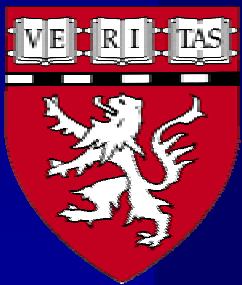


Differential Diagnosis in Bone Marrow Pathology: Reactive versus Neoplastic

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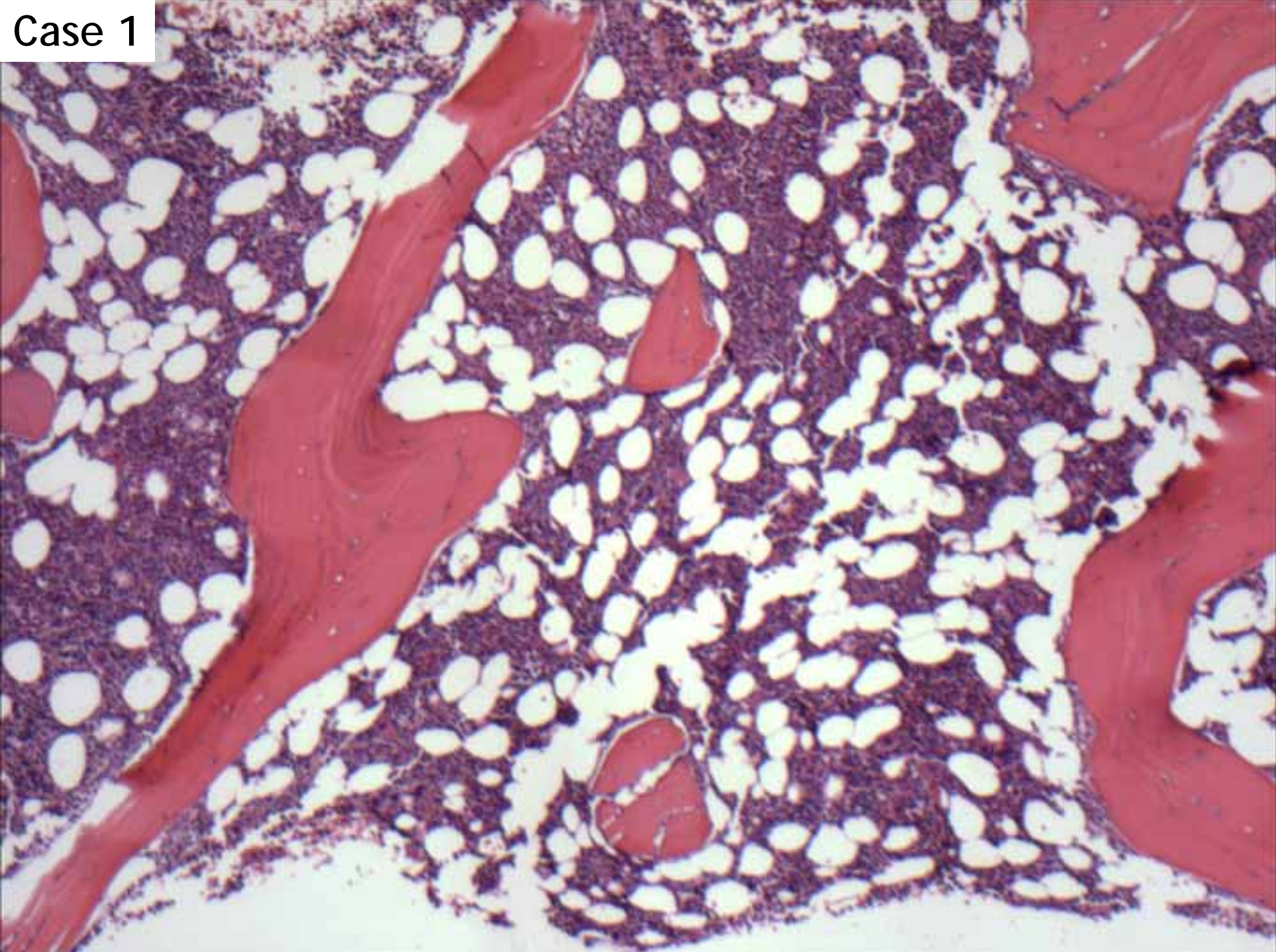


Assistant Professor
Harvard Medical School

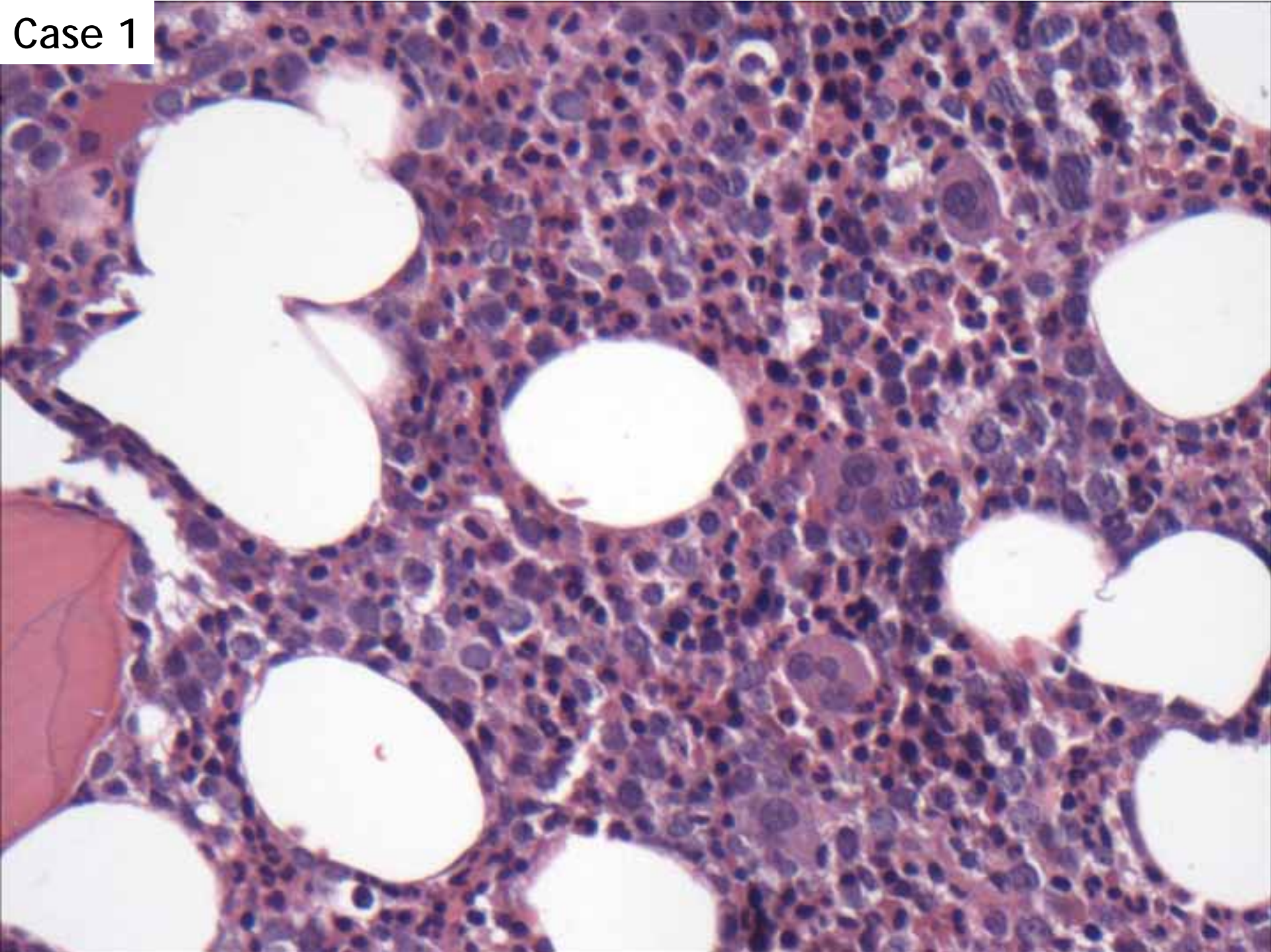
Case 1

- 39 year-old HIV+ man presents with pancytopenia
- CBC results are not available

