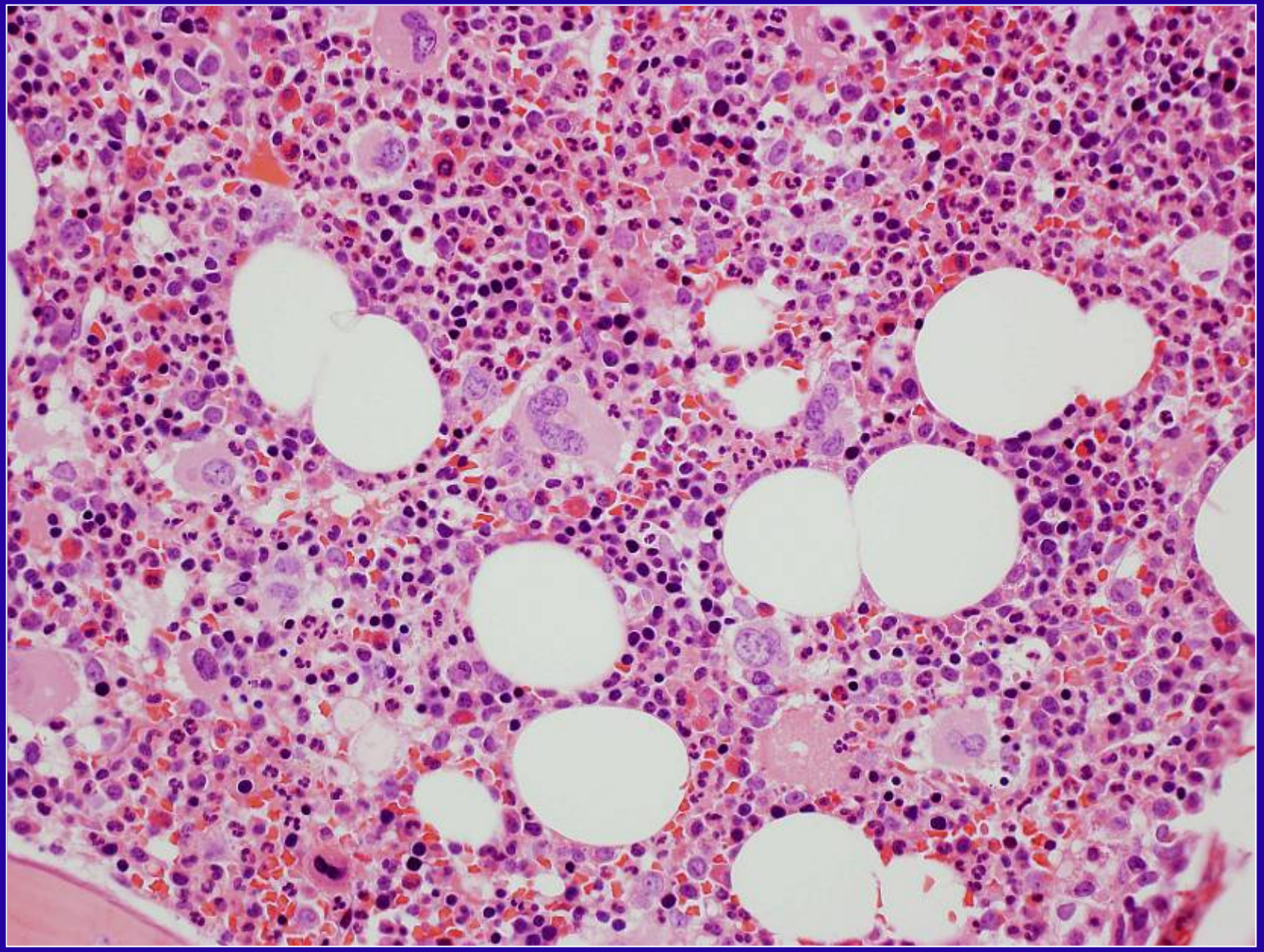


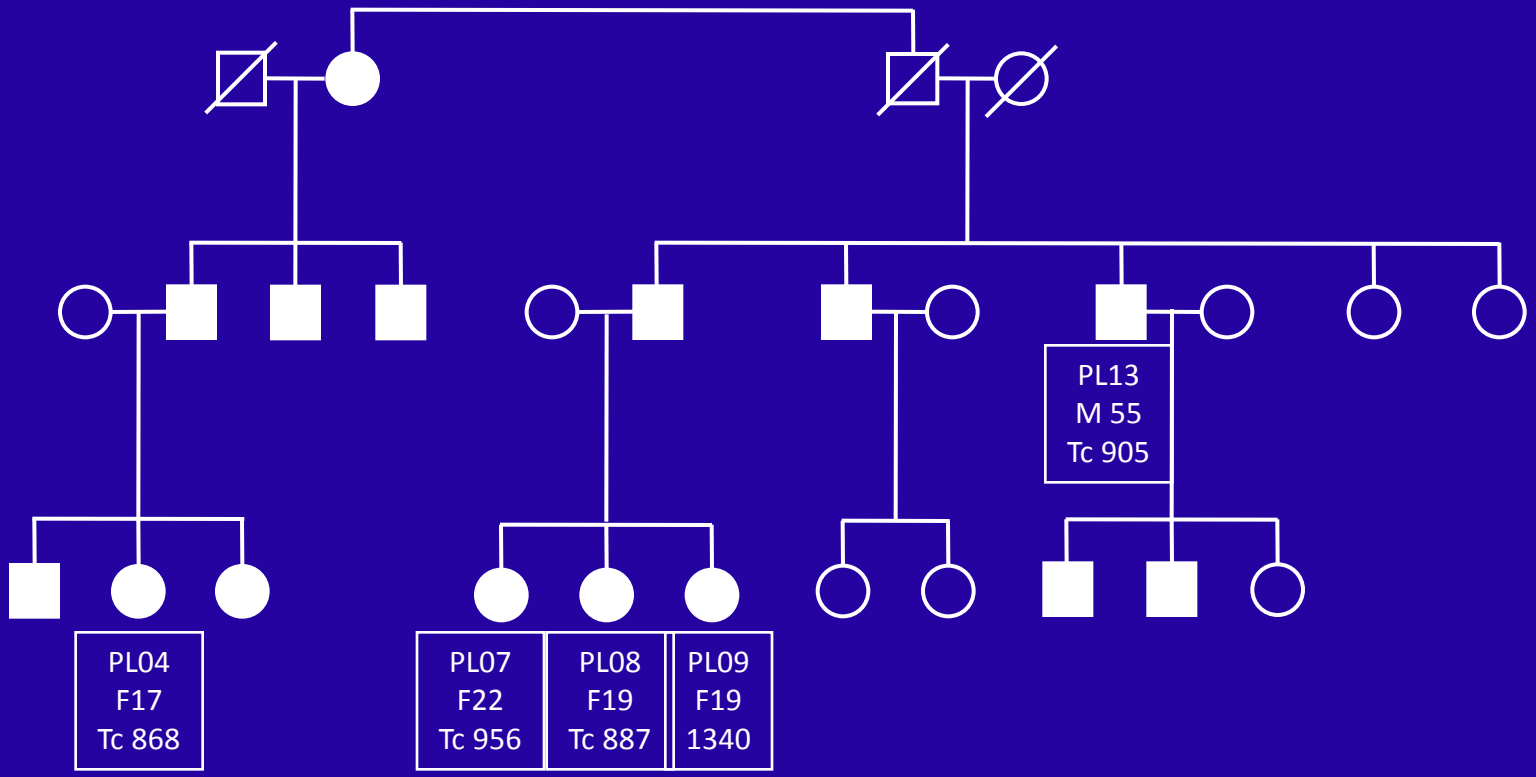

And finally, we divide all diseases into those which are acquired and...
new British – too bright for Europe?...

