MHICC Case 1

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*M*ulti-institutional *H*ematopathology *I*nteresting *C*ase *C*onference

University Health Network

University of Toronto

August 2025

Clinical history

- 49M presenting with bicytopenia (anemia, thrombocytopenia)
- History of multiple myeloma, diagnosed and treated mainly in Philippines
  - 2019: diagnosed with IgG kappa myeloma
  - 2019-2021: received multiple lines of therapy, including proteosome inhibitors, immunomodulatory drugs, anti-CD38 monoclonal antibodies
  - June 2021: allogeneic SCT, complicated by chronic GVHD and CMV colitis
  - Subsequent biochemical relapse, treated with chemotherapy and radiation

Labs

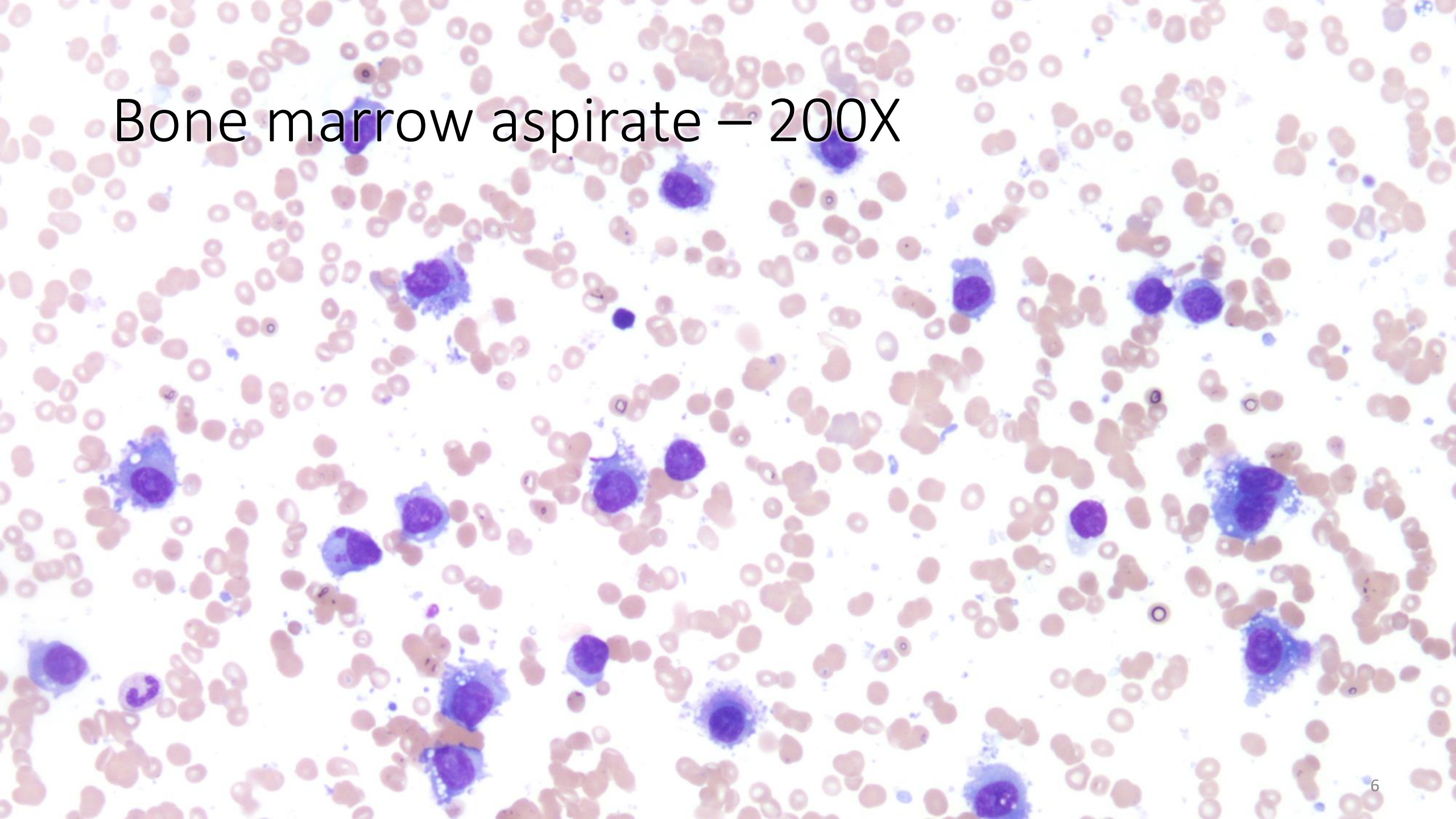
Test	Result
WBC	6.7x10e9/L
RBC	3.15x10e9/L (L)
Hgb	**118 g/L (L)**
Hct	0.34 L/L (L)
MCV	108.6 (H)
MCH	37.5 pg (H)
MCHC	345 g/L
Platelets	**43x10e9/L (L)**
Creatinine	57 umol/L (L)
Calcium	2.26 mmol/L
LDH	271 U/L

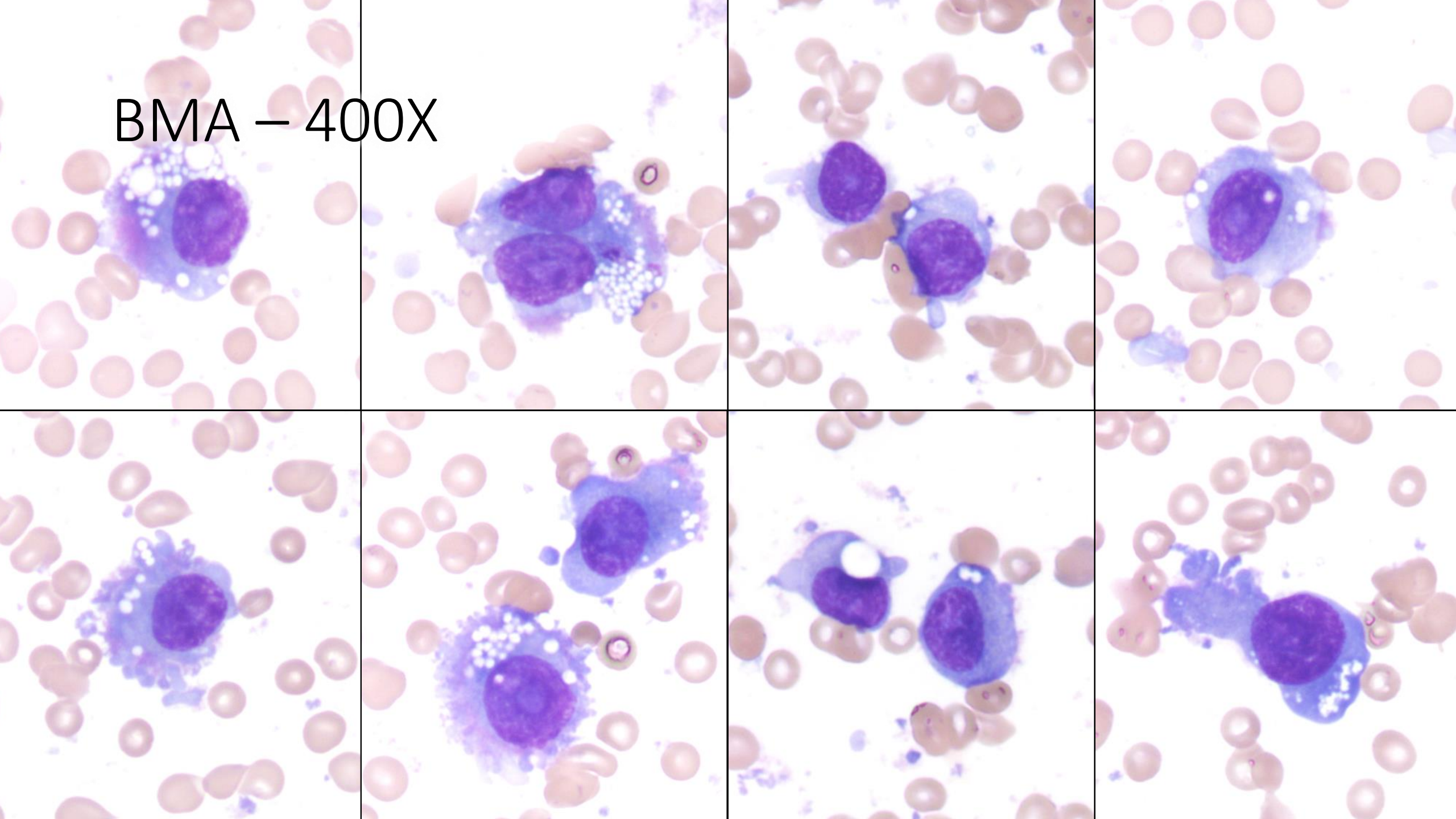
Test	Result
SPEP	M-protein, 11.1 g/L
Free kappa	162.0 mg/L (H)
Free lambda	2.3 mg/L (L)
Kappa/lambda	70.43 (H)
IgG	19.1 g/L (H)
IgA	<0.02 g/L (L)
IgM	<0.10 g/L (L)