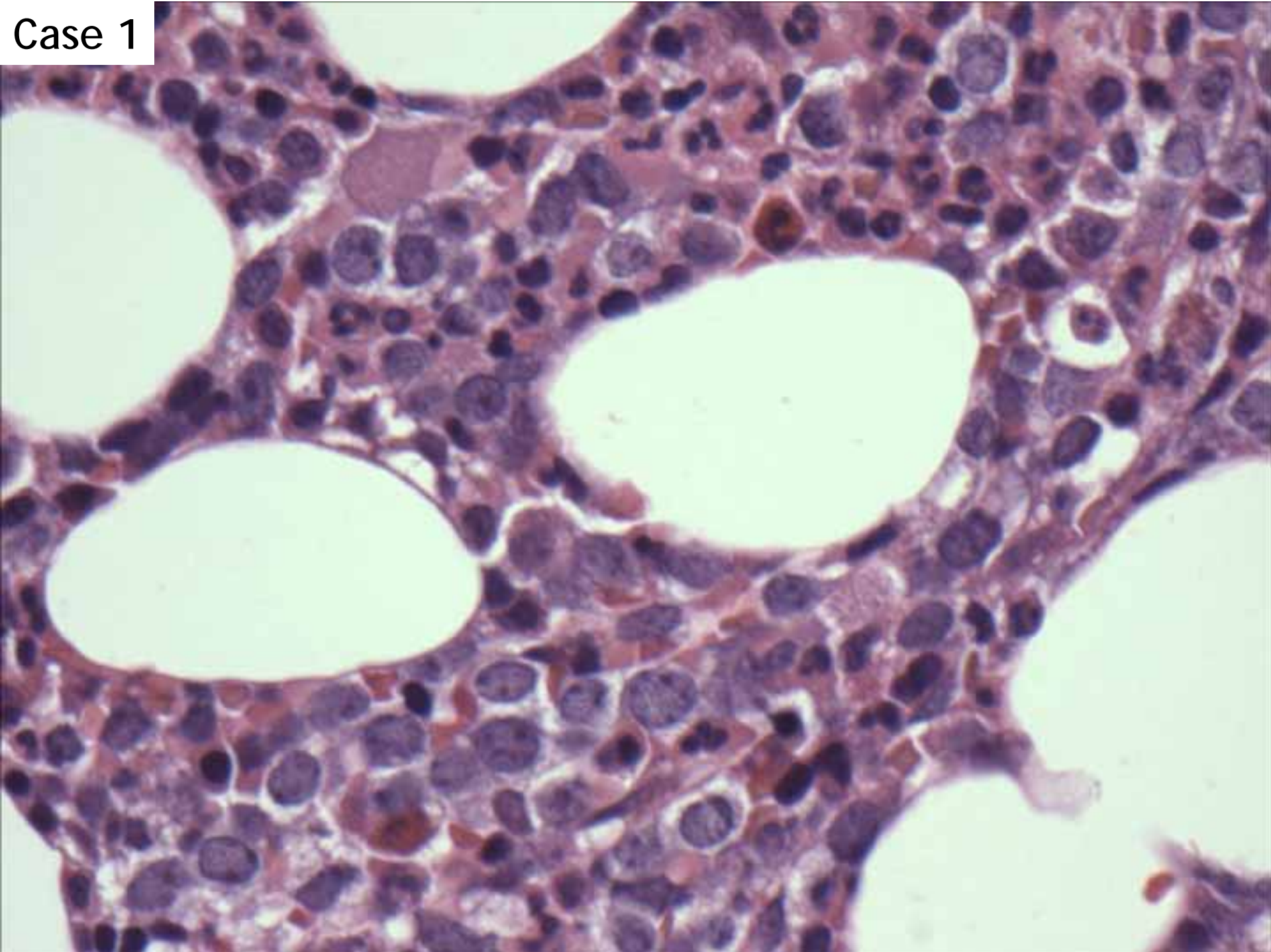
Case 1



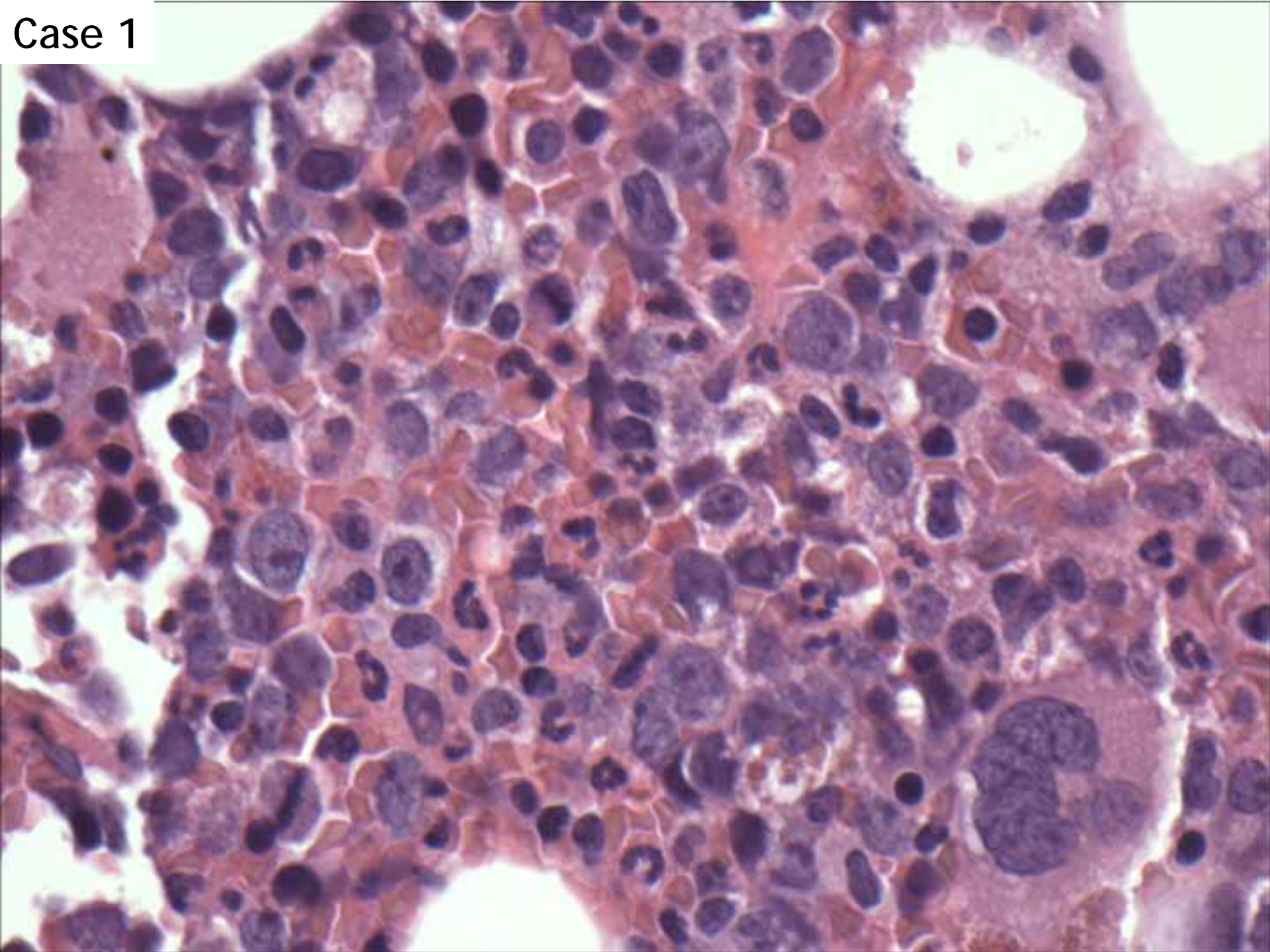
Case 1



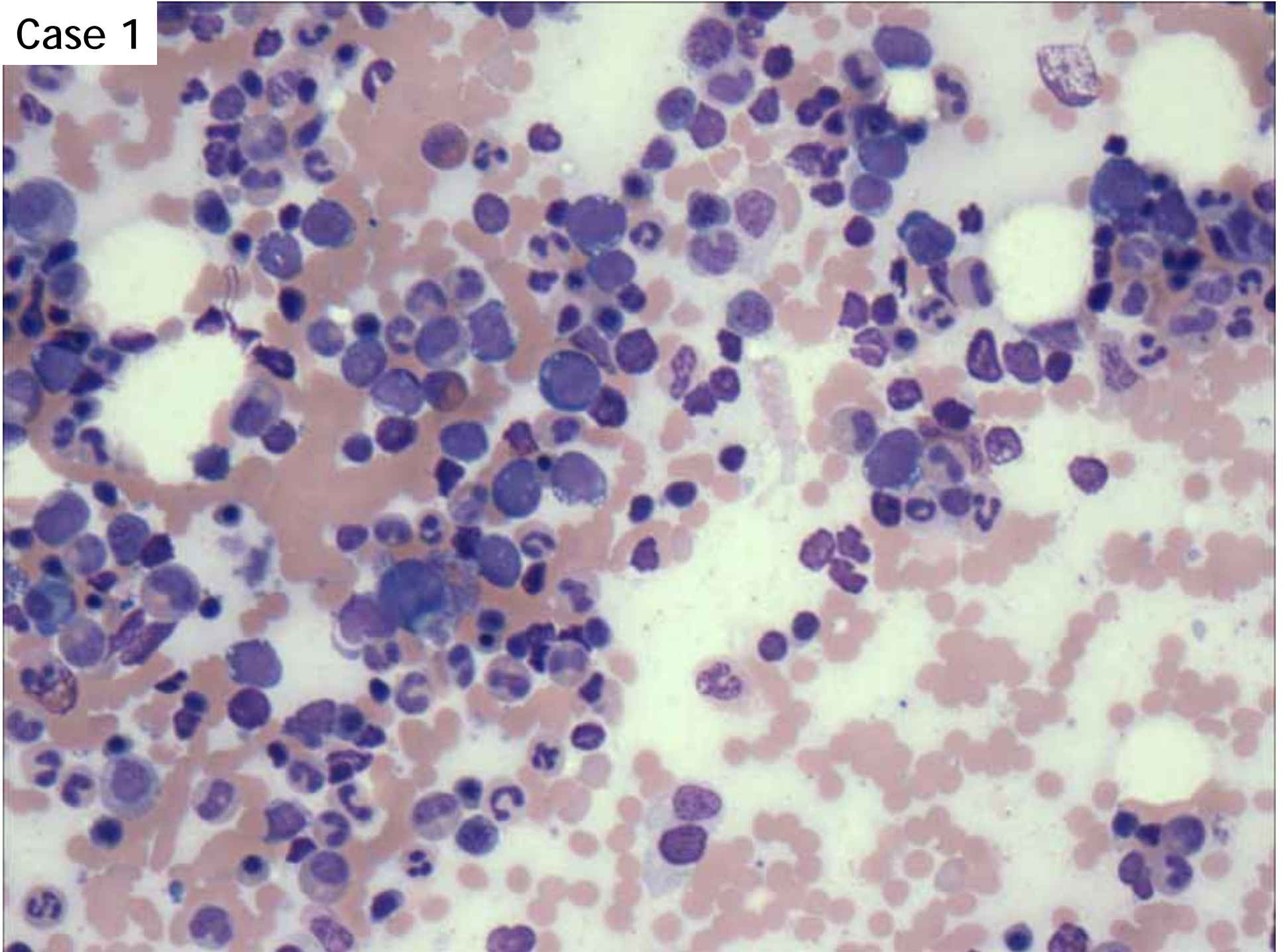
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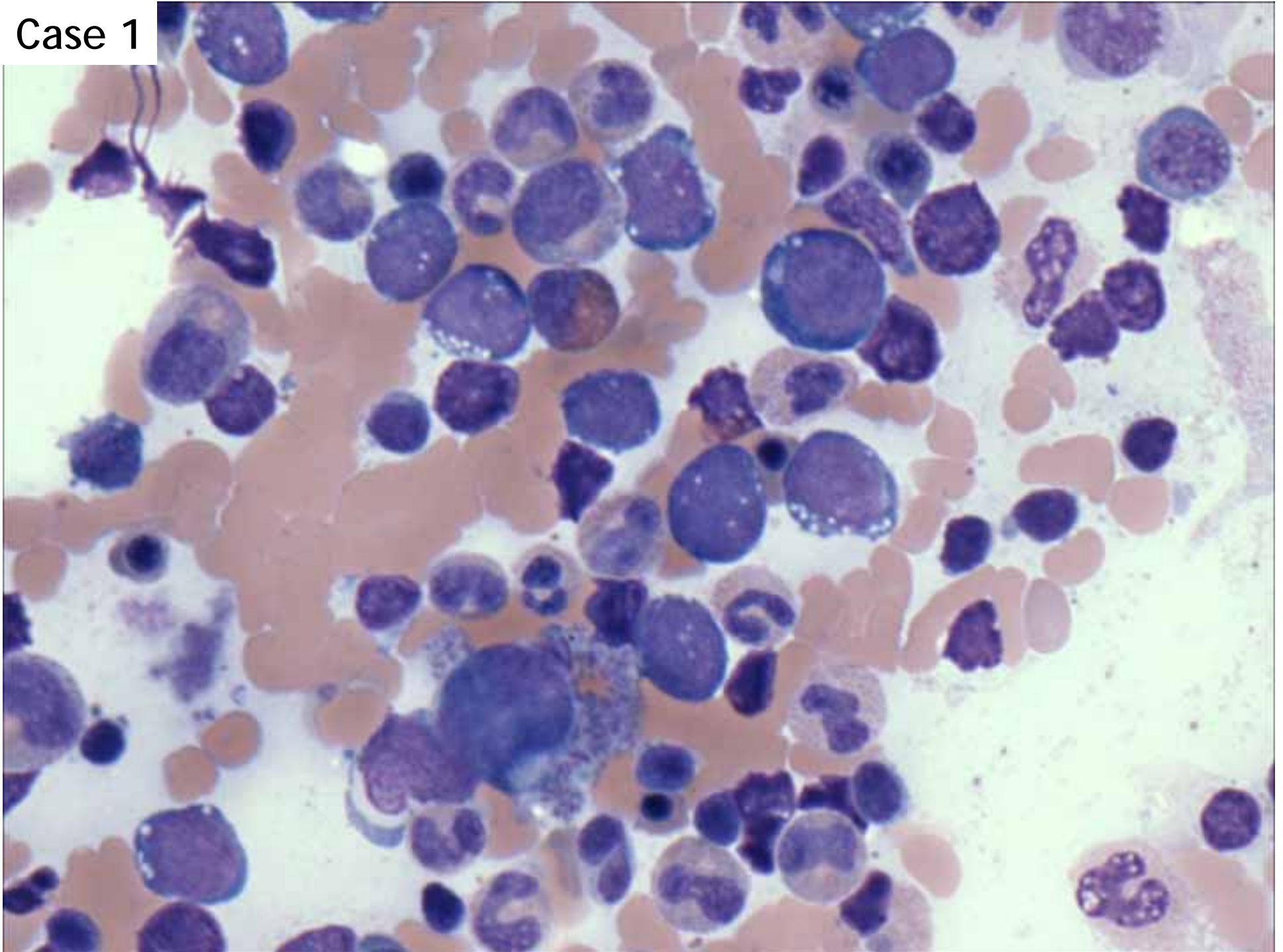
Case 1



