V SIMPOSIUM DEL GRUPO DE ESTUDIO LATINOAMERICANO DE **LINFOPROLIFERATIVOS**

COMITÉ ORGANIZADOR: JUNTA DIRECTIVA GELL 2021 -2023

GELL
Grupo de Estudio Latinoamericano de Linfoproliferativos

Linfoma Folicular. Caso Clínico

Dra. Maria Alejandra Torres Viera

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Agosto 2019

Masculino 61 años, Médico Mastólogo

Sindrome depresivo crónico en tratamiento sertralina. No otros dx

Historia de febriculas vespertinas y sudoración nocturna 1 mes evolución

Adenopatias cervicales ,axilares e inguinales, crurales palpables, indoloras

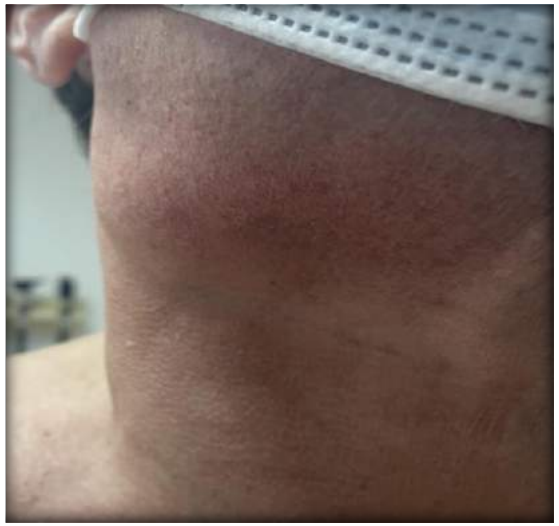
No visceromegalias

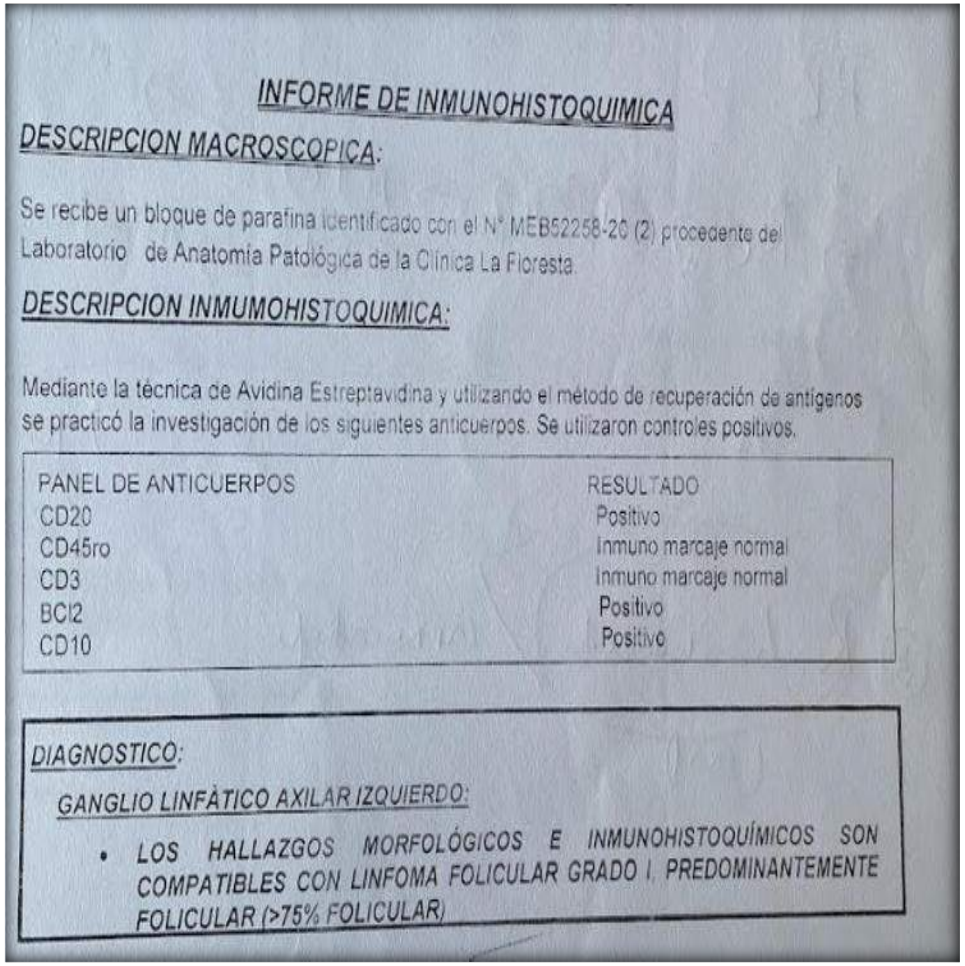
HB 14,5 gr/dl, GB 7.600 mm3, linfocitos 30% (no linfocitosis) Plaquetas 256 x10^3

