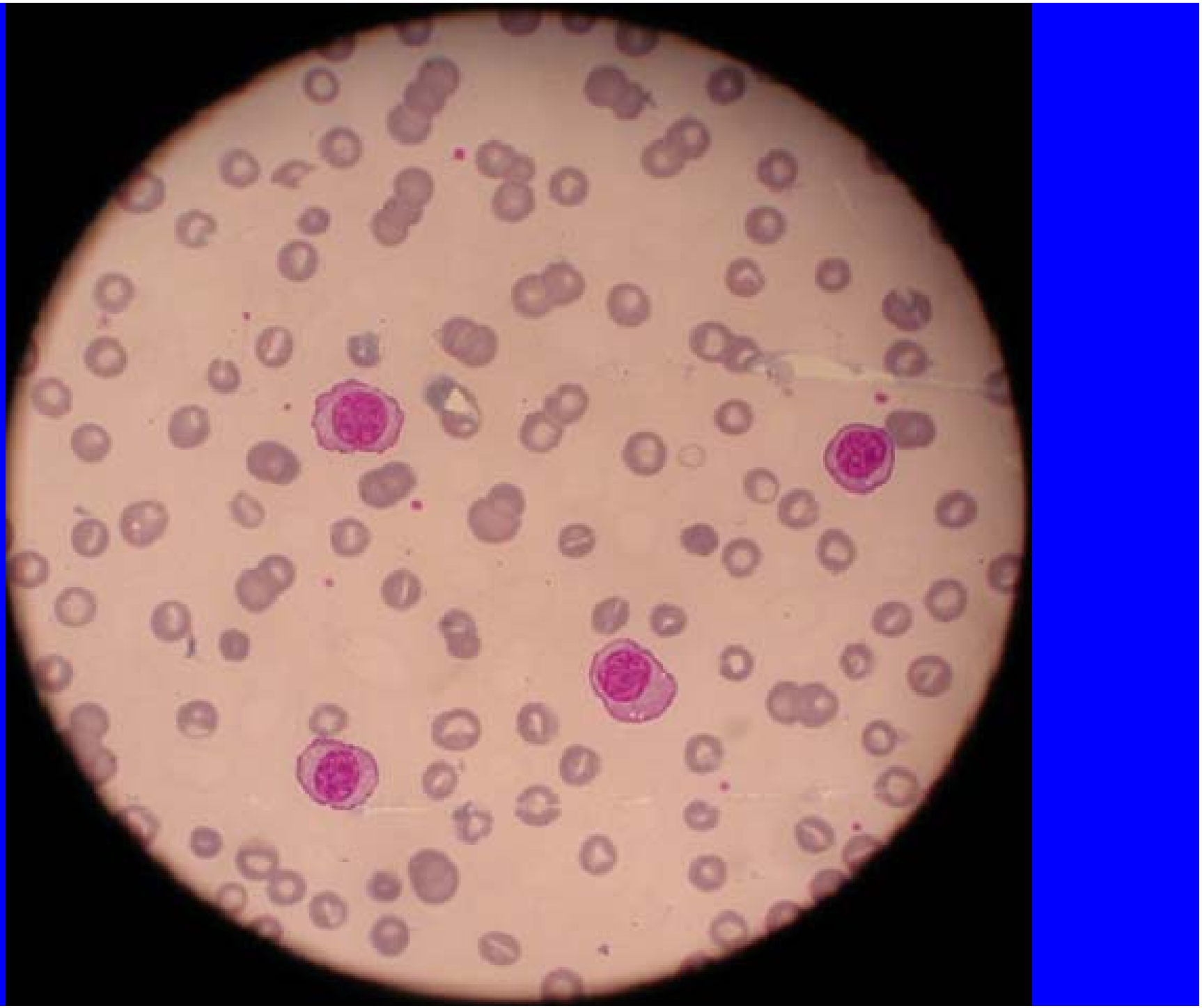
Caso Clinico: Mujer 48 años.

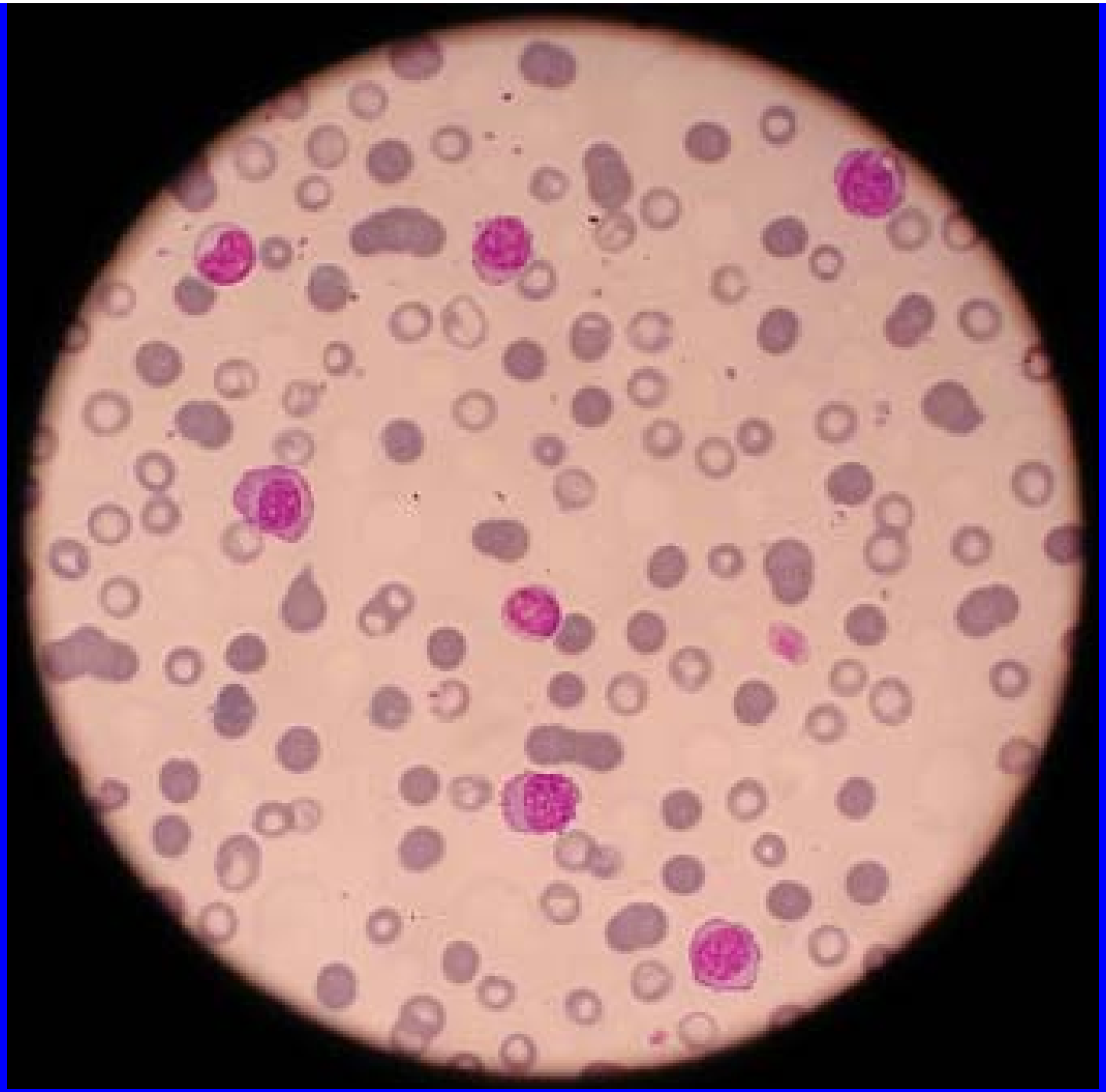
- Fatigabilidad y palidez progresivas, nauseas, dolor en parrillas costales. ExF.palidez.

