



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

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)

Methods

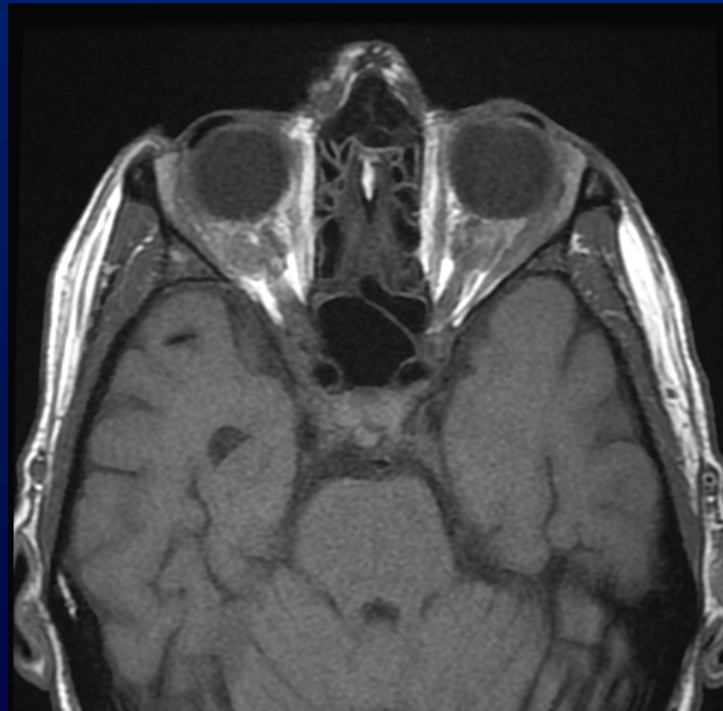
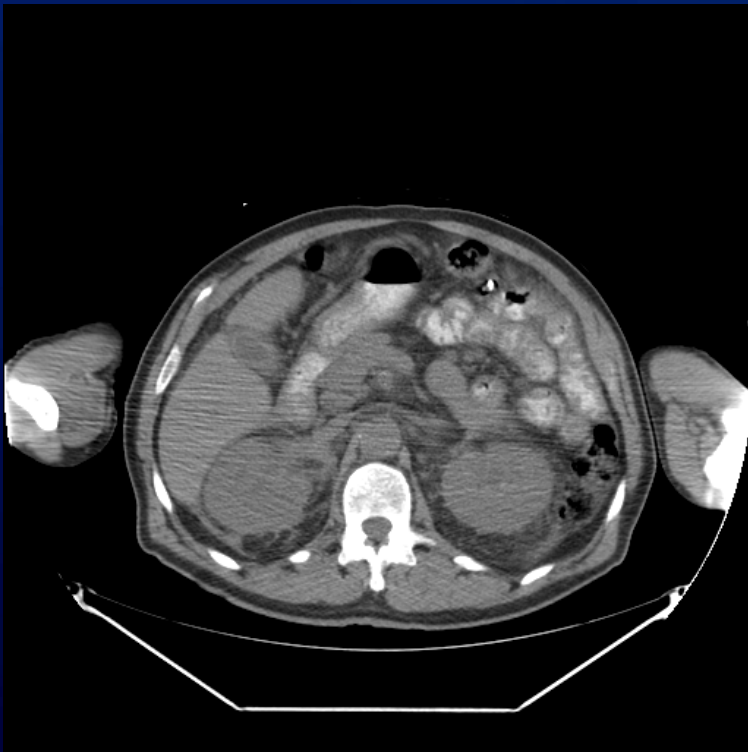
- Retrospective study of ECD patients diagnosed from 1998 to 2016 at Mayo Clinic
- The diagnosis was made using clinical criteria in conjunction with histopathologic findings
- Pathology slides were independently reviewed at our institution

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%)