F 19, plt 1340, dgn.: ET, put on Hydroxycarbamide



Her 17-year old cousin, plt 840, dgn.: ET (in another hospital)





Original Article

A *de novo* splice donor mutation in the thrombopoietin gene causes hereditary thrombocythemia in a Polish family

Kun Liu,[1] Robert Kralovics,[1]* Zbigniew Rudzki,[2] Barbara Grabowska,[3] Andreas S. Buser,[4] Damla Olcaydu,[5] Heinz Gisslinger,[5] Ralph Tiedt,[1] Patricia Frank,[1] Krzysztof Okoń,[2] Anthonie P.C. van der Maas,[6] and Radek C. Skoda[1]

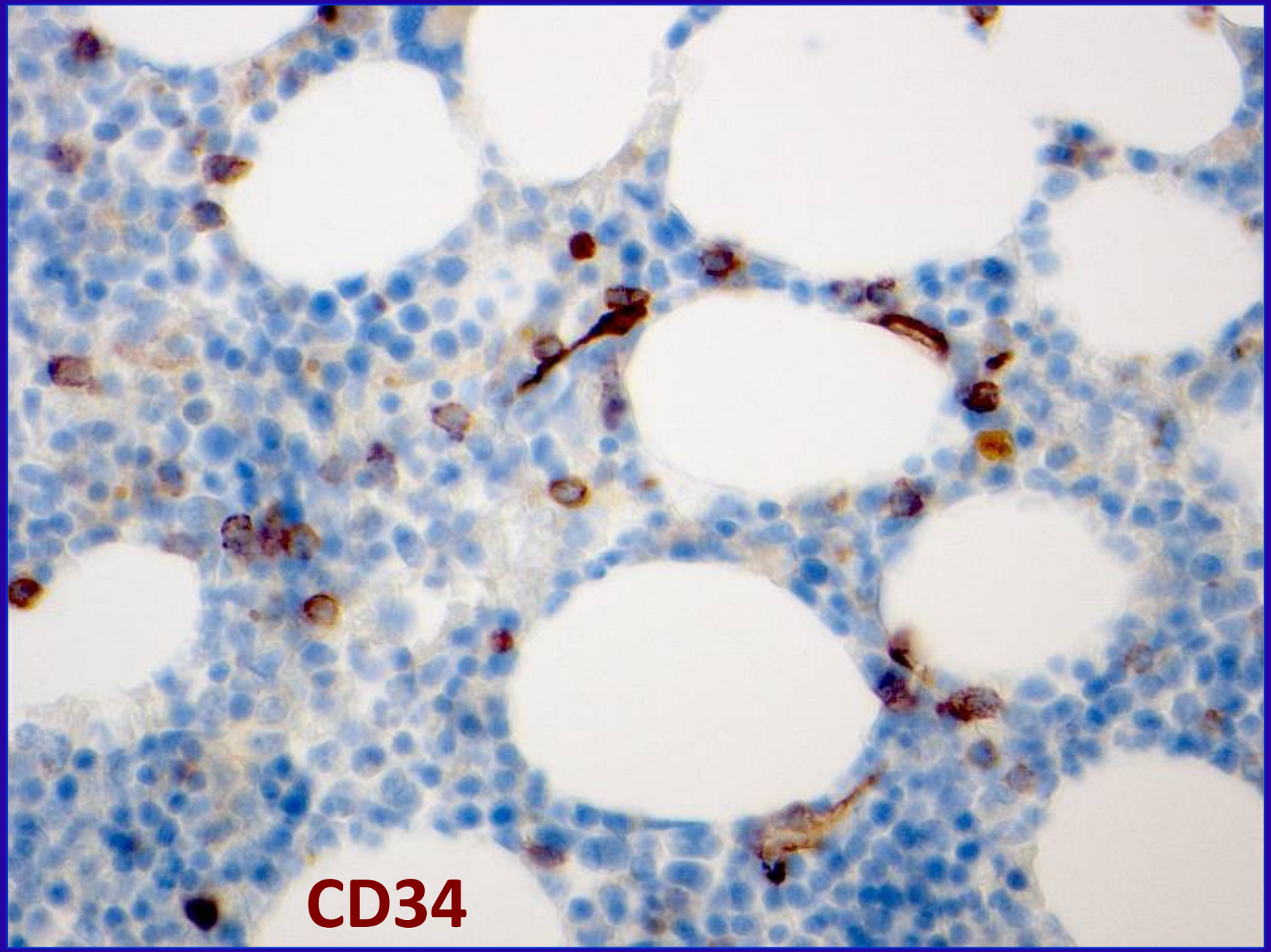
[1]Experimental Hematology, Department of Biomedicine, Basel University Hospital, Basel, Switzerland, [2]Department of Pathomorphology, Collegium Medicum, Jagiellonian University, Kraków, Poland, [3]Department of Hematology, Ludwik Rydygier Memorial District Hospital, Kraków, Poland, Clinical Hematology, [4]Basel University Hospital, Basel, Switzerland, [5]Department of Internal Medicine I, Division of Hematology and Blood Coagulation, Medical University of Vienna, and [6]Department of Internal Medicine, Medical Centre Haaglanden, The Hague, The Netherlands