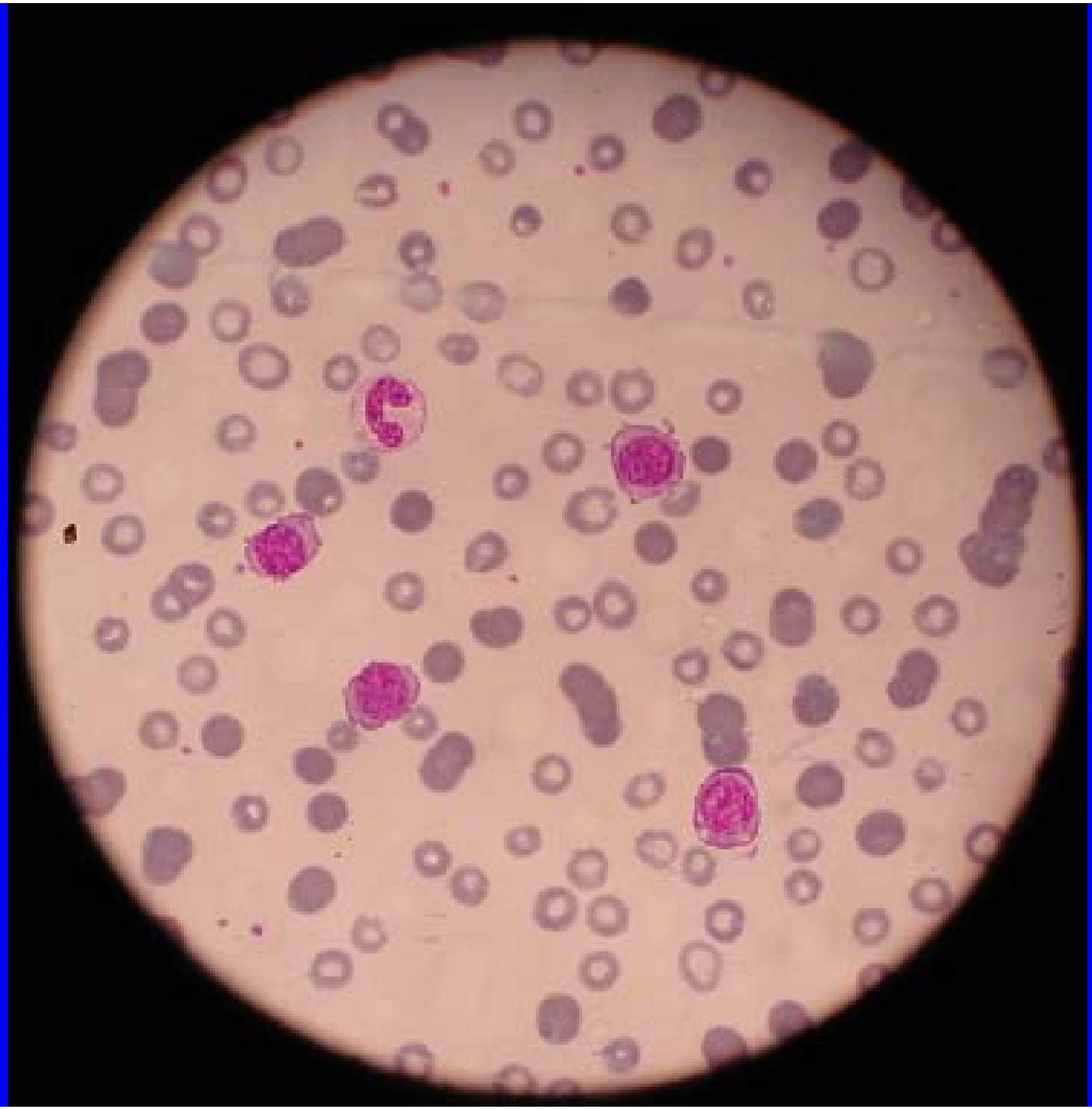
- Hb 5.9 g/dL, Hto 17.7%, Leucocitos 16300/mm3: 80% plasmocitos inmaduros. Plaquetas normales. ESR 140mm/h.
- Paraproteina 7 g/dL, IgG lambda, BJ lambda en orina.
- Creatinina 1.3 mg/dL, B2microglobulina 9 mg/dL, CRP 1.9 mg/dL, Ca 10.2 mg/dL, Albumina 2.5 g/dL, ac. Urico 8.7 mg/dL (N< 6.2) LDH normal. IgE total normal.

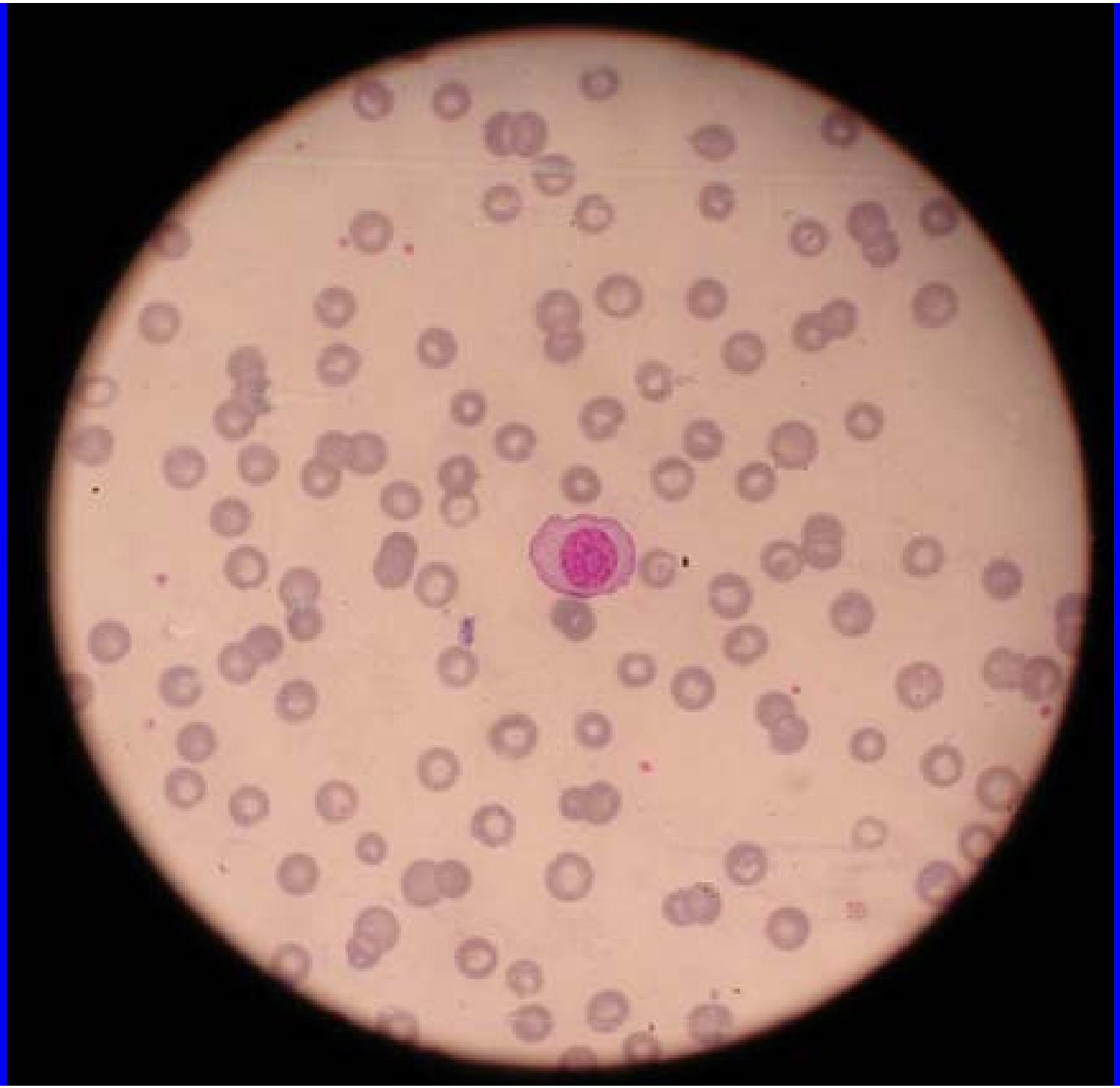
- Mielograma: 90% plasmocitos inmaduros.
- FISH interfase del Cr13 MOsea: 8.5% (limite de significacion).
- Rx Oseas: Osteolisis multiple en craneo y femures. Osteopenia en columna y costillas
- Citometria MO : 70%: CD45-,CD19-,CD38+,CD56+/-,CD20+,CD22-,CD23-,sIg-