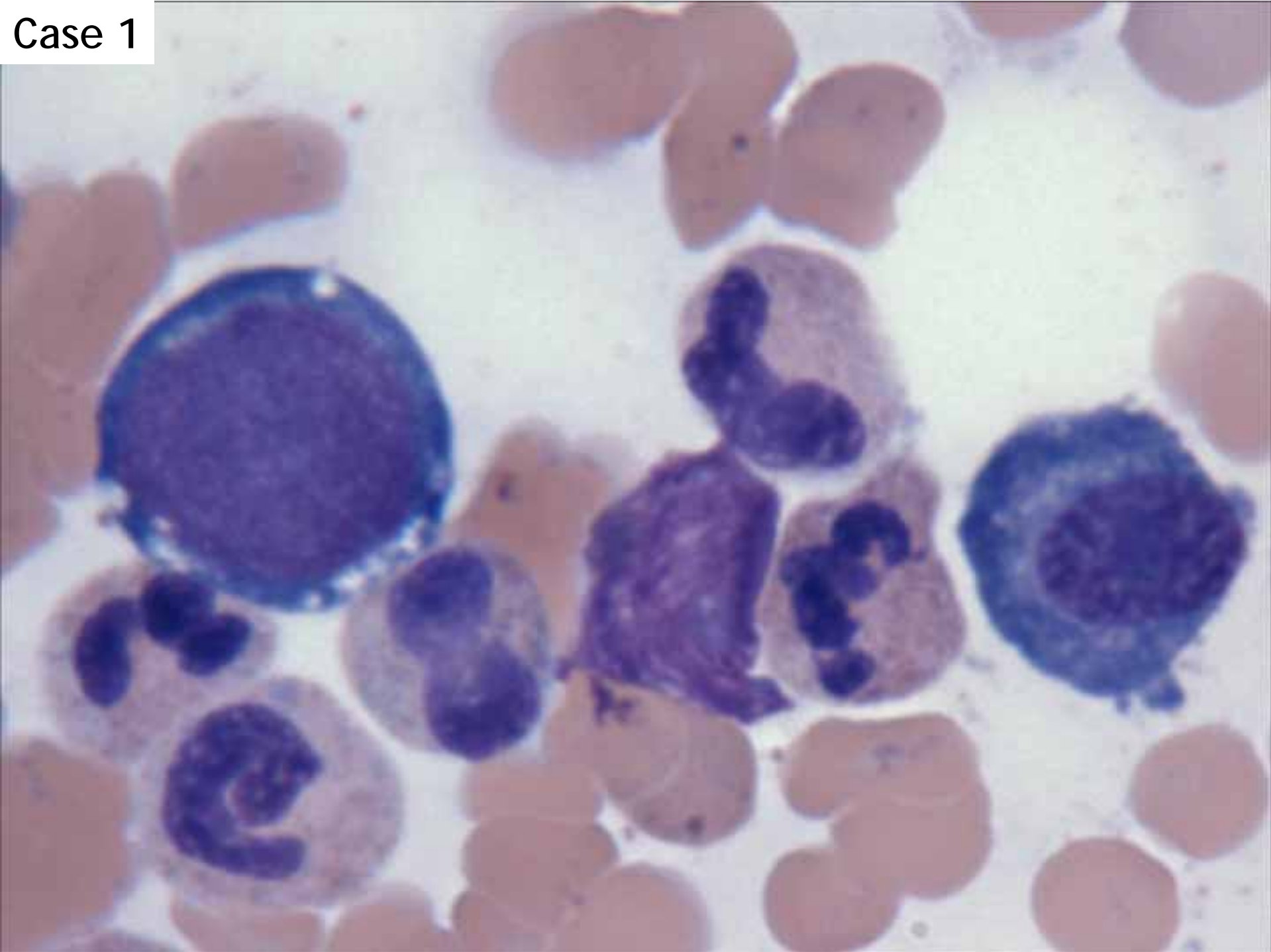
Case 1



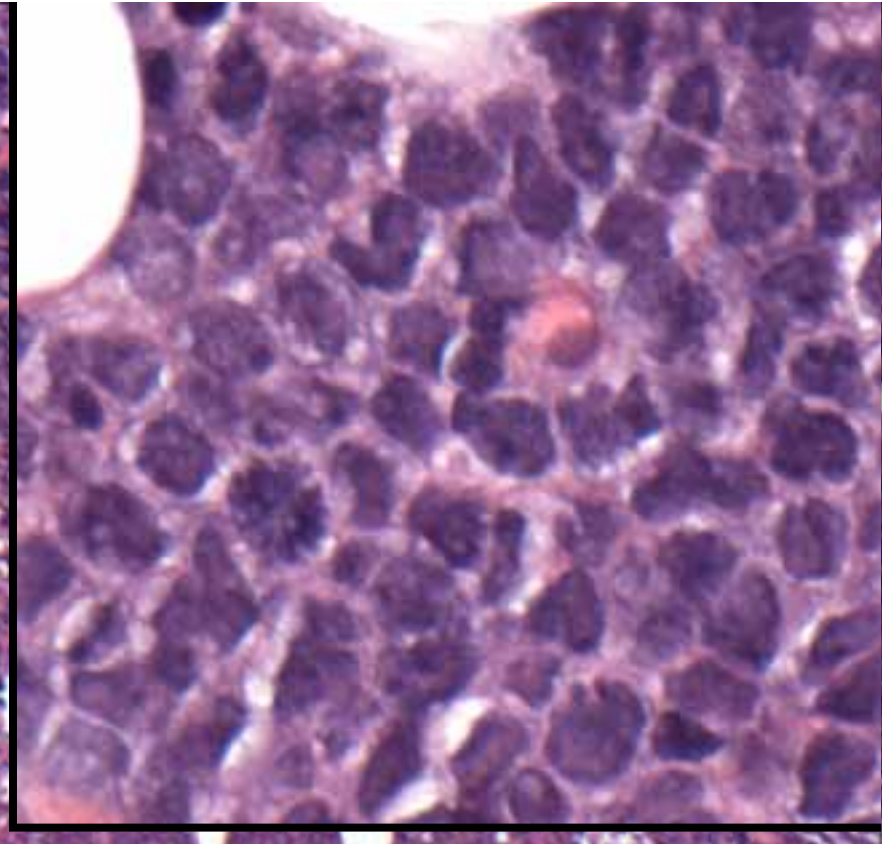
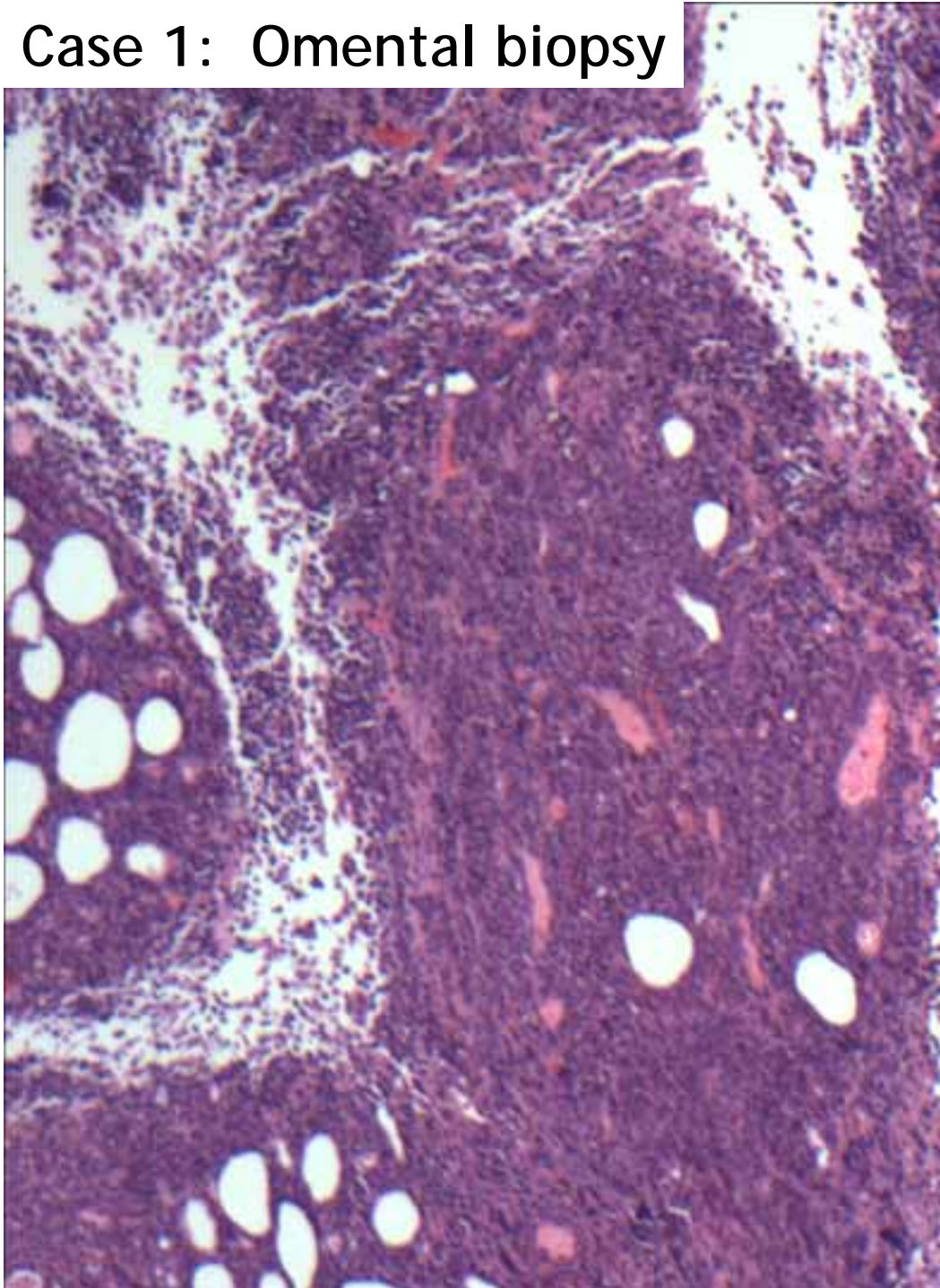
Case 1



Case 1



Case 1: Omental biopsy



**Immunohistochemistry of
omental lymphoma:**

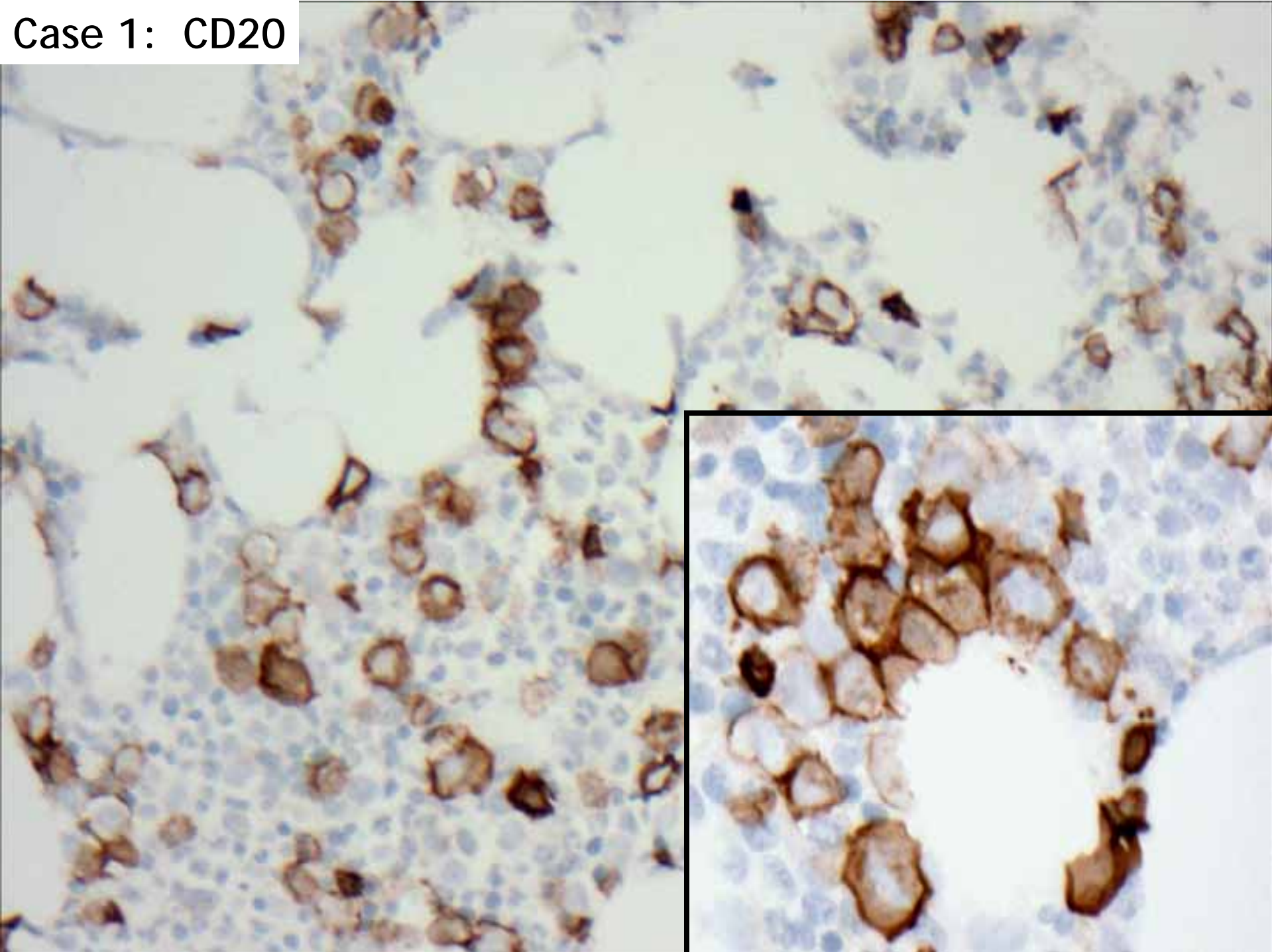
CD20 positive

BCL6 positive

BCL2 negative

Ki67 proliferation fraction 98%

Case 1: CD20



Patterns of high grade lymphoma in marrow

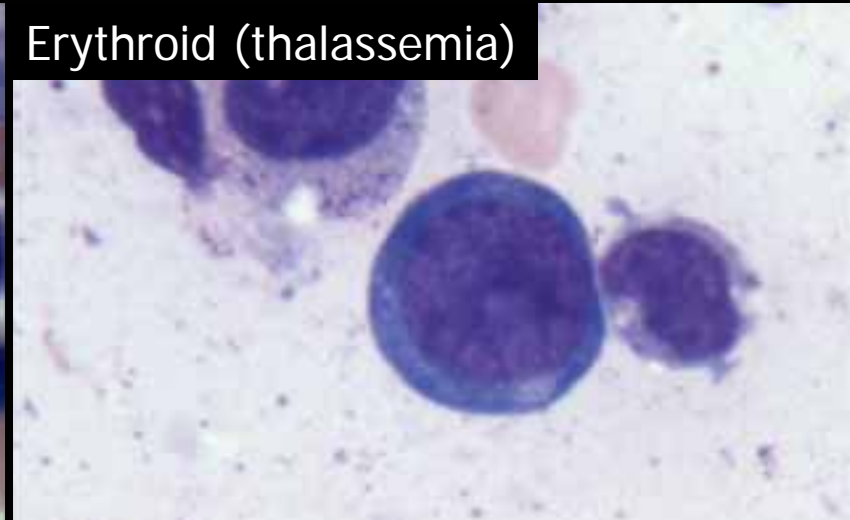
- Nodular aggregates of small lymphocytes
 - 'Discordant' marrow involvement may reflect an underlying systemic low grade lymphoma
- Large lymphoid cells in sheets or as an interstitial infiltrate
 - May be minimal and subtle
 - Cytomorphology resembles erythroblasts
- High grade lymphomas may present in the bone marrow of immunosuppressed patients

Differential diagnosis of large basophilic cells in marrow

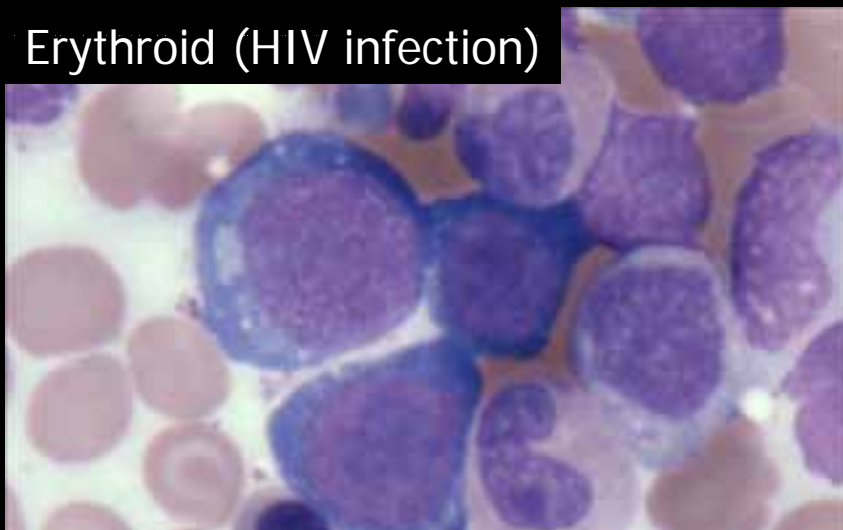
Erythroid (alcohol toxicity)



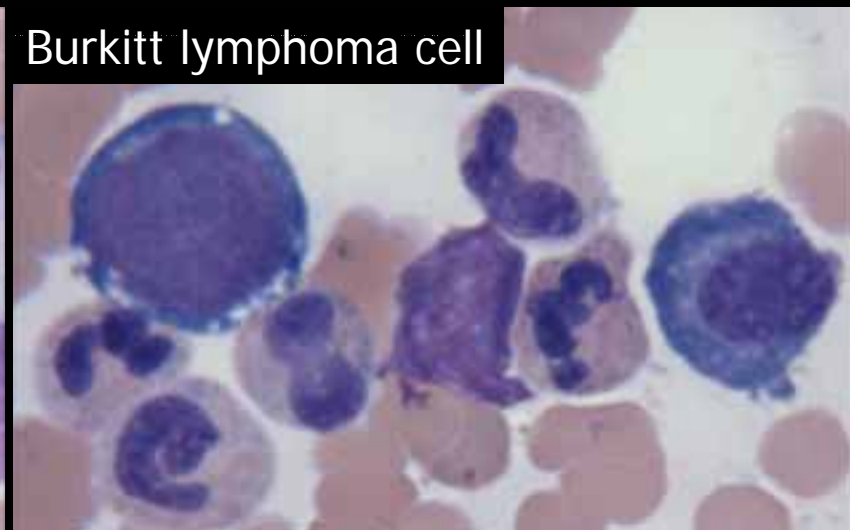
Erythroid (thalassemia)