Imaging

- July 2024: CT whole body low dose
  - Nonspecific tiny lytic lesions in the calvarium
  - Suspicious lytic lesions in T10 and T12 vertebral bodies, bilateral ilia
  - No extraosseous soft tissue masses

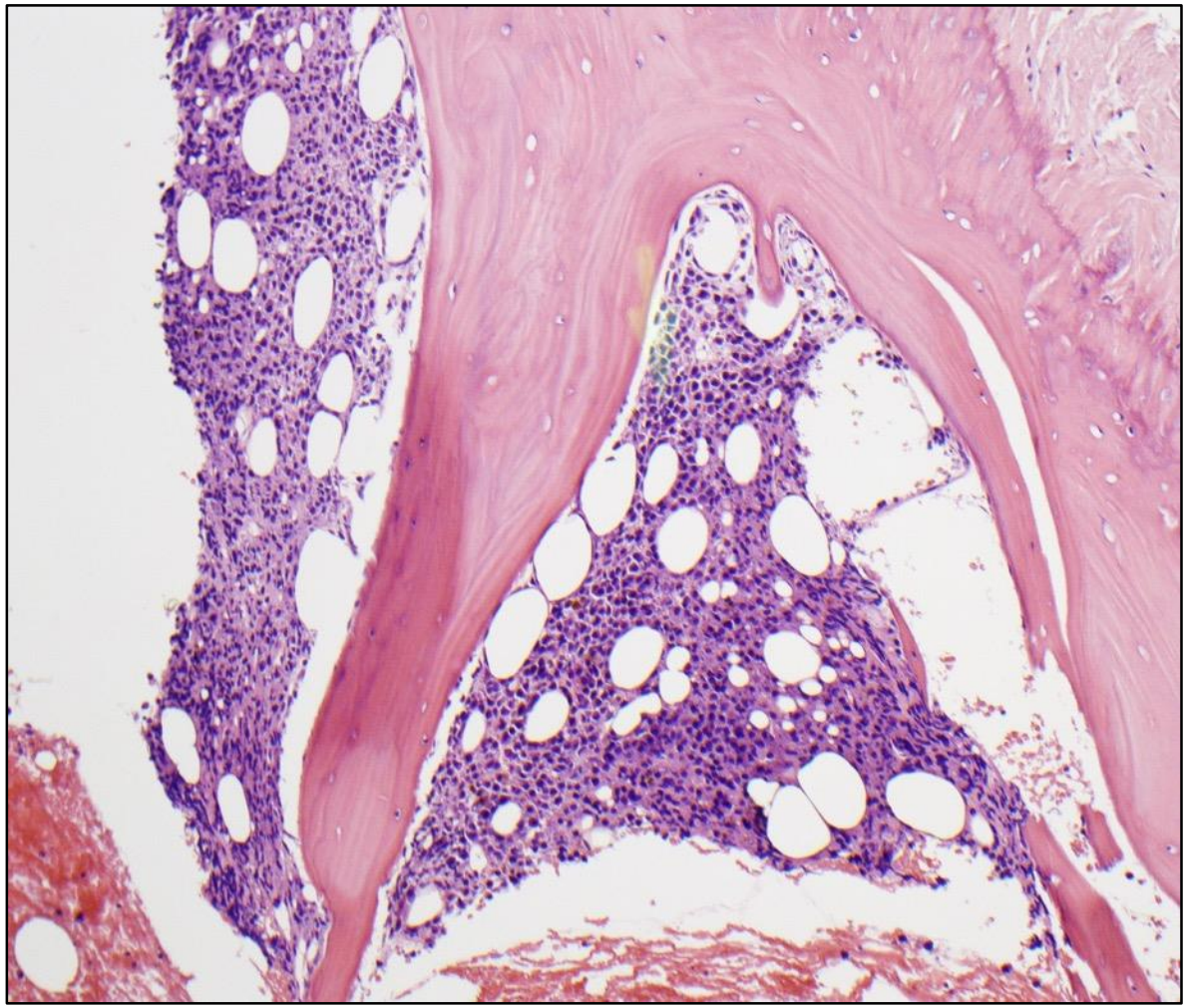
Bone marrow aspirate – 200X



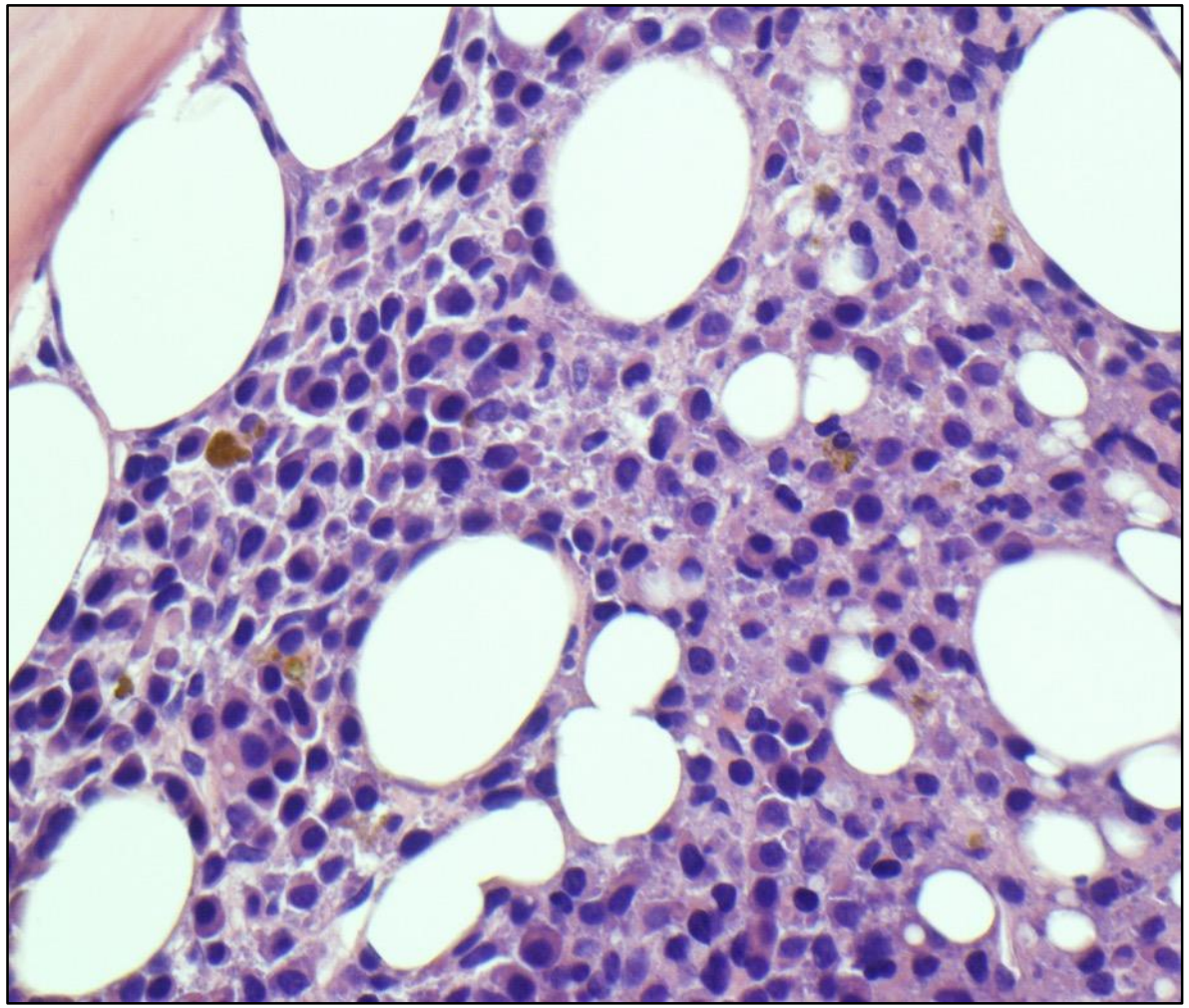

BMA – 400X

Bone marrow biopsy

H&E 100X

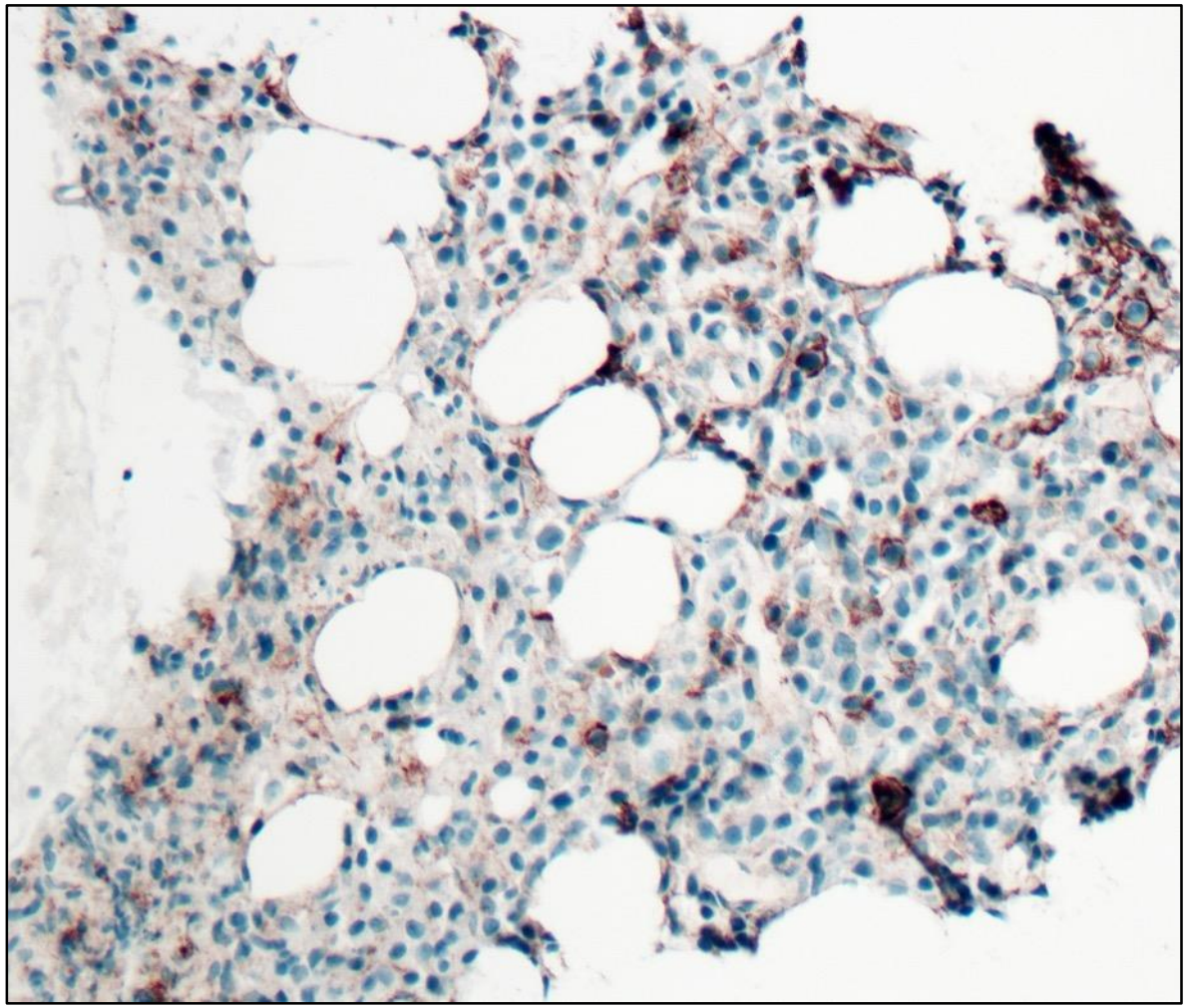


H&E 400X

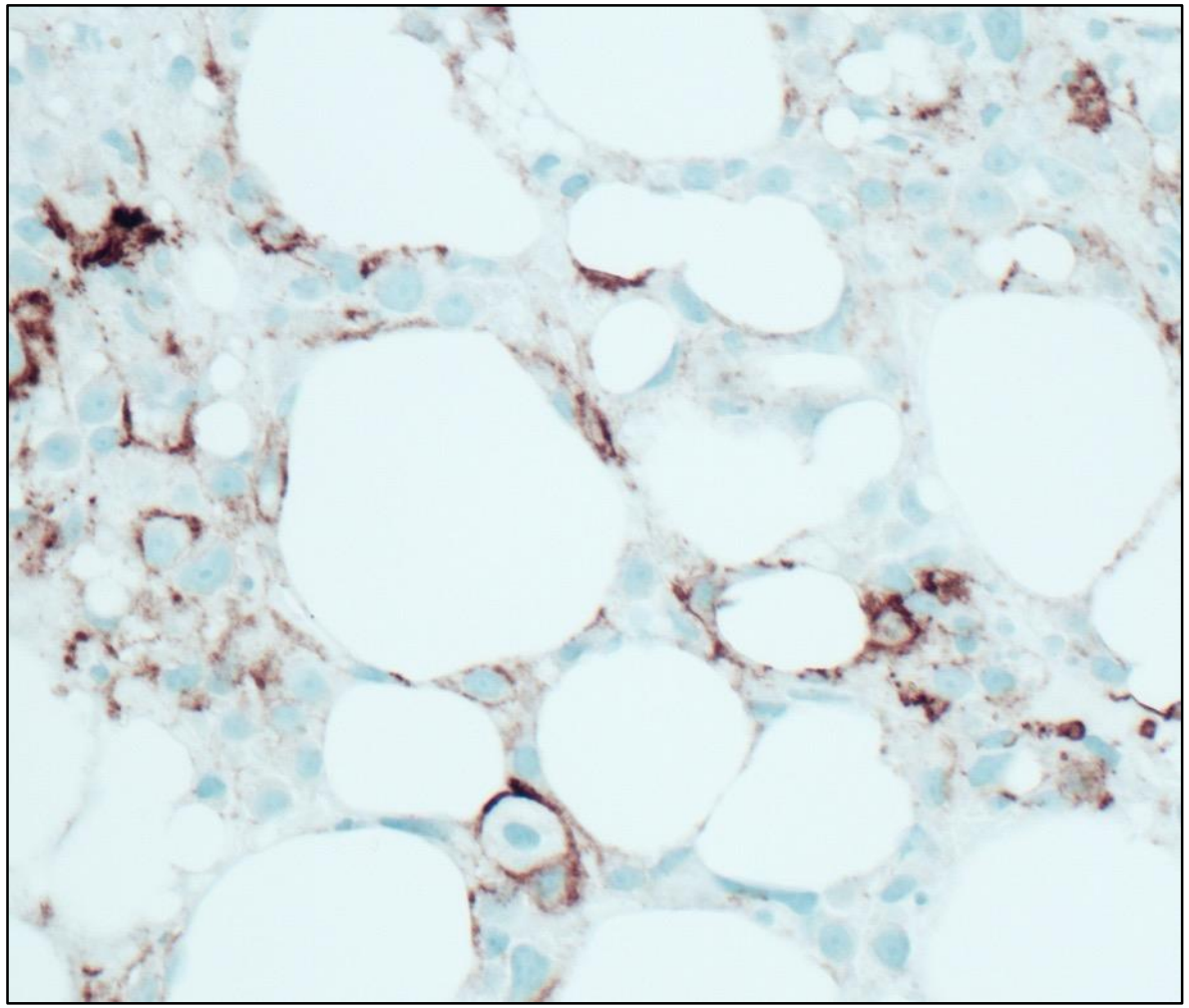


Bone marrow biopsy - immunophenotype

CD138 200X

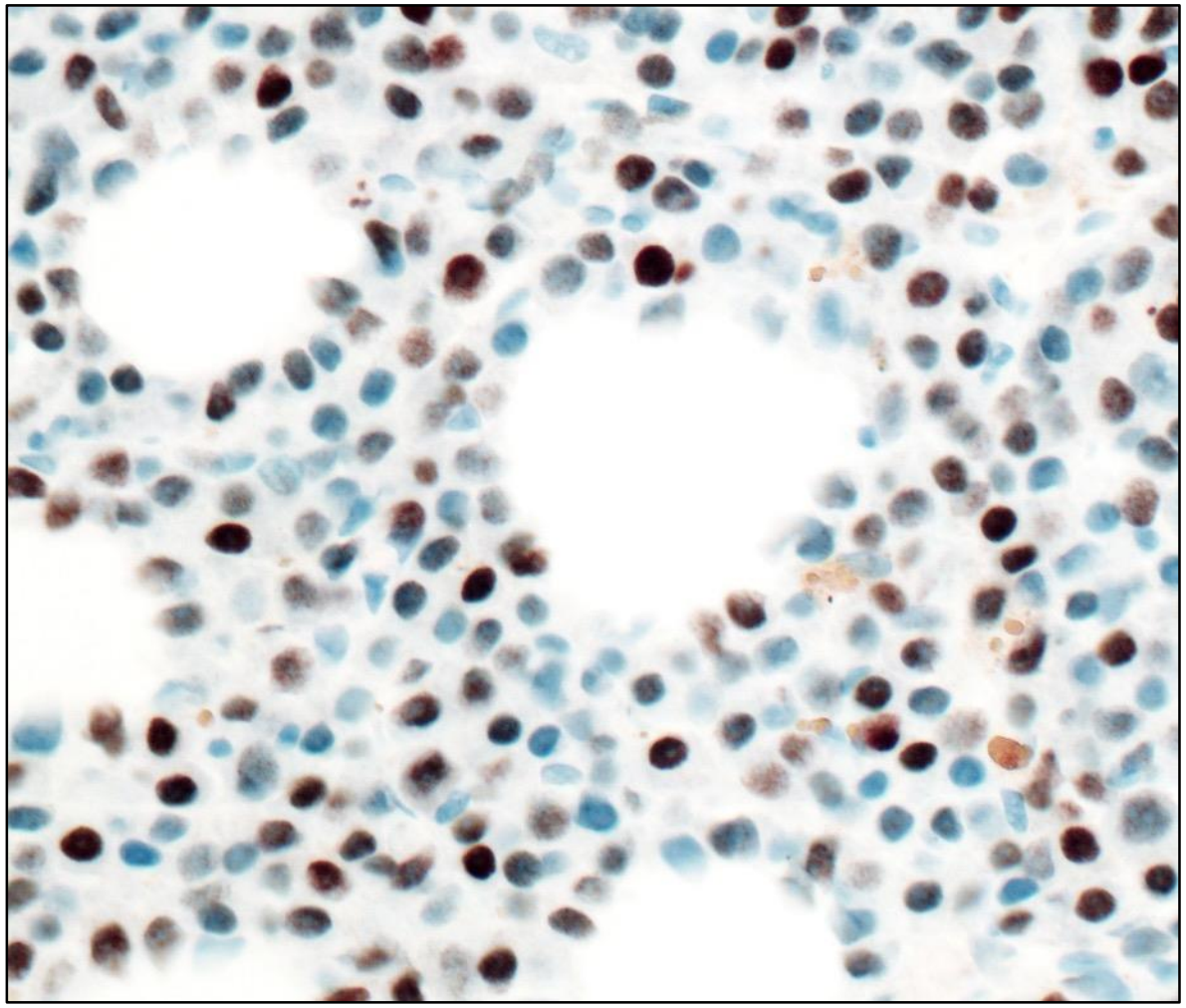


CD138 400X

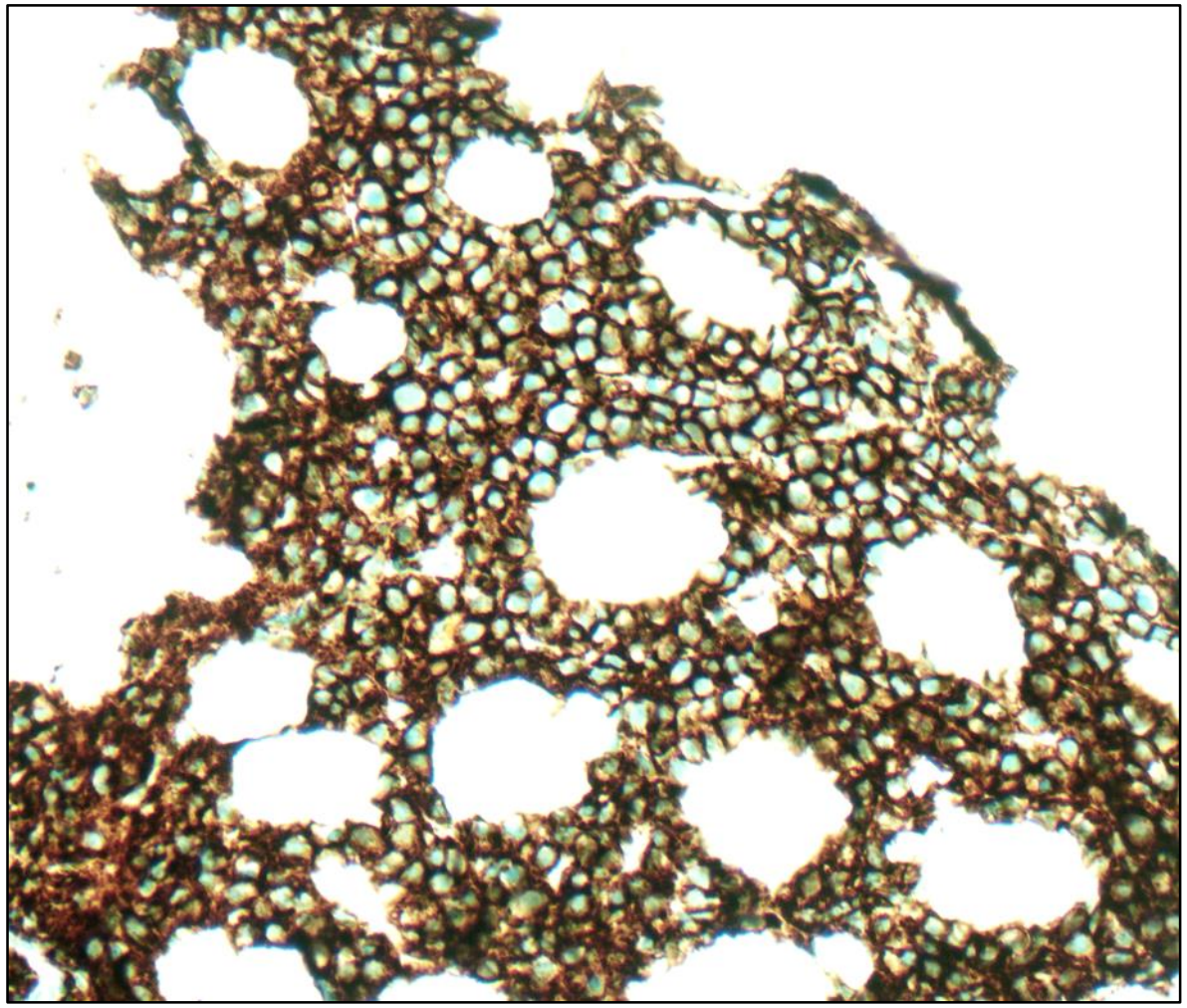


Bone marrow biopsy - immunophenotype

MUM1/IRF4 400X

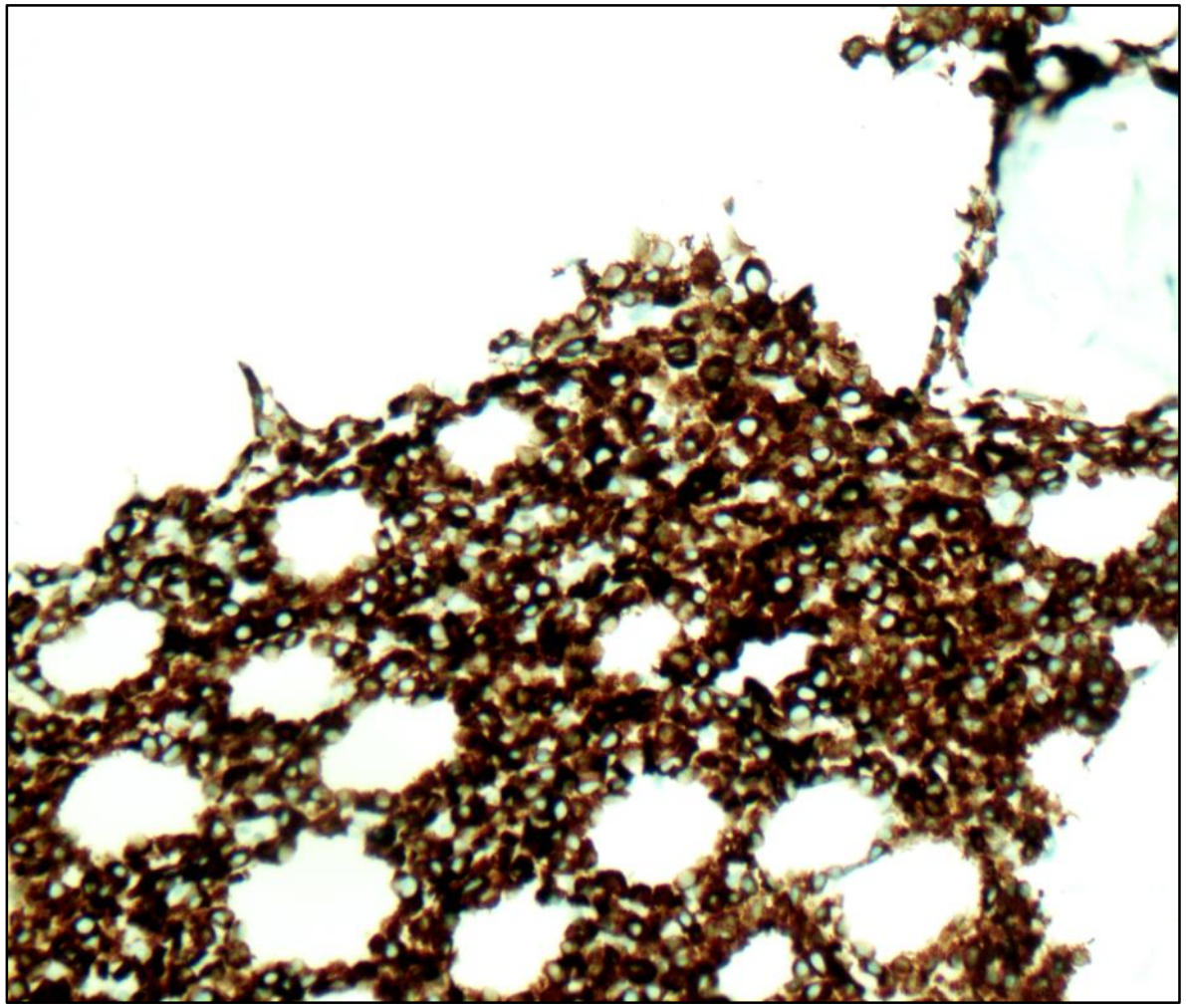