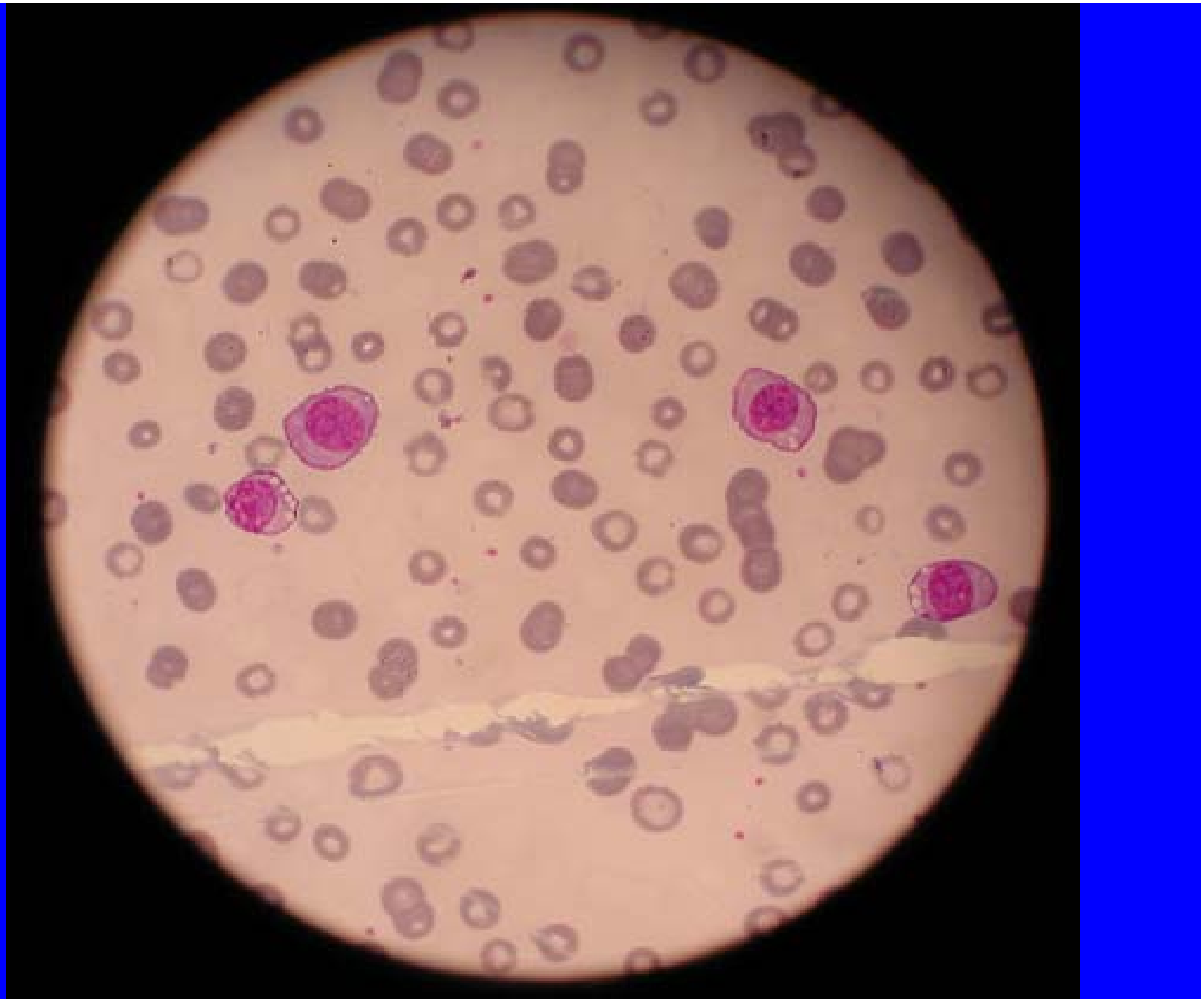
- Dg: Mieloma IgG lambda, BJones lambda+,IIIA(DS),IPSS III.
  Leucemia Plasmocitica primaria.

