CASO 2

122º Reunión Territorial Valenciana de la Sociedad Española de Anatomía Patológica

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VARON, 79 AÑOS

APP:
-MIELOMA IGA en terapia con lenalidomida.
-Hiperparatiroidismo primario.
-ERC estadio 3ª

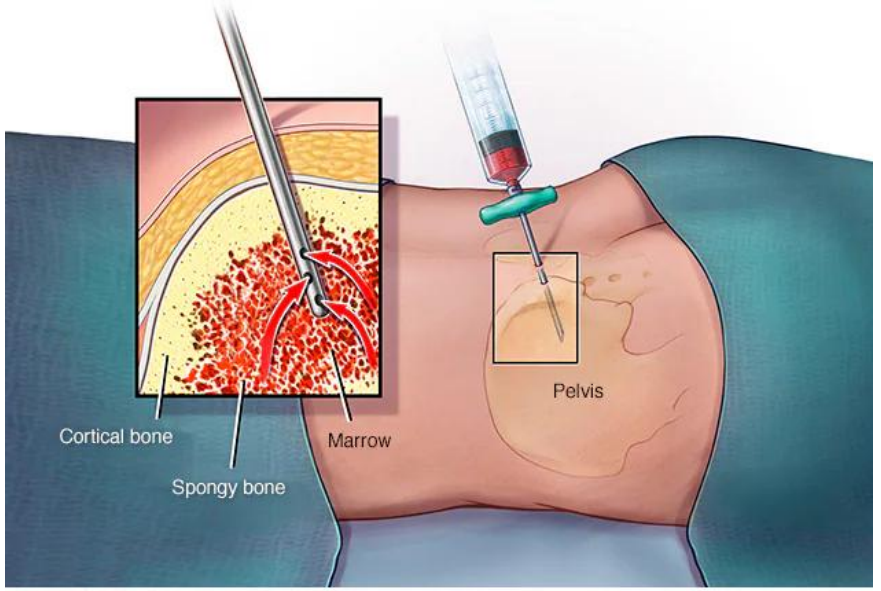
Historia clínica:
-Acude a urgencia por astenia de 4 días, fue intervenido de paratiroidectomía hace 5 días.

-Hemograma:
*Eritrocitos: 2,33 x10e3
*Leucocitos: 1,73 x10e3
*Plaquetas: 58 x10e3
*Hb: 8,1 g/dL

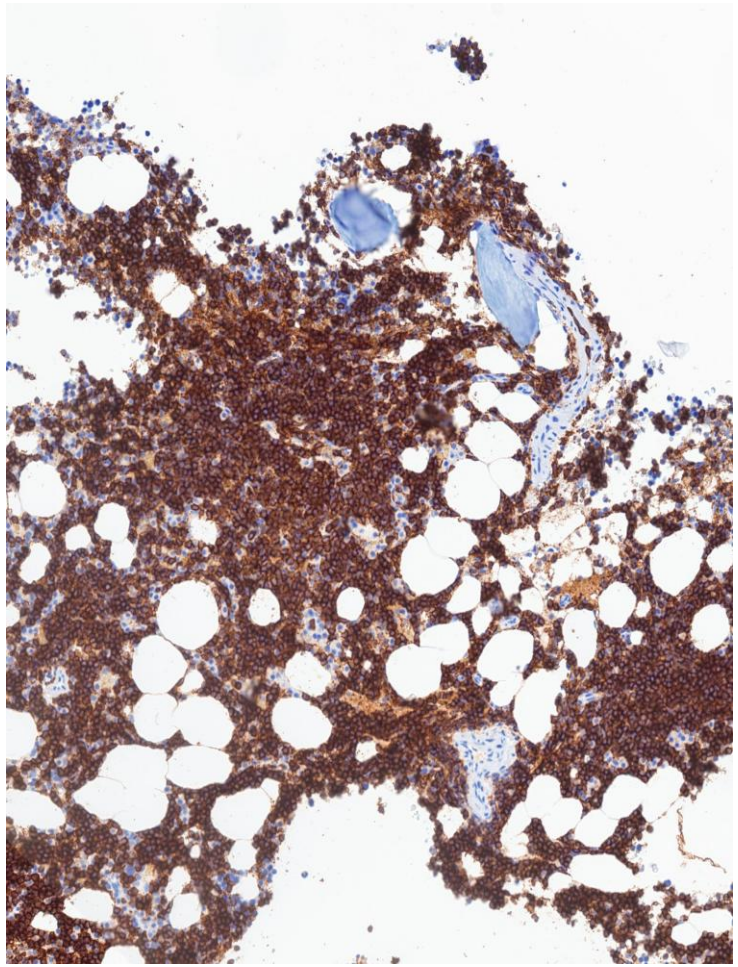
Pancitopenia

-Tiene historia de citopenias persistentes tras 2 dosis de Daratumumab.

