Increased prevalence of myeloid neoplasms in patients with Erdheim-Chester disease

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Background

- Several case reports of concomitant/secondary hematological neoplasms with LCH
  - Acute myeloid leukemia
  - Non-hodgkin lymphoma
  - Histiocytic sarcoma
- Case report of ECD following JAK2 V617F essential thrombocytosis

Edelbroek JR et al. Br J Dermatol. 2012;167(6):1287-1294
Arico M et al. Med Pediatr Oncol.1993;21(4):271-273
Egeler RM et al. Med Pediatr Oncol. 1994;23(2):81-85
Lurlo A et al. Medicine (Baltimore). 2016 May;95(20):e3697

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Background

- Recent study showed high prevalence of myeloid neoplasms in ECD and mixed histiocytosis:
  - 10.1% in the entire cohort (n=189)
  - 7.8% in ECD cohort
  - 25% in mixed histiocytosis cohort
- Common myeloid neoplasms
  - Myeloproliferative neoplasm (MPN)
  - Myelodysplastic syndrome (MDS)
  - MDS/MPN overlap (including CMML)

Papo M et al. Blood. 2017 Aug 24;130(8):1007-1013.

Methods

- Retrospective study of ECD patients diagnosed from 1998 to 2016 at Mayo Clinic
- The diagnosis was made using clinical criteria in conjunction with histopathologic findings
- Pathology slides were independently reviewed at our institution

Diamond EL et al. Blood 2014 Jul 24; 124(4): 483-492.

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Results

Total ECD patients (1998-2016)	72
Mixed histiocytosis	1
Median age	55 years (range, 34-80)
Bone marrow biopsies	22 (30%)
Indications for bone marrow biopsy	
Abnormal peripheral blood count	15
Aid diagnosis of ECD	6
Rule out metastatic prostate cancer	1
Myeloid neoplasm	3 (4%)
Diagnoses	
CMML	2
MPN, NOS	1
ECD involving the marrow	6 (27%)

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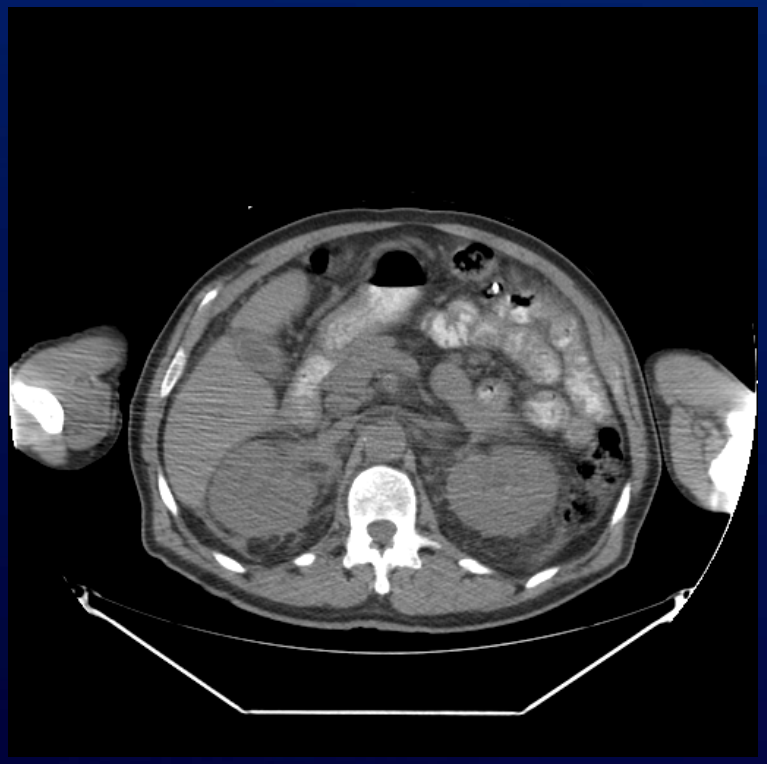
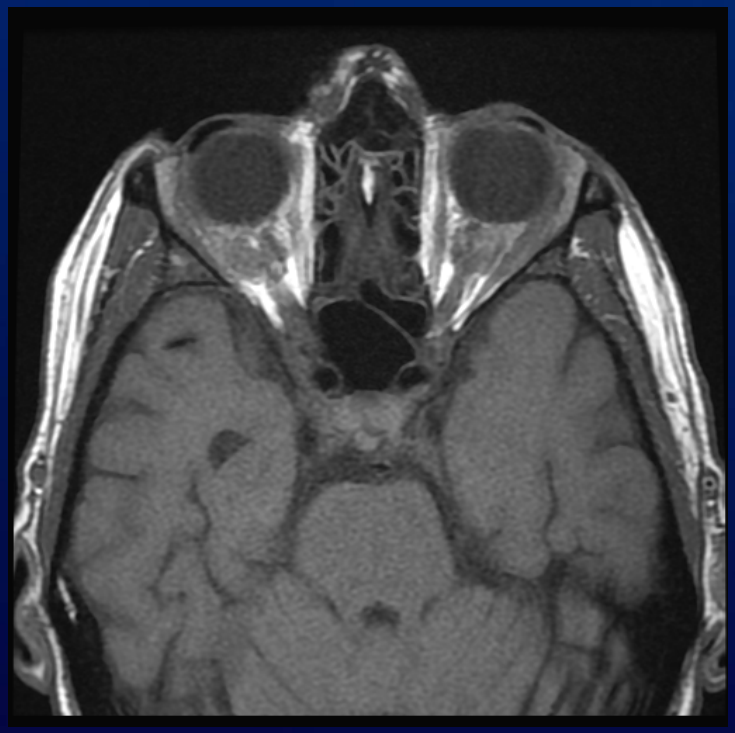
Case 1

- A 75y/o M with known MDS-single lineage dysplasia in 2009
- Not on treatment for the MDS
- December 2013: presented with chronic fatigue, unintentional weight loss of 9 pounds, abdominal pain, progressive ataxia