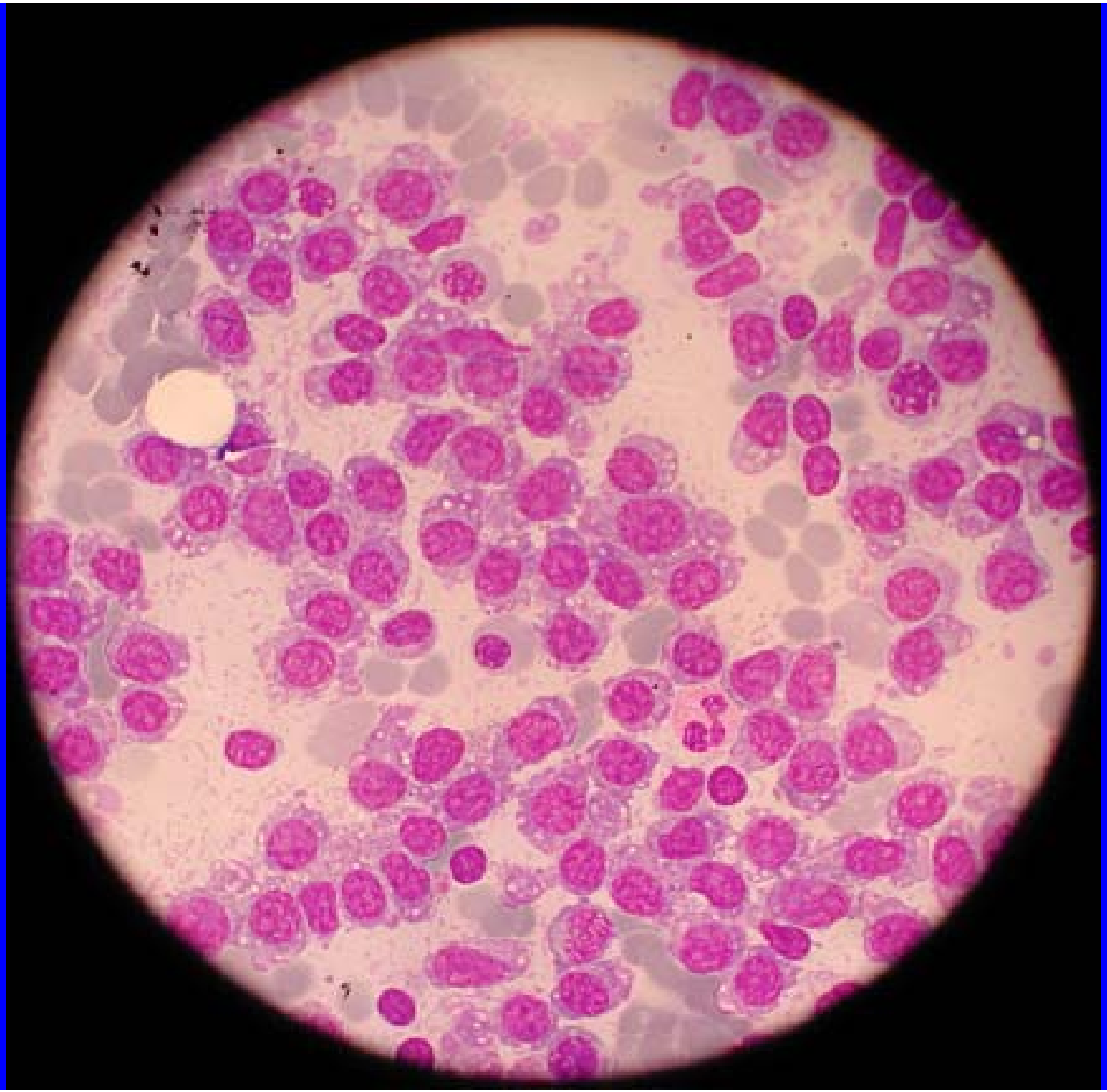


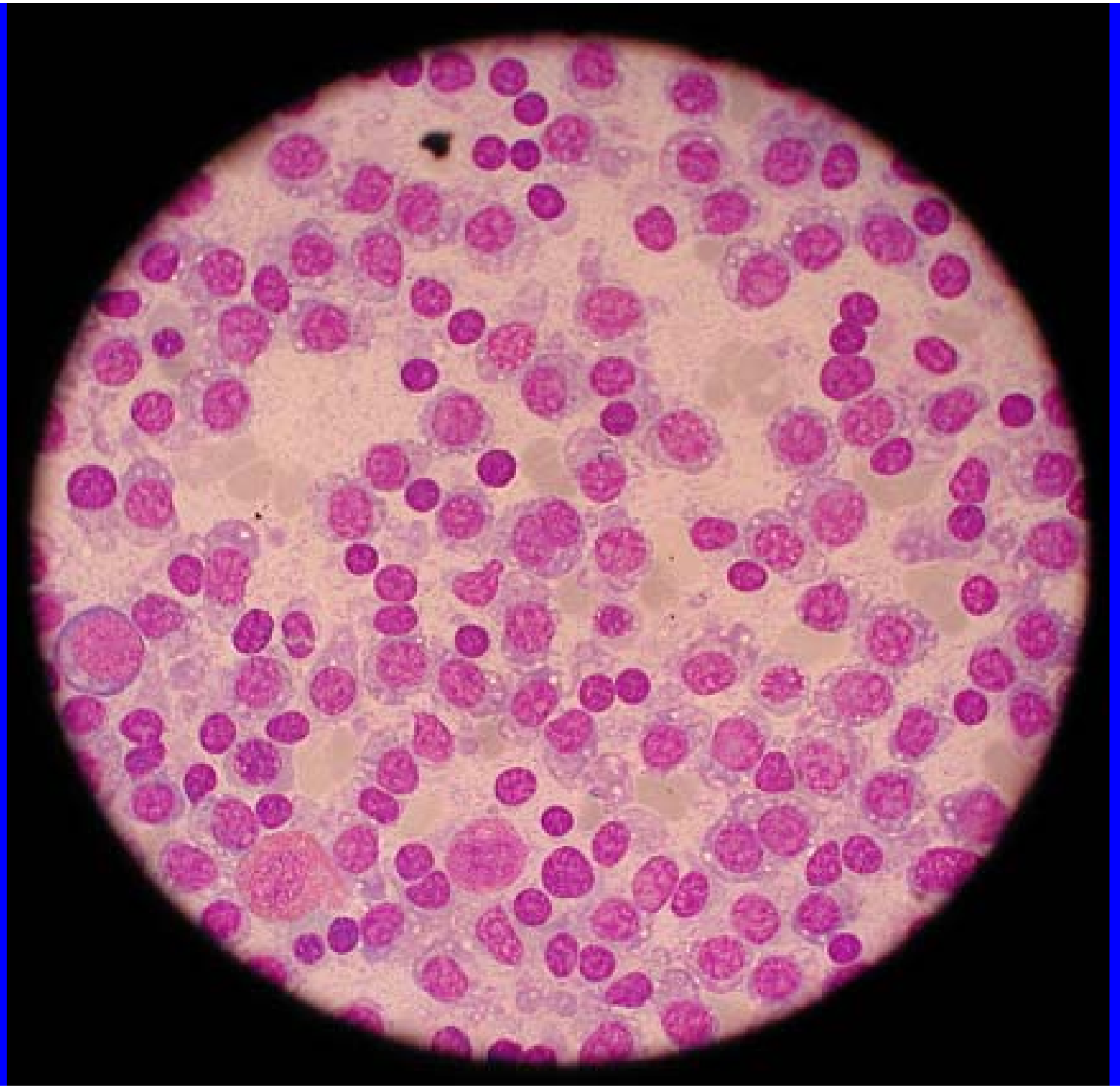












PLASMA CELL LEUKEMIA (PCL)

(Mayo Clinic 1987): 43 patients.

58% Primary PCL

42% Secondary PCL

(N.P. Kyle Am J Med 1987, 83(6): 1062)

Pronostico de la Leucemia Plasmocitica primaria:

- 1.- Muy malo, similar a Leucemia Plasmocitica secundaria.
- 2.- Mejor que la Leucemia Plasmocitica secundaria.
- 3.- Peor que un Mieloma Multiple sin compromiso de sangre periferica.
- 4.- 2 y 3.
- 5.- 1 y 3.