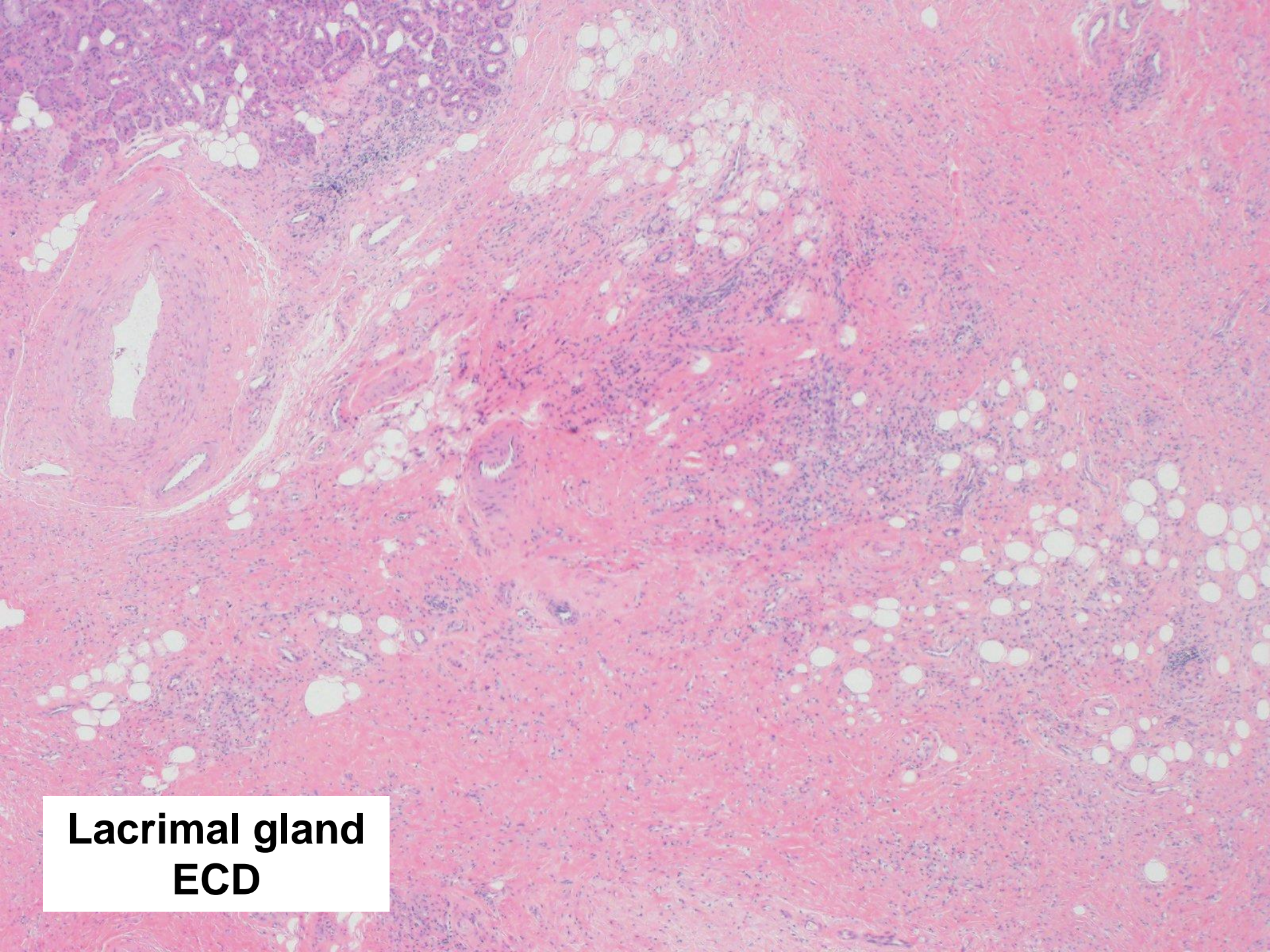
Case 1

- 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

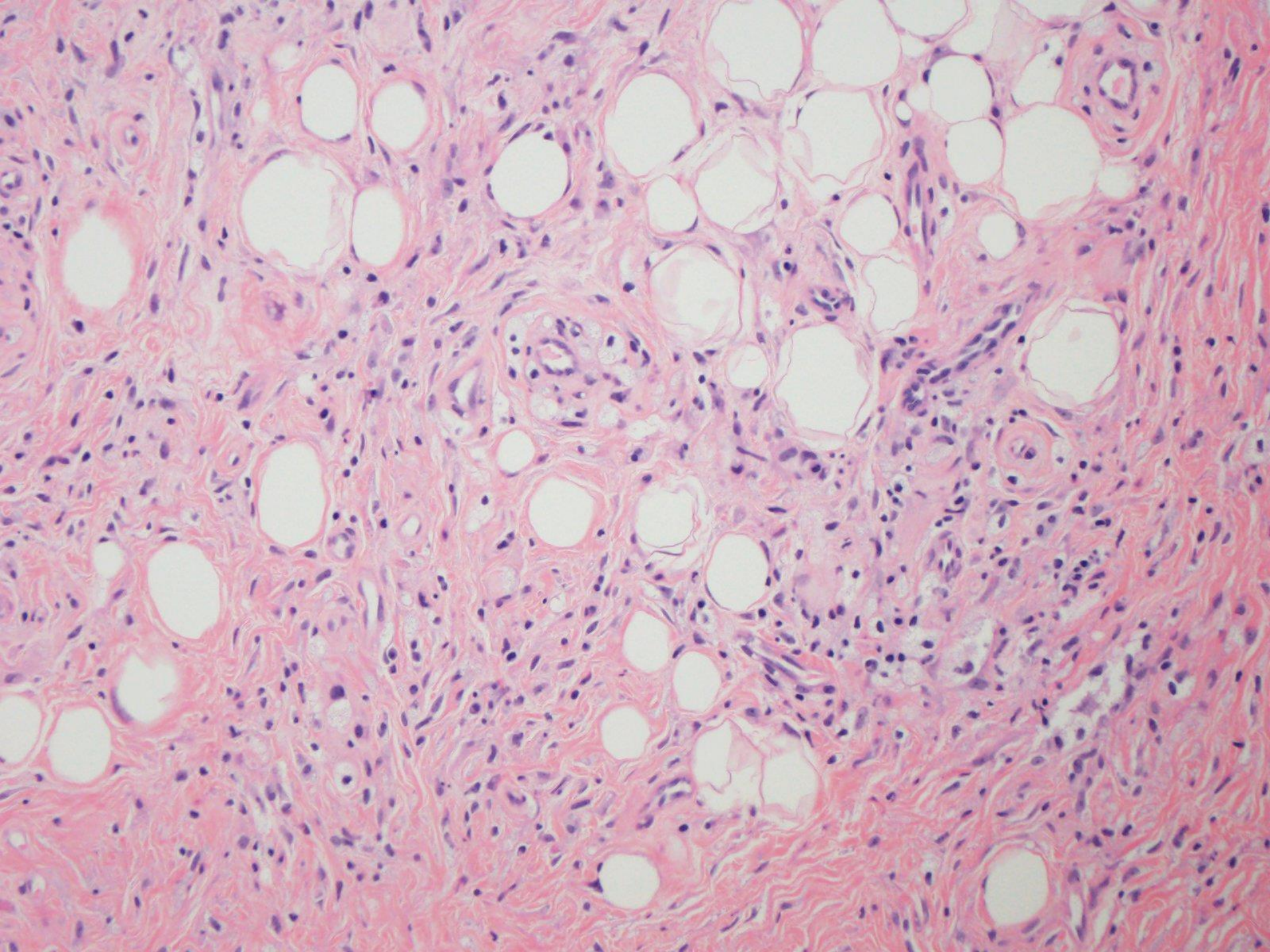


Case 1 continued

- Lacrimal gland pathology consistent with ECD, *BRAF-V600E*
- Monocytosis $2.2 \times 10^9/L$
- 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

