MDS case study:
80-year-old female with macrocytic anemia

MDS case study

Consultation: a 80-year-old woman was referred to our institution in 2006 because of a persistent macrocytic anemia. She presented with tiredness and dizziness.

Medical history:

No allergies. Non-smoker.

- Mild vitamin B12 deficiency and macrocytic anemia diagnosed in 2005. Despite of the correct treatment with intramuscular vitamin B12, the anemia persisted.
- Chronic atrophic gastritis.
- Hypertension.

Physical examination: skin pallor with no other significant abnormalities.

MDS case study

Blood tests (I):

• RBC 91x10^9/L, **Hb 7.4 g/dL**, Htc 22.9%, **MCV 119.9 fL**, MHC 38.7pg, WBC 5.14x10^9/L, platelets 306x10^9/L. Reticulocytes: 2.59 %, total 49.5x10^9/L.

• Glucose 120 mg/dl, Creatinine 0.99 mg/dl, LDH 329 UI/L, Bilirrubin 0.53 mg/dl, AST 12 UI/L, ALT 9 UI/L, GGT 60 UI/L, AF 40 UI/L, Total proteins 6.9 g/dL, Albumin 4.4 g/L, EPO 678 mU/mL, Vitamin B12 464 pg/mL, Folic acid 10.9 ng/mL, Ferritin 126 ng/mL.

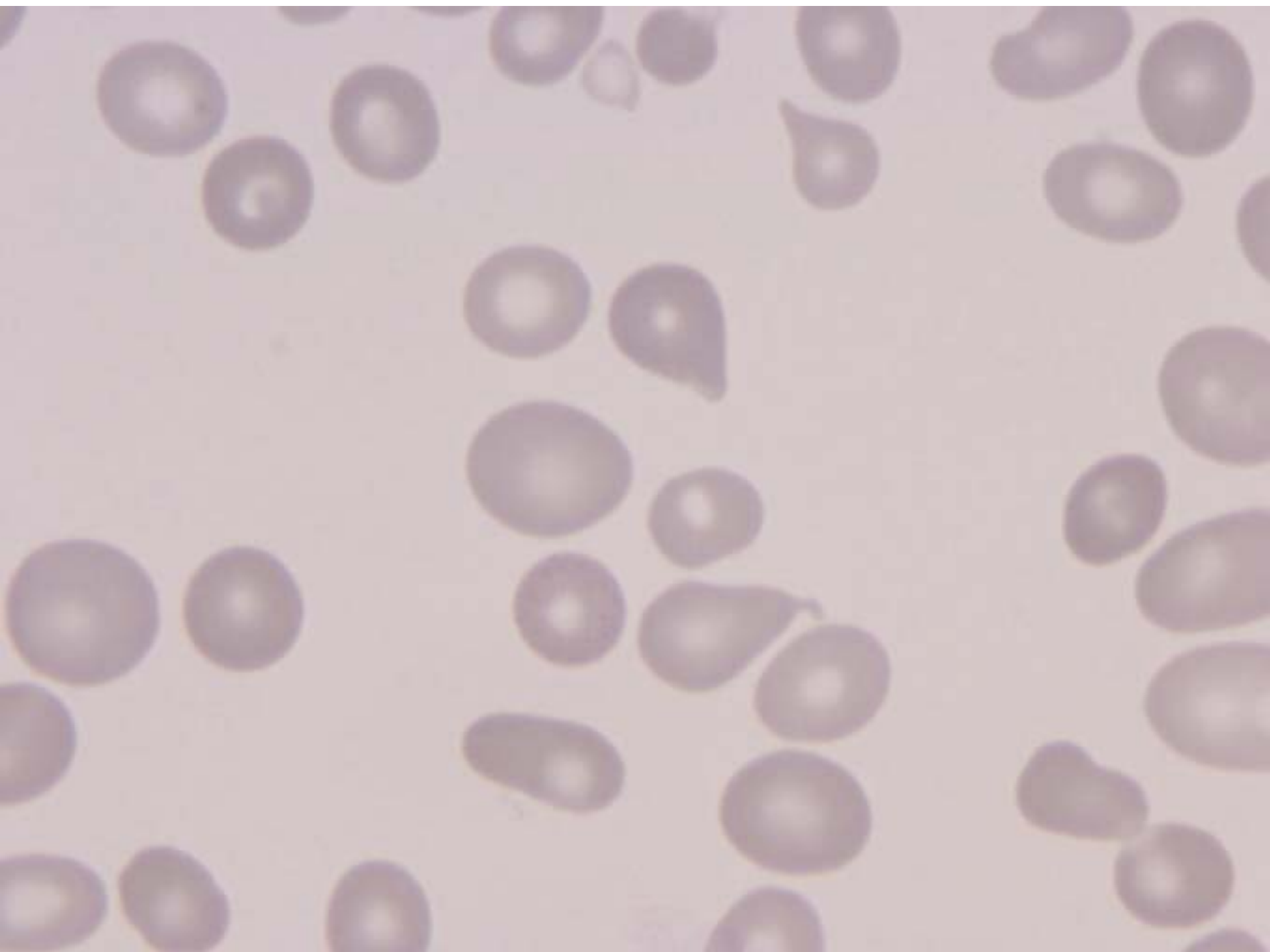
• HBV, HCV, HIV negatives.