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Case 1 continued

- Lacrimal gland pathology consistent with ECD, *BRAF-V600E*
- Monocytosis 2.2 x 10^9/L
- Bone marrow: CMML-0 and ECD
- Treatment:
  - Steroid, Anakinra (1 month Rx): Progressive disease
  - Vemurafenib (6 months Rx): intolerance– fatigue
  - Dabrafenib (4 months Rx): partial response but intolerance
- October 2016: hospitalization for multi-organ failure, pancytopenia → death

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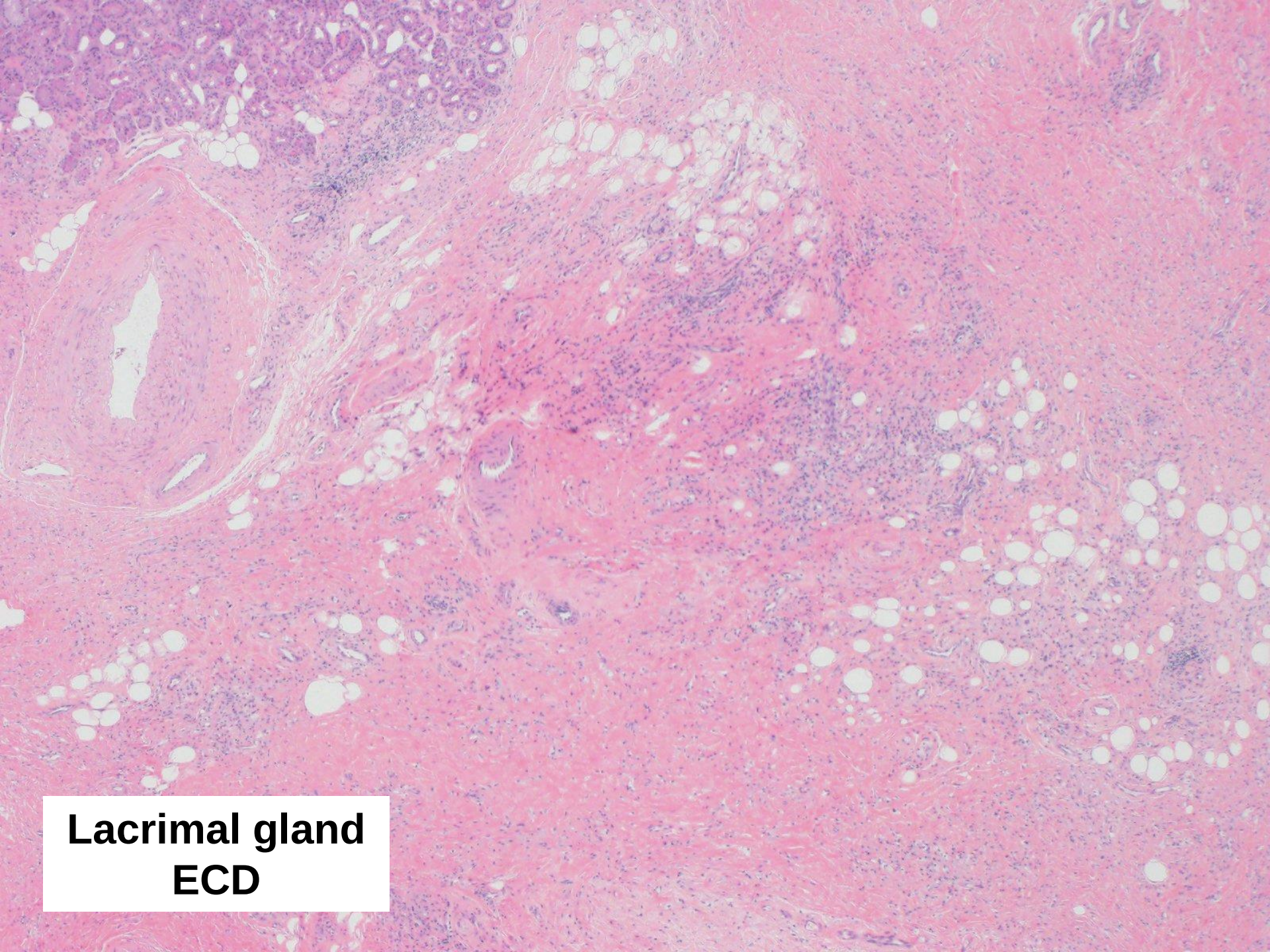
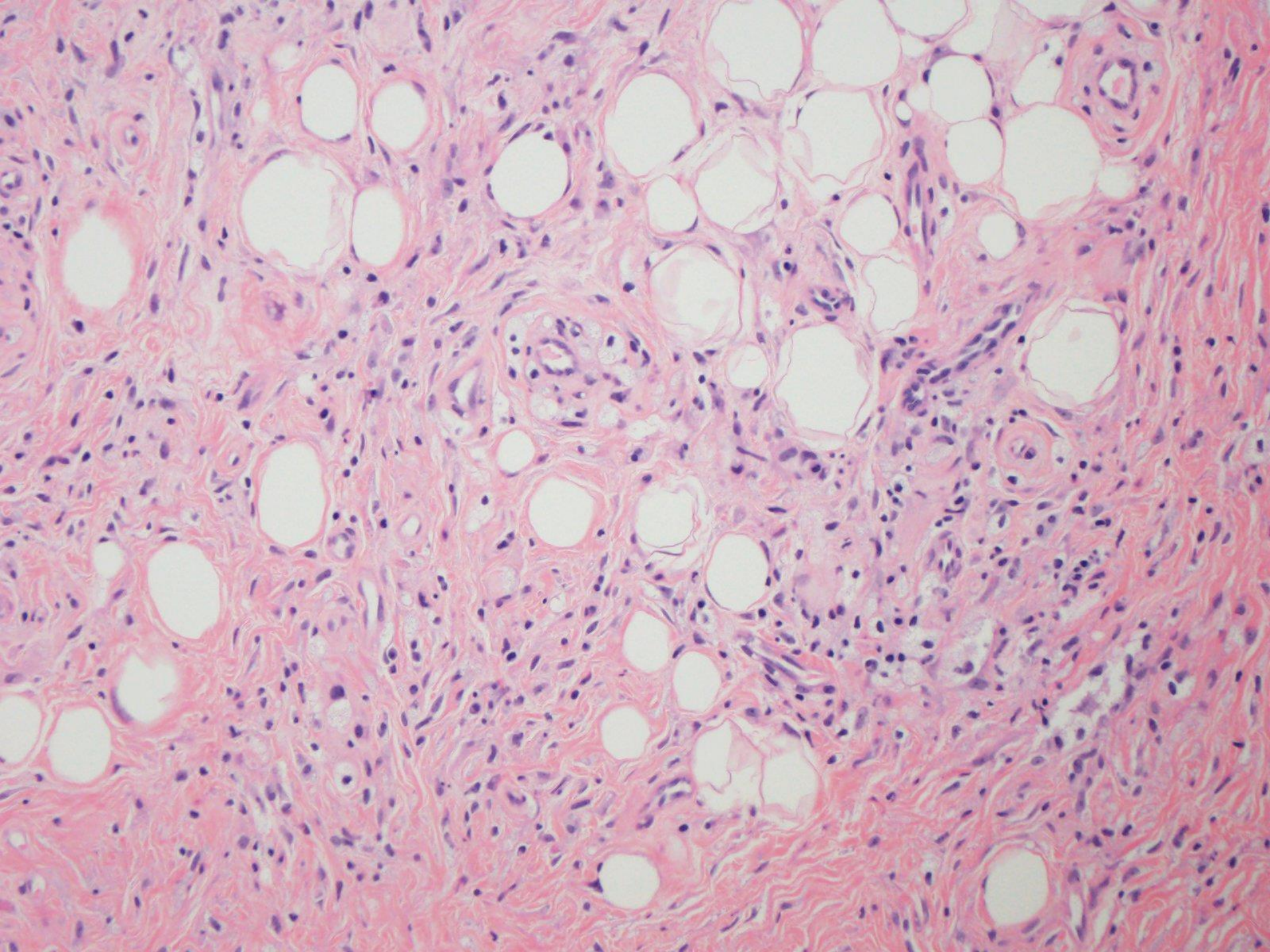
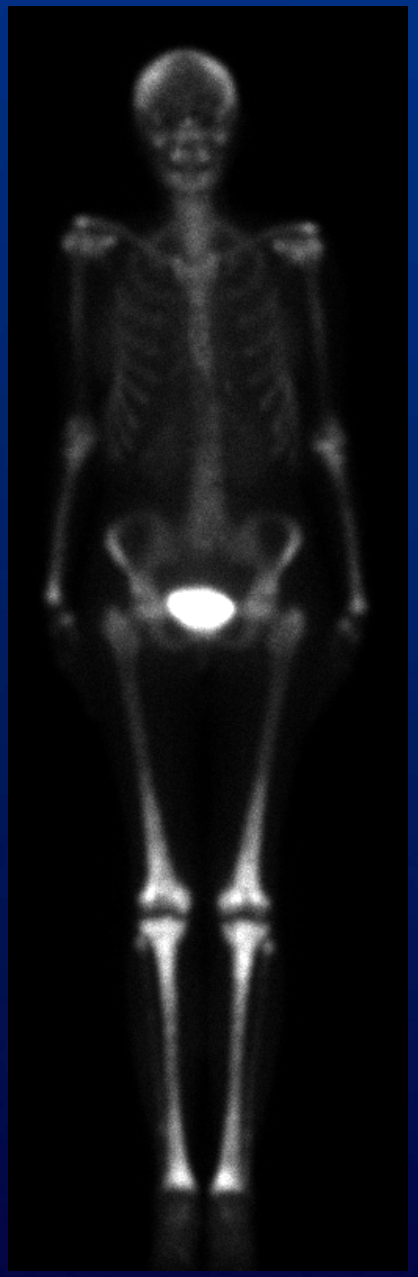