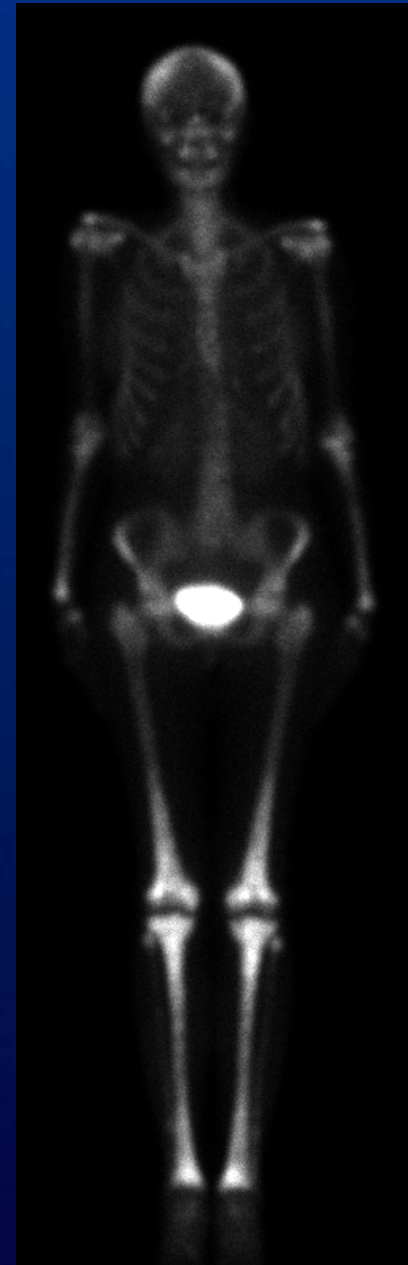


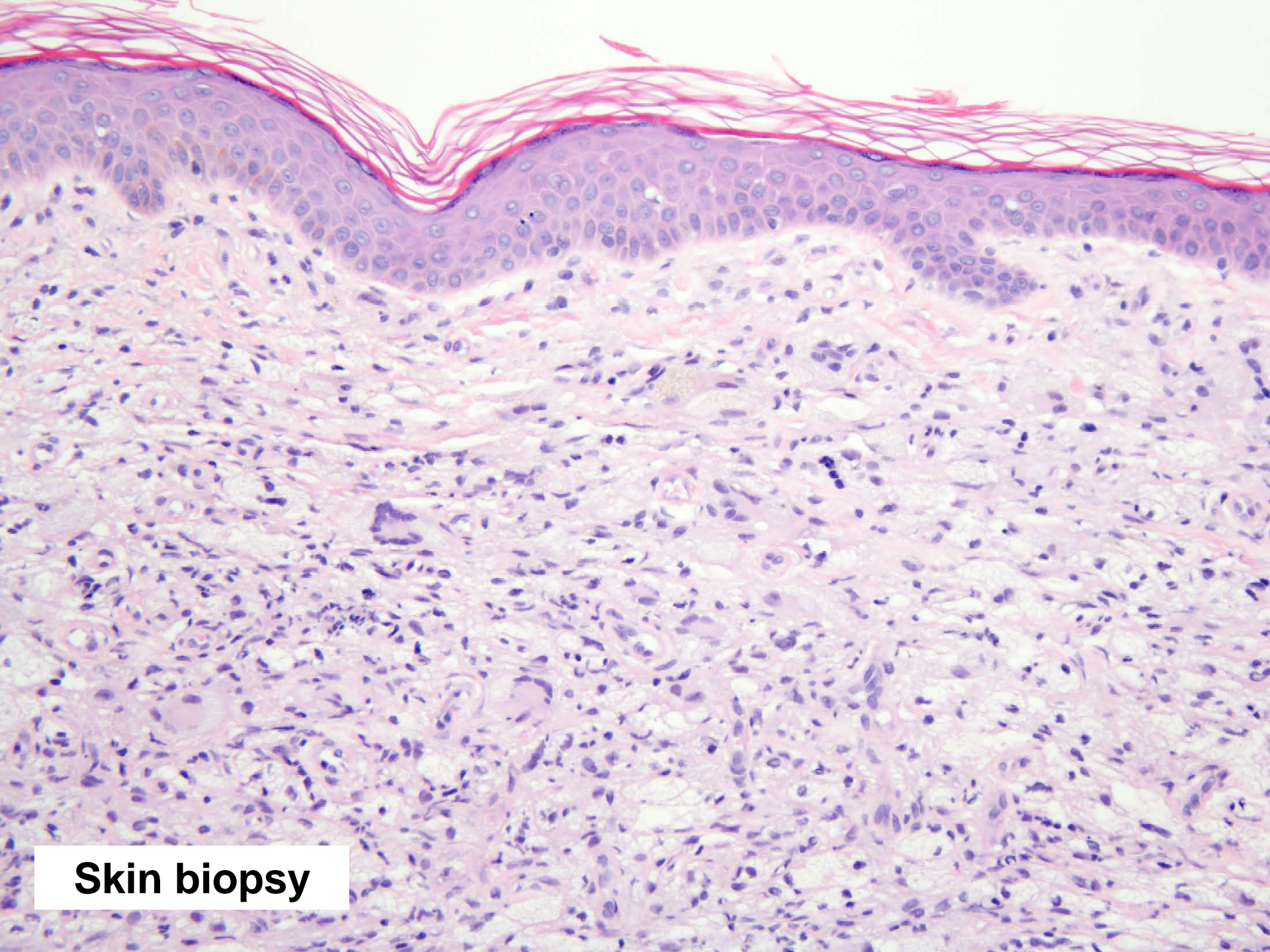
**Lacrimal gland
ECD**



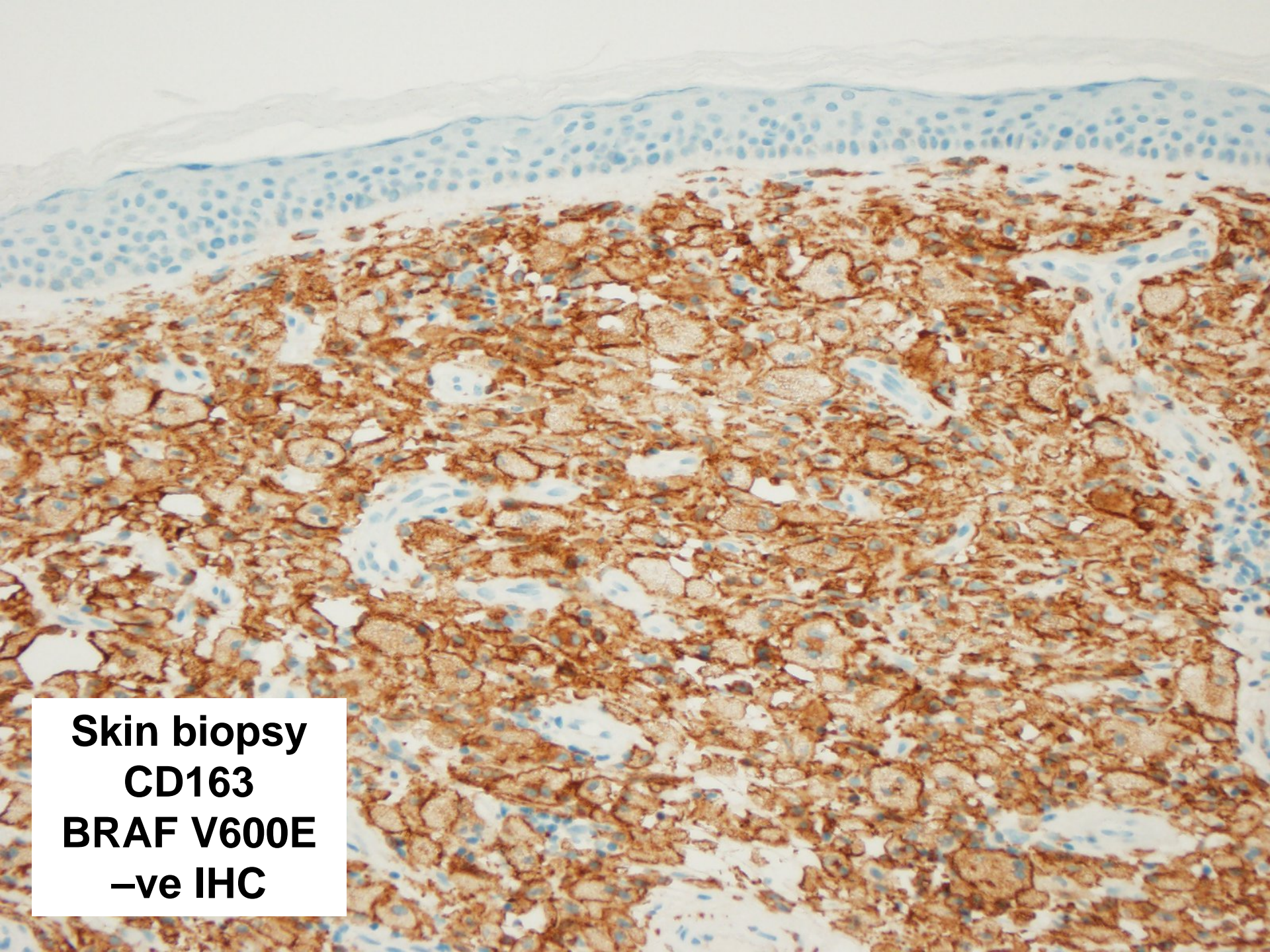
Case 2

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





Skin biopsy