Erythroid (HIV infection)



Burkitt lymphoma cell



Case 1 Diagnosis:

Burkitt lymphoma (atypical variant)
involving bone marrow

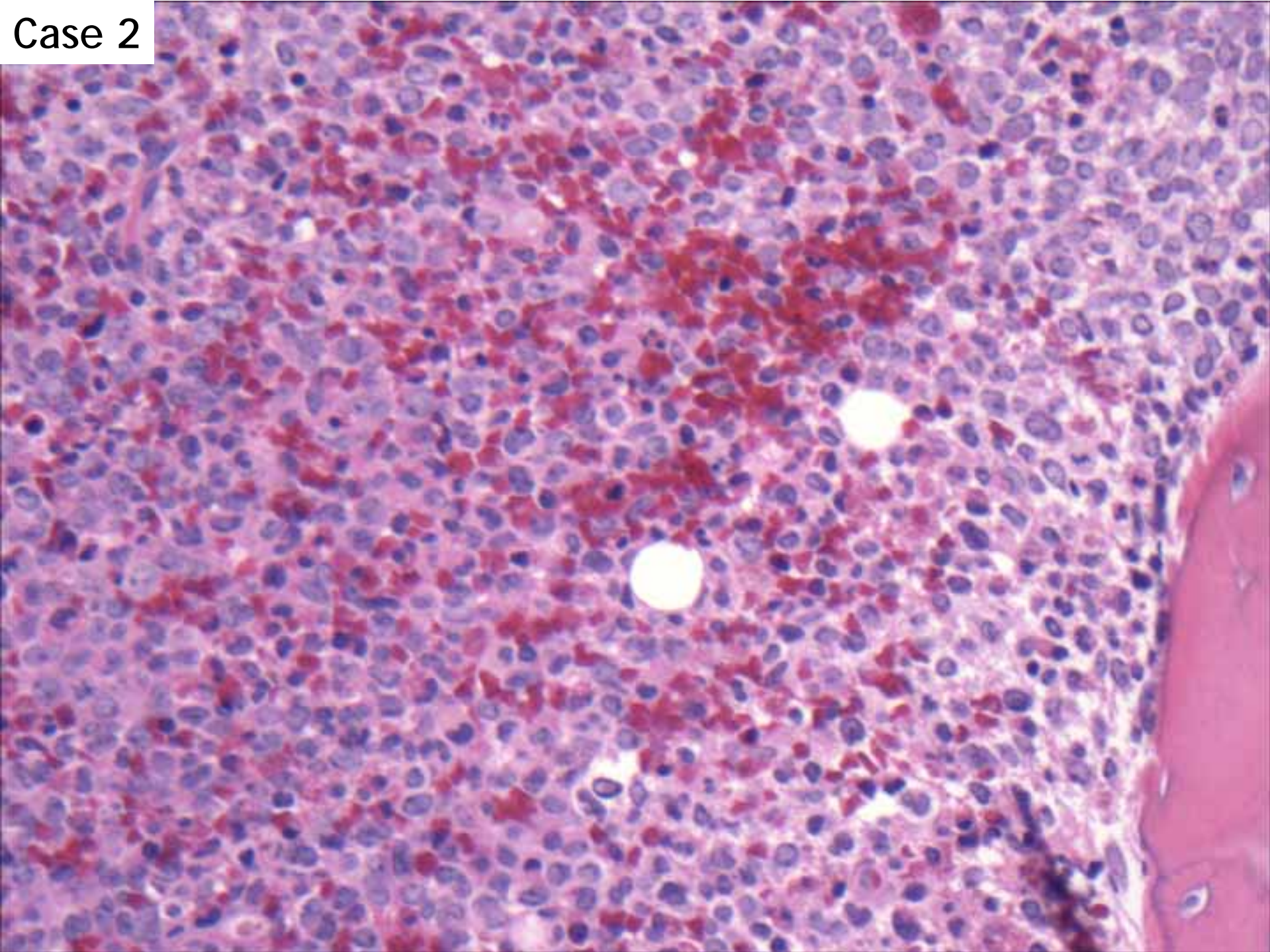
Teaching point:

High-grade lymphomas may involve marrow as interstitial large cells resembling early erythroids

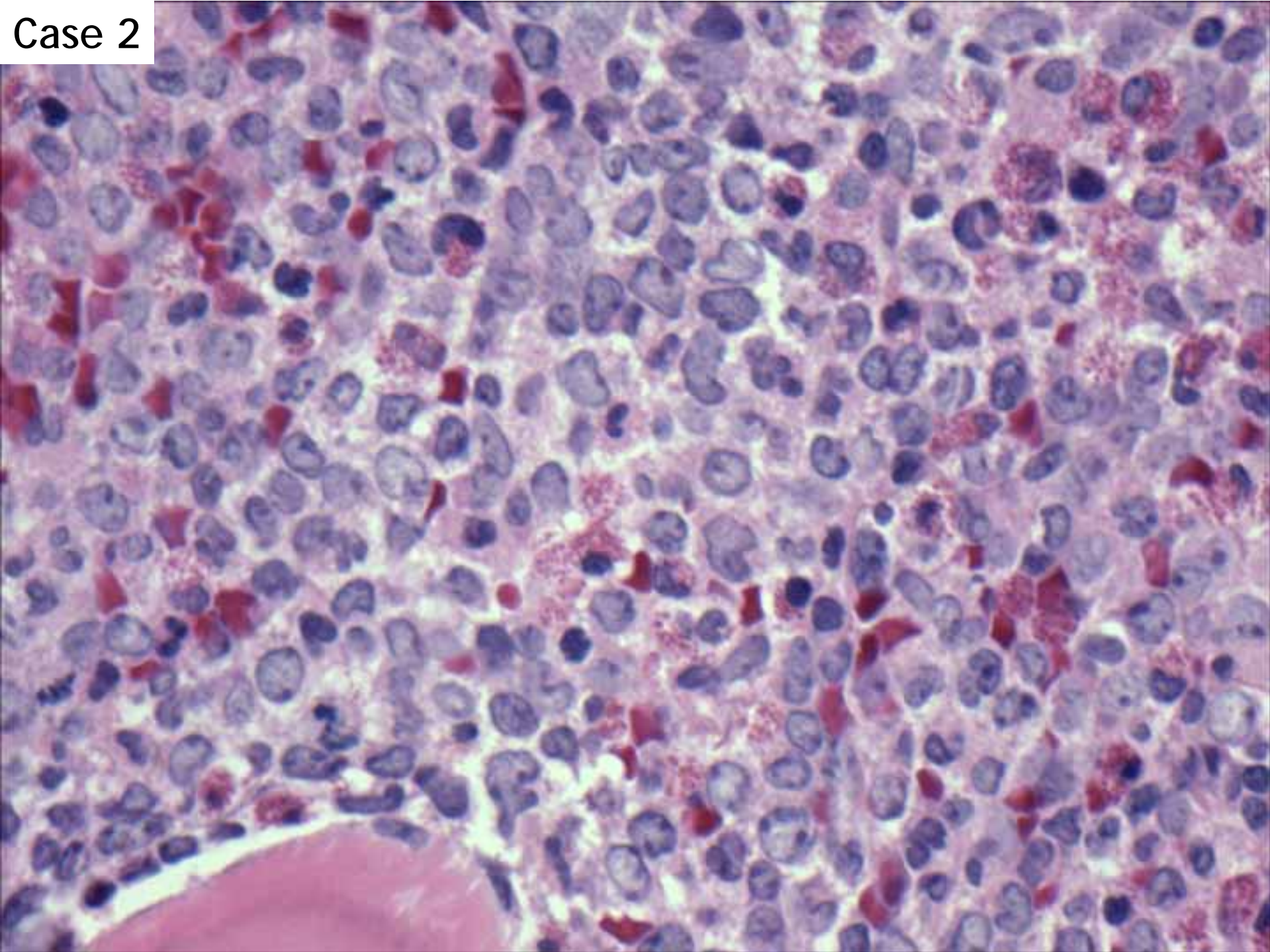
Case 2

- 40 year-old woman with progressive leukopenia and thrombocytopenia.
- CBC results
 - WBC=3.2 x 10⁹/L
 - 38% neutrophils, 12% monocytes, 41% lymphocytes, 1% eosinophils, 1% basophils, 7% blasts
 - HCT=32.0%
 - PLT= 57 x 10⁹/L