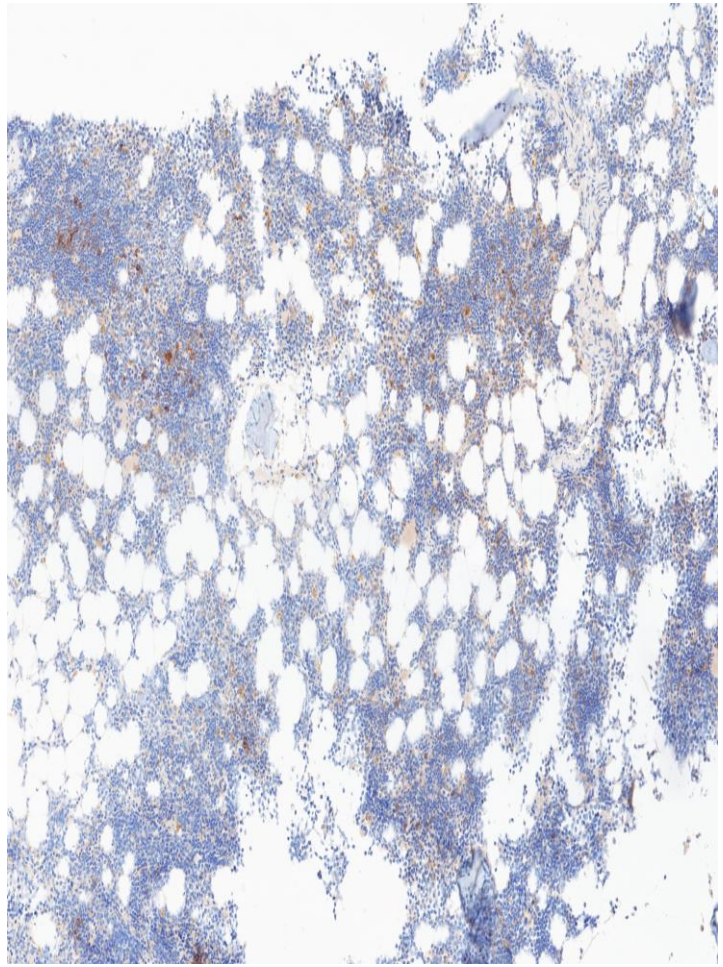
-Se realiza BMO:
https://pathpresenter.net/public/display?token=d36d1c03