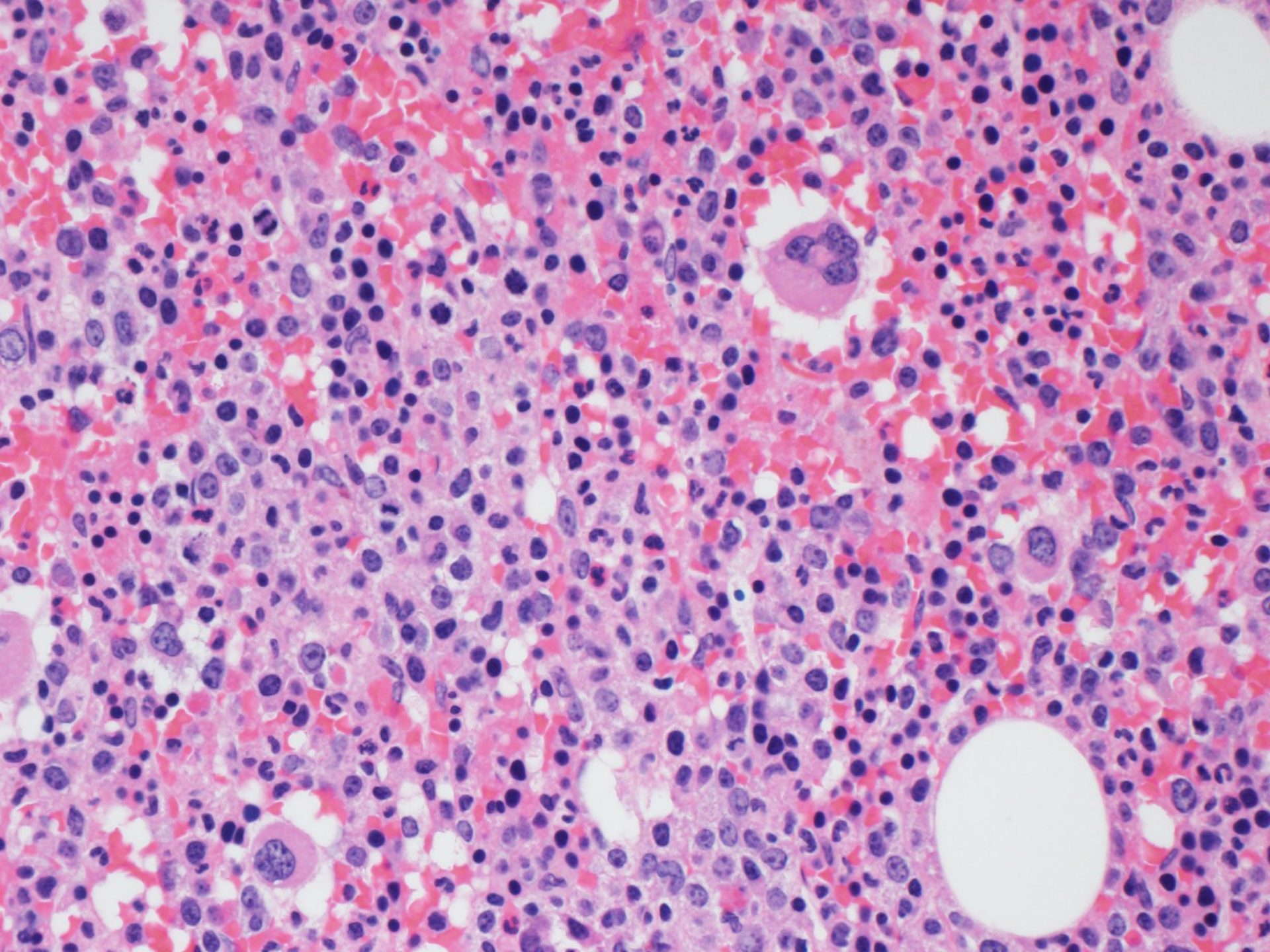


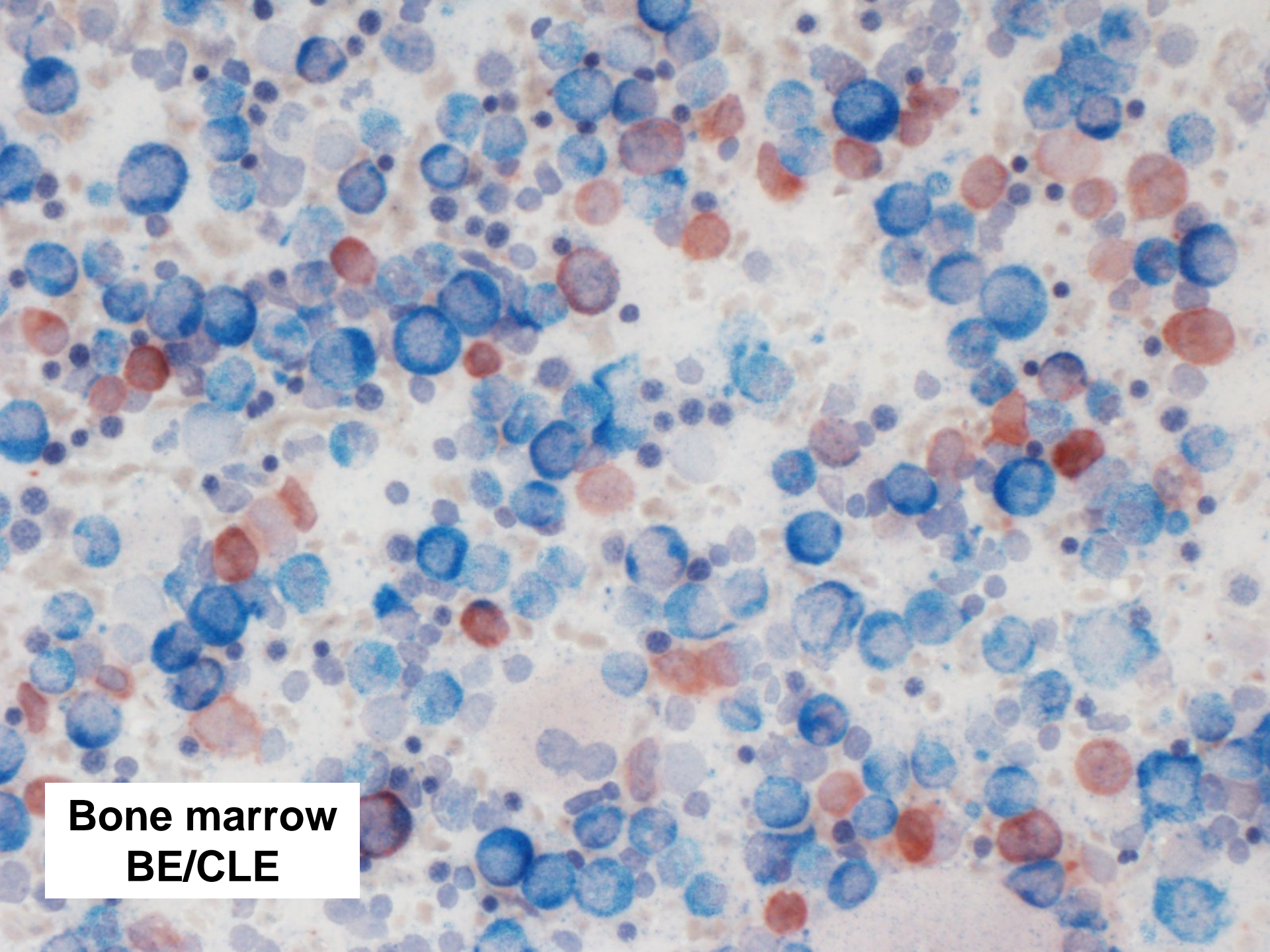
Skin biopsy
CD163
BRAF V600E
-ve IHC



This histological image shows a section of bone marrow stained with hematoxylin and eosin (H&E). The marrow is