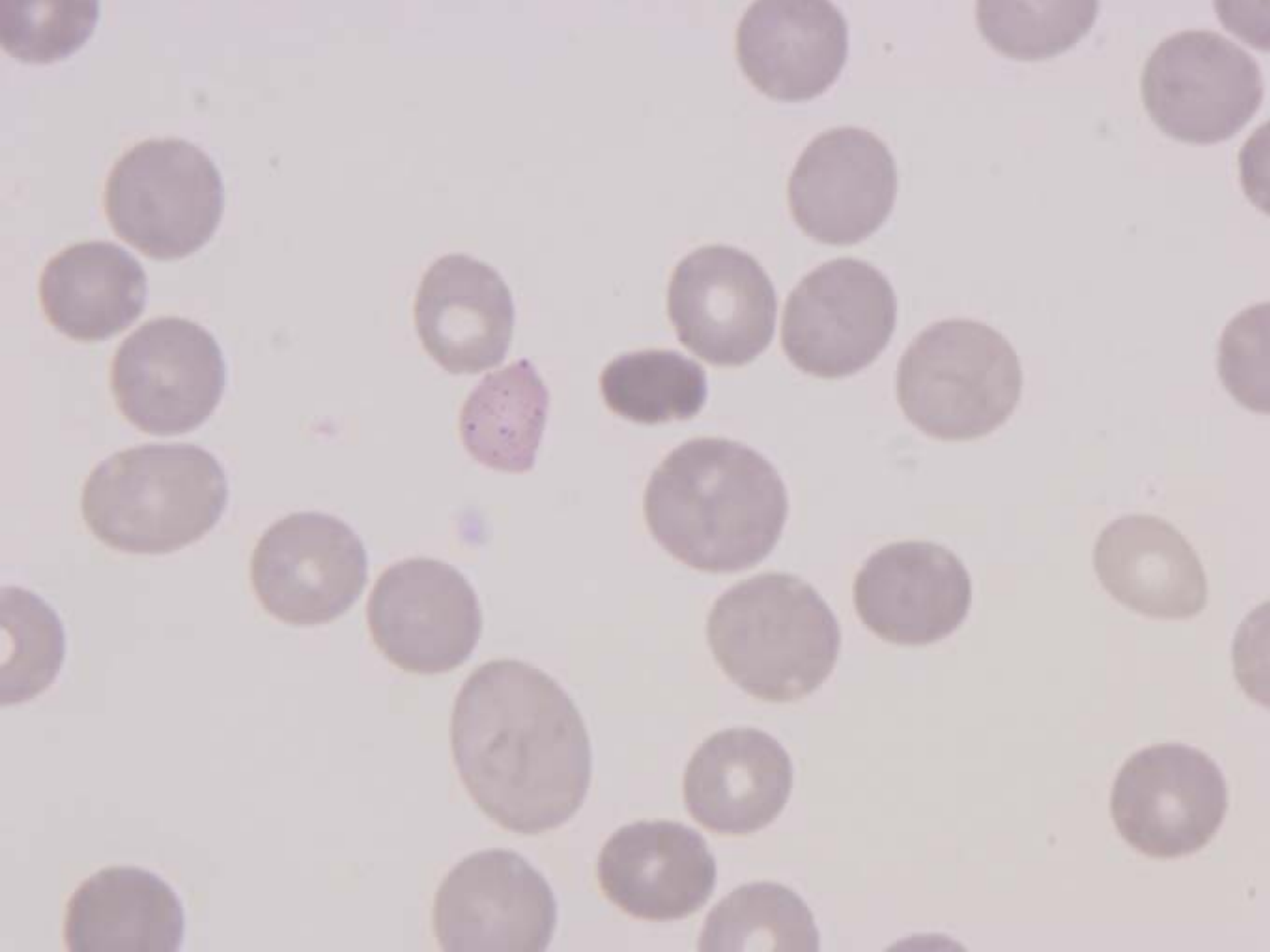
• Prothrombin rate 71%, aPTT 27 seg.

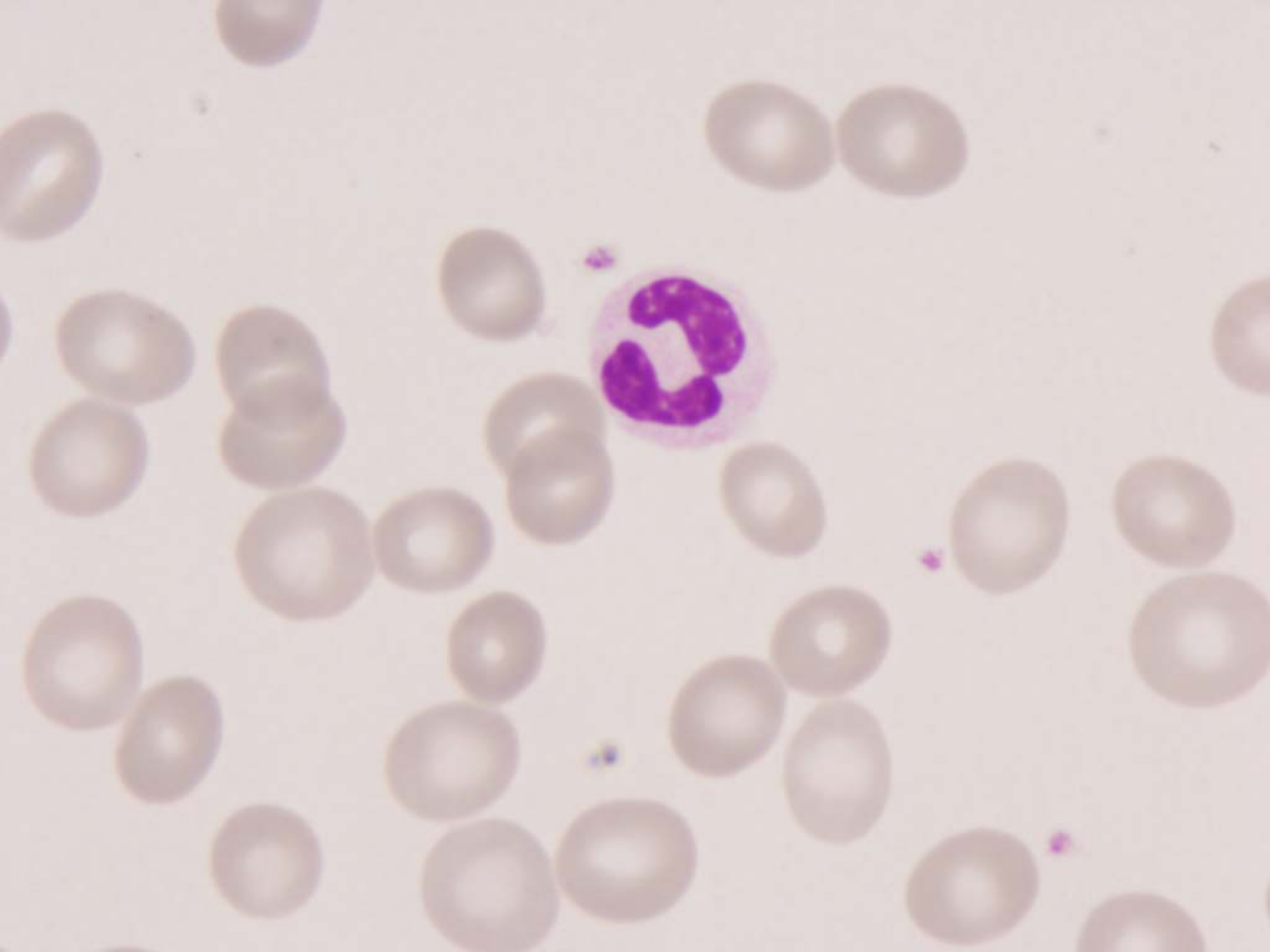
MDS case study

Blood tests (II):

- Peripheral blood smear:
  - WBC differential count: 64N, 4Eo, 0B, 28L, 4M.
  - Anisopoikilocytosis, macrocytosis, polycromasia, basophilic stippling. Some schistocytes, elliptocytes and dacryocytes.
  - Anisocytosis of platelets.
  - Doble population of neutrophils: coexistence of normal and marked hypogranulated elements.







MDS case study

Bone marrow aspirate:

Hypercellular.

Megakaryopoiesis: abundant**. 58%** of dysmorphic elements: small megakaryocytes **with hypo- or monolobated nucleus.**

Erythropoiesis: **15%.** Asynchronic maduration, nuclear budding, altered mitosis, irregular distribution of hemoglobin and presence of Höwell-Jolly bodies.

Granulopoiesis: 61%. Hypogranulated neutrophils with Döhle bodies.