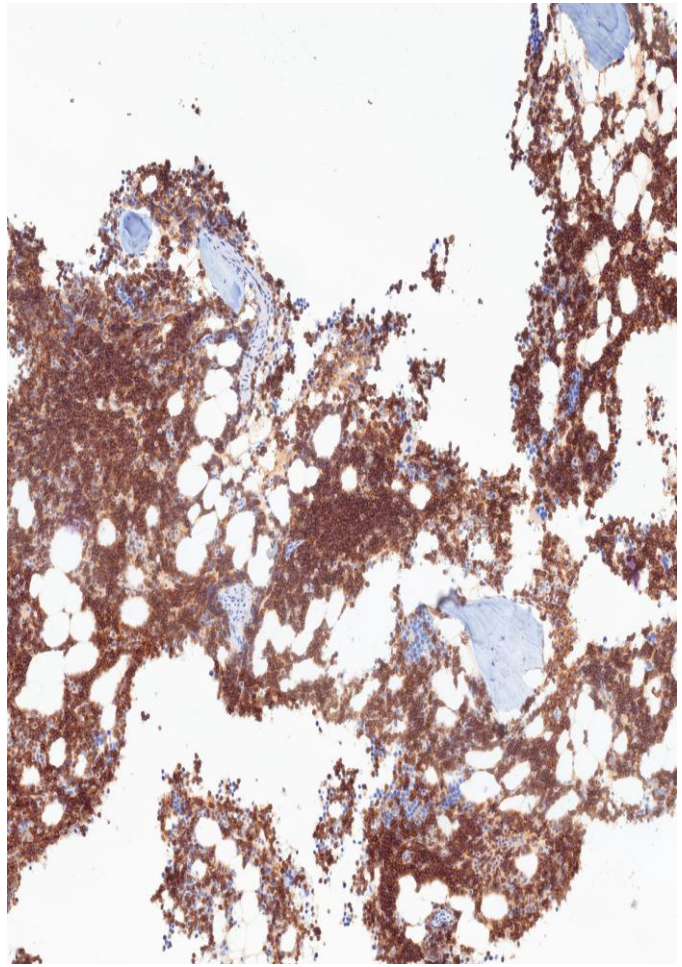
CD20



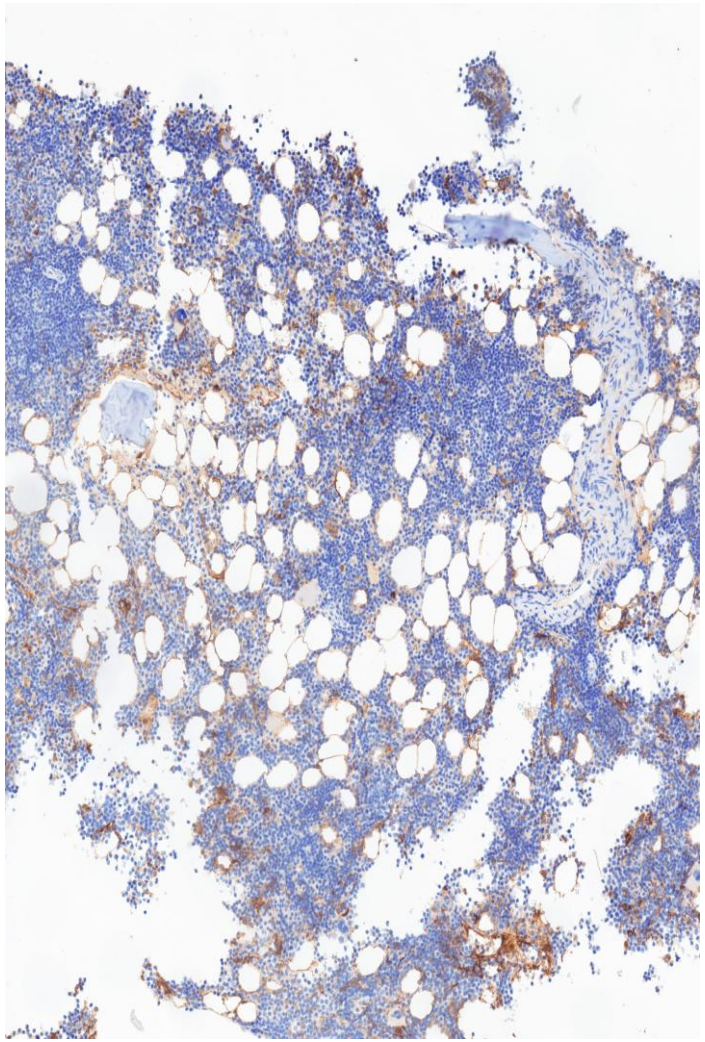
CD23



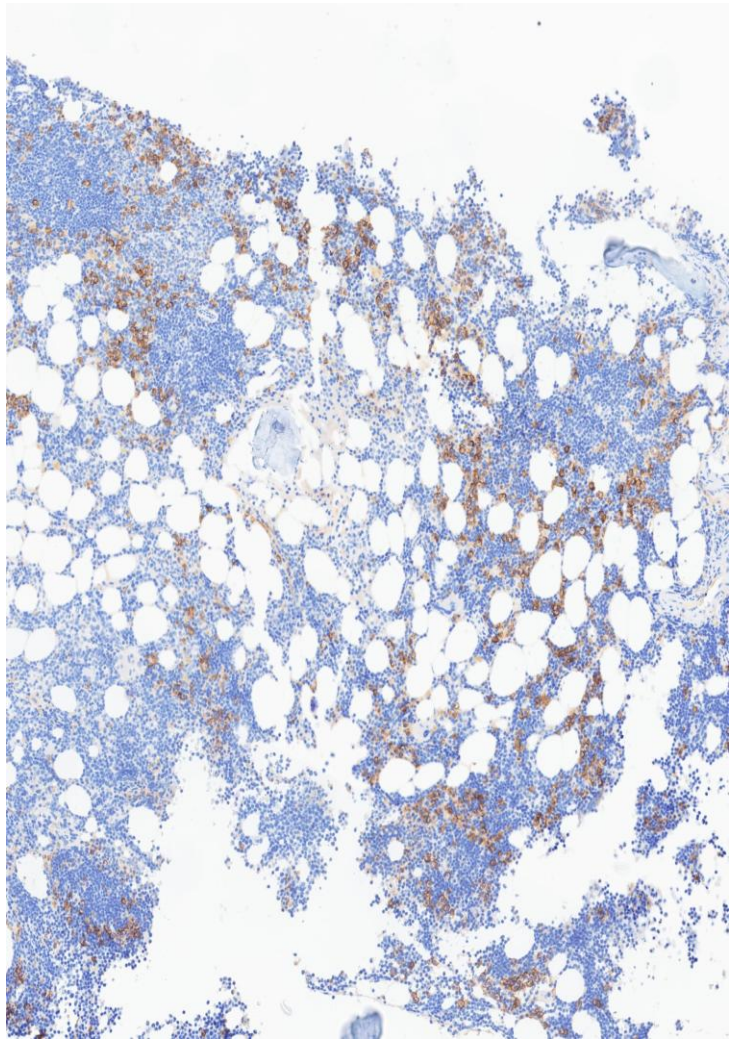
CD5



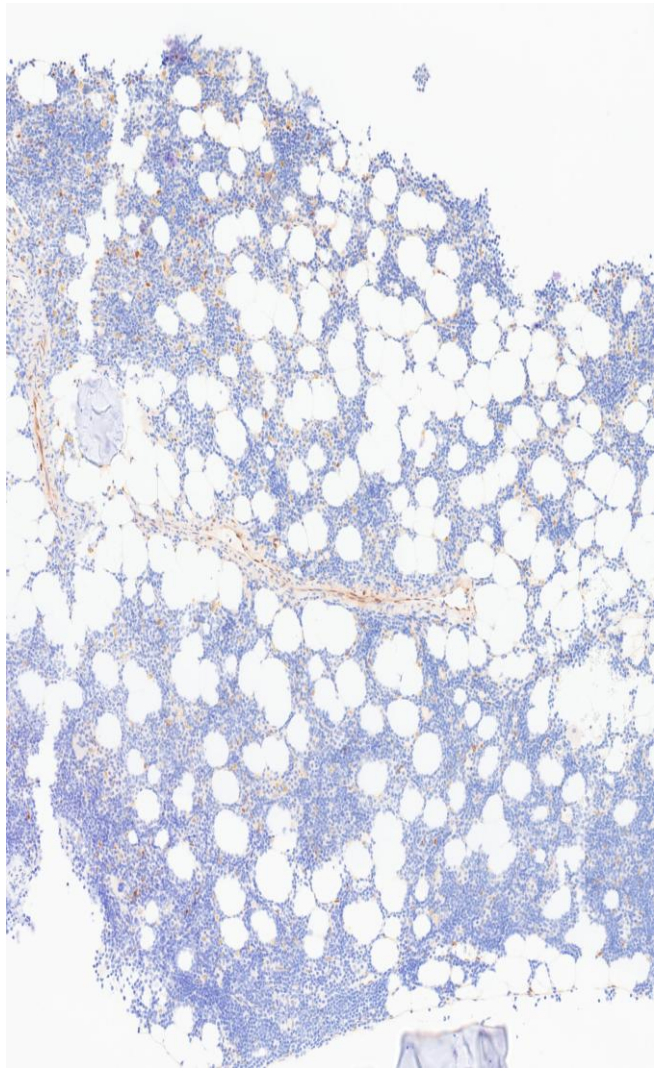
CD10



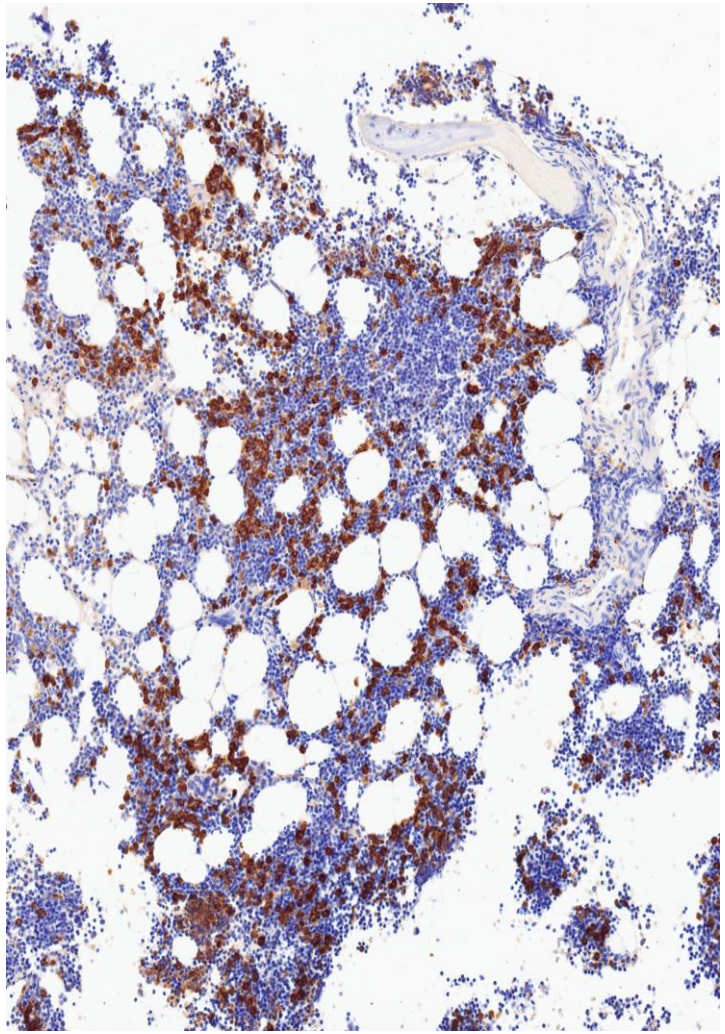
CD138



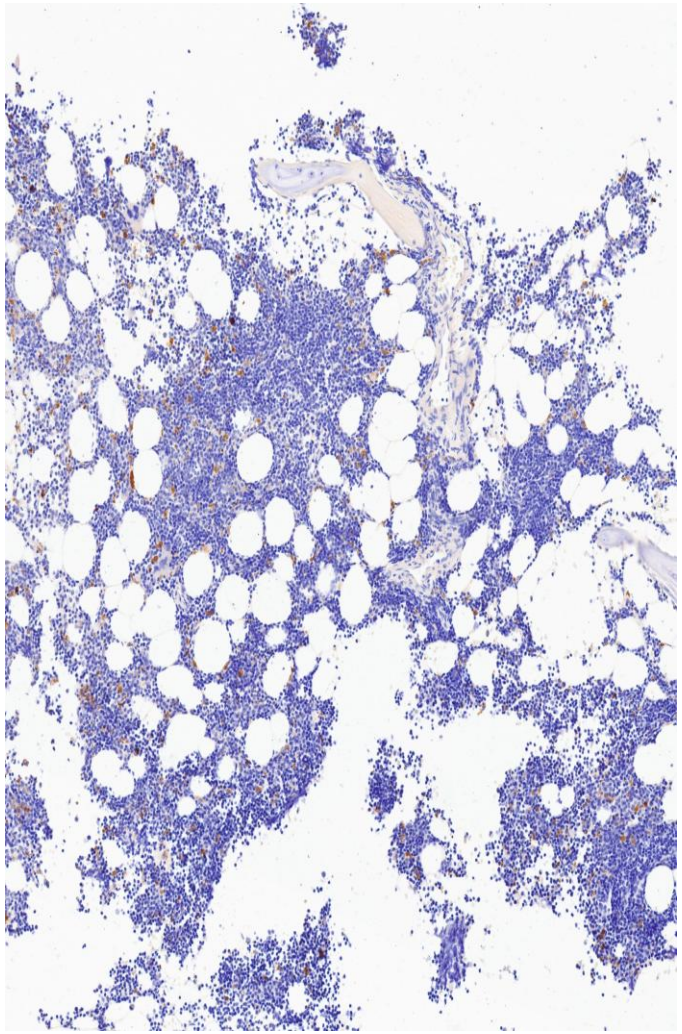
CICLINA D1



KAPPA



LAMBDA



Dx: LLP/LLC concomitante con Mieloma Múltiple

Característica	LLC / LLP (CLL / SLL)	Mieloma Múltiple
Célula de origen	Linfocito B maduro CD5+ CD23+	Célula plasmática neoplásica
Fenotipo IHQ / FC	CD19+, CD20 (bajo), CD5+, CD23+, cadenas ligeras kappa/lambda restringidas.	CD138+, CD38++, MUM1+, CD56 (variable), ciclina D1 (si t(11;14)), cadenas ligeras restringidas
Genética típica	Del(13q), del(11q), del(17p)/TP53, trisomía 12	t(11;14), t(4;14), t(14;16), del(17p), hiperdiploidía
Manifestaciones clínicas	Linfocitosis, adenopatías, esplenomegalia, citopenias por infiltración o autoinmunidad	CRAB: hipercalcemia, insuf. renal, anemia, lesiones óseas líticas