Table 1. Clinical and Biologic Data for the MM and Primary PCL Cases

Parameter	MM (n = 664)	PCL (n = 26)	*P*
Age ≥65 years (median)	65.0% (68 ± 10)	50.0% (66 ± 10)	.12216
Male	53%	46%	.49355
ECOG ≥2	33%	58%	.01993
Extramedullary involvement	4%	23%	.01407
Bone scale ≥2	67%	48%	.17767
Hemoglobin <8.5 g/dL	31% (10.1 ± 2.7)	54% (8.2 ± 2.3)	.01451
Platelets <100 × 10^9/L	9% (209 ± 83)	48% (123 ± 88)	<.00001
Stage III	59%	92%	.00093
BM PCs ≥40%	43%	92%	<.00001
LDH ≥460 U/L	9%	48%	<.00001
Albumin <3.5 g/dL	46%	52%	.58077
Type of monoclonal component			
IgG	55%	54%	.00027
IgA	30%	4%	
IgD	1%	8%	
Bence Jones	13%	31%	
Nonsecretory	1%	4%	
Monoclonal proteinuria	40%	68%	.00068
Creatinine ≥2 mg/dL	21%	44%	.00634
Calcium ≥11.0 mg/dL	20%	48%	.00071
β_2-Microglobulin ≥6 mg/mL	27%	65%	.00012
C-reactive protein ≤6 mg/dL	18%	61%	.00015
S-phase PCs ≥3%	32%	71%	<.00001
S-phase residual BM cells <4.5%	26%	83%	<.00001
Global response	63%	38%	.01330
OR and complete response	40%	29%	.27427

Table 3. S-Phase Cells and DNA Ploidy by Flow Cytometry in MM and Primary PCL

Parameter	MM (n = 404)	PCL (n = 22)	*P*
S-phase $CD38^{+++}$ (PCs)	2.9%	4.5%	.0038
S-phase $CD38^{-/+}$ (residual normal cells)	7.4%	2.7%	<.0001
DNA index			
<1	1.5%	4.8%	
=1	42.5%	95.2%	<.0001
>1	56.0%	0%	

Table 4. FISH Results Using Centromeric Probes in 13 Primary PCL Cases and 56 MM Cases

Chromosome	PCL Patients (n = 13)		MM Patients (n = 56)	
	Monosomy	Trisomy	Monosomy	Trisomy
1	14%	43%	3%	37%
3	0%	0%	0%	31%
6*	0%	0%	0%	32%
7	0%	0%	0%	28%
8	0%	0%	5%	8%
9*	0%	0%	0%	52%
10	0%	0%	0%	8%
11	0%	0%	3%	33%
12	0%	0%	0%	3%
13*	86%	0%	26%	0%
15	0%	0%	0%	48%
17	0%	0%	0%	22%
18	0%	43%	6%	24%
X	25%†	0%	32%†	6%‡
Y	0%	0%	0%	0%

Results are expressed as a percentage of trisomic/monosomic cases for MM patients.

*Chromosomes in which the incidence of numeric aberrations was different between PCL and MM ($P < .05$).

†Calculated only in females (0% in males).

‡Calculated only in males (0% in females).

Table 2. Immunophenotypical Results in MM and Primary PCL

Immunophenotype	MM	PCL	*P*
BB4+	99%	100%	.90482
CD10+	6%	6%	.72808
CD13+	31%	23%	.40456
CD15+	7%	8%	.60321
CD20+	17%	50%	.00139
CD38+	100%	100%	—
CD56+	70%	45%	.02217
CD9+	78%	46%	.01984
CD117+	43%	0%	.03646
DR+	56%	21%	.01549