densely infiltrated with a population of small, dark-staining cells, characteristic of myeloid cells in chronic myelomonocytic leukemia (CMML). These cells are distributed throughout the marrow space, which is also filled with numerous large, pale, circular adipocytes. The overall architecture of the marrow is disrupted by the dense cellular infiltration.

**Bone marrow
c/w CMML**

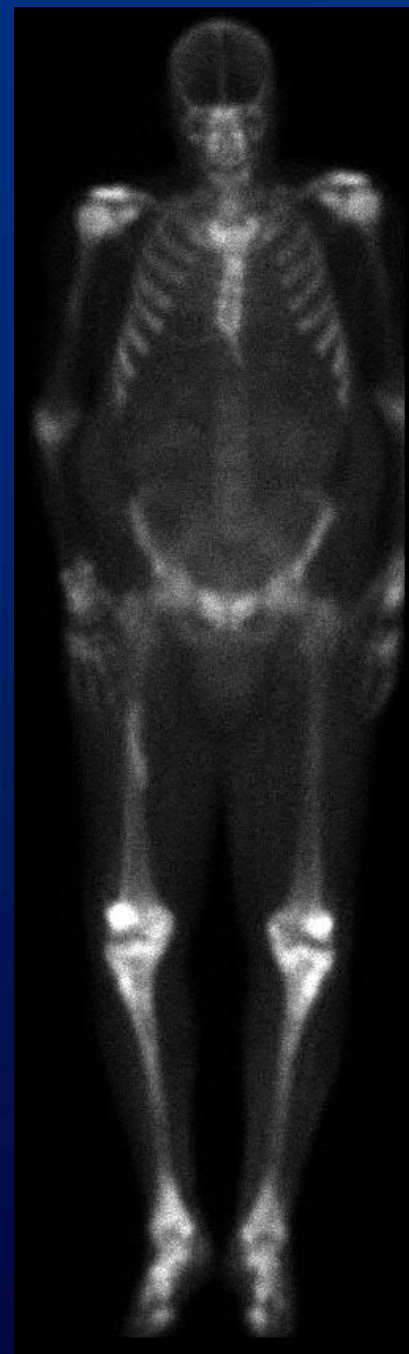
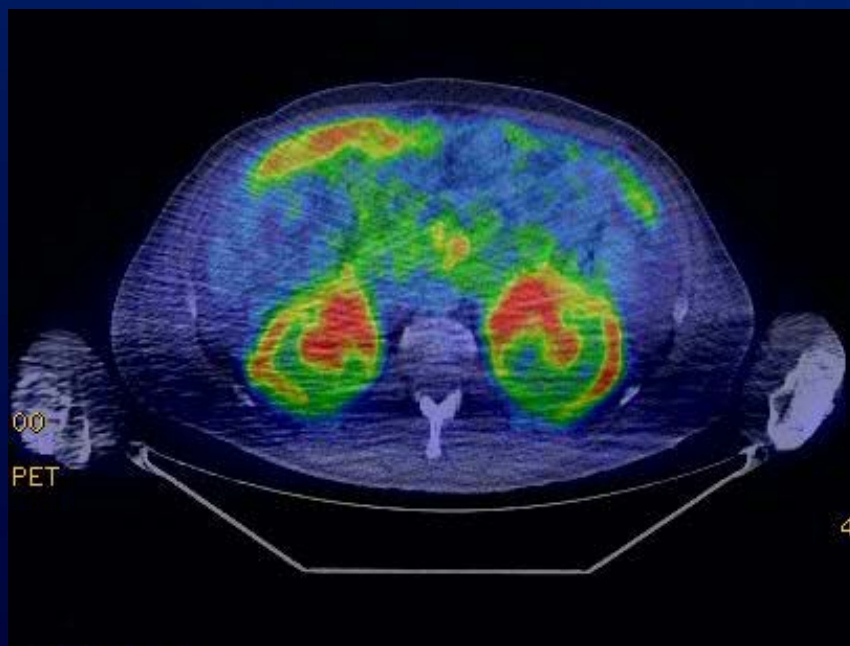