Proteína monoclonal	Habitualmente ligera (pico pequeño), hipogammaglobulinemia	Pico M claro (IgG, IgA, cadenas ligeras)
Morfología típica	Linfocitos pequeños, escaso citoplasma, núcleos redondos, centros proliferativos con paraimputación	Plasmocitos maduros/atípicos, núcleos excéntricos, cromatina en rueda, citoplasma basófilo
Tratamiento inicial	Observación (estadios Binet A / Rai 0), BTK inhibitors, venetoclax	Bortezomib + lenalidomida + dexametasona (VRd) ± trasplante
Pronóstico	Depende de TP53, IGHV mutado, complejidad cariotípica	Depende del riesgo citogenético (IMWG), respuesta profunda (MRD–)

Diagnostic and Clinical Considerations in Concomitant Bone Marrow Involvement by Plasma Cell Myeloma and Chronic Lymphocytic Leukemia/Monoclonal B-Cell Lymphocytosis

A Series of 15 Cases and Review of Literature

Christopher L. Alley, MD; Endi Wang, MD, PhD; Cherie H. Dunphy, MD; Jerald Z. Gong, MD; Chuanyi M. Lu, MD; Elizabeth L. Boswell, MD; James Burchette, MT(ASCP); Anand S. Lagoo, MD, PhD

• *Context.*—Plasma cell myeloma and chronic lymphocytic leukemia are both common hematologic malignancies, sharing many epidemiologic features. Concomitant detection of the 2 conditions poses special diagnostic challenges for the pathologist.

Objective.—To describe the pathologic findings in cases of concomitant bone marrow involvement by myeloma and $CD5^+$ monoclonal B cells and to outline the differential diagnostic possibilities, suggest a workup for correct diagnosis, and examine clinical outcome.

Design.—Fifteen cases that met the diagnostic criteria were identified from pathology databases at 4 participating institutions. Morphologic findings were reviewed, additional immunohistochemical stains performed, and flow cytometric, cytogenetic, and relevant laboratory and clinical information was summarized. Previously published cases were searched from electronic databases and cross-references.

Results.—Most patients (13 of 15) were older males, yet had both monotypic plasma cells and B cells in the diagnostic marrow. In 4 patients, myeloma developed 24 months or later after chronic lymphocytic leukemia. In 7 patients, myeloma and $CD5^+$ B cells showed identical immunoglobulin light-chain restriction. Primary differential diagnoses include lymphoplasmacytic lymphoma, marginal zone lymphoma, and chronic lymphocytic leukemia with plasmacytoid differentiation. CD56 and/or cyclin D1 expression by plasma cells was helpful for correct diagnosis. Most patients in our cohort and published reports were treated for plasma cell myeloma.

Conclusions.—Concomitant detection of myeloma and chronic lymphocytic leukemia in the bone marrow is a rare event, which must be carefully differentiated from lymphomas with lymphoplasmacytic differentiation for correct treatment.