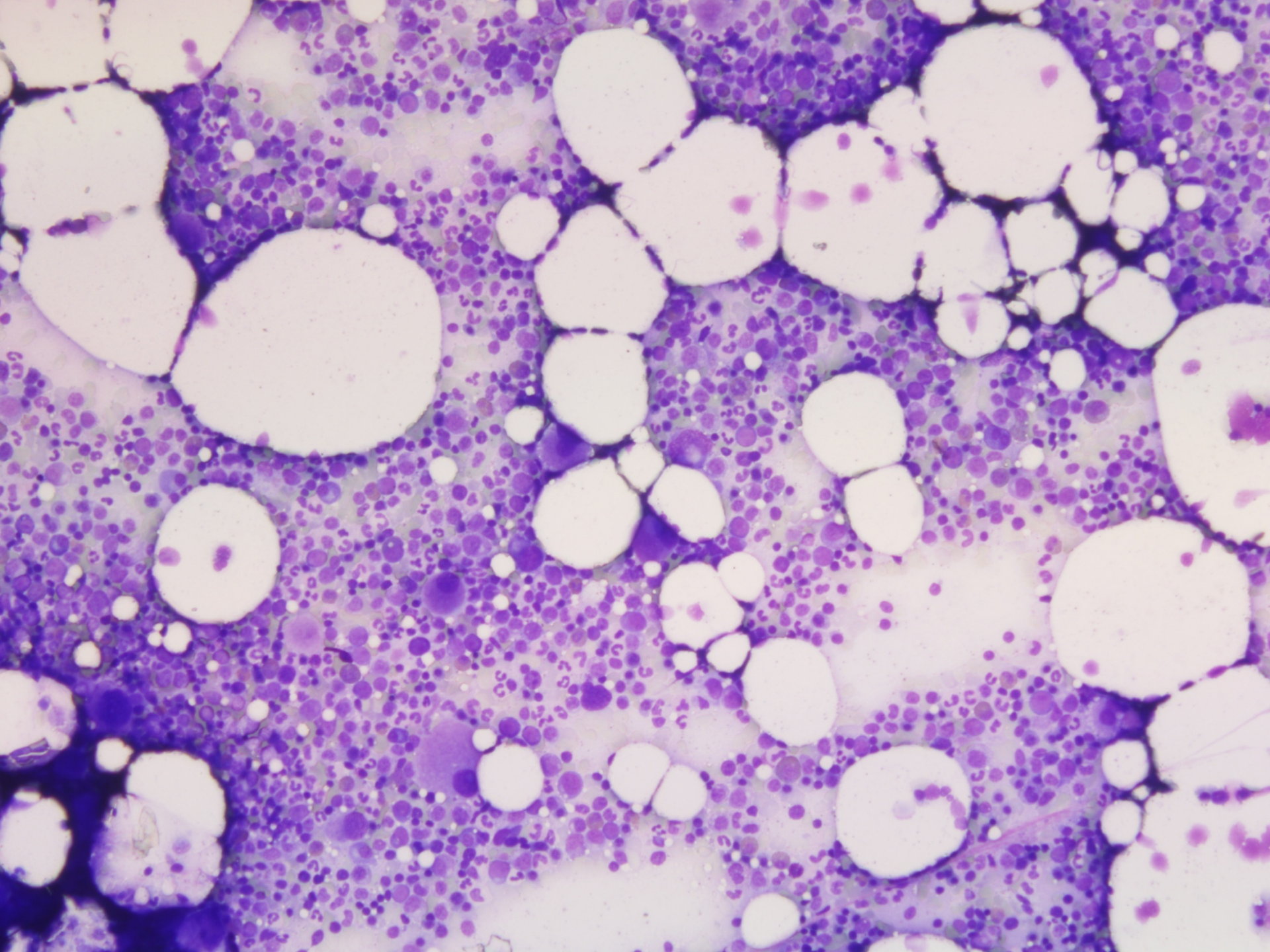
6% blasts (3% type I and 3% type II).

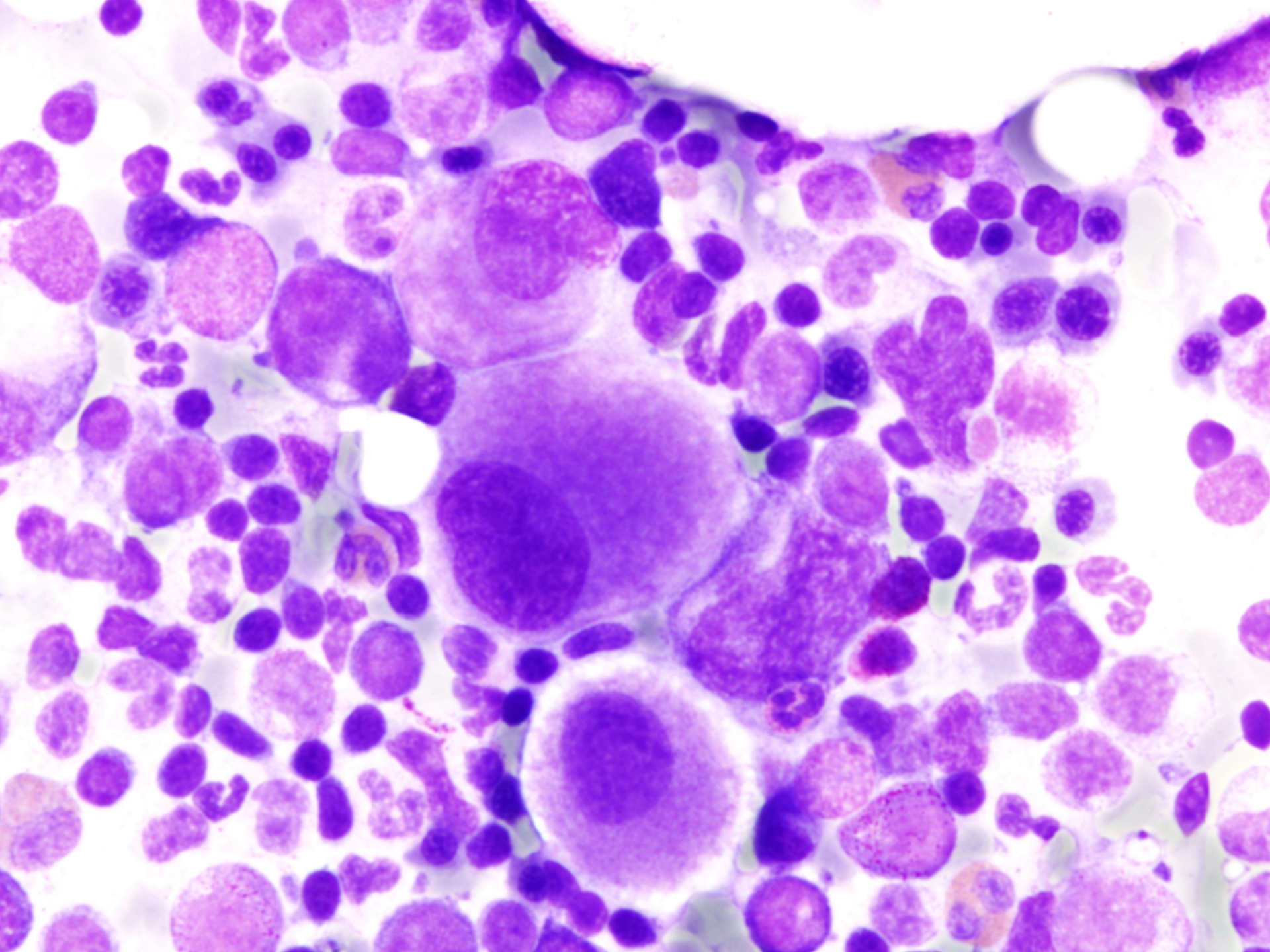
Mononuclear phagocytic system : 3%.