CD20 200X

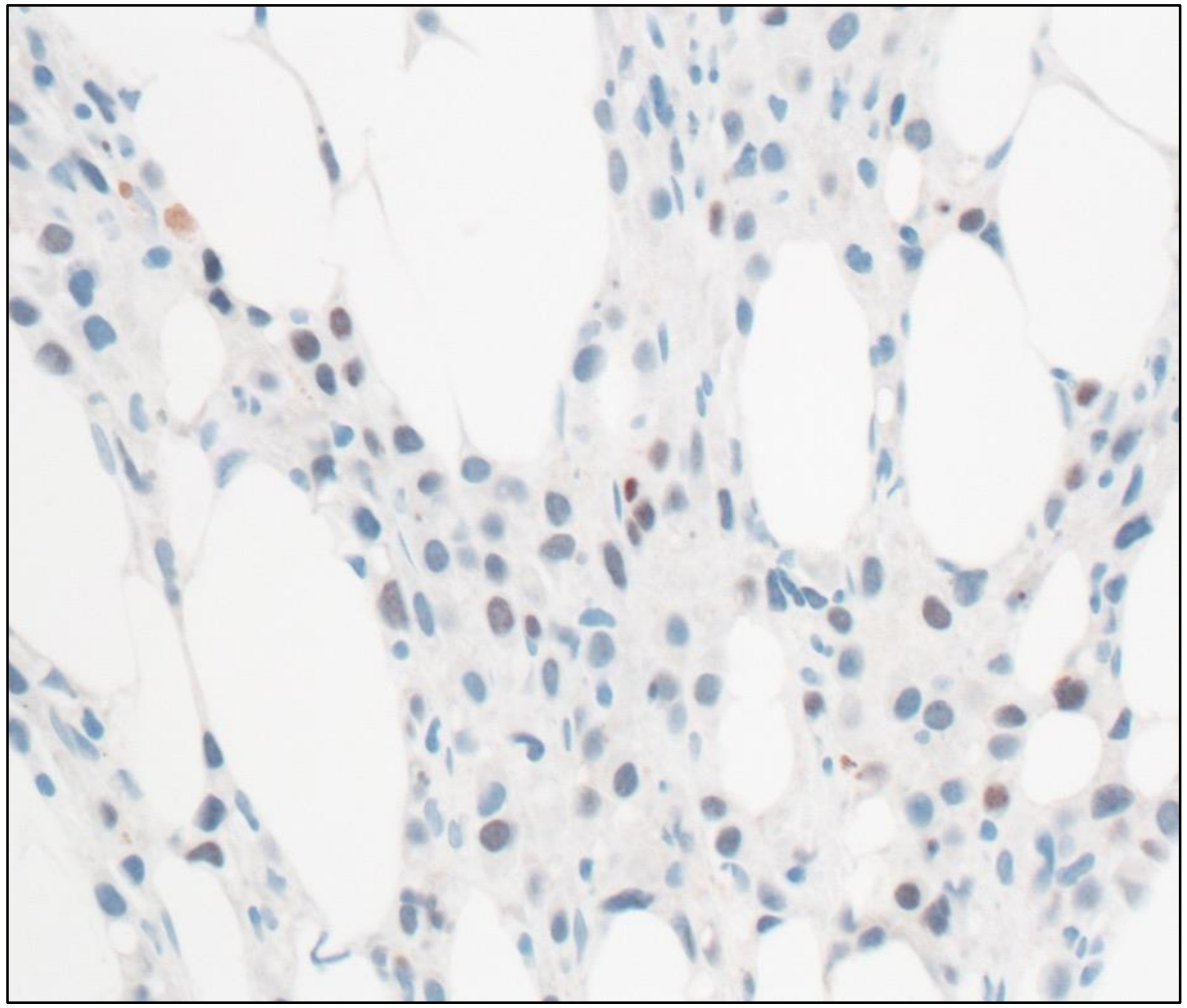


Bone marrow biopsy - immunophenotype

CD79a 200X

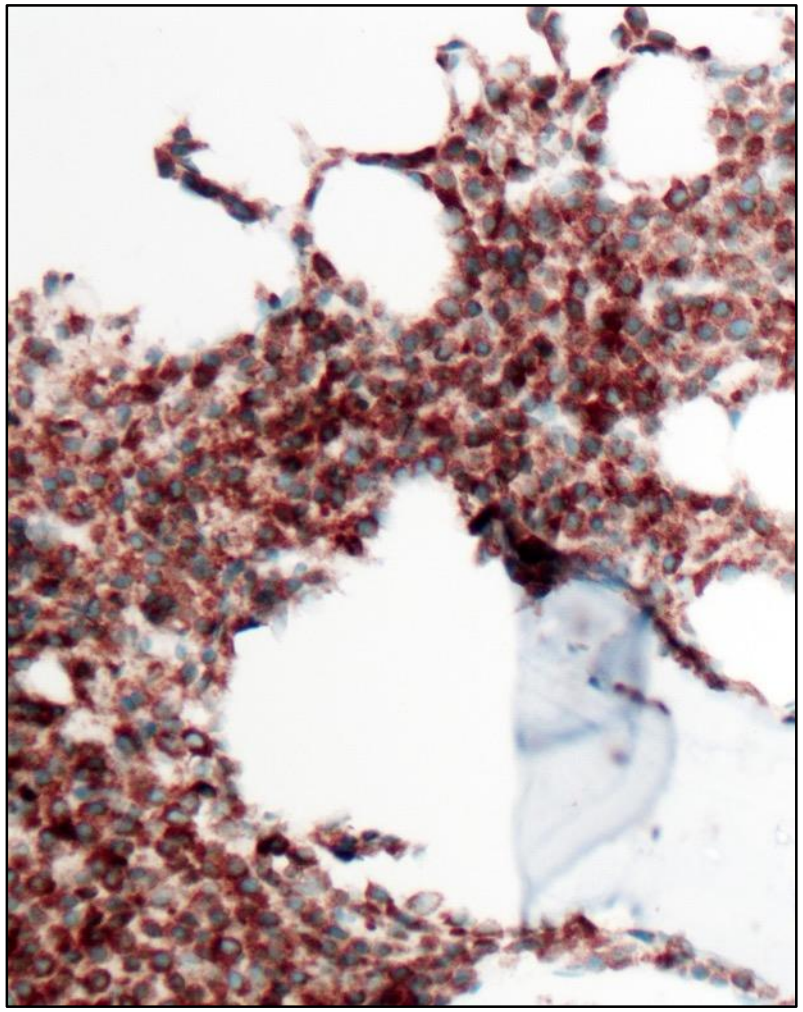


PAX5 400X

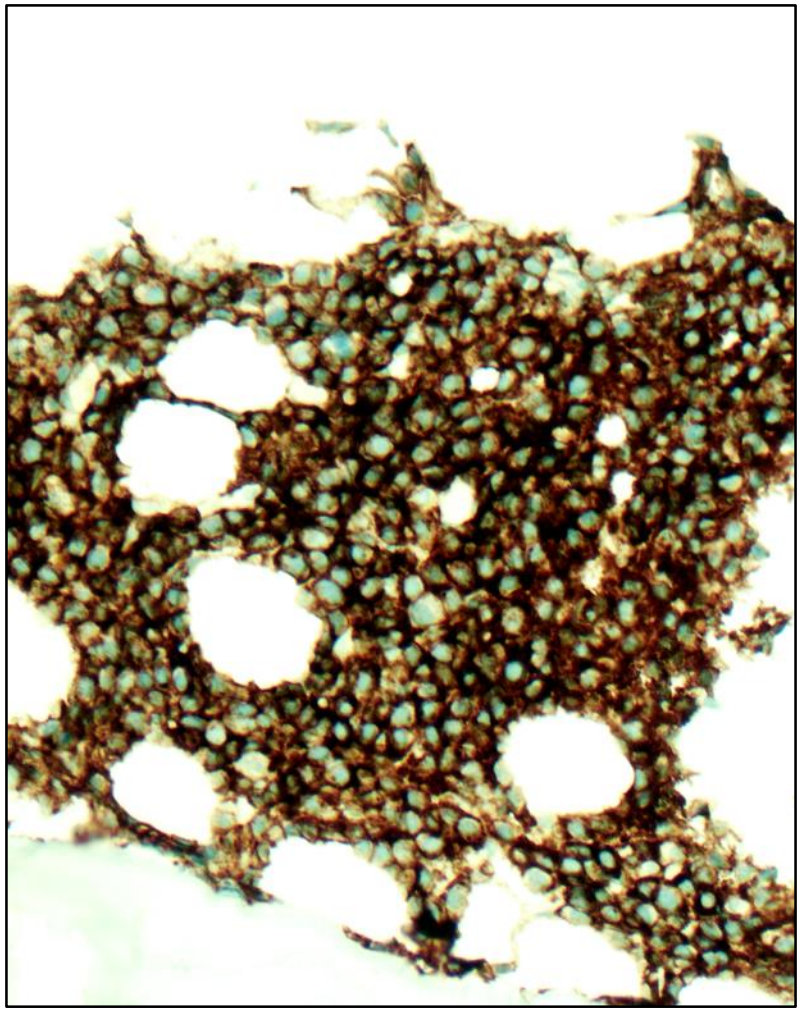


Bone marrow biopsy - immunophenotype

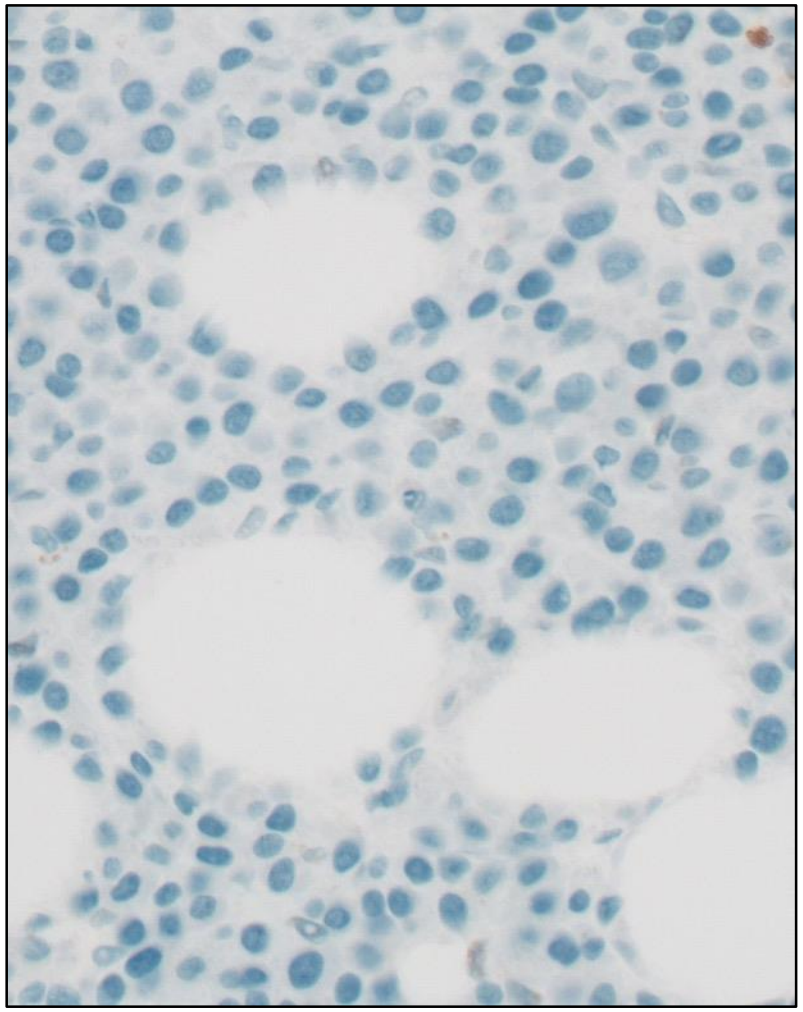
BCL2 200X



CD10 200X

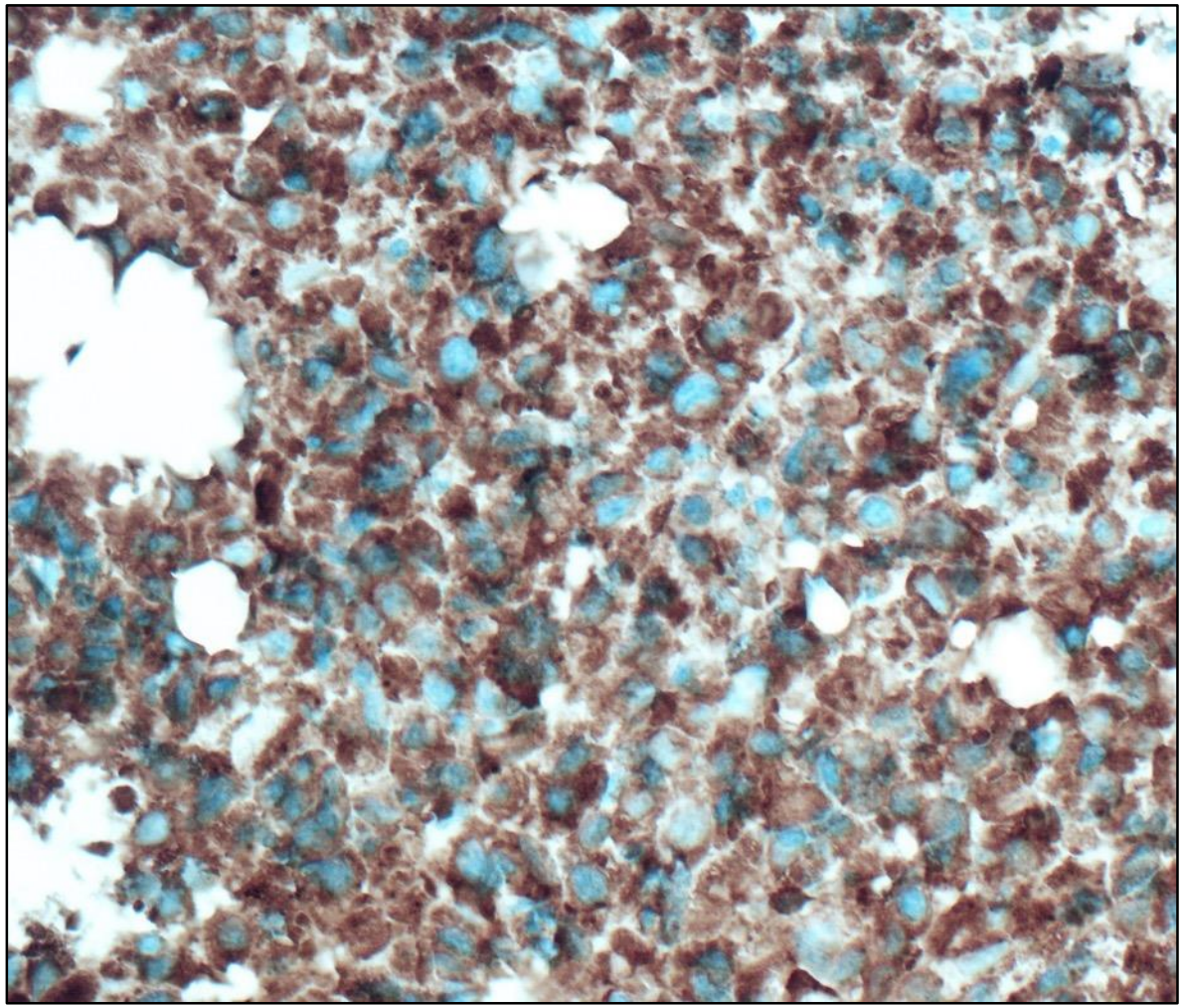


BCL6 400X

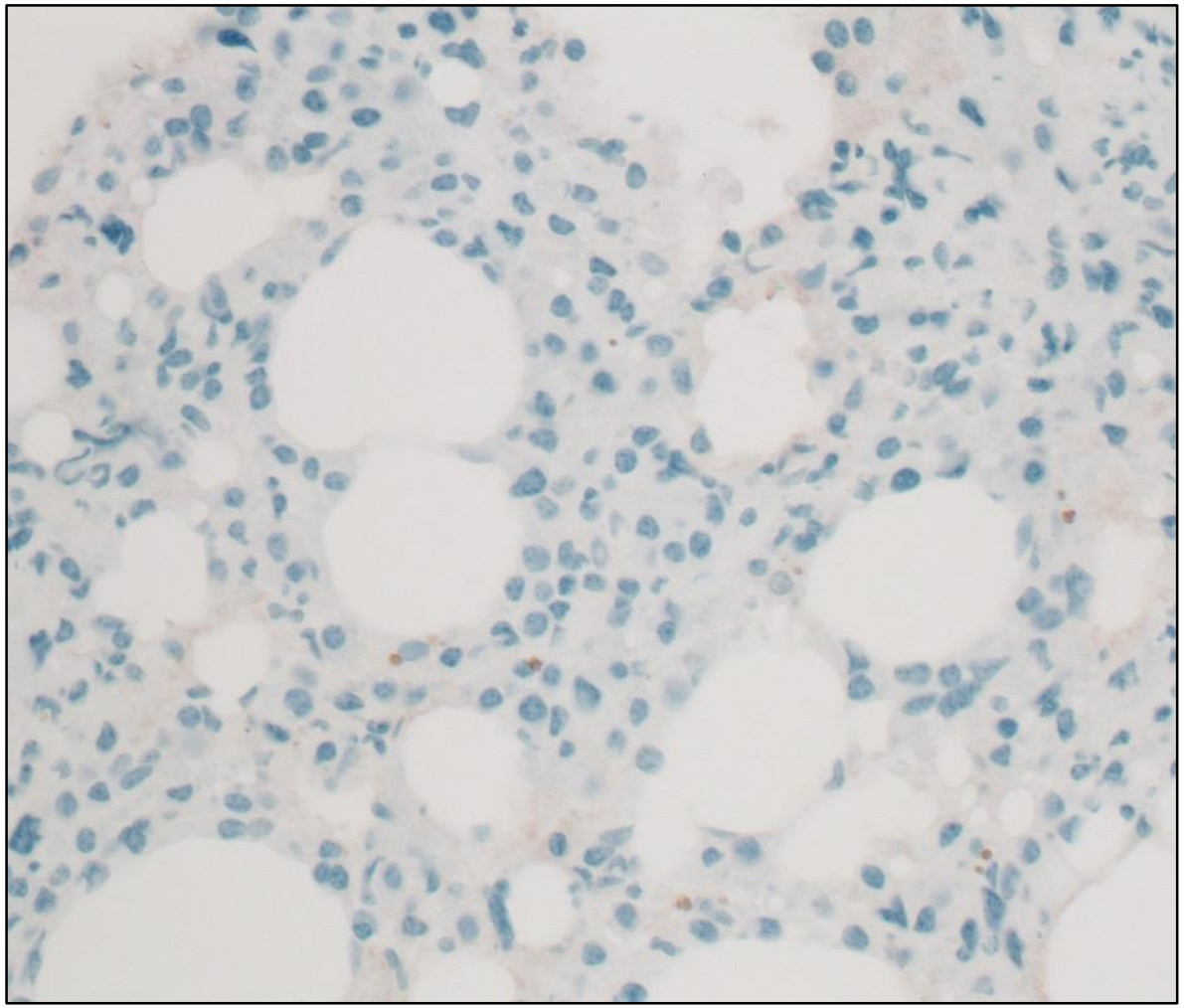


Bone marrow biopsy - immunophenotype

Kappa 400X

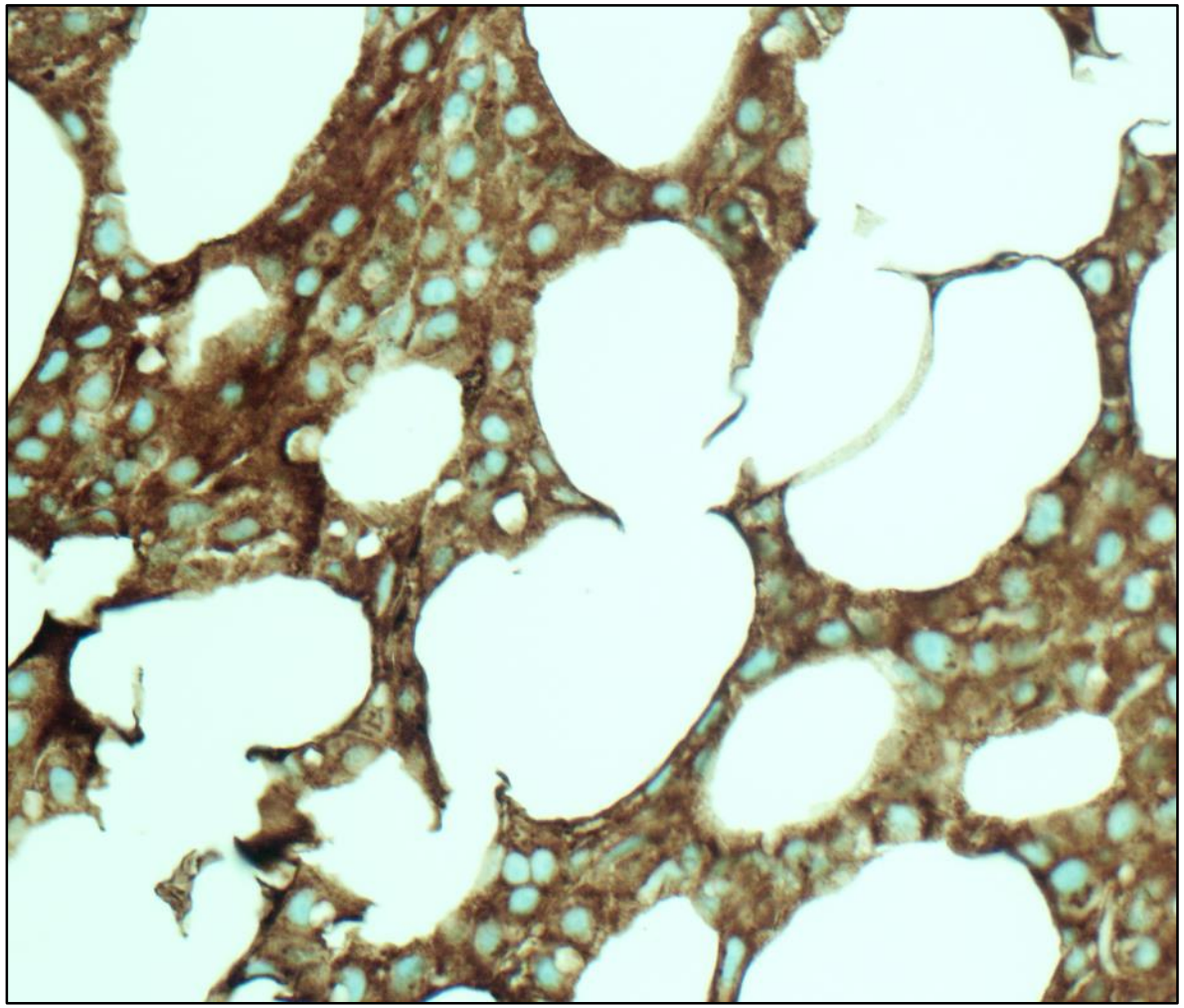


Lambda 400X

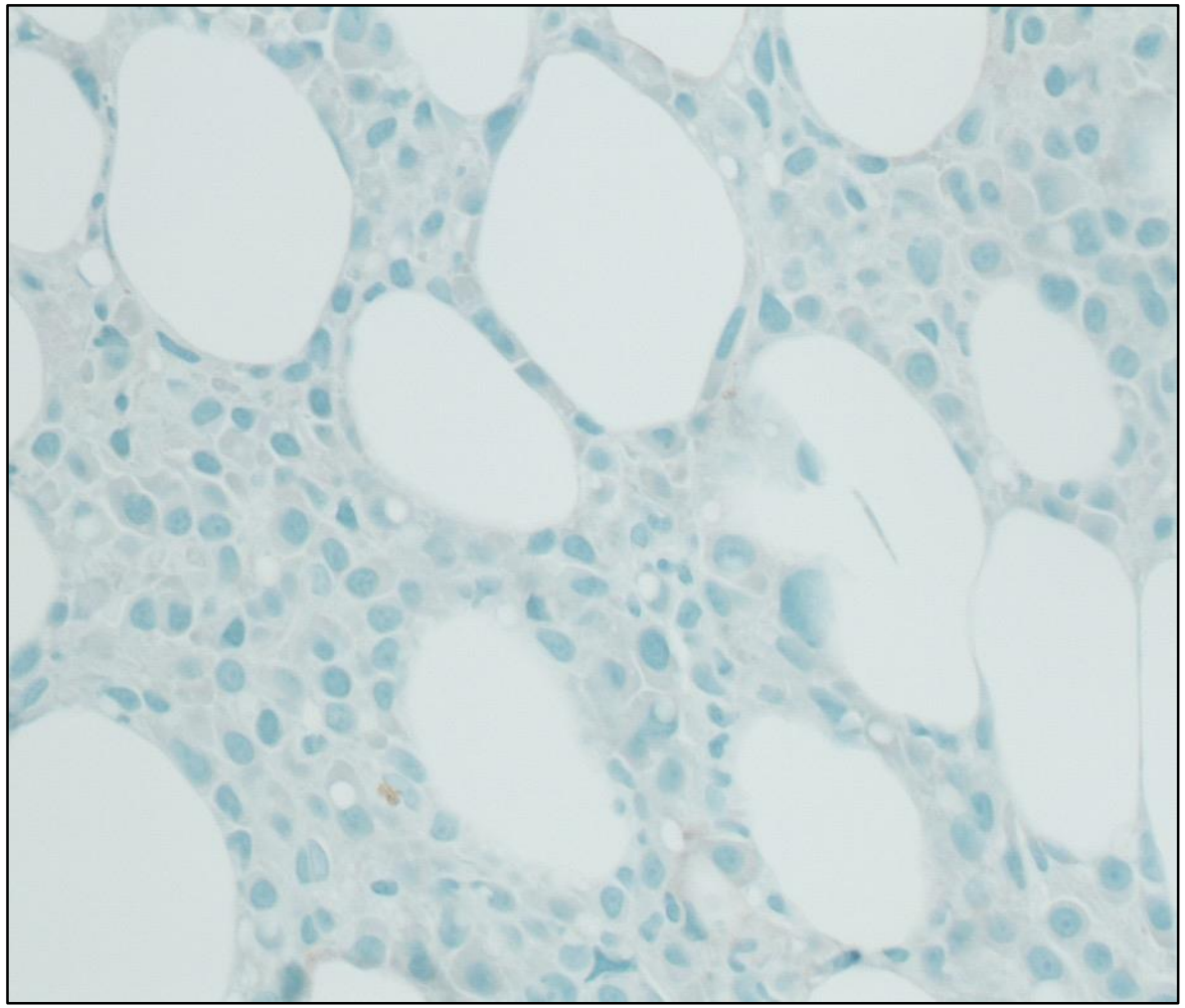


Bone marrow biopsy - immunophenotype

IgG 400X



IgM 400X



Summary of findings

Morphology

Specimen	Results