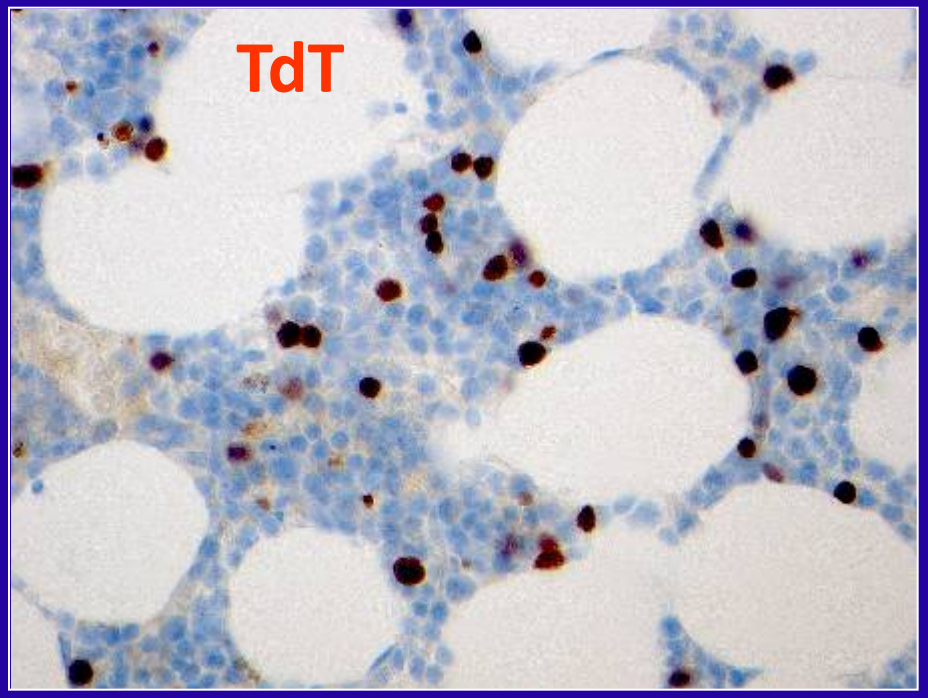
Haematologica 2008;93:706-14

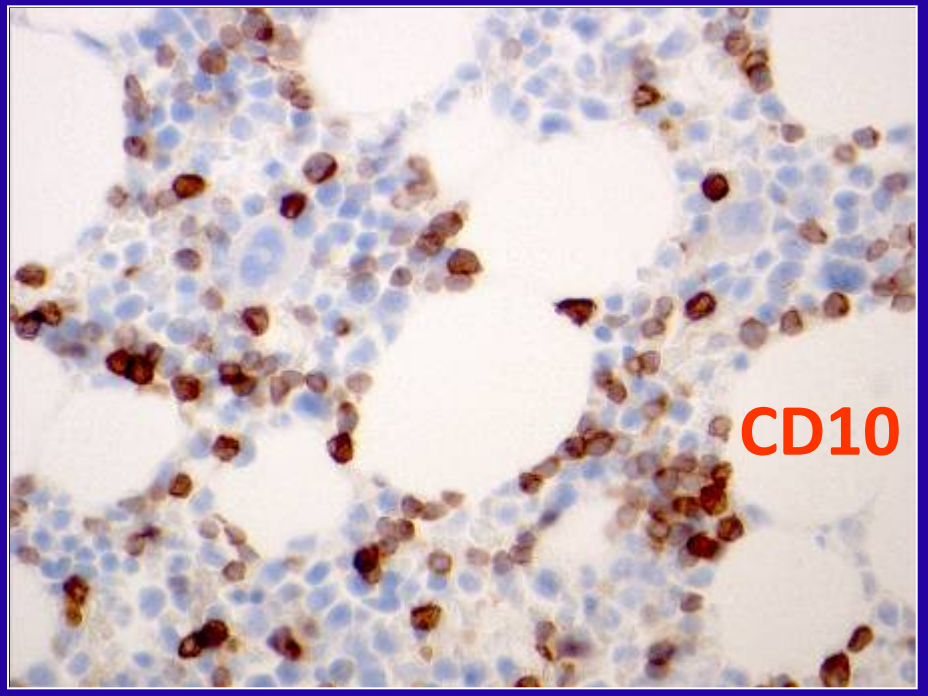
Summary

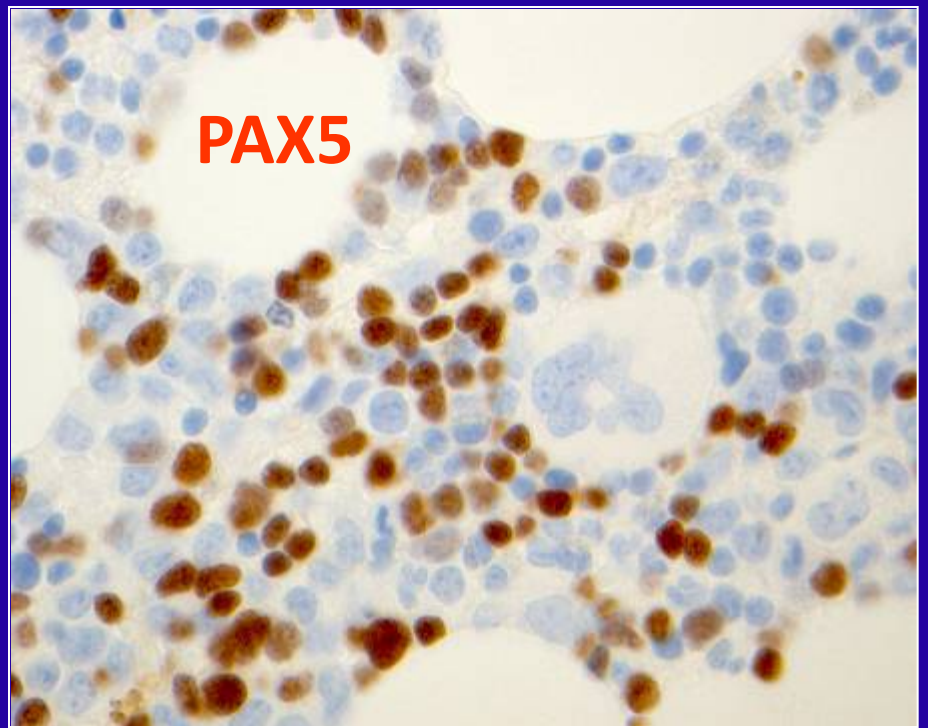
- Think twice before diagnosing 'unusual' MPN, MDS/MPN
- Have a mimic checklist
- CNL mimics are probably much more frequent than genuine CNL
- No excess of blasts – suspect a mimic ...

CD34+ (?) blasts 6 months post alloSCT for AML









CD10 ≥ PAX5 > CD79a > CD20 ≥ TdT > CD34

Summary

- Think twice before diagnosing 'unusual' MPN, MDS/MPN
- Have a mimic checklist
- CNL mimics are probably much more frequent than genuine CNL
- No excess of blasts – suspect a mimic (remember haematogones)
- Very ugly “MDS”, not-that-ugly blood counts - suspect a mimic

- **Check the clinical history** (referral cases!)

- Never believe self-professed teetotallers