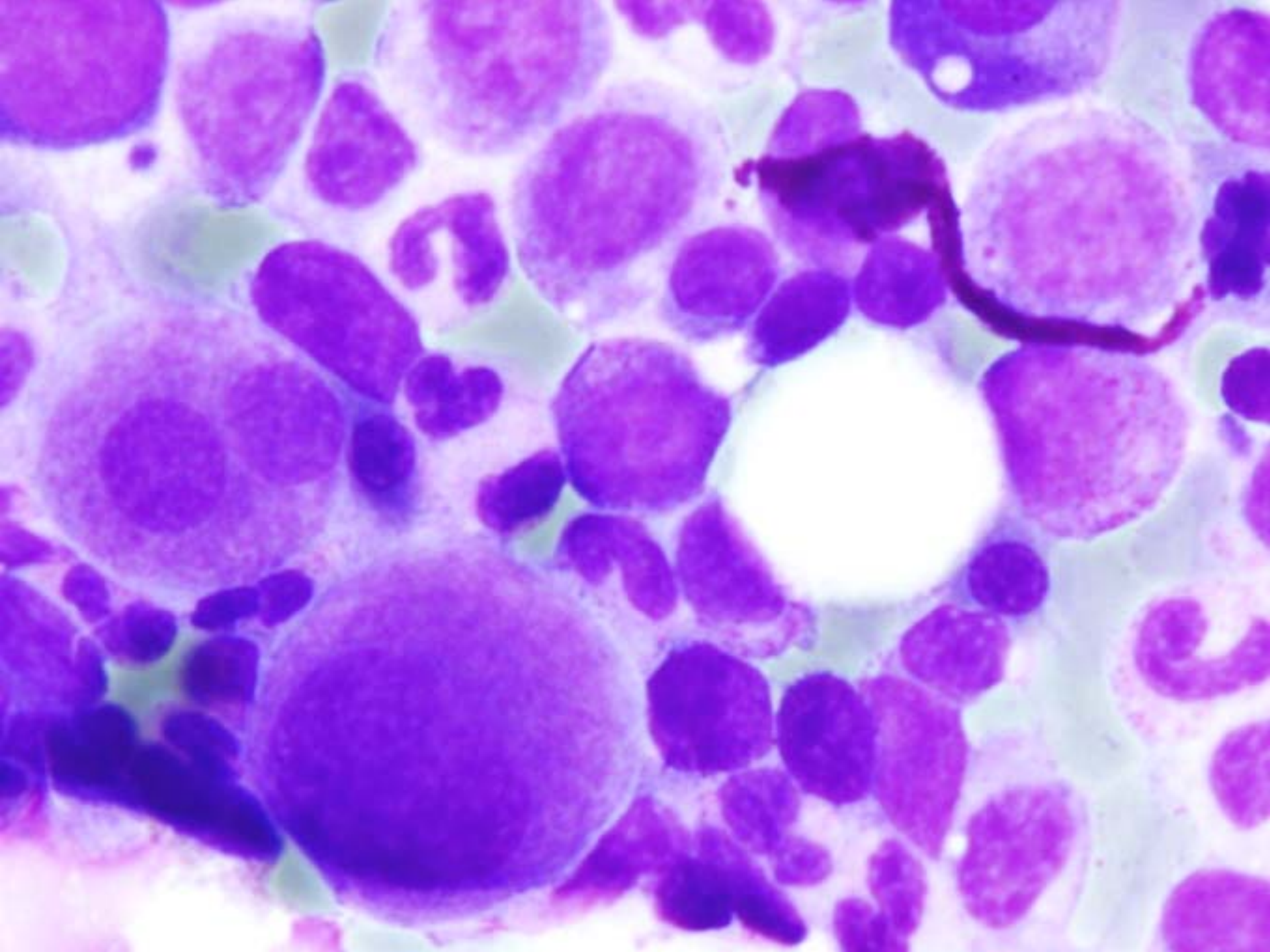
Lymphocytes:19%.