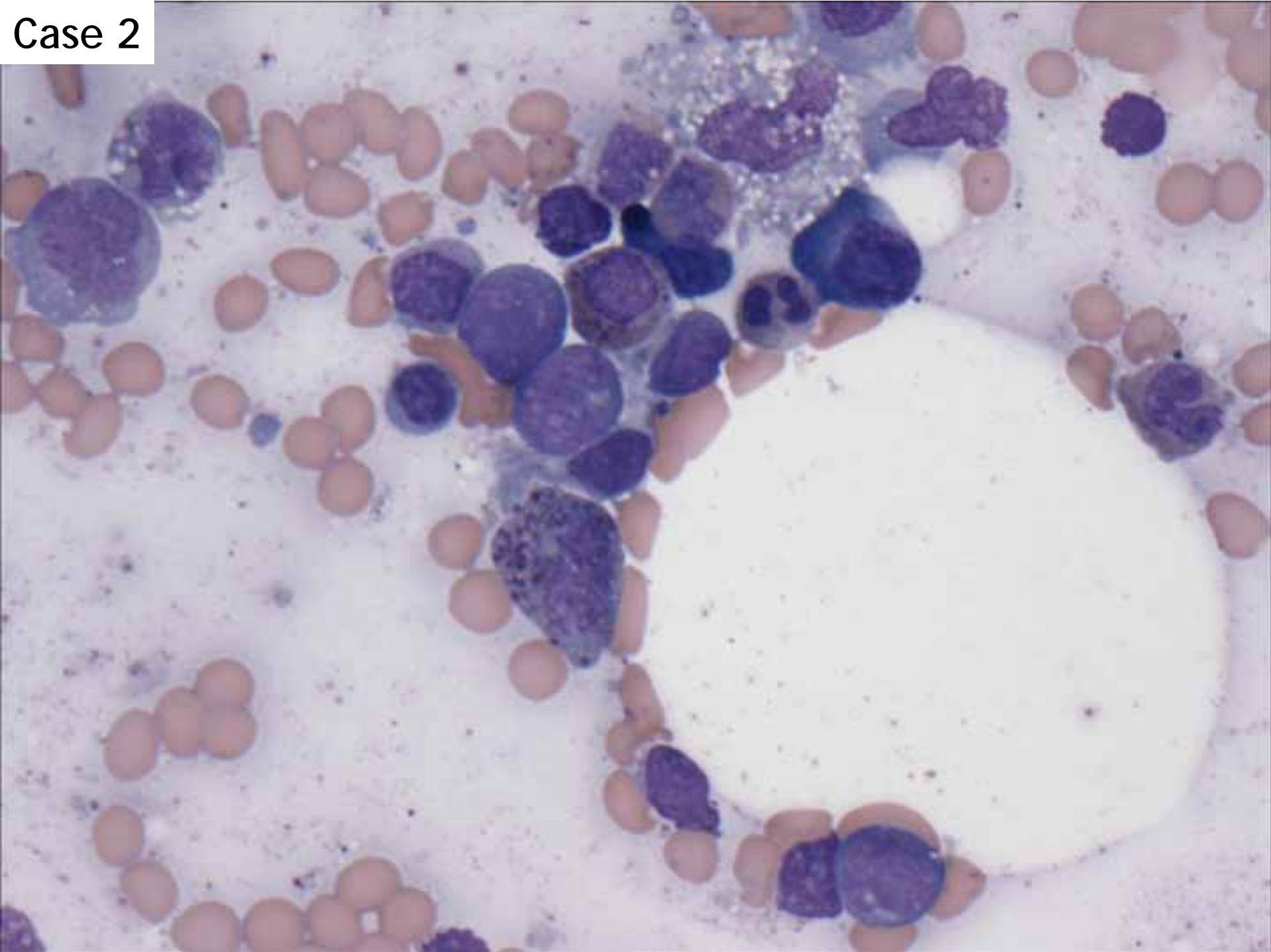
Case 2



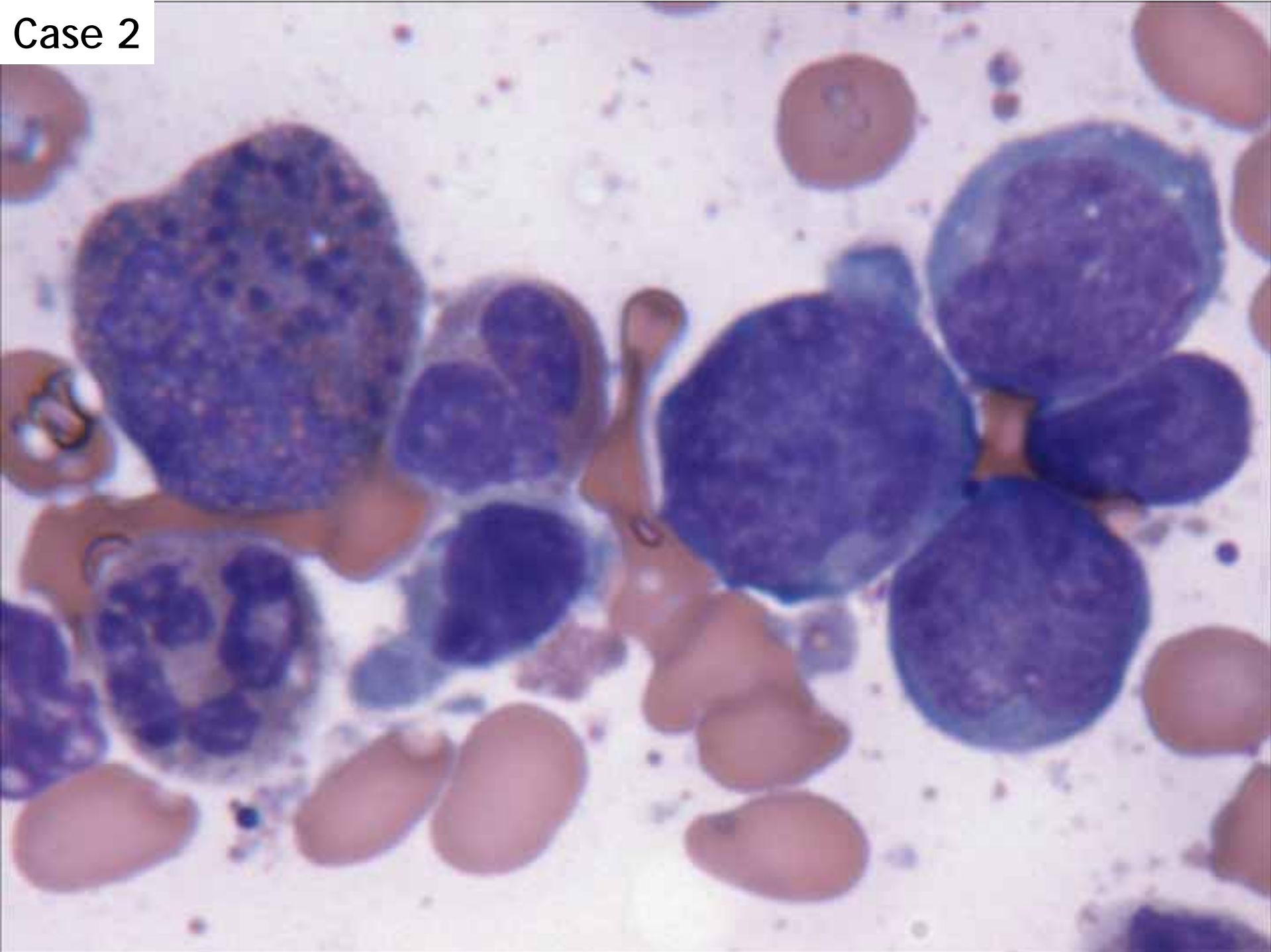
Case 2

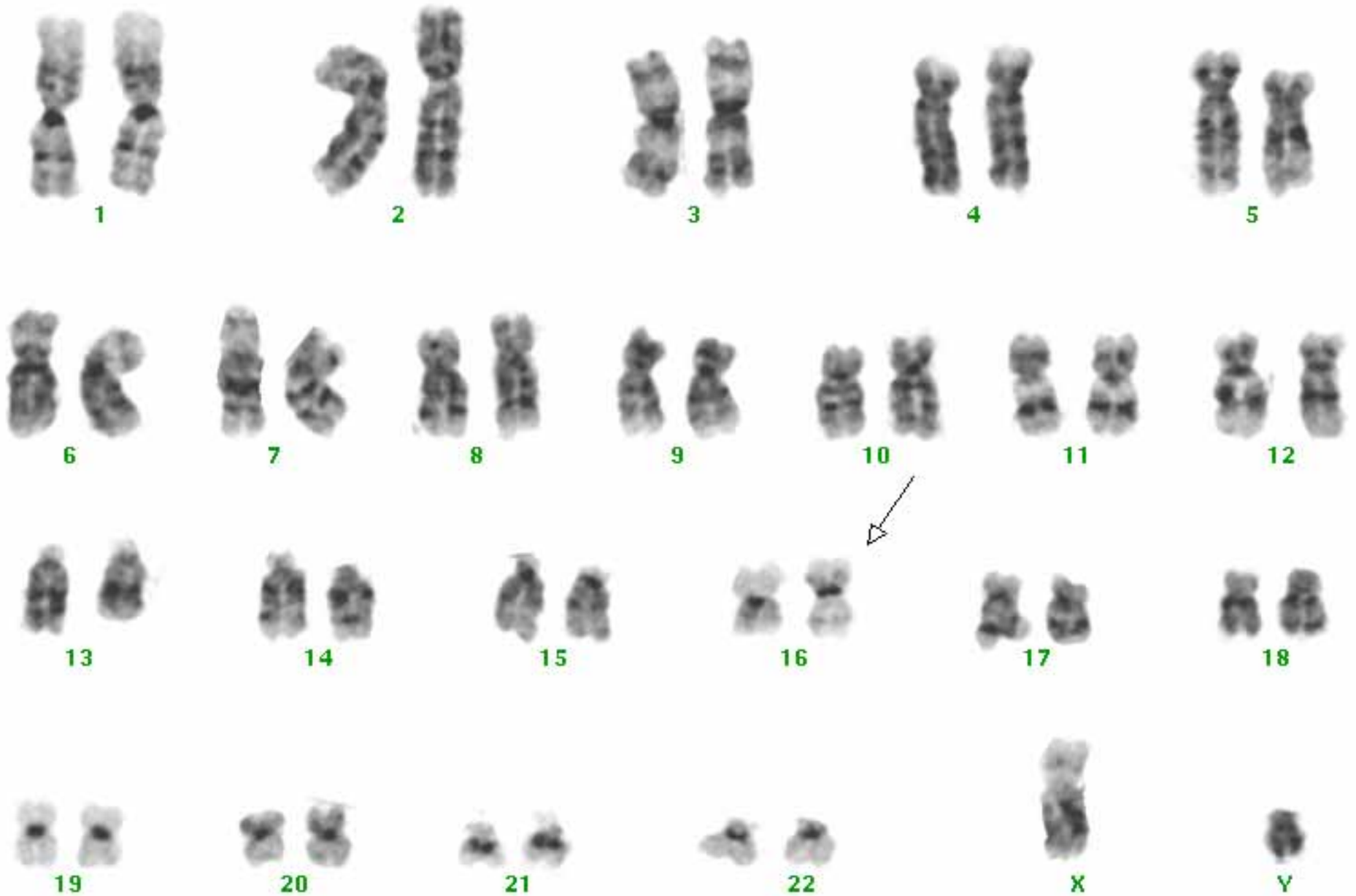


Case 2



Case 2



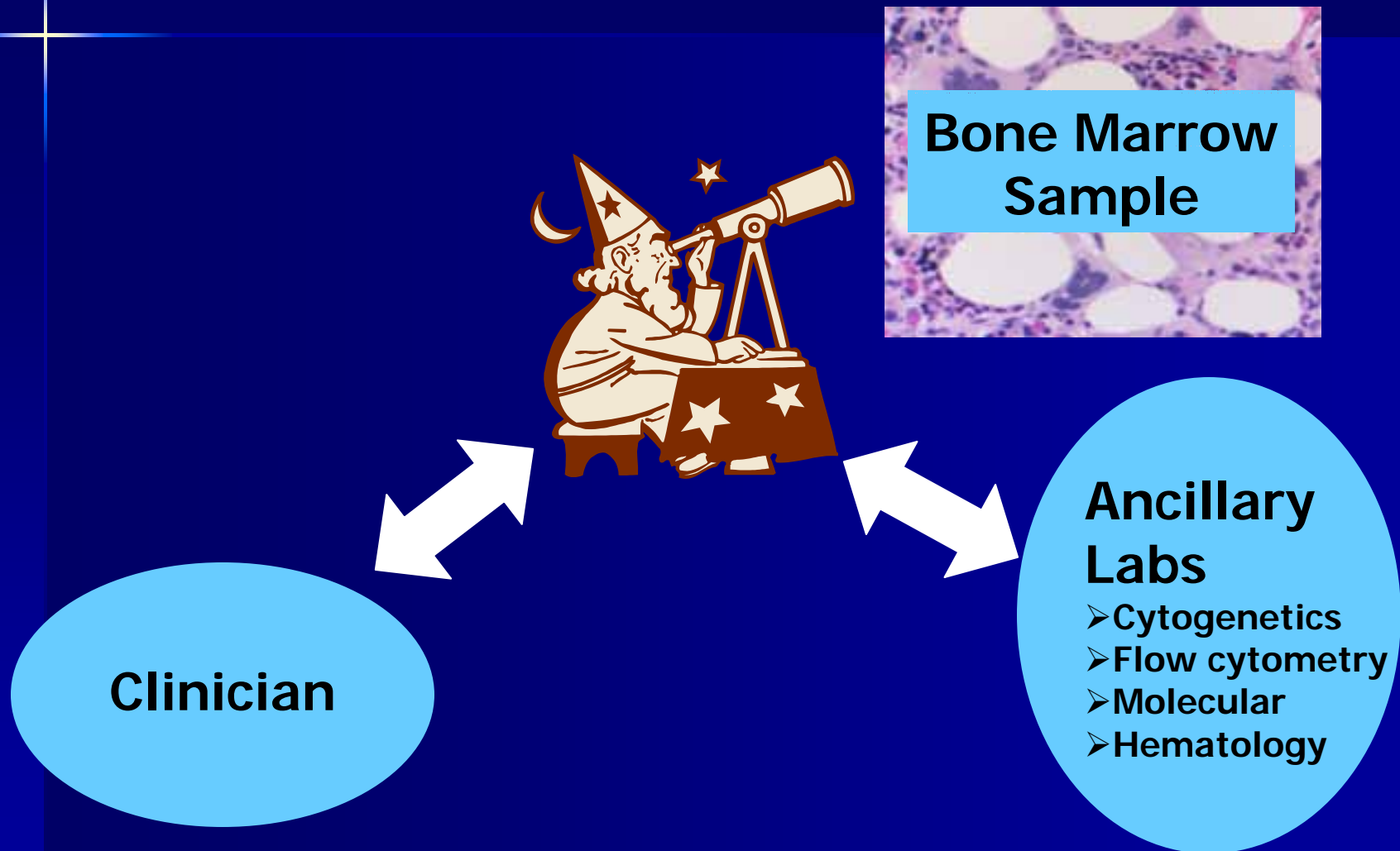


46, XY, inv(16)(p13q22) in all 20 metaphases

Implications of AML with inv(16)(p13q22)

- Relatively good prognosis
- Usually myelomonocytic leukemia with abnormal bone marrow eosinophils (FAB 'M4Eo')
 - No peripheral eosinophilia
 - Occasional cases may lack classic morphology
- Cytogenetic finding is subtle!
 - Can investigate by FISH if cytogenetics fails

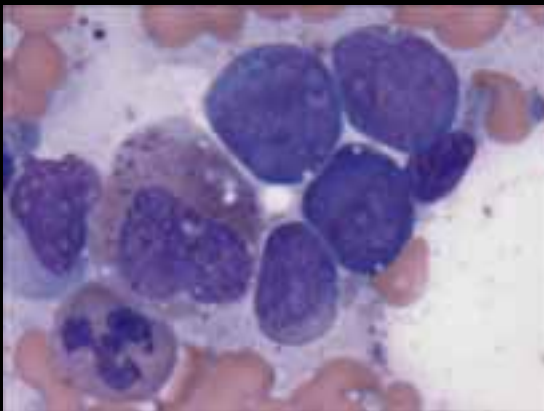
Pathologist can save the day in case of subtle cytogenetic finding



Differential diagnosis of eosinophilia

■ Neoplastic eosinophils

- Hypereosinophilic syndrome/CEL
- AML with inv(16)
 - Eosinophil/basophil cells in marrow
- Some types of MDS
 - Dysplastic eosinophils
- CML



■ Reactive eosinophils

- Drug, infection, allergy
- Reactive to a neoplasm
 - ALL with eosinophilia
 - T-cell lymphomas
 - Hodgkin lymphoma
 - Mast cell disease



Case 2 Diagnosis:

Acute myeloid leukemia with inv(16)

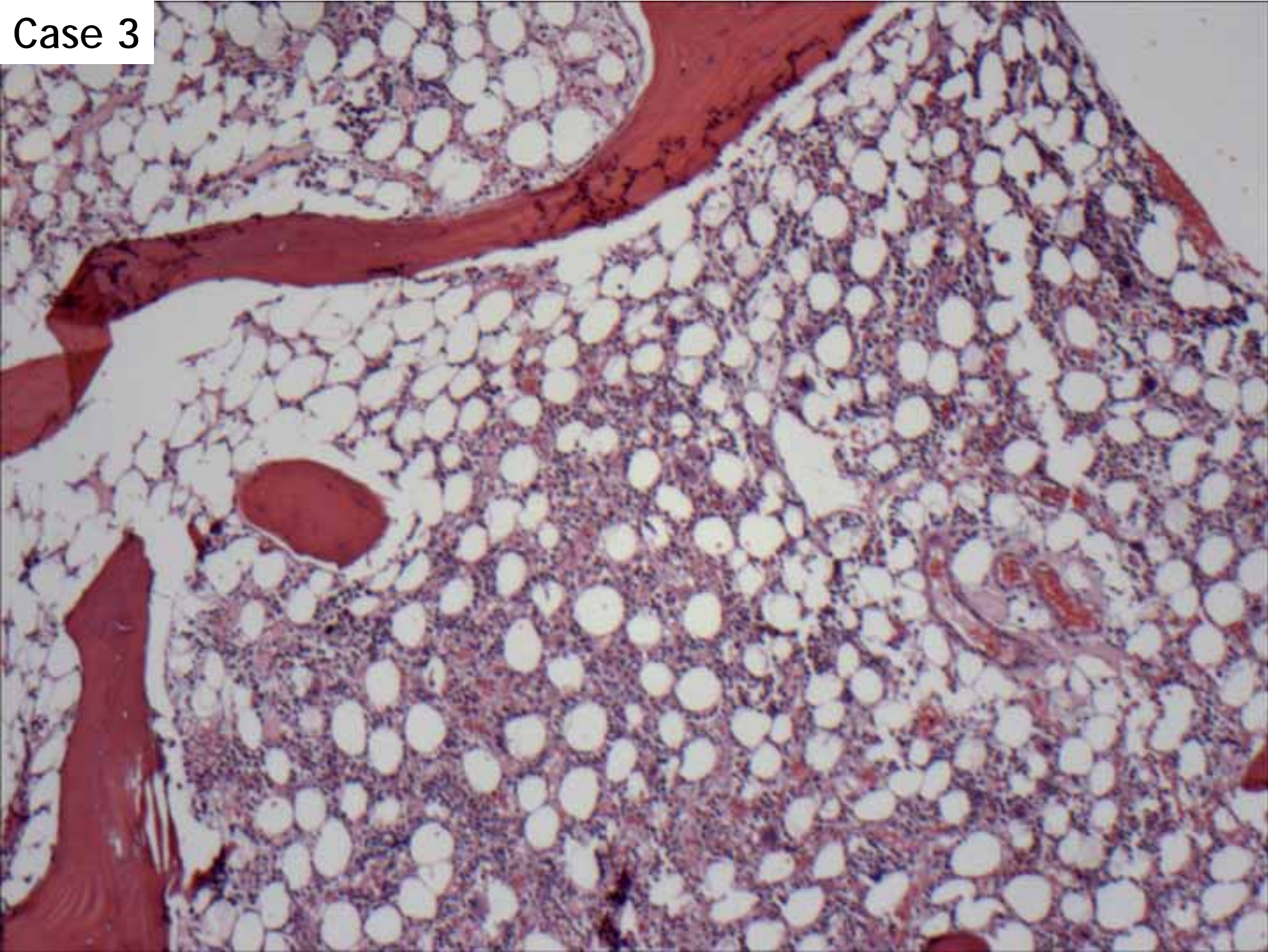
Teaching point:

Acute leukemias may present with marrow and/or peripheral eosinophilia

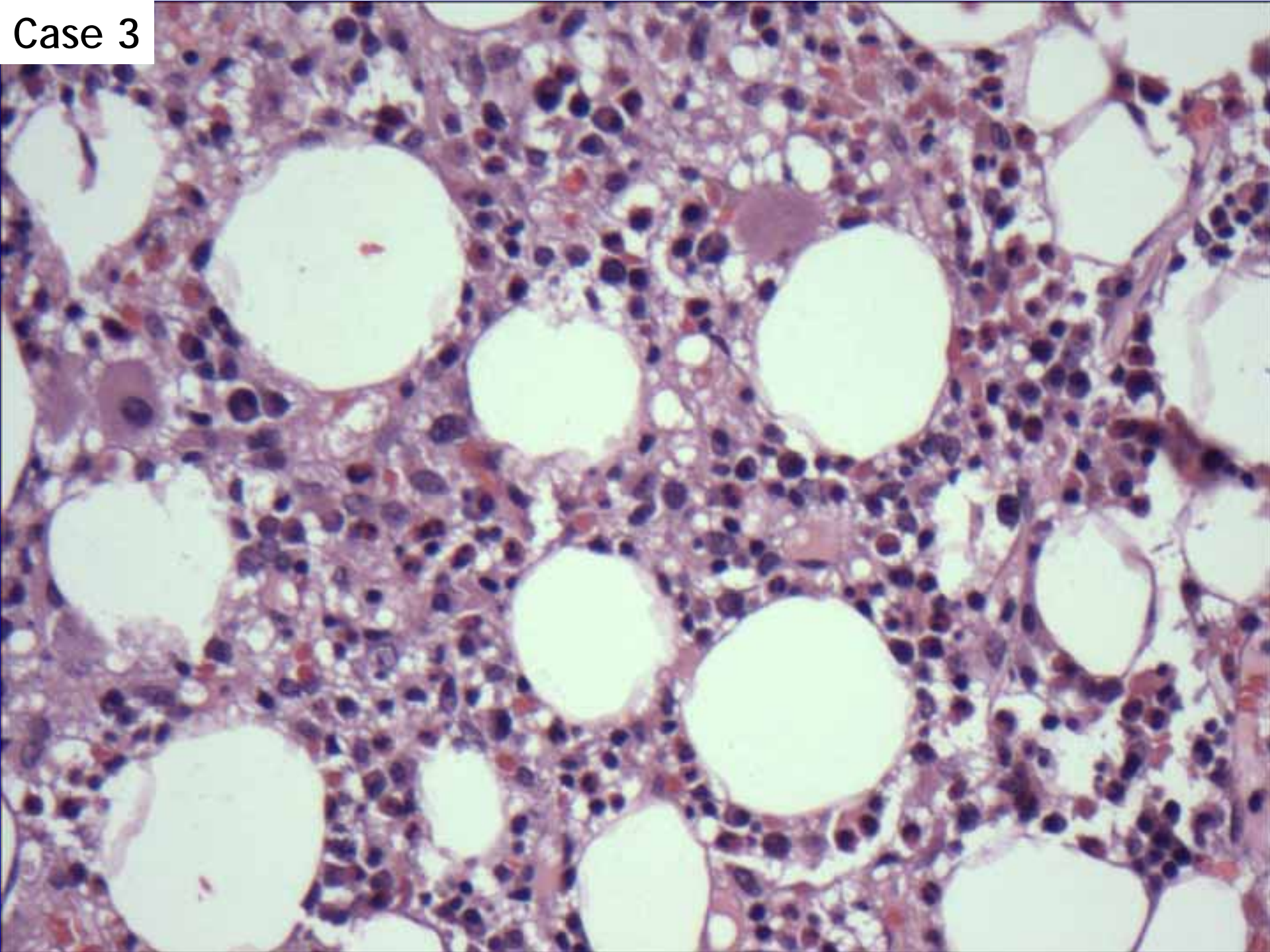
Case 3

- 82 year-old woman with agranulocytosis and sepsis
- CBC results
 - WBC=0.6 x 10⁹/L
 - 1% neutrophils, 94% lymphocytes, 4% eosinophils
 - HCT=30.8%
 - PLT=83 x 10⁹/L