LDH normal. Beta dos 2,6 mg/dl (hasta 2,1 mg/dl)

Albúmina 4,2 gr/dl

MO positiva





INFORME DE INMUNOHISTOQUIMICA

DESCRIPCION MACROSCOPICA:

Se recibe un bloque de parafina identificado con el N° MEB52258-20 (2) procedente del Laboratorio de Anatomía Patológica de la Clínica La Floresta.

DESCRIPCION INMUMOHISTOQUIMICA:

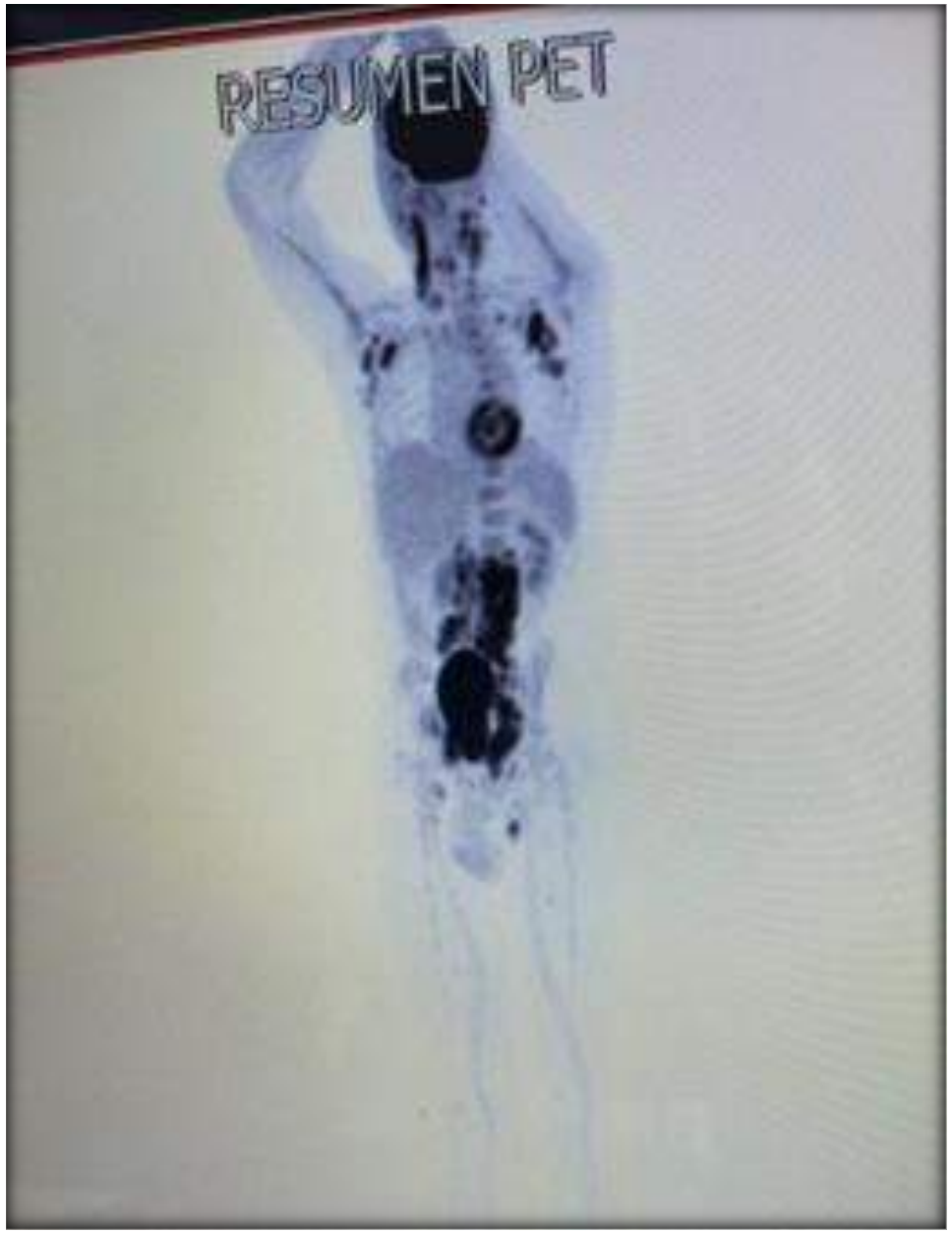
Mediante la técnica de Avidina Estreptavidina y utilizando el método de recuperación de antígenos se practicó la investigación de los siguientes anticuerpos. Se utilizaron controles positivos.