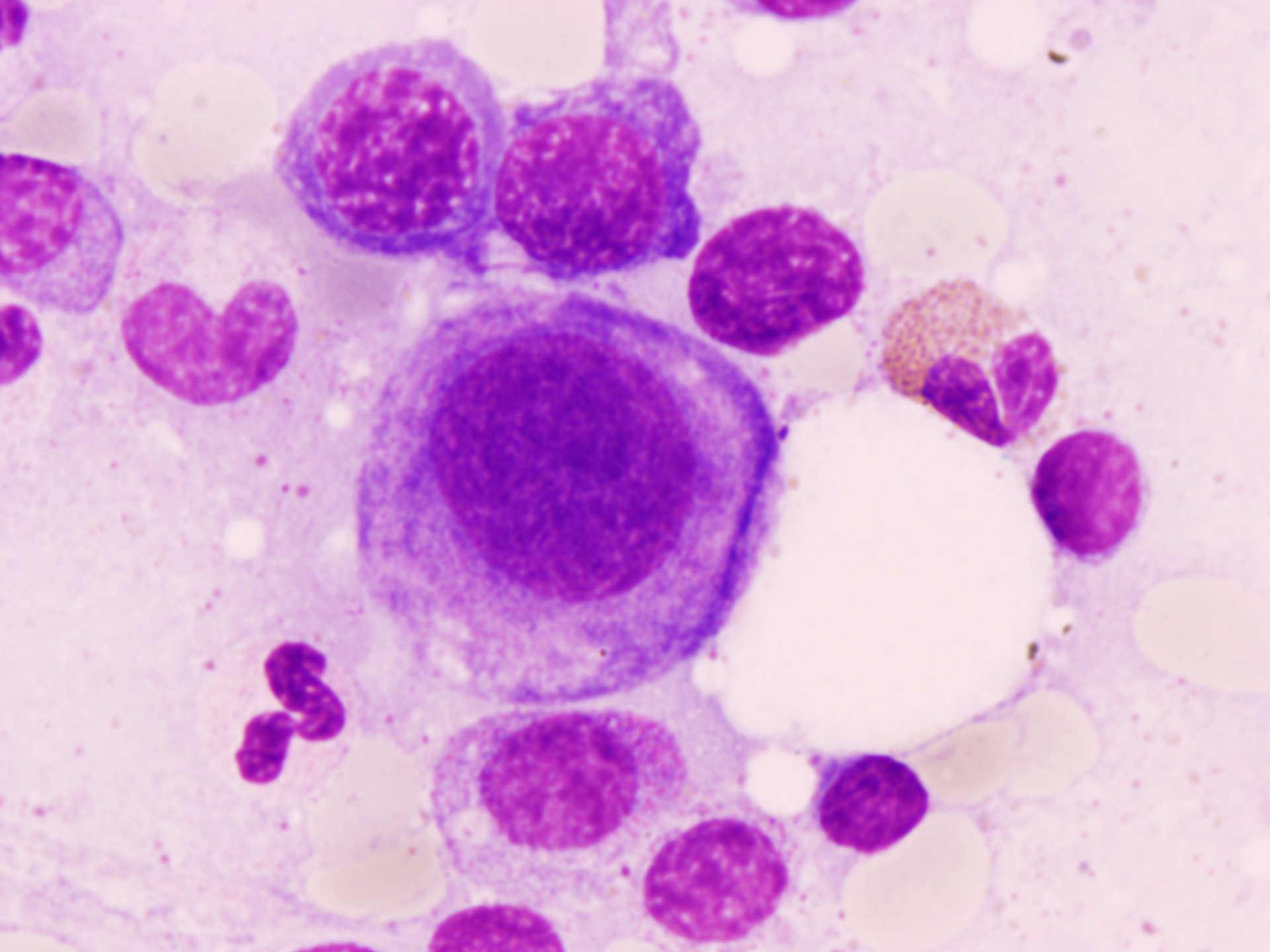
Plasma cells: 2%

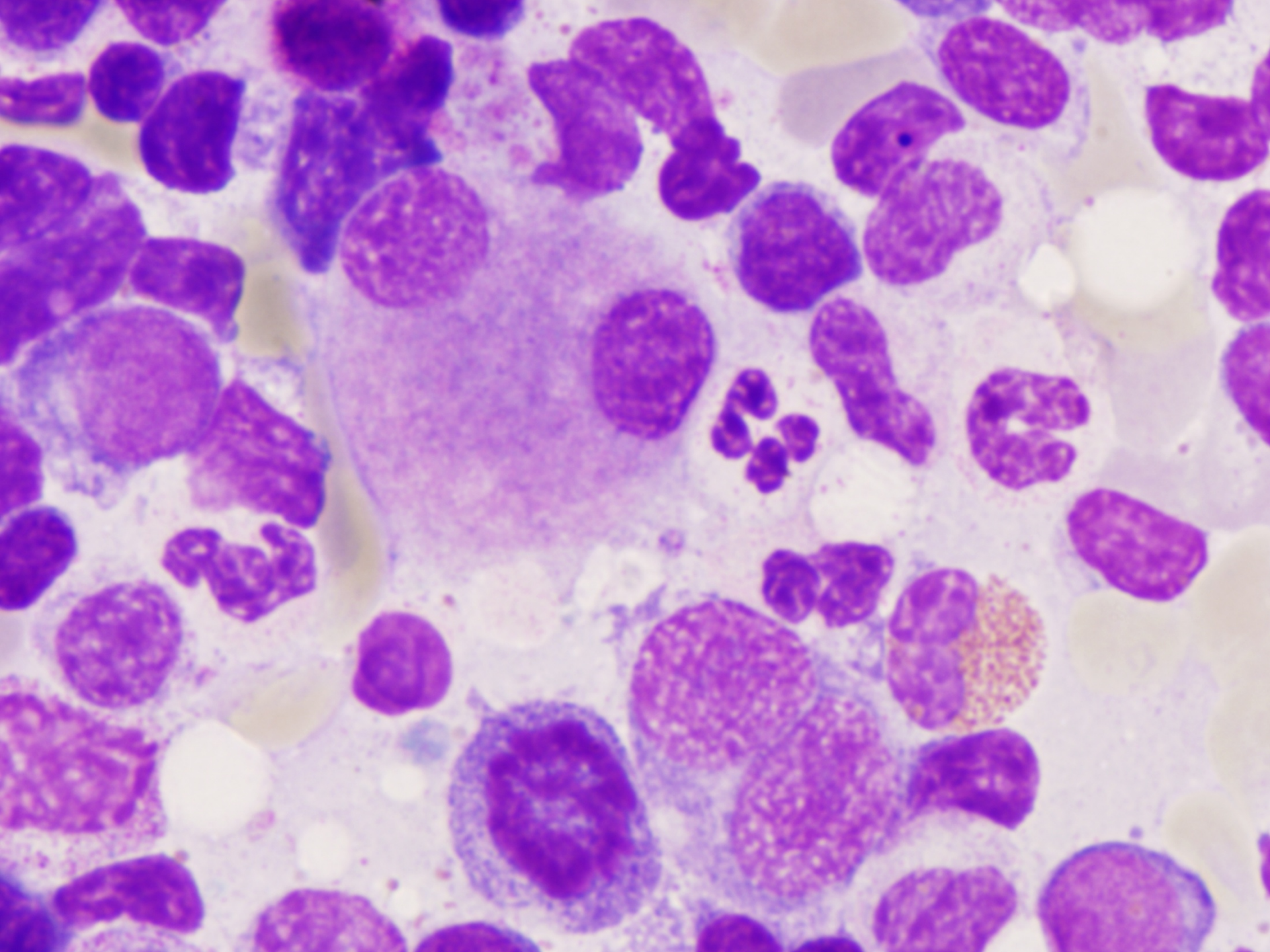
Normal macrophagic iron store. Sideroblasts type I and II: 48%. No ring sideroblasts.