**Bone marrow
BE/CLE**

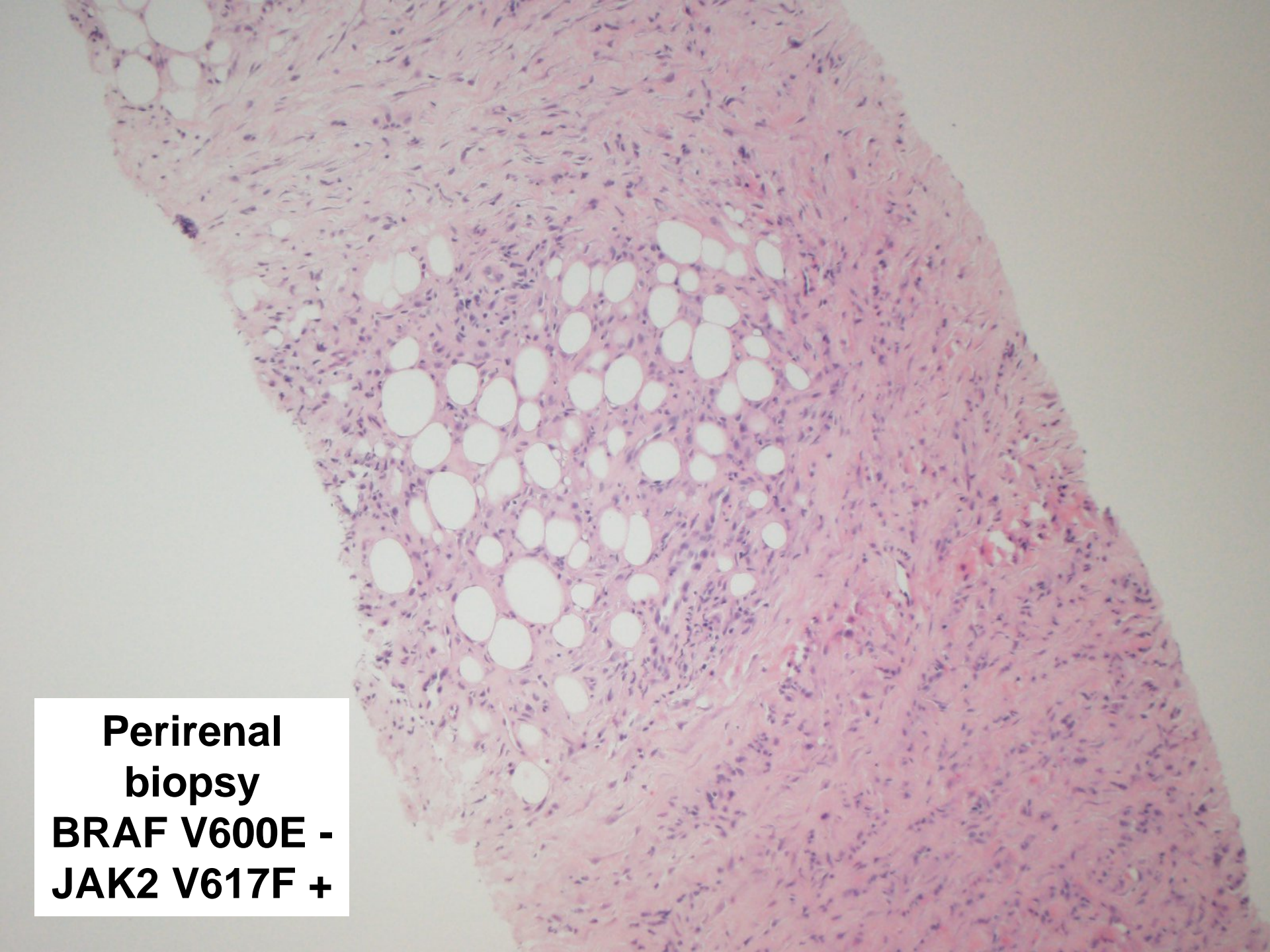
Case 3

- 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

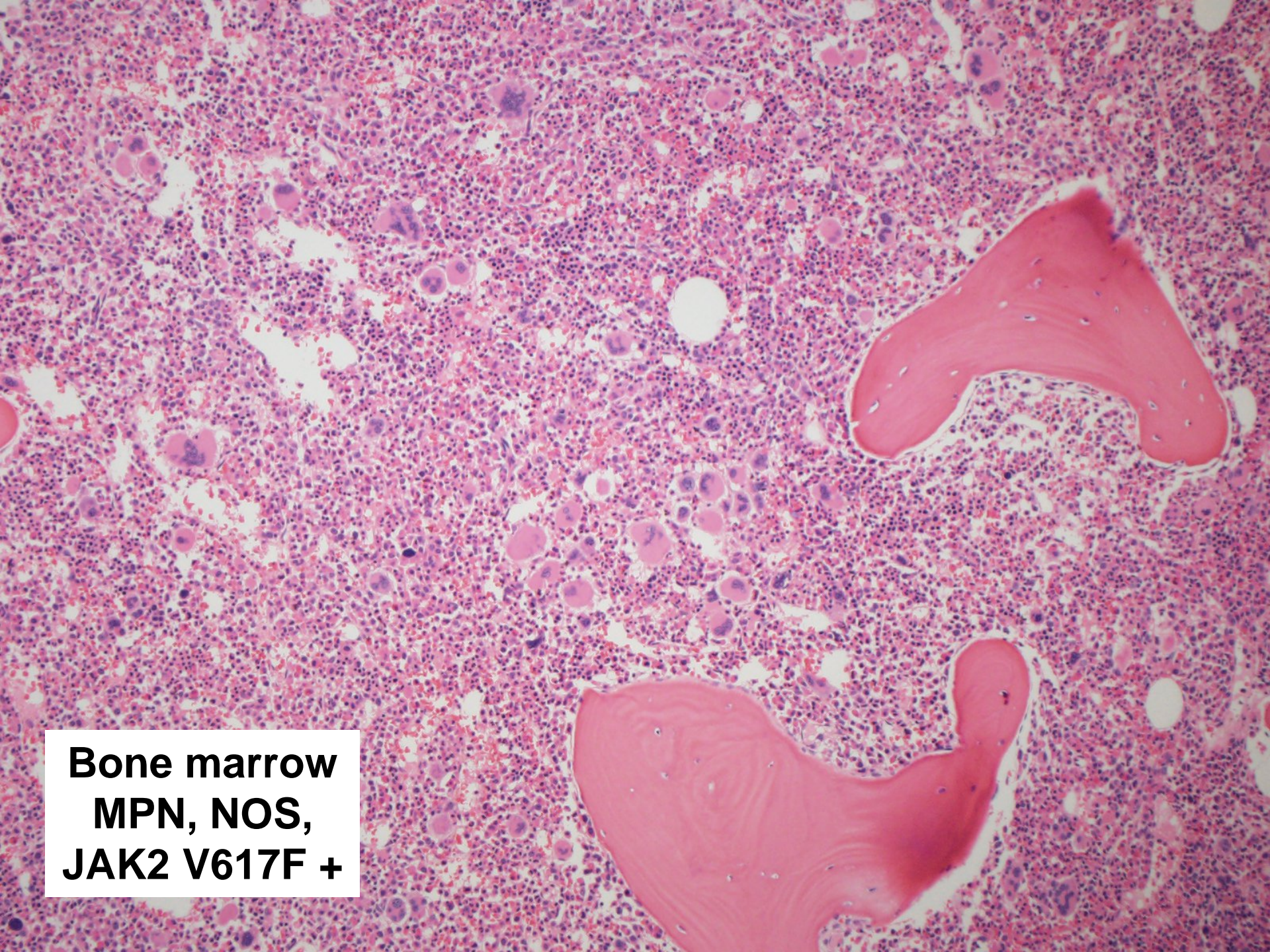


Case 3 continued

- 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)



**Perirenal
biopsy
BRAF V600E -
JAK2 V617F +**



This histological image shows a section of bone marrow stained with hematoxylin and eosin (H&E). The marrow is densely populated with cells, including numerous small, dark-staining nuclei and larger, pale-staining cells with prominent nucleoli. There are several large, irregular, eosinophilic (pink) structures scattered throughout the field, which appear to be areas of necrosis or large, atypical cells. The overall architecture is disrupted, consistent with a myeloid neoplasia.

**Bone marrow
MPN, NOS,
JAK2 V617F +**



This image is a high-magnification micrograph of a bone marrow section stained for CD163. The tissue is densely populated with cells. The CD163-positive cells, which are macrophages or monocytes, are stained a dark brown color. These cells are distributed throughout the field of view, often appearing as small, rounded or elongated cells with prominent brown staining. The background consists of numerous smaller, lighter-colored cells, likely hematopoietic precursors or other marrow cells, which are stained a pale blue or purple. The overall texture of the image is granular and complex, reflecting the cellular diversity of the bone marrow.

Bone marrow
CD163

Results

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

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



Thank you

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