Bone marrow aspirate	Plasmacytoid cells with cytoplasmic vacuolation and blebbing; occasional flame-cell-like change
Bone marrow biopsy	Interstitial infiltrate by small to medium plasmacytoid cells (~70-80% of total cellularity)

Immunophenotype (bone marrow biopsy)

Category	Results
Plasma cell	CD138 mostly −, MUM1 variable
Clonality	Kappa restricted (Lambda –)
Pan-B-cell	CD20+, CD79a+, PAX5−

Category	Results
GC markers	CD10+, BCL6−
Isotype	IgG+, IgM−
Other	BCL2+

Differential diagnosis

Entity	Supportive findings	Discordant findings
Lymphoplasmacytic lymphoma	Plasmacytoid morphology CD20+, CD79a+	IgM–, PAX5– Cytoplasmic light chain restriction
Follicular lymphoma	CD10+, BCL2+	Interstitial infiltrate PAX5–, BCL6– Cytoplasmic light chain restriction
Plasma cell neoplasm (recurrence)	Plasmacytoid morphology Cytoplasmic light chain restriction IgG+	CD20+, CD10+

Additional findings

- **Flow cytometry**:
  - Subset of plasma cells with dim CD138, CD38 expression appears to show kappa restriction
  - No immunophenotypic evidence of non-Hodgkin B-cell lymphoproliferative disorders
- **Molecular testing**:
  - Negative for *MYD88* L265P

Additional findings (cont'd)

- **FISH**:
  - TP53 negative
  - t(11;14) negative
  - t(14;16) negative
  - t(4;14) negative

Diagnosis

- Plasma cell neoplasm with aberrant CD20 and CD10 expression

Myeloma with aberrant CD20 expression

- **Frequency**: ~9% by flow[1], ~8-18%[2,3] by IHC