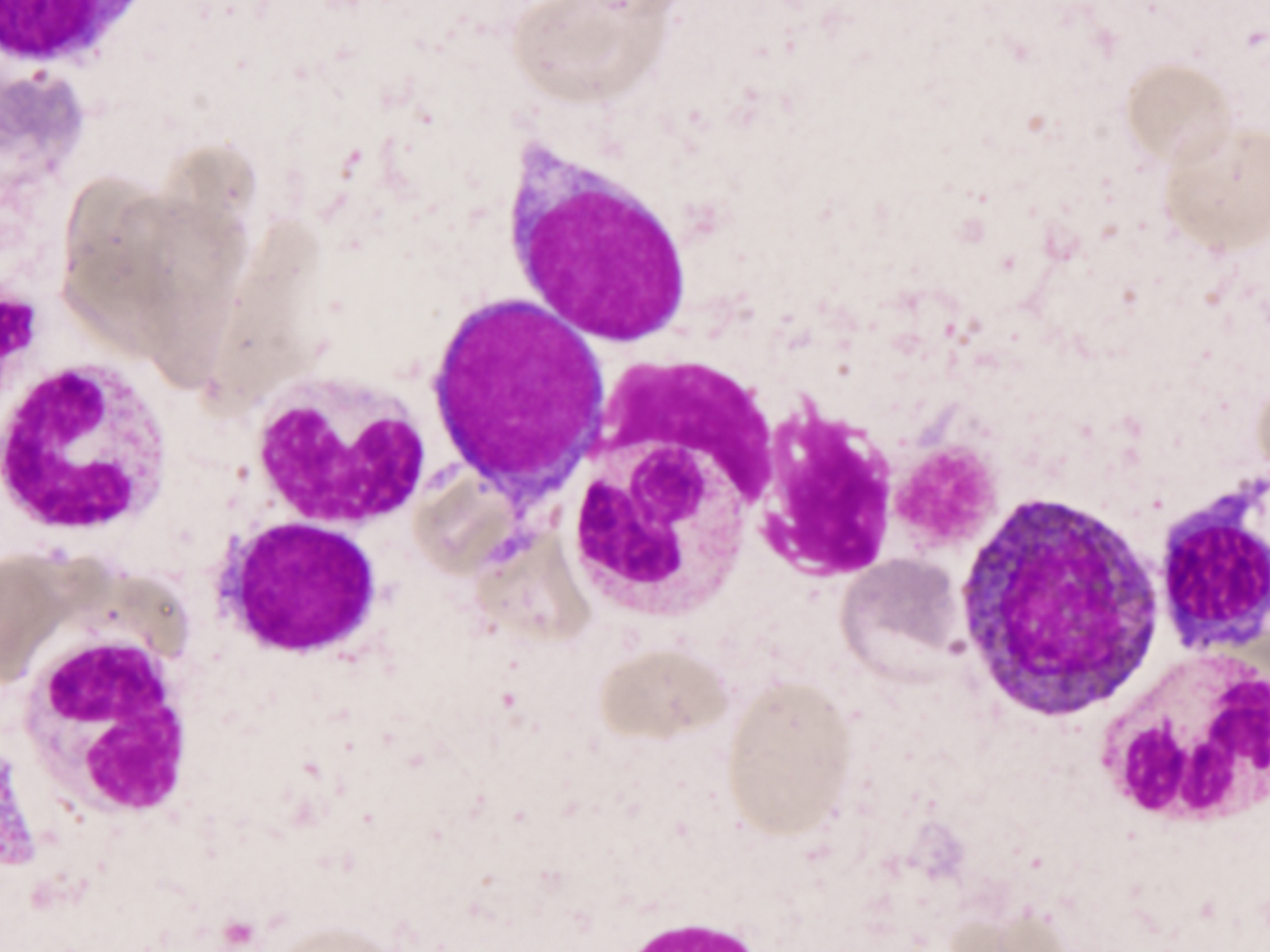


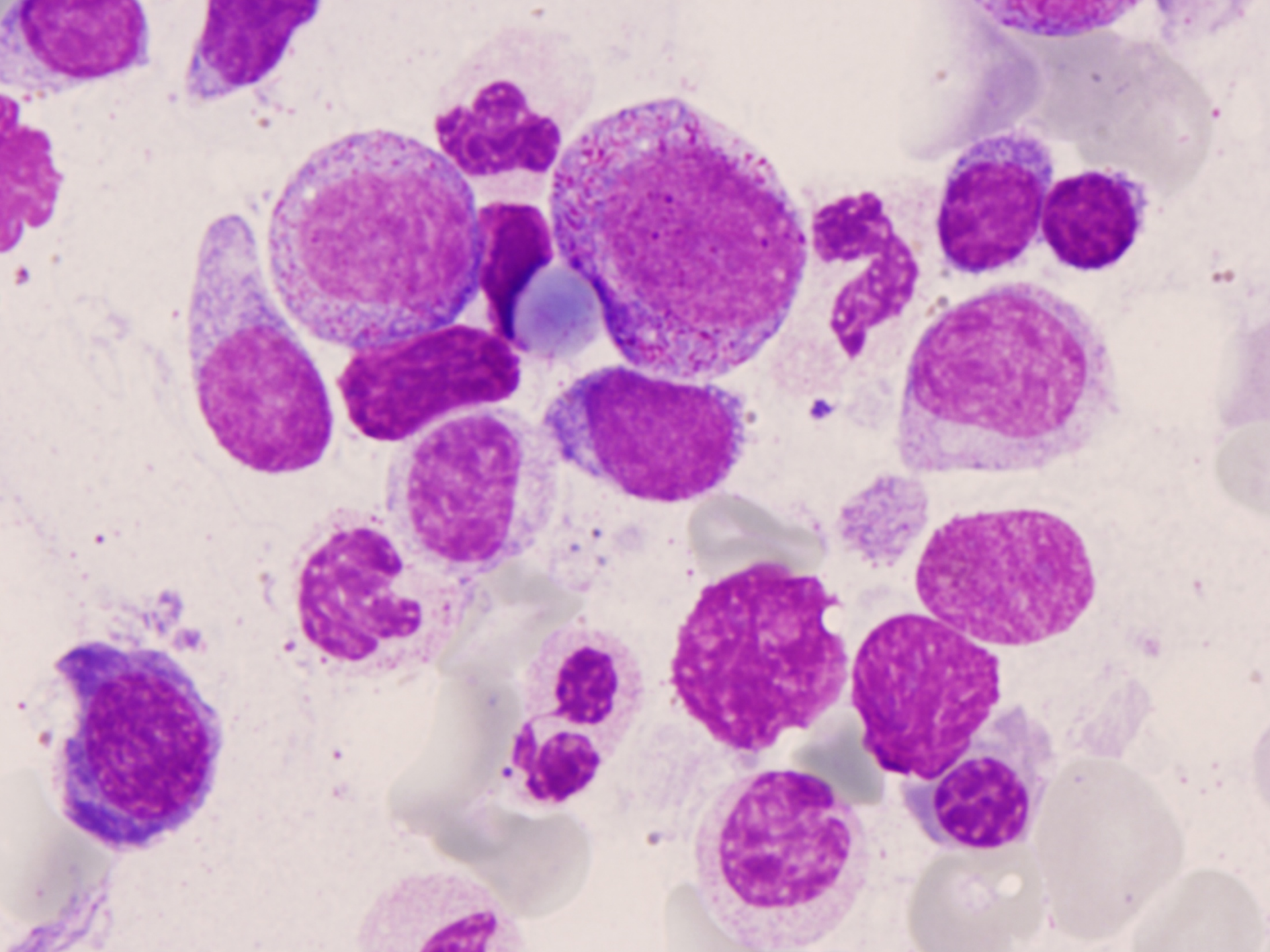








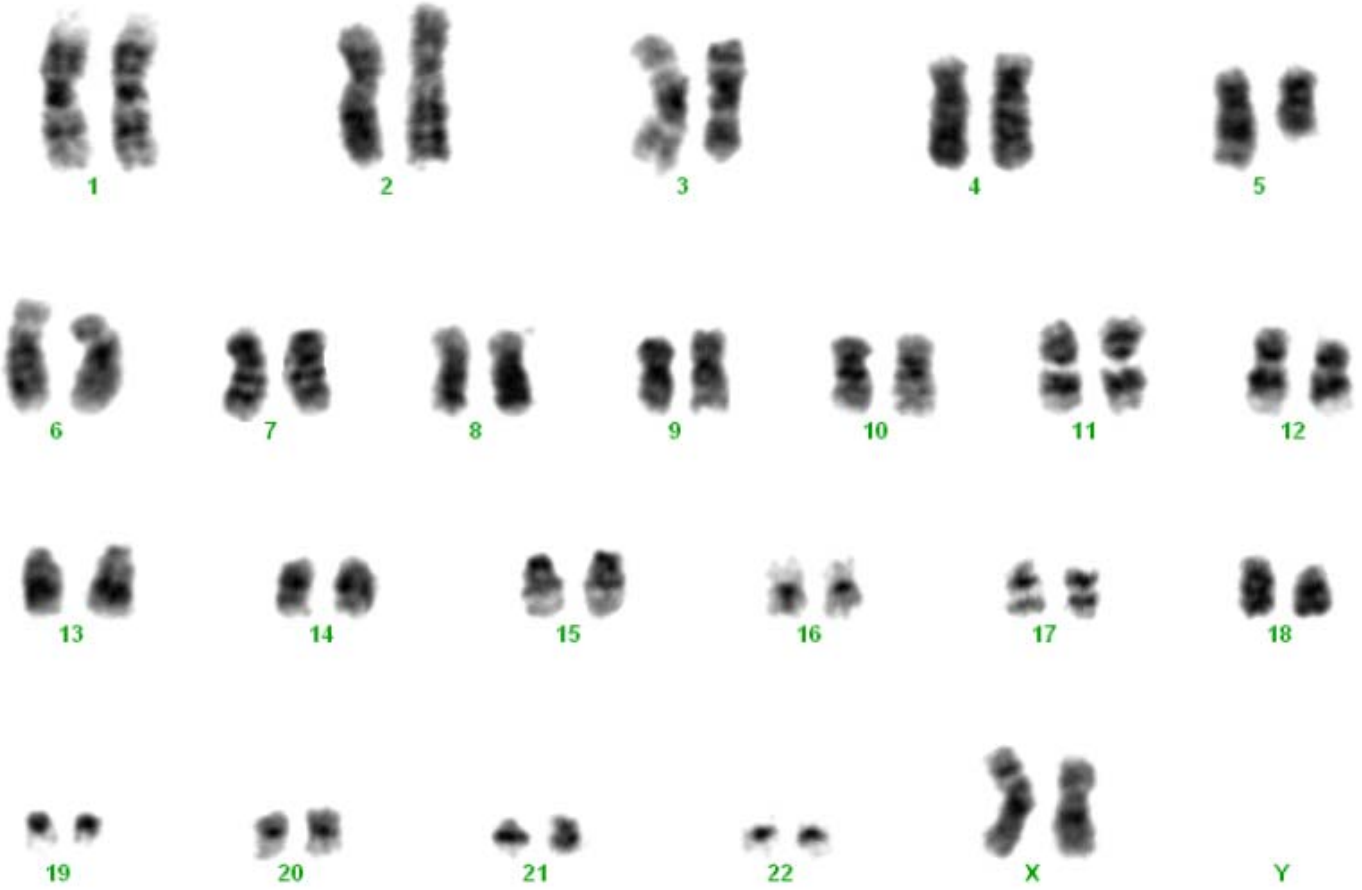




MDS case study

Bone marrow karyotype:

46,XX,del(5)(q13q33)[14]/46,XX[6]



MDS case study

Diagnosis:

Myelodysplastic syndrome with isolated del (5q)

vs

Refractory anemia with excess blasts type I (6% blasts in BM)

Classification of MDS: WHO 2008

Subtipo	Cytopenia	Blasts PB (%)	Blasts BM %	% ring SB in BM	Dysplasia
RCUD	1 or 2 cytopenias	<1	<5	<15	1 cell line
RARS	Anaemia	0	<5	≥15	Erythroid
RCMD	Cytopenia/s	<1	<5 No Auer R.	<15 o ≥15	≥2 líneas
RAEB-1	Cytopenia/s	<5	5-9 No Auer R.	Indifferent	Indifferent
RAEB-2	Cytopenia/s	5-19 (+/- Auer R.)	10-19 +/- Auer R.	Indifferent	Indifferent
MDS associated with isolated del(5q)	Anaemia	<1	<5	Indifferent	Indifferent