Lacrimal gland
ECD



Case 2

- A 59y/o F with skin lesions
- Skin biopsy Nov 2009: Xanthogranuloma, ECD diagnosis, *BRAF V600E* negative by IHC
- Monocytosis 1.15 x 10^9/L, splenomegaly
- Bone marrow: CMML-1
- Treatment: Hydroxyurea in April 2013 for CMML
- Death within 3 months of initiation of hydroxyurea (July 2013)



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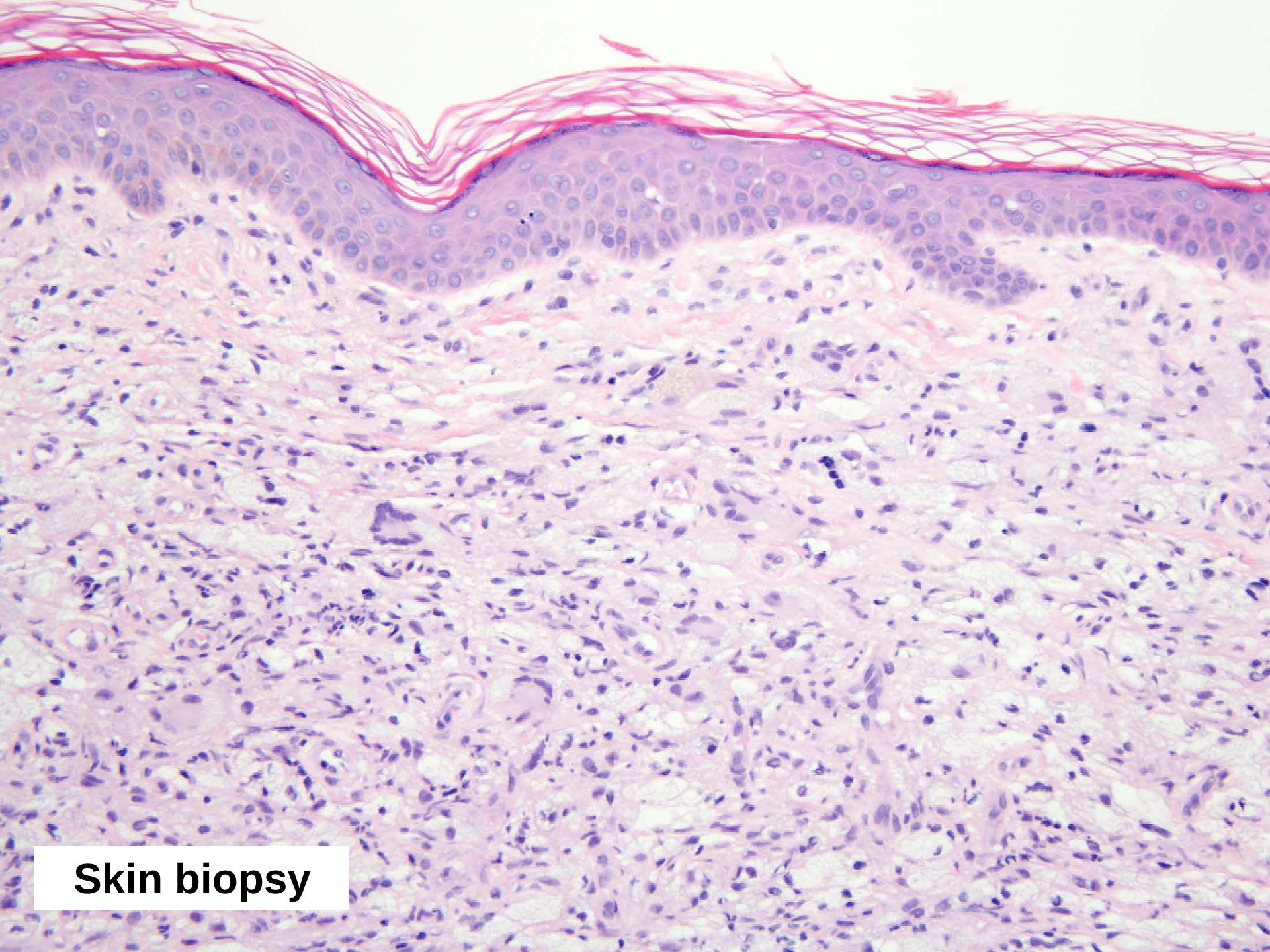
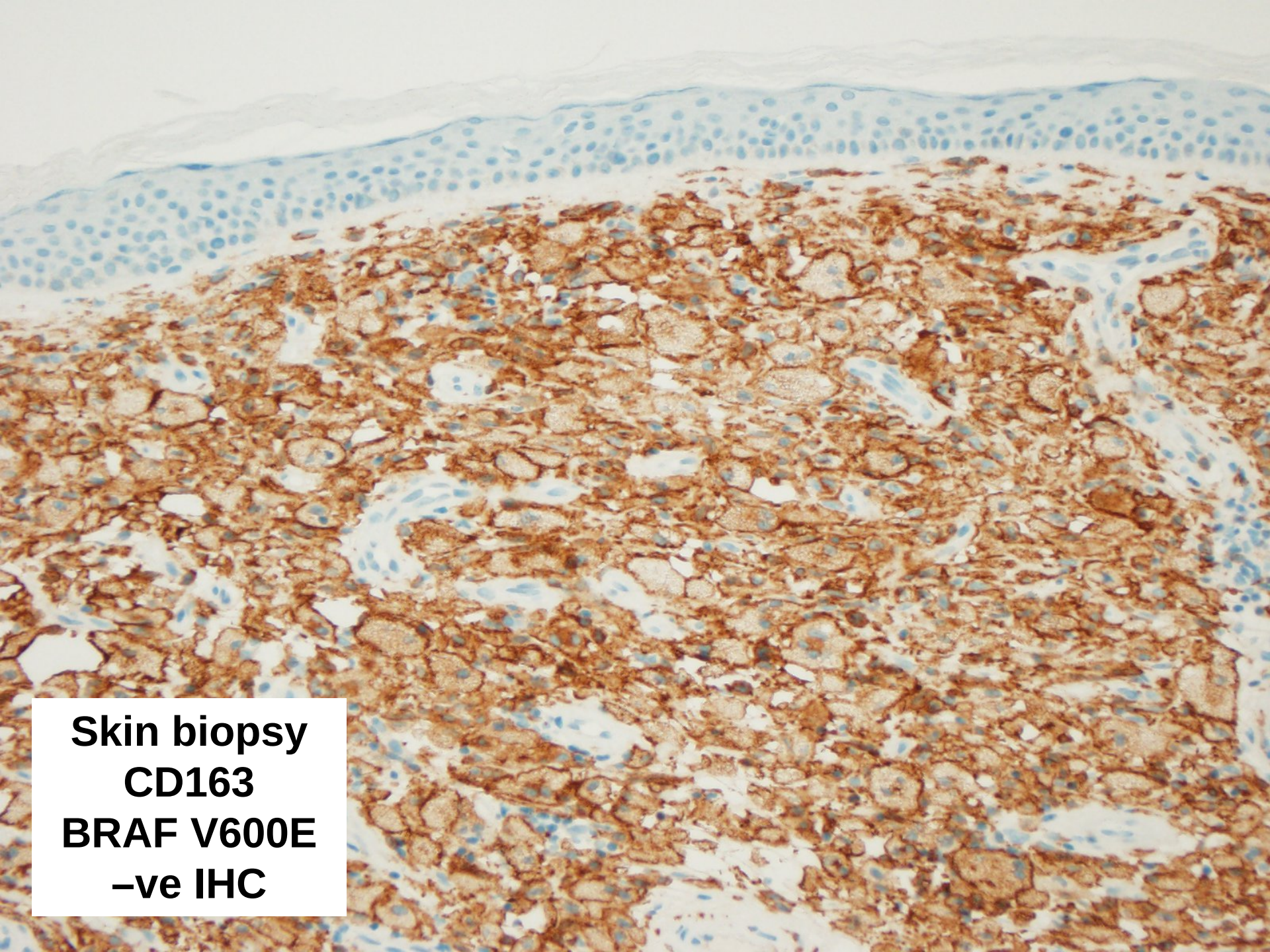
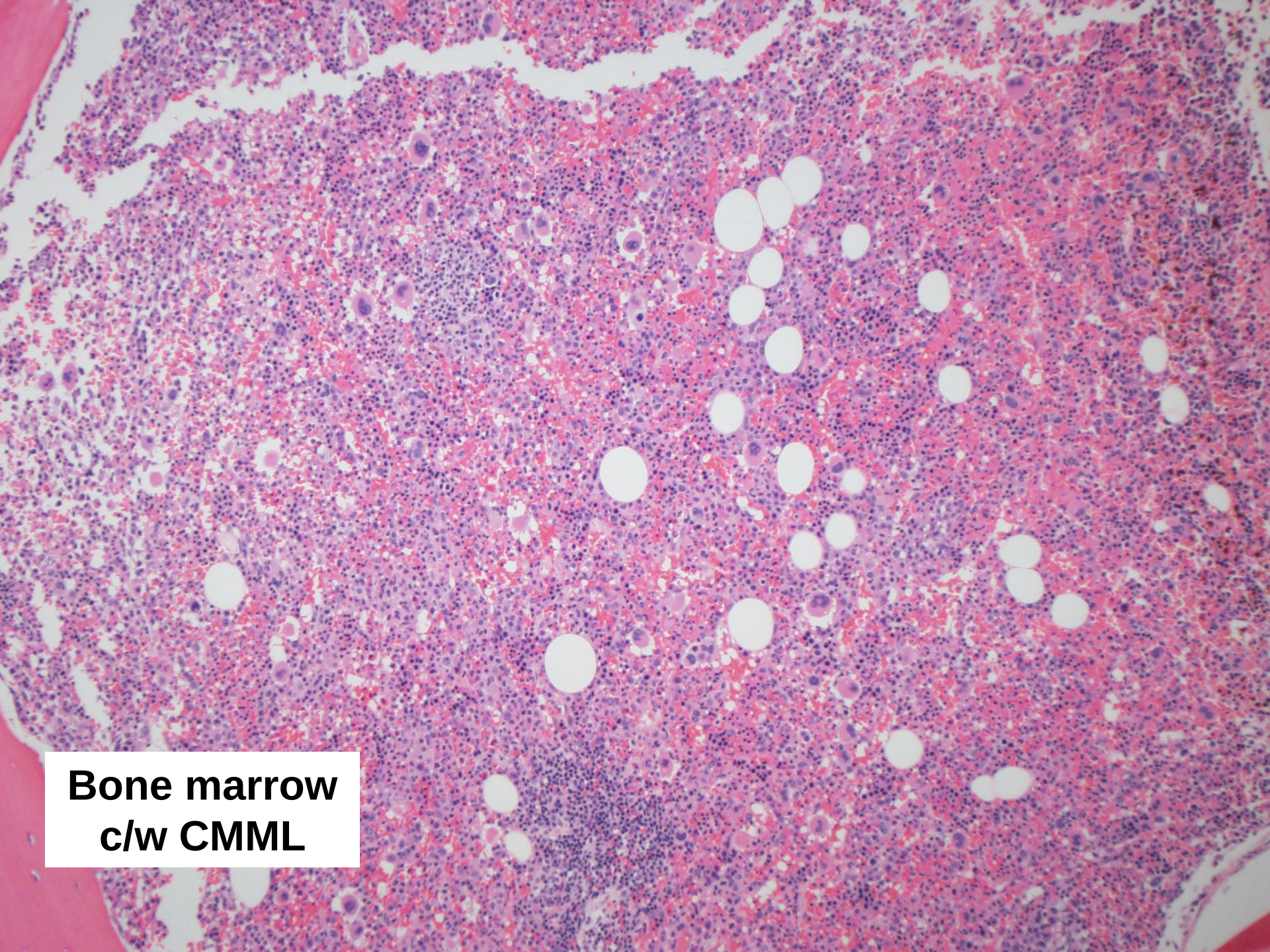
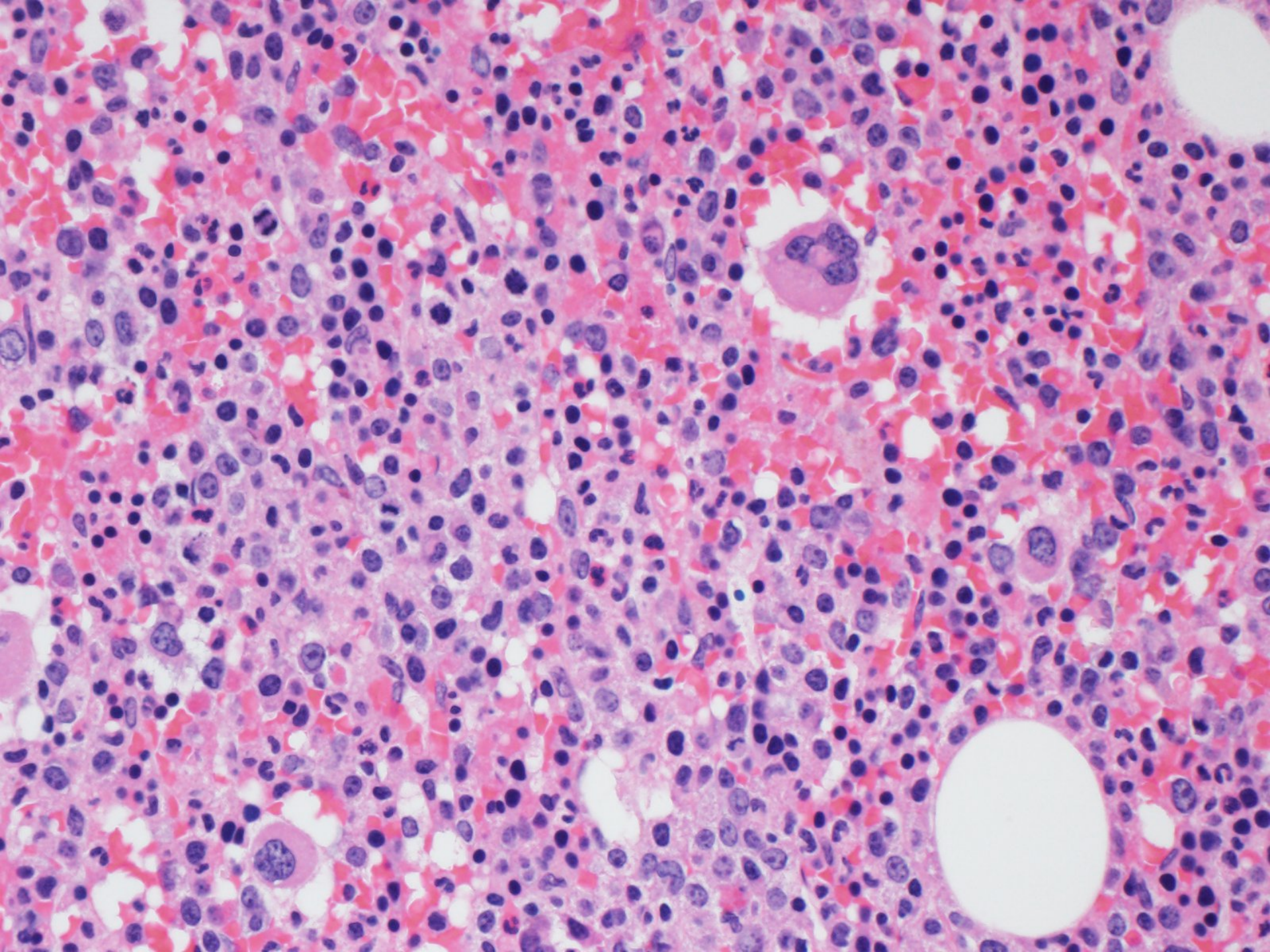
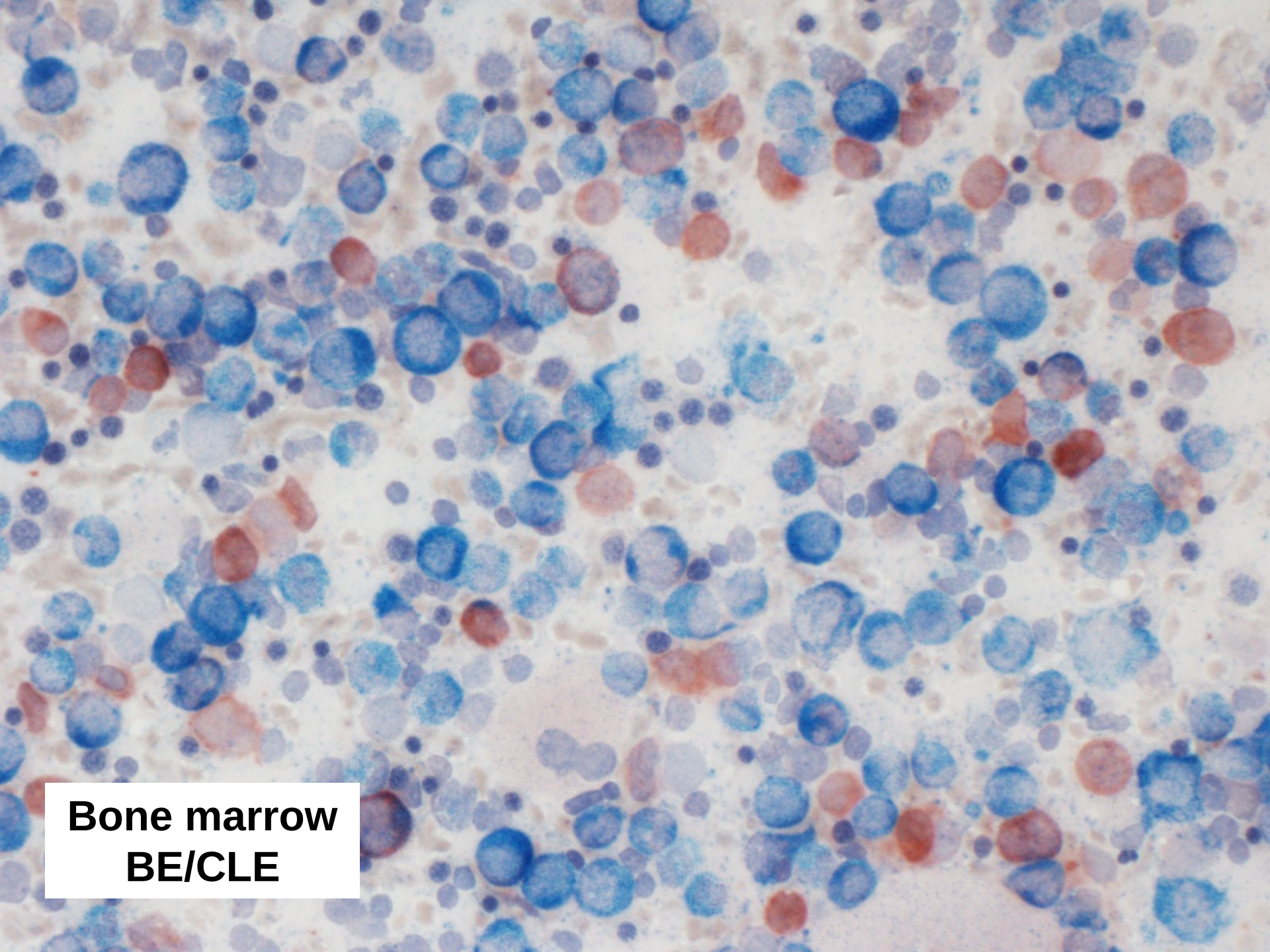