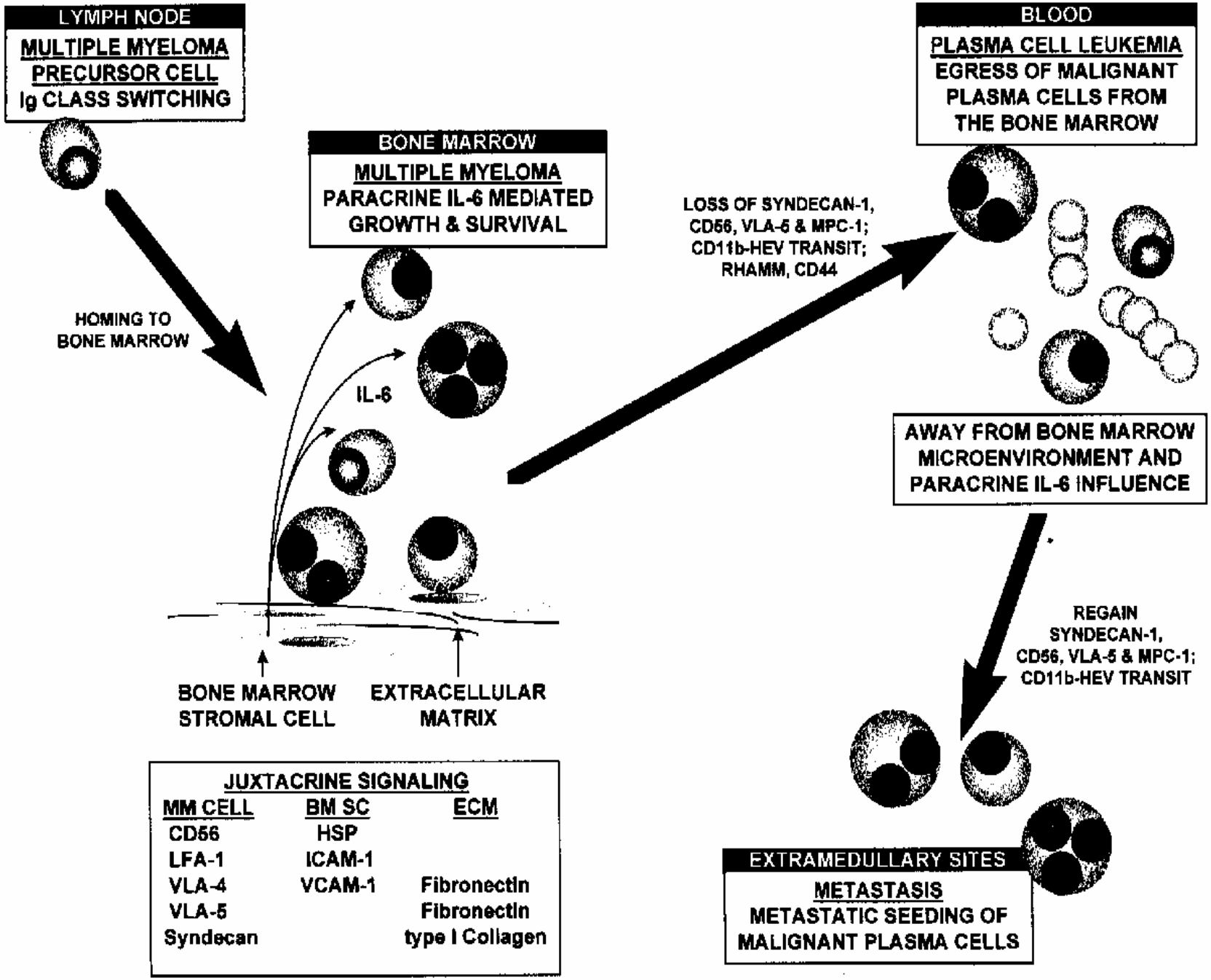


Figure 2. *See legend on opposite page*

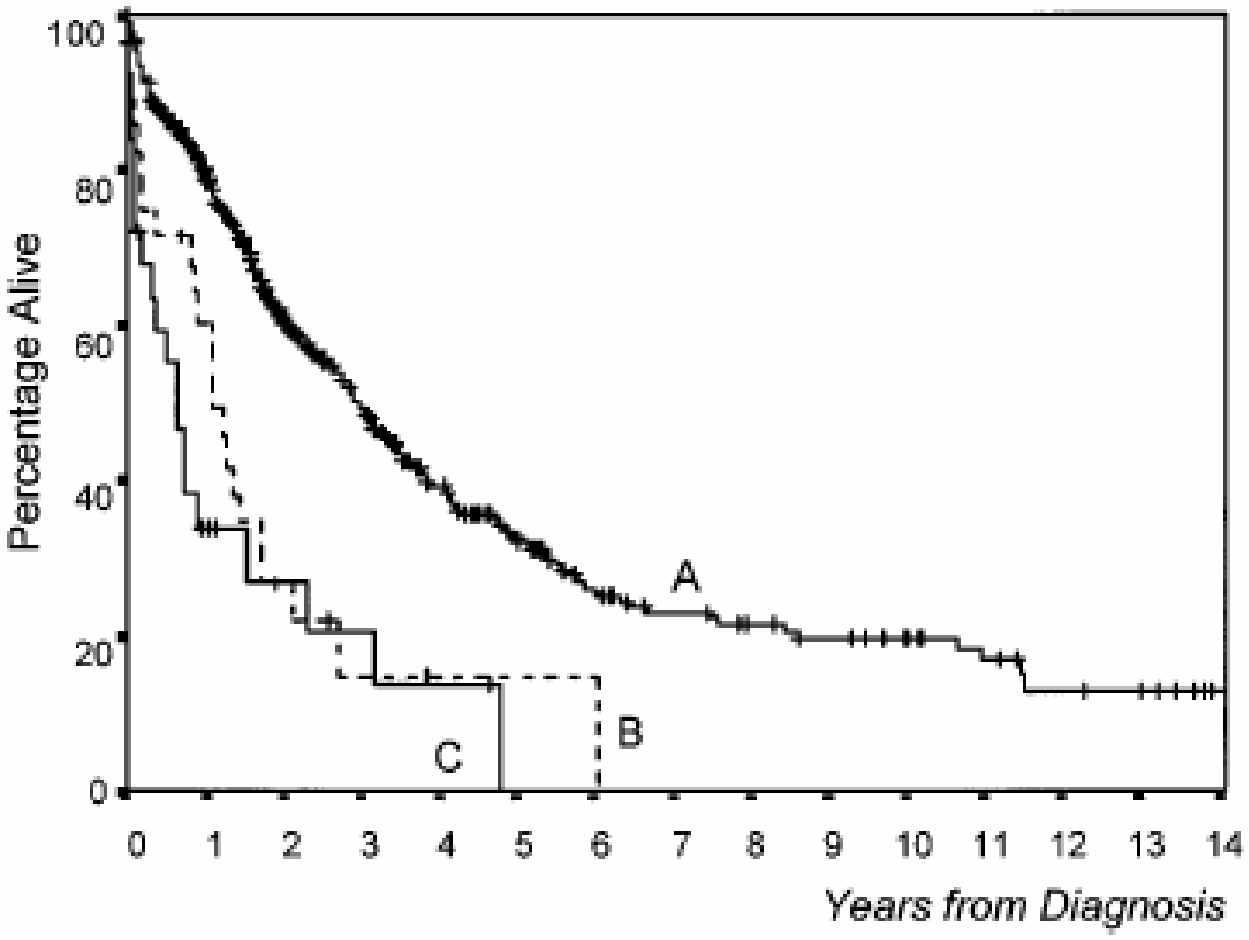


Fig 1. Survival differences between MM and primary PCL: (A) 664 MM patients (mean survival, 36 months), (B) 28 MM patients with poor prognostic features (S-phase PCs > 3%, β_2-microglobulin > 6 mg/mL, and stage III) (mean survival, 13 months), and (C) 26 PCL patients (mean survival, 8 months). 664 MM versus 26 PCL, $P < .0001$; 28 poor-prognosis MM versus 26 PCL, $P = .2989$.

Table 5. Analysis of Prognostic Factors for Overall Survival in PCL Patients

Variable	No. of Patients	Median Survival (d)	Univariate *P*	Multivariate *P*
β_2-Microglobulin				
<6 mg/L	8	560	.0252	.0037
≥6 mg/L	15	138		
S-phase plasma cells				
<4.5%	12	266	.0459	.0200
≥4.5%	9	184		
ECOG scale				
<2	11	1,157	.0014	NS
≥2	15	138		
Protein C reactivity				
<6 mg/dL	7	1,157	.0051	NS
≥6 mg/dL	11	62		
Platelets				
$<100 \times 10^9$/L	12	116	.0014	NS
$\leq 100 \times 10^9$/L	13	560		
Therapy				
Polychemotherapy	14	560	.0137	NS
MP	12	116		

Tratamiento:

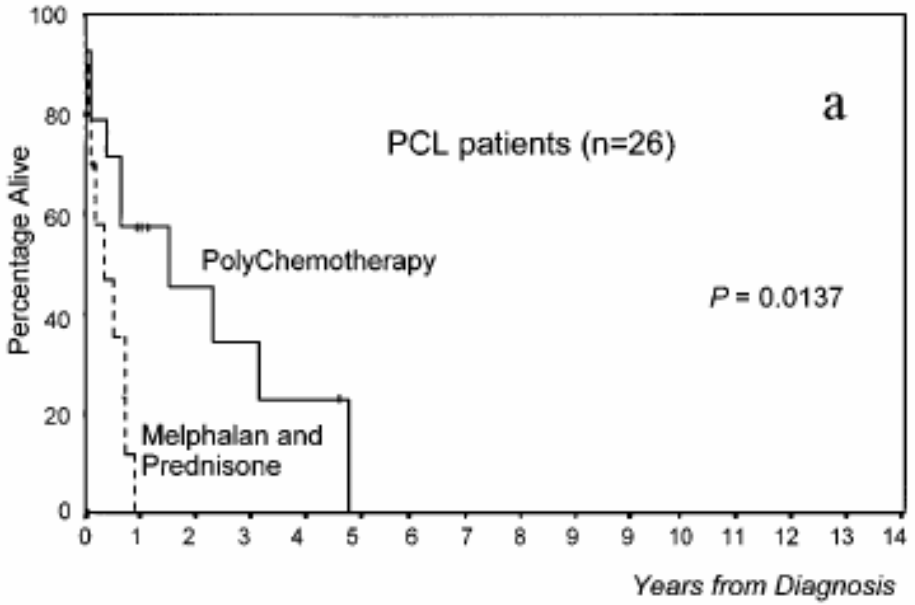
- 1.-Melphalan + Prednisona.
- 2.- VAD y Tx autologo de P.Hematopoyeticos (TxAPH).
- 3.- Thalidomide + Dexametasona y TxAPH.
- 4.- DT-PACE y TxAPH.
- 5.- HyperCVAD.
- 6.- Quimioterapia o Thalidomide+Dexa seguido mini TxalloPH.
- 7.- Combinaciones con Bortezomib.