- **Morphology**: enriched in small mature plasma cells[3]; overall heterogeneous[2]
- **Immunophenotype**:
  - CD19–, CD22–, CD10–, sIg–; retains plasma cell markers (CD38++, CD138+)[1]
  - PAX5: usually negative; minority aberrantly positive[2,4]
- **Genetics:** associated with t(11;14)[3,5]
- **Prognosis**: appears favourable with t(11;14)[5]; no consistent effect otherwise
- **Therapy**: rituximab responses generally limited[6]

1. Lin P et al. Am J Clin Pathol 2004
2. Grigoriadis N et al. Pathology 2012
3. Robillard N et al. Blood 2003
4. Lin P et al. Mod Pathol 2004
5. Jian Y et al. Front Oncol 2022
6. Kapoor P et al. Br J Haematol 2008

Myeloma with aberrant CD10 expression

- Normal plasma cells are CD10 negative (GC marker, shut off with plasma cell differentiation)
- **Frequency**: rare[1]
- **Morphology**: associated with plasmablastic/immature plasma cells[2,3]
- **Prognosis**: early studies noted associated with aggressive behavior[2,3], but recent studies limited
- Raises the possibility of germinal-center derived lymphomas, e.g. follicular lymphoma

1. WHO5R 2022
2. Durie and Grogan Blood 1985
3. Tamura et al. Blut 1989

Expression of B-cell markers in myeloma

CD79a/b

Marker	Biology	Detection	Expression in myeloma	Diagnostic value
CD79a	Part of BCR complex; downregulated in plasma cells (PC)	IHC	Variable; positive in ~50%, weak in 15%, negative in ~35%[1]	Positivity not aberrant Loss supports PC > lymphoma
CD79b		Flow	Consistently negative	Negativity helps distinguish PC (–) from lymphoma (+)

PAX5

Biology	Expression in myeloma	Diagnostic value
B-cell lineage transcription factor; represses plasma cell differentiation	<5%, usually in CD20+ cases[2;] normally negative	Positivity in myeloma = aberrant

1. Tanaka et al. Pathol Int 2009

2. Lin P et al. Am J Clin Pathol 2004

3. Grigoriadis N et al. Pathology 2012

Summary

- Plasma cell myeloma may retain B-cell markers (CD20, CD79a) and can rarely aberrantly express PAX5, CD10
- These cases can mimic B-cell lymphomas
- Integrating clinical and laboratory findings with morphology, clonality, isotype, and molecular studies is essential