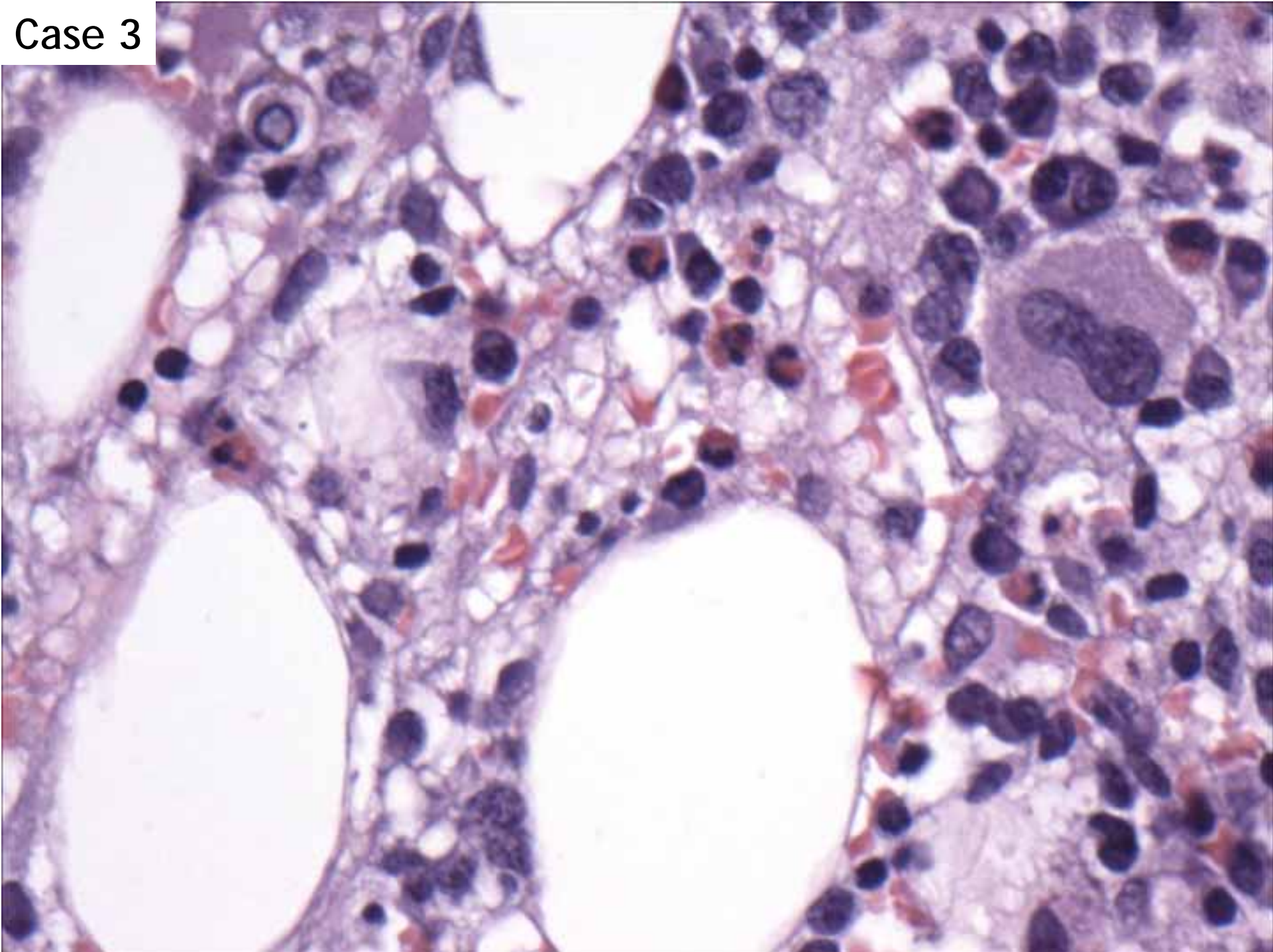
Case 3



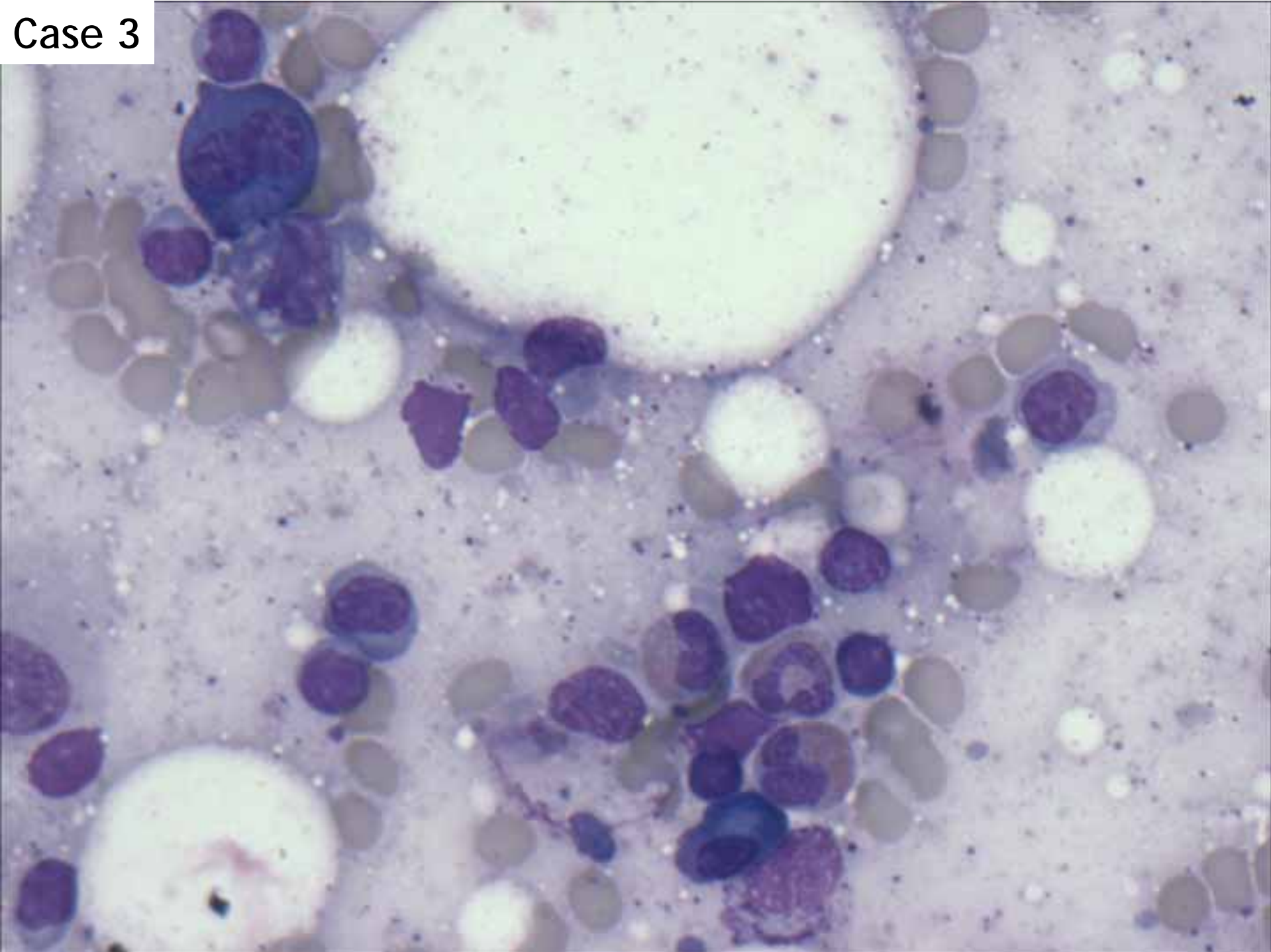
Case 3



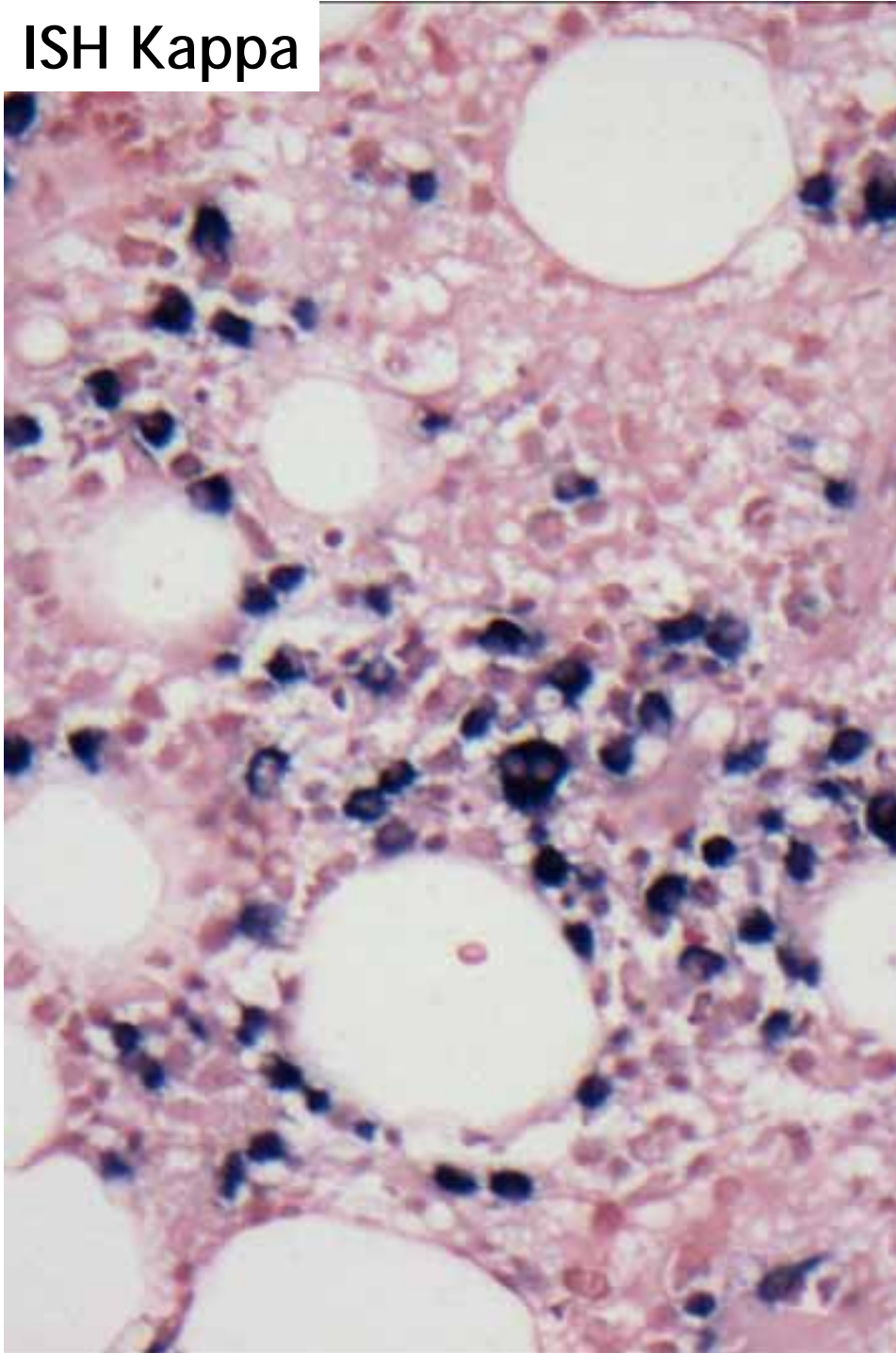
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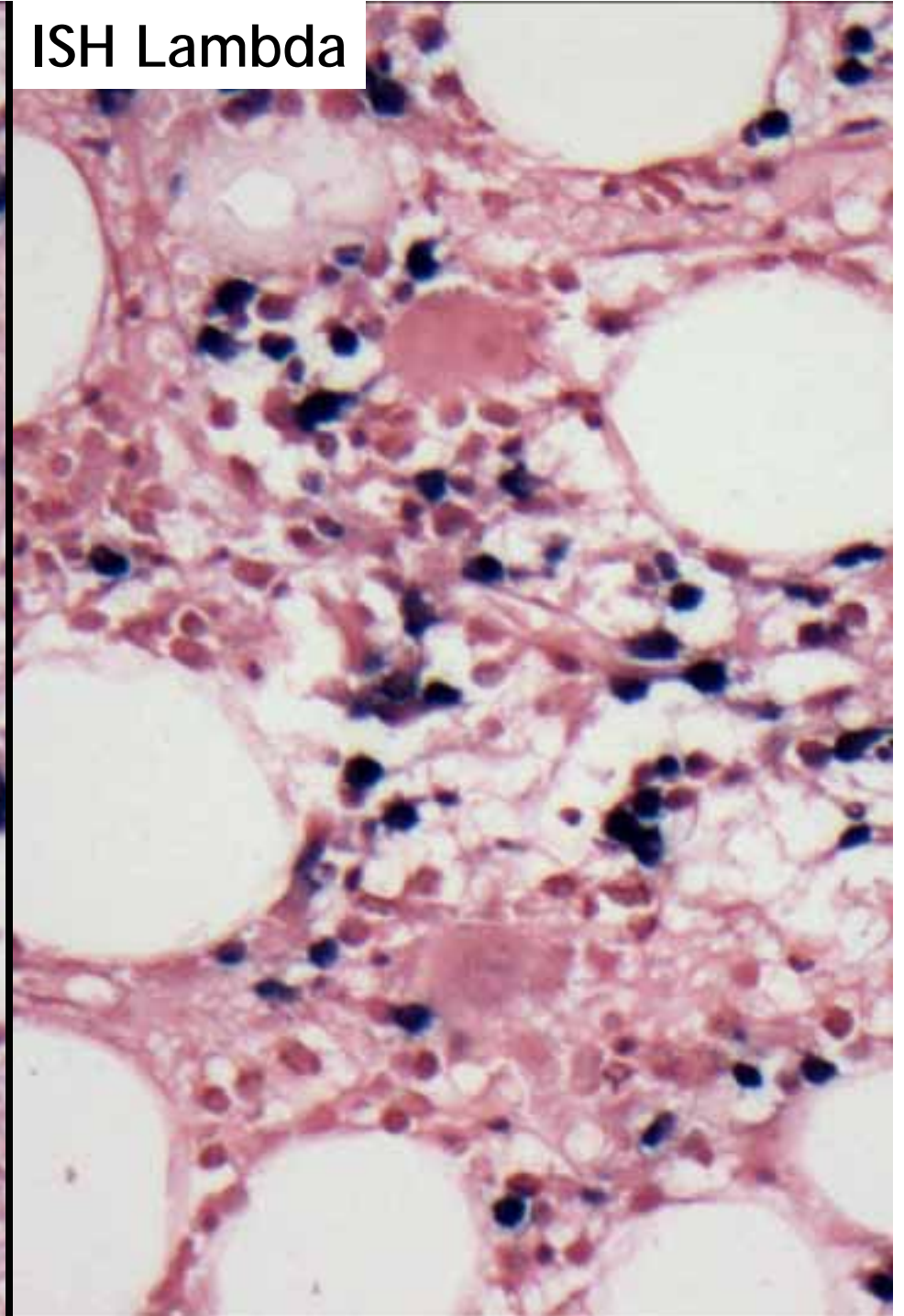
Case 3



ISH Kappa



ISH Lambda



Patterns of marrow reaction to injury

- Hypercellularity with left shift
- Hypocellularity with apoptotic figures and cell debris (fibrillary eosinophilic material) if acute
 - Usually no significant reticulin fibrosis
- Increase in plasma cells, eosinophils, mast cells, lymphocytes, histiocytes, siderophages

Case 3 Diagnosis:

Acute marrow injury secondary to sepsis

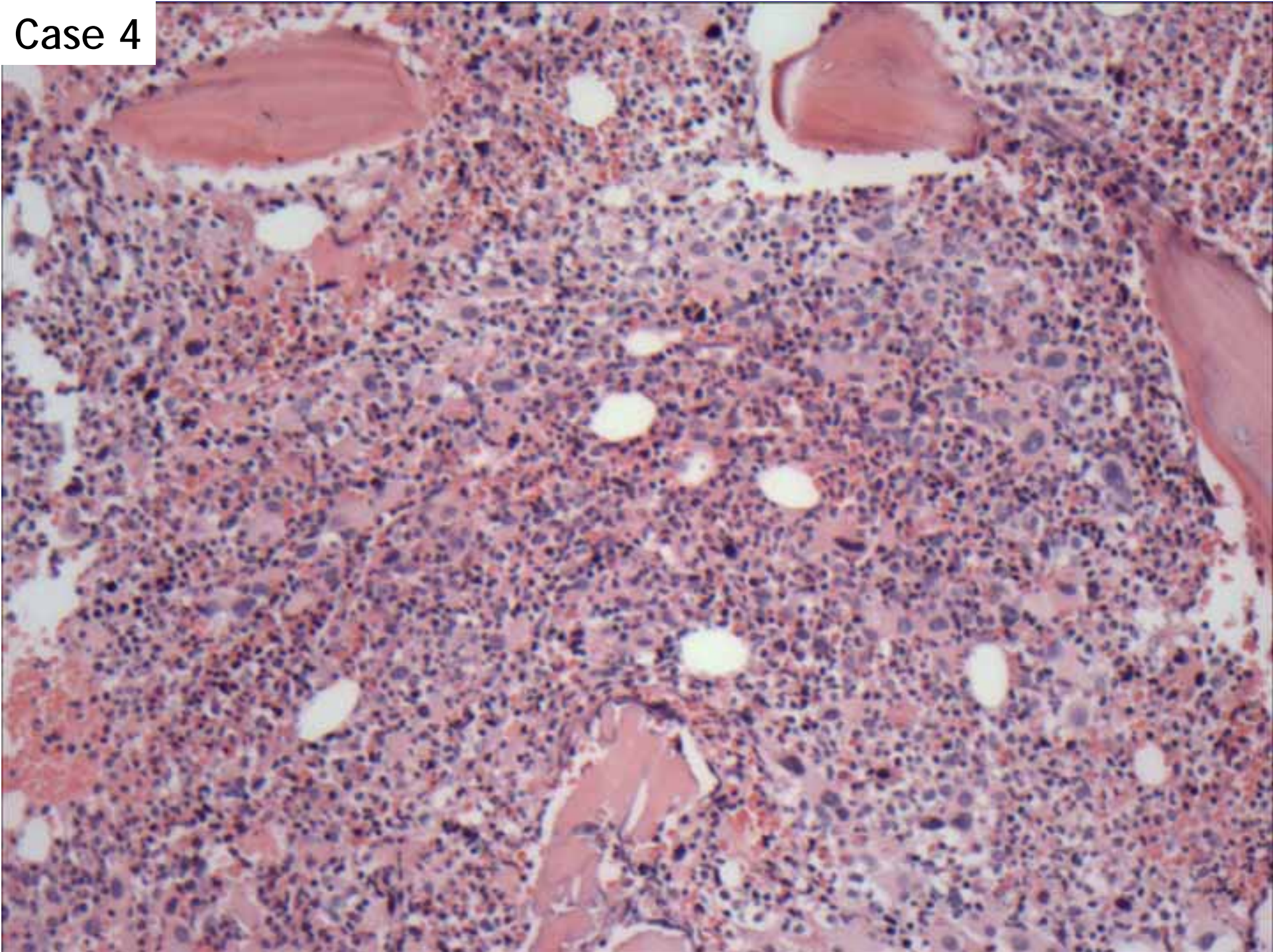
Teaching point:

Injury to marrow secondary to a toxic or infectious insult may mimic a primary marrow disease

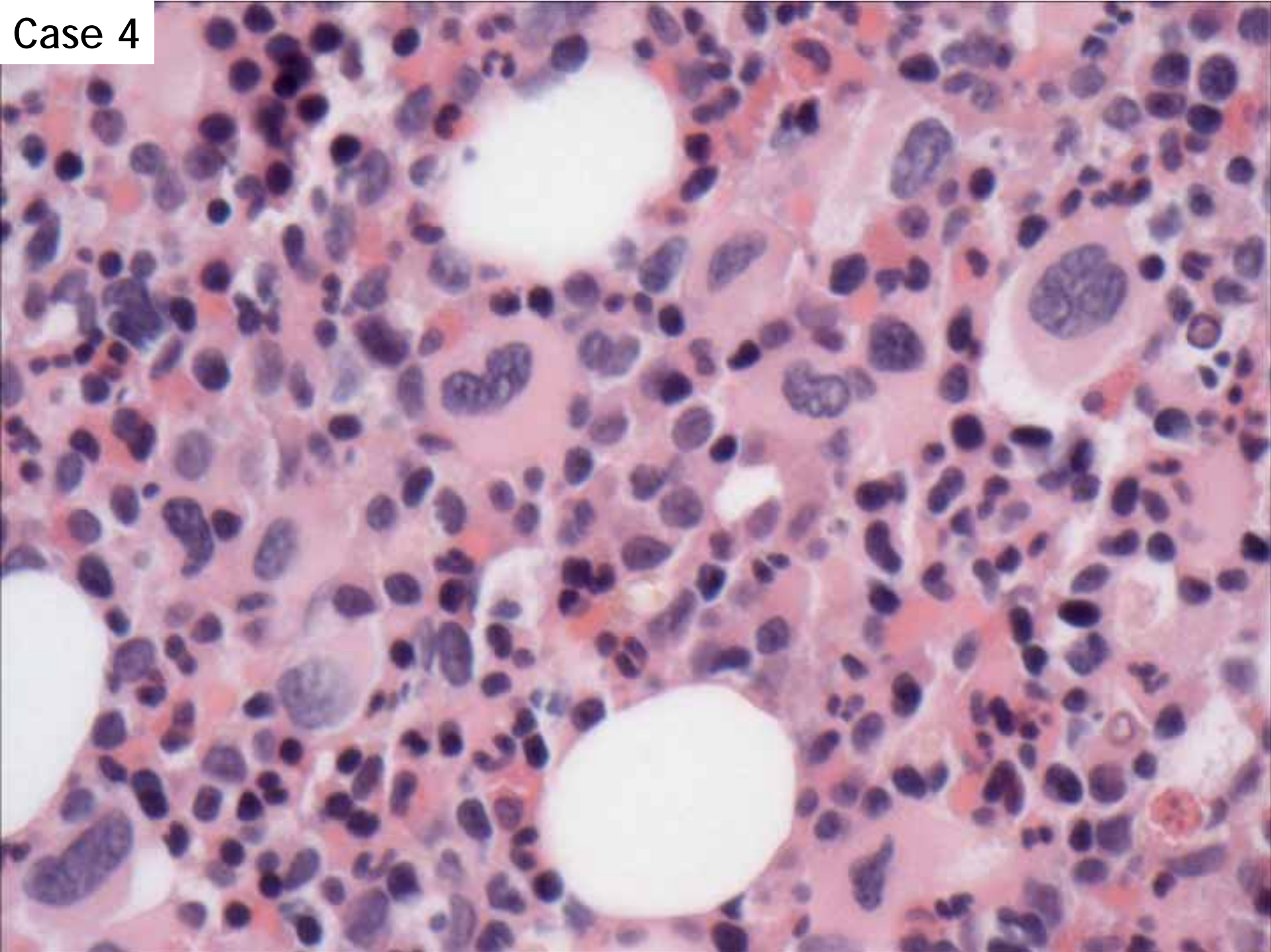
Case 4

- 73 year-old man with marked thrombocytosis
- CBC results
 - WBC=0.6 x 10⁹/L
 - 1% neutrophils, 94% lymphocytes, 4% eosinophils
 - HCT=30.8%
 - PLT=83 x 10⁹/L