PLASMA CELL LEUKEMIA (PCL)

(Mayo Clinic 1987): 43 patients.

	x O.S.
58% Primary PCL	6.8 m
42% Secondary PCL	1.3 m

(N.P. Kyle Am J Med 1987, 83(6): 1062)



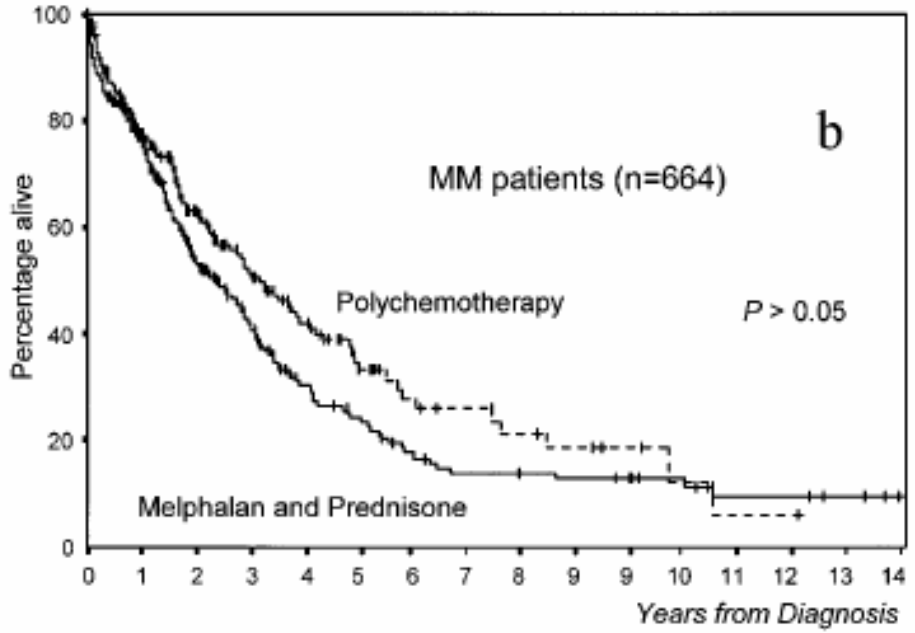


Fig 2. Survival according to treatment in (a) 26 primary PCL patients and (b) 664 MM patients.

Table 2. Case reports of high dose chemotherapy with autologus hematopoietic stem cell support in plasma cell leukemia (PCL)

Reference	Number of patients	Age and sex	Myeloablative regimen	Outcome
44	1	34M	Melphalan 140mg/m²	In renussion at 1 year
45	1	24F	Melphalan 180 mg/m², TBI	In remmission at 23 months
46	1	44M	Melphalan 140mg/m², TBI	Alive with persistent monoclonal component at 22 months
47	3	58 years old (median), all women	Melphalan 200mg/m²	2 patients alive at 14 and 26 months, one patient dead 3 months after transplantation

TABLE III. Published Data on Patients With PPCL Who Underwent BMT or SCT

Case no.	Age at diagnosis	Transplant type	Survival after diagnosis (months)	Year of publication	Ref. no.
1	34	Autol. BMT	30[a]	1983	16
2	20	Allog. BMT	3	1989	17
3	42	Allog. BMT	13[a]	1989	18
4	44	Autol. SCT	106+[b]	1996	20
5	58[c]	Autol. SCT	83[d]	1997	21
6	58[c]	Autol. SCT	46[d]	1997	21
7	58[c]	Autol. SCT	11[d]	1997	21
8	58	Autol. SCT	101+[e]	1998	22
9	44	Allog. BMT	22	1999	23
10	68	Autol. SCT	22	1999	23
11	62	Autol. SCT	36[a]	1999	24
12	45	Autol. SCT	18[a]	1999	1
13	NR	Autol. SCT	20	2001	25
14	NR	Allog. BMT	27	2001	15
15	NR	Autol. BMT	7	2001	15
16	NR	Autol. SCT	40.8	2002	6
17	NR	Allog. SCT	NR[f,g]	2002	6
18	61	Autol. SCT	22[a]	2002	26
19	31	Autol. SCT	72[a]	2002	27
20	44	Autol. SCT	9	2002	28
21	55	Autol. SCT	33[h]	2002	29
22	53	Autol. SCT	19[a]	2003	19

[a]Final survival may be longer as no follow-up after publication is available.
[b]Personal communication, P. Musto.
[c]Median is given for 3 cases.
[d]Personal communication, S. Hovenga.
[e]Personal communication, S. Sica.
[f]NR, not reported.
[g]Died 15 days after transplant.
[h]Personal communication, F. Cremer.

Tratamiento:

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- 3.- Thalidomide + Dexametasona y TxAPH.
- 4.- DT-PACE y TxAPH.
- 5.- HyperCVAD + o – TxAPH.
- 6.- Quimioterapia o Thalidomide+Dexa seguido de mini TxalloPH.
- 7.- Combinaciones con Bortezomib. + o - TxAPH

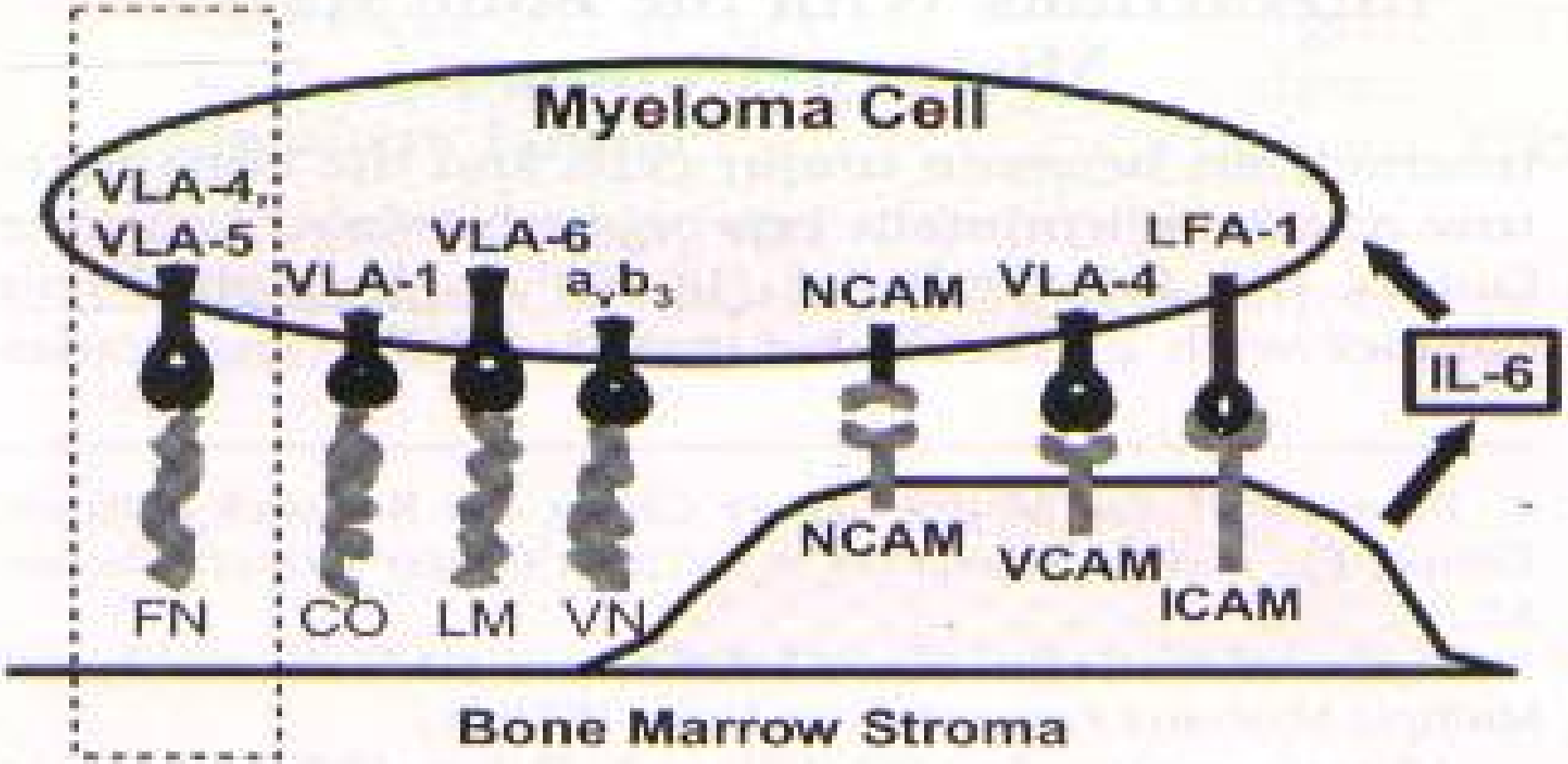


Figure 2. Cell–cell and cell–matrix interactions in the bone marrow microenvironment. CO, collagen; FN, fibronectin; ICAM, intercellular adhesion molecule; IL-6, interleukin-6; LFA, leukocyte function-associated antigen; LM, laminin; NCAM, neural cell adhesion molecule; VLA, very-late antigen; VN, vitronectin. Reproduced from Shain KH et al.[5]