Skin biopsy


Skin biopsy
CD163
BRAF V600E
–ve IHC

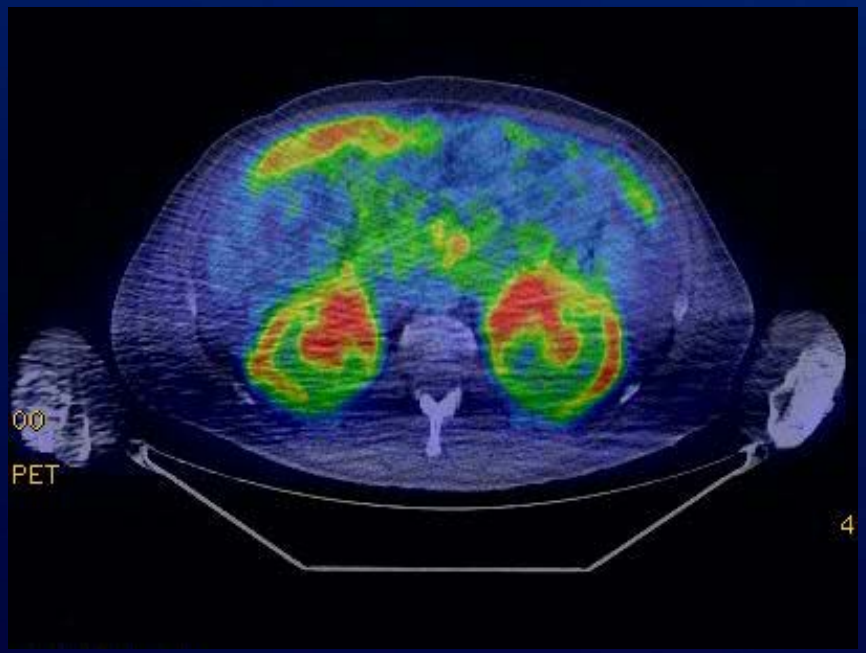

Bone marrow
c/w CMML

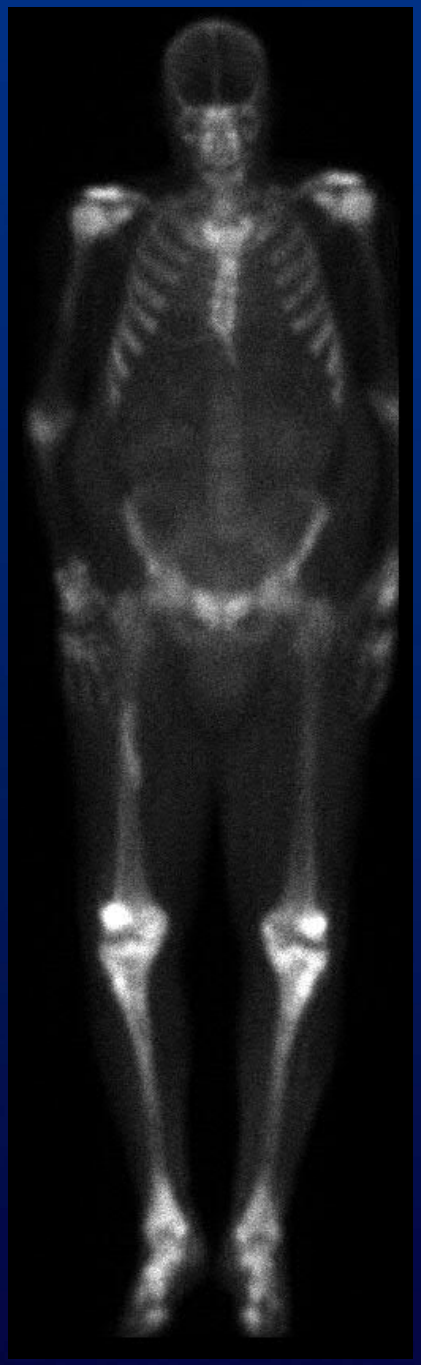



Bone marrow
BE/CLE

Case 3

- A 51 y/o M with *JAK2 V617F* essential thrombocytosis in 1995
- Treatment with hydroxyurea
- ECD diagnosis (peri-renal tissue) in Sep 2012, *BRAF-WT*





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Case 3 continued

- Bone marrow 10/2012: MPN, not otherwise specified, *JAK2 V617F*
- Peri-renal biopsy positive for *JAK2 V617F* (suboptimal sample)
- Treatment and follow-up
  - Interferon alfa: Progressive disease Sept 2013
  - Subsequent follow-up at an outside facility
- Passed away in June 2016 (exact cause unknown)