Unclassified MDS	Cytopenias	=1	<5		<10% in ≥ 1 cell lines and CG abnormality
ICUS (provisional)	Cytopenias **> 6 months**	0	<5	0	NO displasia NO CG abnormality

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MDS case study

Diagnosis:

Myelodysplastic syndrome with isolated del (5q)

vs

Refractory anemia with excess blasts type I (6% blasts in BM)

Prognosis:

IPSS: intermediate risk-I (score 0.5 for blasts count).

WPSS: high risk (score 3 for WHO subtype and transfusion requirement).

MDS case study

Outcome:

• Initially, she was treated only with supportive therapy.

• On April 2008 the patient started treatment with lenalidomide with no transfusion requirement since then.

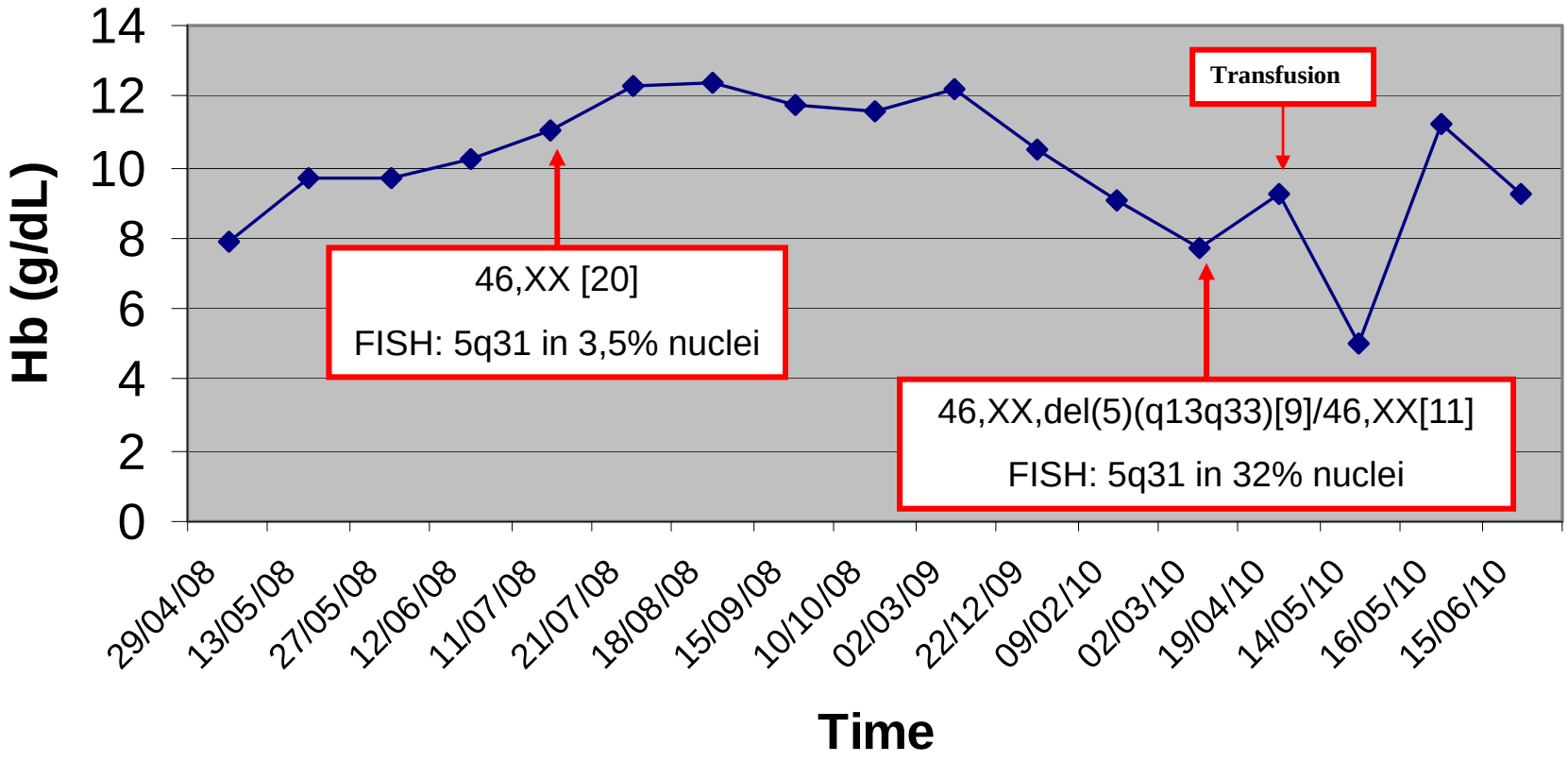
• Bone marrow study in July 2008:

- reduction of dismorphic features (<10% monolobated megakaryocytes).
- karyotype: 46,XX[20].
- FISH: 5q31 in 3.5% nuclei.

• On March 2009, the patient presented exacerbation of the anemia (Hb 7.7 g/dL). Bone marrow study showed:

- Karyotype: 46,XX,del(5)(q13q33)[9]/46,XX[11].
- FISH: 5q31 in 32% nuclei.

MDS case study



MDS case study

MDS associated with isolated del(5q)

MDS characterizaid by:

- Anemia whit or without cytopenias and/or thrombocytosis
- Blasts in bone marrow <5%
- Blasts in PB<1%
- No Auer rods
- Isolated del(5q)

5q- Syndrome

- Clinical picture described by Van den Berghe in 1974
- Higher incidence in older women
- Macrocytic anemia
- Normal o elevated platelet count
- Erythroid hypoplasia
- Blasts in bone marrow <5%
- Blasts in PB<1%
- Isolated del(5q)

MDS case study

- The commonly deleted region in patients with the 5q- syndrome was mapped to a region of 1.5 MB between 5q31 and 5q33

- Sequencing of genes located in these regions did not reveal mutations, suggesting that haploinsufficiency of one or more genes contributes to the development of the disease

GENES IMPLICATED IN THE PATHOGENESIS OF MDS

Genes	Chr. Localitation	% (MDS)
TET2	4q24	25
RPS14	5q32	15
CTNNA1	5q31	15
Mir145/146[a]	5q33	15
AXL1	20q11.21	10
N-RAS	1p13.2	10
P53	17p13.1	5-10
RUNX1/AML1	21q22.3	5-10
NPM1	5q35	5
JAK2	9p24	5
FLT3	13q12	2-5
C/EBPalpha	1913.1	1-4
EVI-1	3q26	2
CBL	11q23.3	1-2
EZH2	20	6

Its presence indicates clonality

Jansen JH. EHA 2010

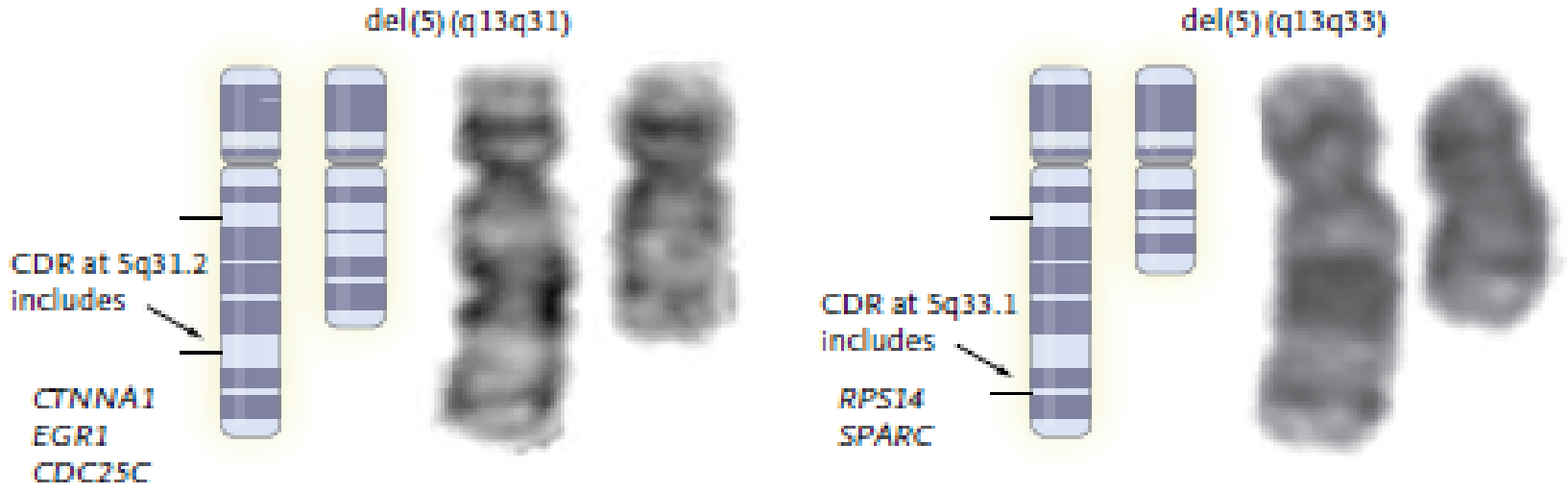


Figure 4. Ideograms and Commonly Deleted Regions Involving Del(5q).

In typical 5q minus syndrome, the commonly deleted region (CDR) has been mapped to 5q33.1 (at right), which contains *SPARC*, the gene encoding osteonectin (secreted protein, acidic, cysteine-rich), and *RPS14*, the gene encoding ribosomal protein S14. In the del(5q)-associated myelodysplastic syndrome–acute myeloid leukemia, the commonly deleted region has been mapped to 5q31.2 (at left), which contains genes encoding catenin alpha 1 (*CTNNA1*), early growth response 1 (*EGR1*), and cell division cycle 25 homologue C (*CDC25C*).

Tefferi A, N Engl J Med 2010