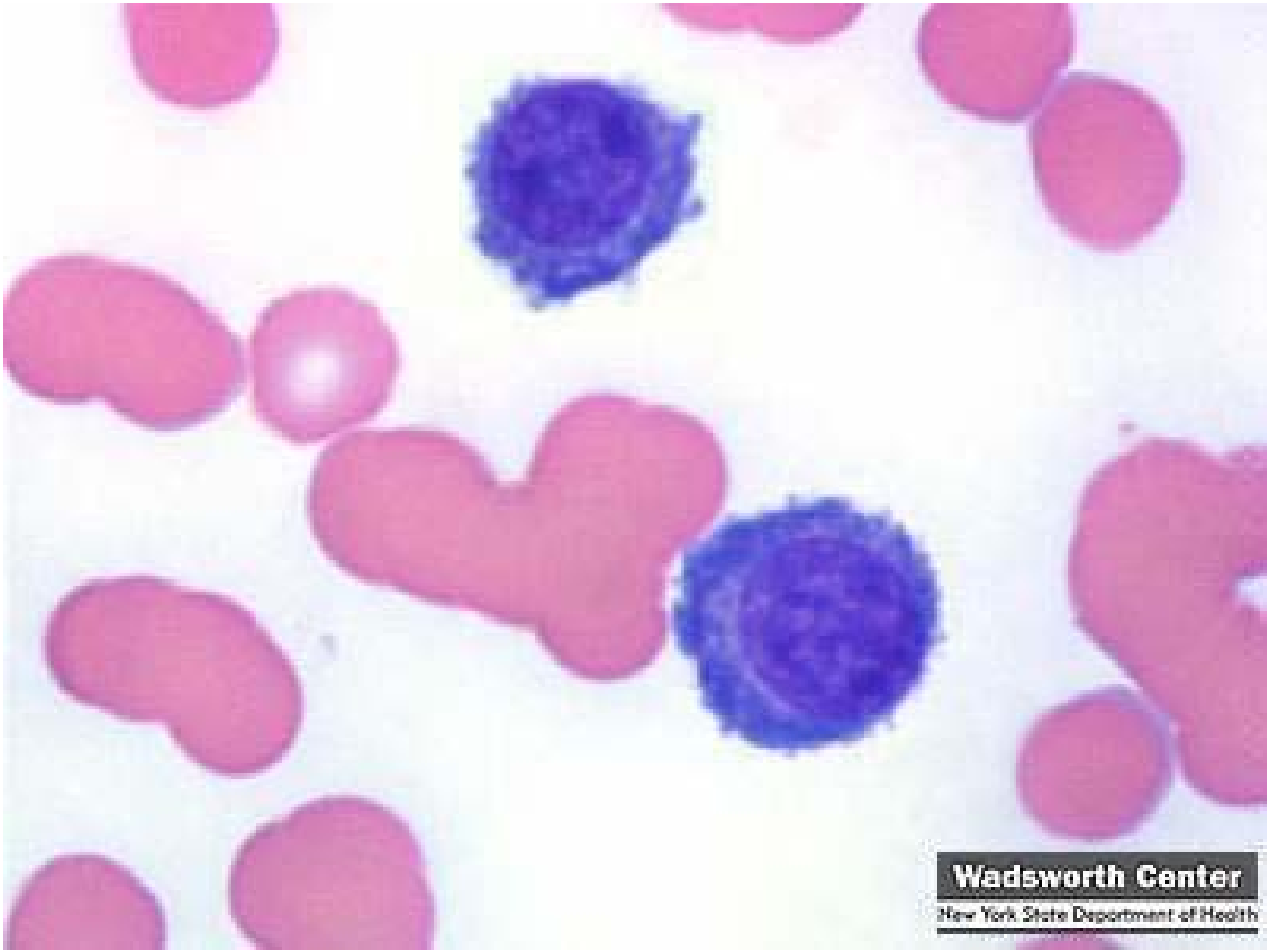
Paciente GRF: MW+Amiloidosis primaria

	K libre (mg/L)	L libre (mg/L)	Relacion K/L
30-04-2005	10.2	110.0	0.0927
Tx APHMel140.18/07/05			
29-07-2005	8.09	49.7	0.163
01-08-2005	9.62	62.6	0.154
17-08-2005	8.1	35.0	0.231
26-08-2005	13.9	25.1	0.554
13-09-2005	10.6	19.4	0.546
04-10-2005	6.98	19.5	0.358
25-10-2005	8.61	19.8	0.435
22-11-2005	12.4	22.3	0.556
31-03-2006	< 5.40	19.1	< 0.28
10-04-2006	8,17	9,24	0,884
18-08-2006	9,56	12,7	0,753
V REF	3.3-19.4	5.7-26.3	0.26-1.65

FGC 55a. XX	K libre	L libre	Relacion K/L
MM Bence Jones K. suero	(mg/L)	(mg/L)	
02-02-2006 ThalDex	> 162	9.1	> 17.8
07-02-2006 ThalDex	> 162	14.7	> 11
17-02-2006 ThalDex	> 162	11.7	> 13.8
08-03-2006 VelcadeDex	61.3	21.2	2.89
21-03-2006 VelcadeDex	60.5	22.3	2.71
27-03-2006 VelcadeDex	34.2	15.9	2.15
25-04-2006 VelcadeDex	37	43,2	0,856
18-05-2006 VelcadeDex	15,3	18,1	0,845
13-06-2006 VelcadeDex	16,2	15,8	1,03
14-07-2006 VelcadeDex	19,6	18,4	1,07
01-09-2006 VelcadeDex	14,8	14,4	1,03
V REF	3.3-19.4	5.7-26.3	0.26-1.65

Table I. Case series of chemotherapy in PCL

Reference	Number of patients	Age and sex	Regimen	Outcome
1	27	Median age 57 years	Alkylating agent and steroids (10 patients) VAD or cyclophosphamide/ etoposide (CE) (17 patients)	Median survival 12 months for entire group. Median survival 2 months and 20 months for alkylating agent plus steroid and CE group respectively
3	15 (8 with primary PCL and 7 with secondary)	Median age 58 years 7M and 8F	Valious, mostly cyclophosphamide and prednisone-based	Median survival 2 months for the entire group. Median survival 10 and 1 month for the primary and secondary PCL groups respectively.
4	25 patients with primary PCL	Median age 53 years 15M and 10F	15 patients melphalan, 6 patients multiple agents The rest did not receive treatment	Median survival 8.7 months and 7.3 months for the melphalan and the multiple agents group respectively.
4	18 patients with secondary PCL	Median age 61 years 11M and 7F	7 patients melphalan and 2 patients multiple agents The rest did not receive treatment	Median survival 3.5 and 6 months for the melphalan and the multiple chemotherapy group respectively


Wadsworth Center
New York State Department of Health