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Concurrent Diagnosis of Chronic Lymphocytic Leukemia and Plasma Cell Myeloma: Report of 2 Cases and Differential Diagnostic Considerations

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Case series
Patients: Male, 82-year-old • Female, 66-year-old
Final Diagnosis: Chronic lymphocytic leukemia and plasma cell myeloma
Symptoms: Osteoarthritis • shortness of breath
Clinical Procedure: —
Specialty: Pathology

Table 4. Summary of Clinical and Pathologic Findings in Published Cases

Case No.	Source, y	Age, y/Sex	Initial Disease[a]	Interval (First and Second Disease), mo	CLL Cells, % of BM Cellularity	PCM Cells, % of BM Cellularity	CLL Ig Isotype	PCM Ig Isotype
1	Vander and Johnson,[34] 1960	72/M	Together	0	60	40	NA	NA
2	Naidu and Rosner,[35] 1971	67/M	Together	0	46	34	NA	IgA λ
3	Shuster and Causing,[39] 1971	54/M	CLL	54	13	64	NA	IgG
4	Fitzgerald et al,[36] 1973	68/F	CLL	96	60	40	NA	IgM κ
5	Narasimhan et al,[33] 1975	67/M	Together	0	46	34	NA	IgG λ
6	Narasimhan et al,[33] 1975	60/M	Together	0	40	30	NA	IgG κ
7	Wash U CPC,[40] 1975	53/F	CLL	44	30	70	NA	IgG κ
8	Crowley et al,[37] 1977	80/F	Together	0	NA	Sheets	sIg negative	IgA κ
9	Hoffman and Rudders,[32] 1977	69/M	CLL	24	NA	Not given	"Different from myeloma"	"Different from CLL"
10	McLaughlin et al,[43] 1978	77/M	Together	0	Extensive	Occasional	NA	IgG κ
11	Zawadzki et al,[38] 1978	48/F	CLL	29	NA	Almost complete	NA	IgG κ
12	Pedersen-Bjergaard et al,[30] 1978	78/M	CLL	18	48	26	κ	λ
13	Kough and Makary,[31] 1978	75/F	CLL	72	30	24	NA	IgA κ
14	Kough and Makary,[31] 1978	58/M	CLL	144	57	20	NA	Not detected
15	Jeha et al,[29] 1981	64/M	Together	0	NA	NA	IgM κ	IgG κ
16	Zalcberg et al,[44] 1982	69/M	PCM	31	30 later	40 initially, 6 when CLL present	κ	IgM λ
17	Kontozoglou and Skinnider,[28] 1983	64/M	Together	0	30	38	NA	IgG κ
18	Bassan et al,[27] 1984	52/M	Together	0	40 (sheets)	50	λ	IgD λ
19	Pines et al,[26] 1984	42/F	CLL	96	NA		IgM κ	IgM κ
20	Fermand et al,[25] 1985	69/F	CLL	120	Not given	Not given	IgG1 κ	IgA κ
21	Brouet et al,[45] 1985	56/M	CLL	132	52	46	NA	κ
22	Brouet et al,[45] 1985	63/F	CLL	48	82	9	NA	IgA λ
23	Brouet et al,[45] 1985	73/M	CLL	24	30–60	4–80	μ-κ	IgA λ
24	Brouet et al,[45] 1985	57/M	CLL	24	20–60	10–80	IgA	IgA

Dx diferenciales

-Linfoma linfoplasmocitico (Macroglobulinemia de Waldestrom):
CD20 (+), CD5 (-), CD23 (+).
Distribución mixta de plasmáticas y linfocitos.
Elevación de IgM y expresa MYD88.

-Linfoma de zona marginal (esplénico):
CD20 (+), CD5 (-), CD23(-)

-LLC con diferenciación a células plasmáticas:
Ciclina D1 (-), CD56 (-), CD138(-)
No manifestaciones clínicas como hipercalcemia o lesión renal.

NUESTRO CASO
CD20 (+)
CD5 (-)
CD23 (-)? (positivo por CMF)
CD 10 (-)
CD138 (FOCOS +)
CICLINA D1 (-)

CONCLUSIONES:

- La aparición simultánea de LLC y PCM es una condición hematológica infrecuente que plantea desafíos diagnósticos críticos para el patólogo.

- Las técnicas de diagnóstico auxiliares (Inmunohistoquímica, citometría de flujo, estudios moleculares e Hibridación Fluorescente in Situ - FISH) son indispensables para establecer un diagnóstico preciso y confiable.

- Los pacientes con este diagnóstico dual a menudo requieren modificación del tratamiento, siendo el PCM el principal determinante del pronóstico

MUCHAS GRACIAS

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