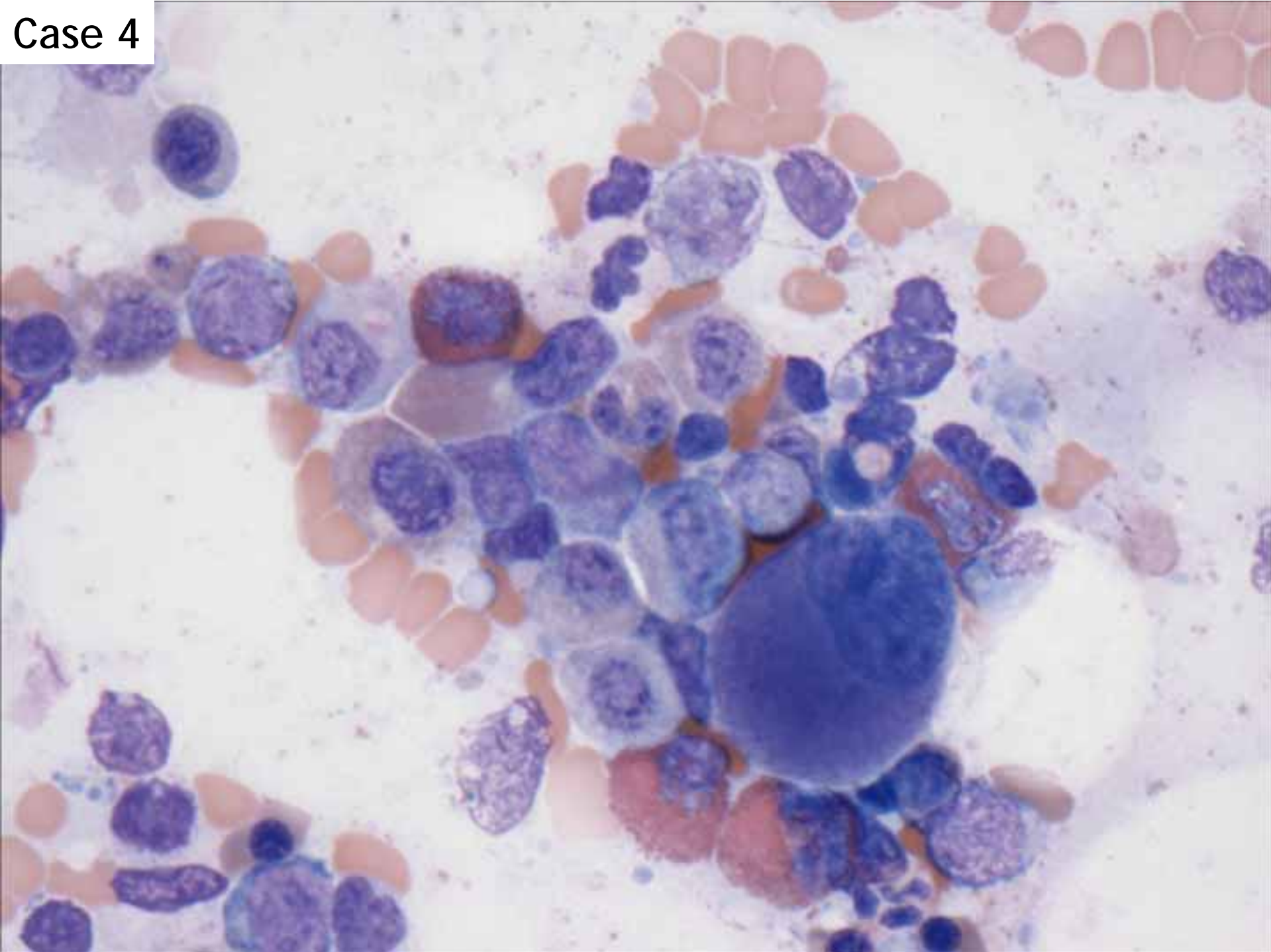
Case 4



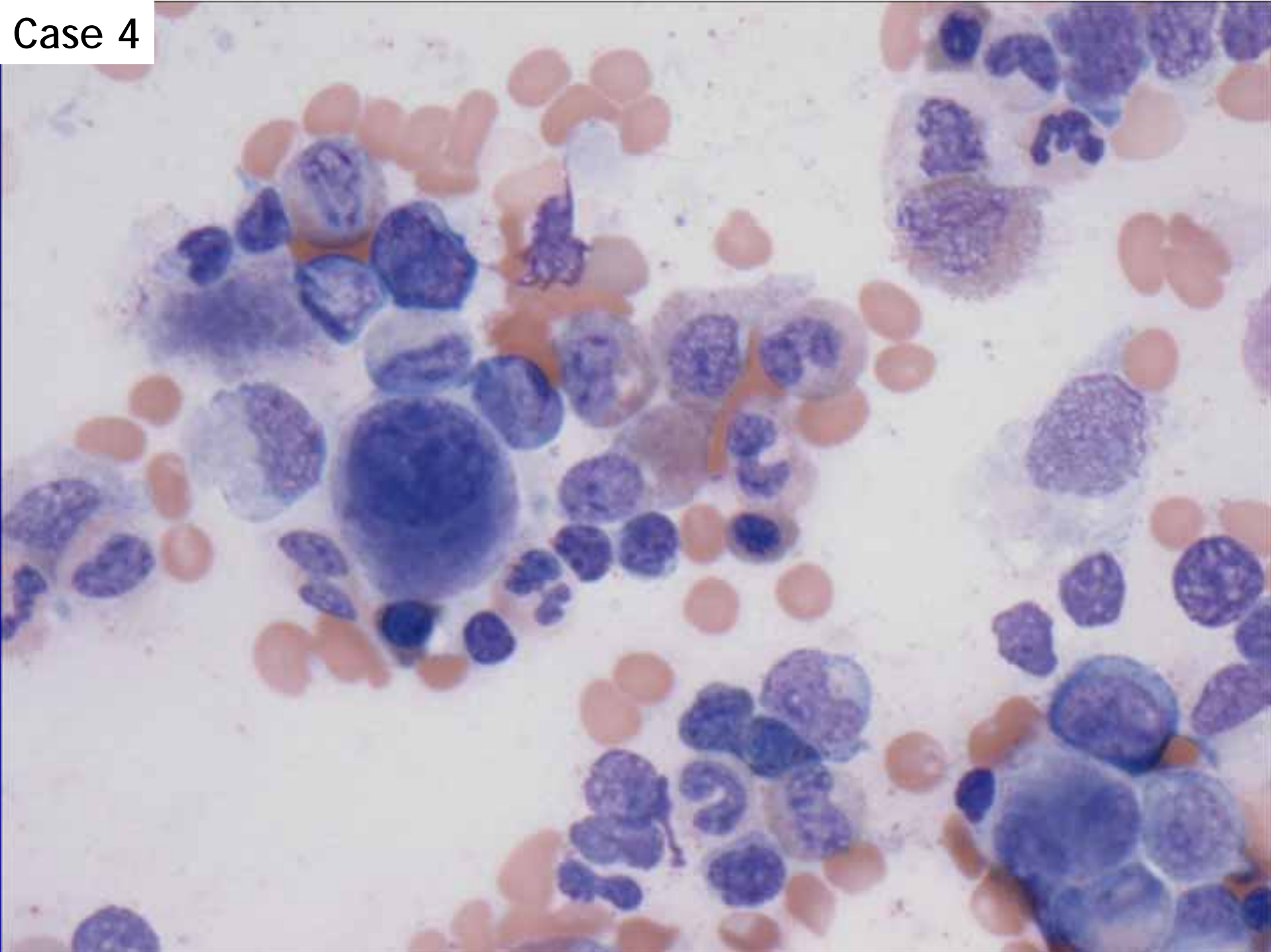
Case 4

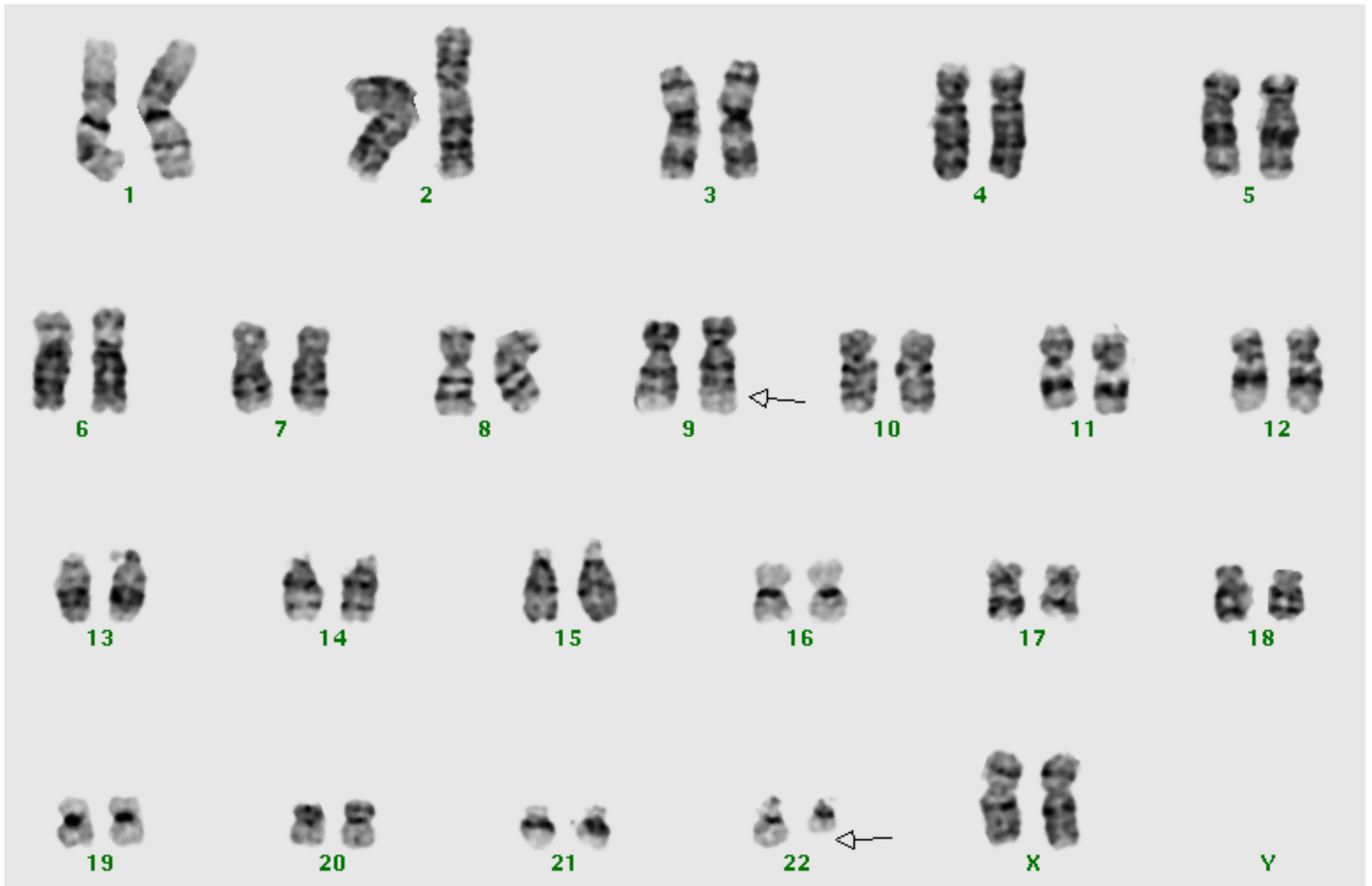


Case 4



Case 4





46, XY, t(9;22)(q34;q11.2) in all 20 metaphases

Always consider atypical presentations of CML

- Myelofibrotic
- With marked eosinophilia
- With thrombocytosis
- With relative erythroid hyperplasia
 - Patients with hemoglobinopathies
- With blunted leukocytosis and macrocytosis due to folate deficiency
- In blast crisis

Case 4 Diagnosis:

Chronic myelogenous leukemia in chronic phase

Teaching point:

Consider atypical presentations of CML in the differential diagnosis of hypercellular marrows