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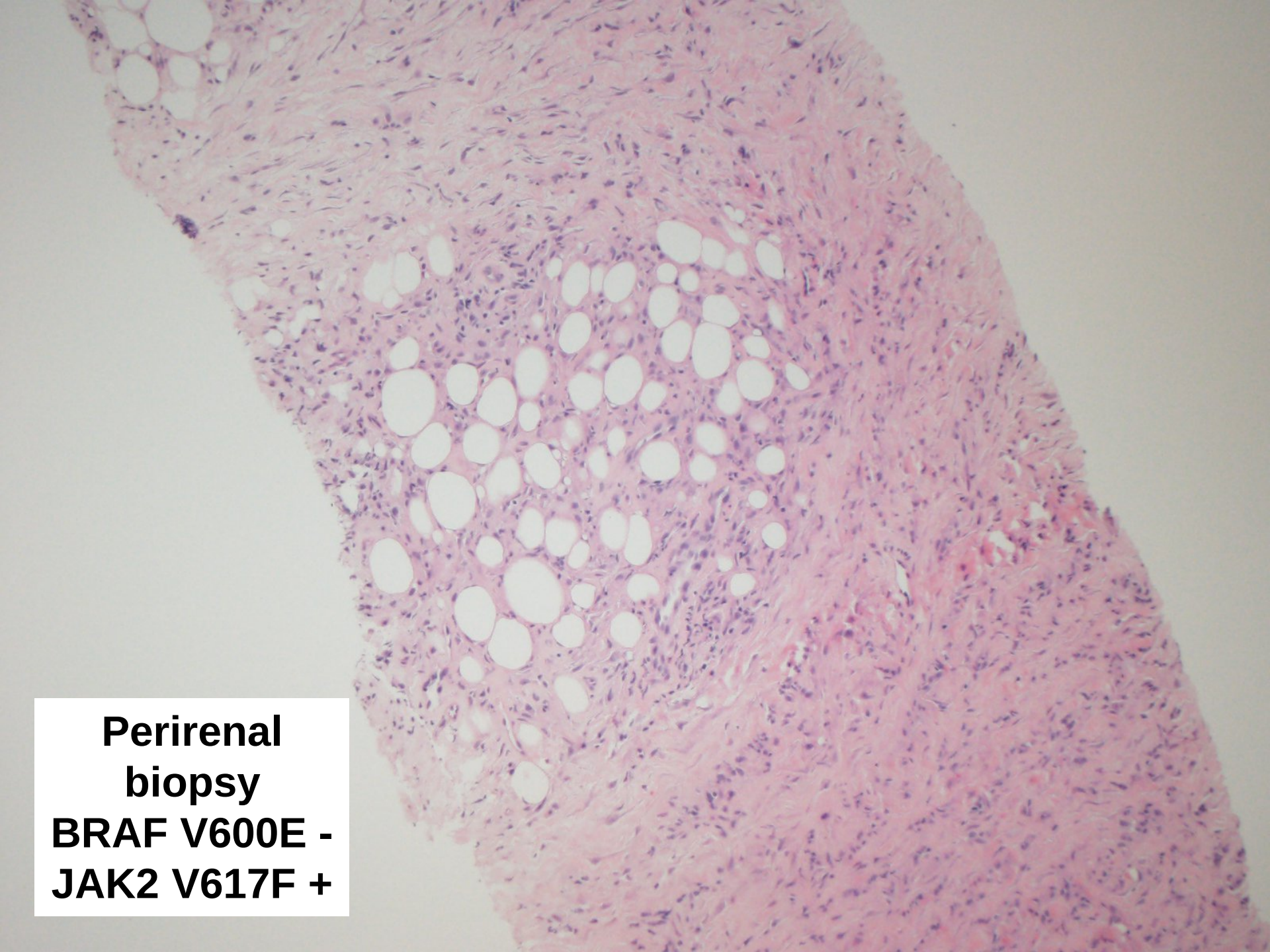
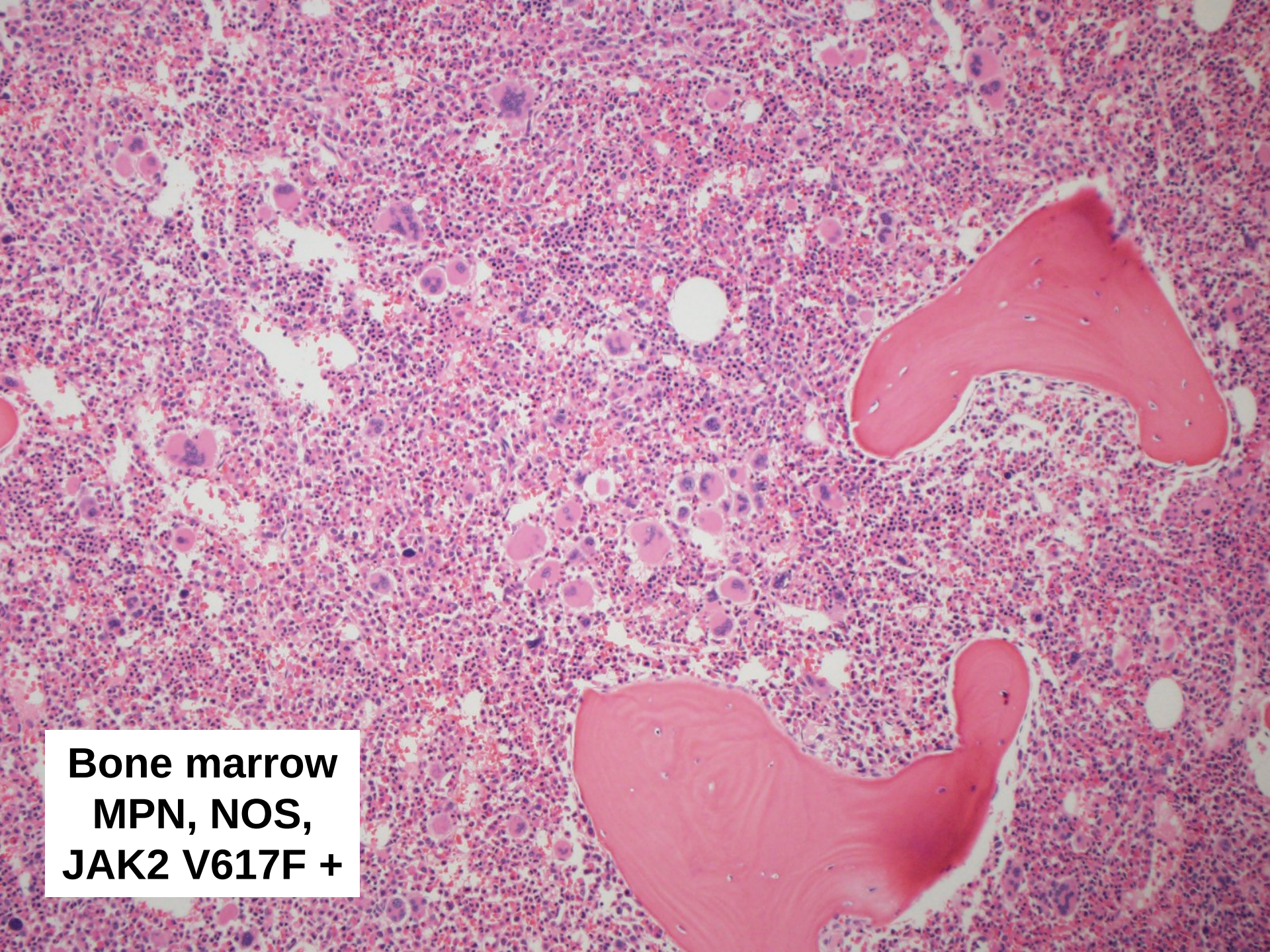

Perirenal
biopsy
BRAF V600E -
JAK2 V617F +


Bone marrow
MPN, NOS,
JAK2 V617F +


Bone marrow
CD163

Results

- 72 patients followed for 256 years
- 3 (4%) developed myeloid neoplasms
- 1.2 myeloid neoplasms per 100-patient years

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Conclusions

- Myeloid neoplasms present in 4% of ECD, higher than expected in general population
- CMML most common myeloid neoplasm.
- All these patients with notable abnormality on their peripheral blood counts.
- May consider bone marrow biopsy in ECD patients with peripheral blood count abnormalities

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Thank you

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