PANEL DE ANTICUERPOS	RESULTADO
CD20	Positivo
CD45ro	Inmuno marcaje normal
CD3	Inmuno marcaje normal
BCl2	Positivo
CD10	Positivo

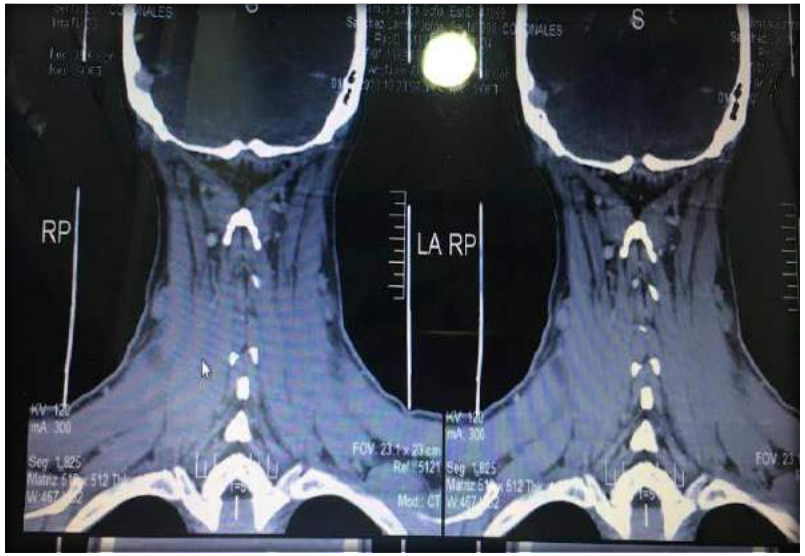
DIAGNOSTICO:

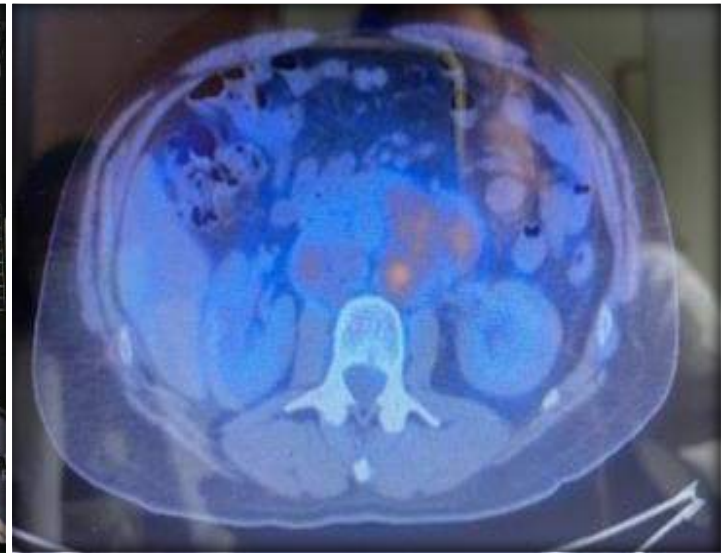
GANGLIO LINFÁTICO AXILAR IZQUIERDO:

- LOS HALLAZGOS MORFOLÓGICOS E INMUNOHISTOQUÍMICOS SON COMPATIBLES CON LINFOMA FOLICULAR GRADO I, PREDOMINANTEMENTE FOLICULAR (>75% FOLICULAR)



CT PET Inicial: Adenopatías en cuello, la mayor 15 mm, axilas positivas en captación, pero de nuevo no voluminosas, captación 4,8. Inguinales e ilíacas positivas, captación 8,9 en retroperitoneo se evidencian ganglios múltiples menores 3 cm, evidencia un plastrón perirenal paraaórtico izquierdo de diametro mayor de 6 cm. cuya captación no supera Suv 8,5. NO HAY captaciones mayores a SUV 10



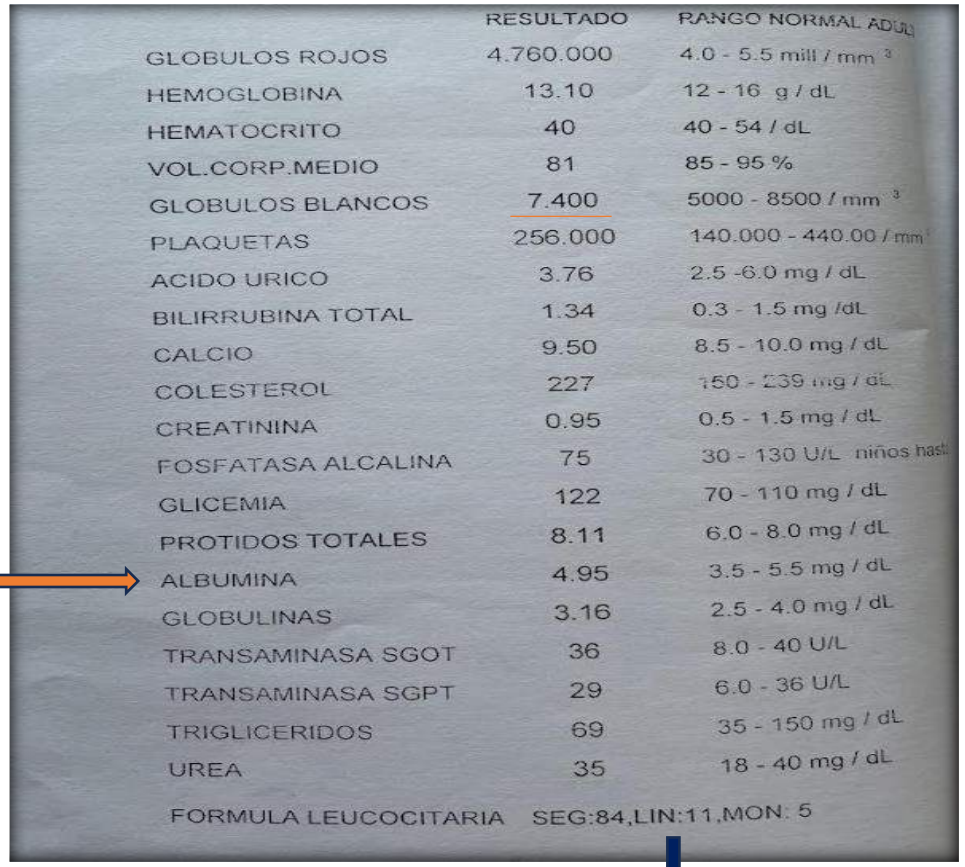


Definiendo Pronóstico

n
> 3 ganglios > 3 cm ≠ áreas
Tumor > 7 cm
Síntomas B
Derrame pleural/Ascitis
Síndrome compresivo
Citopenias
Esplenomegalia > 16cm
Linfocitosis tumoral > 5000/mm³

ECOG status >1, high LDH, presence B symptoms more than 1 extra nodal area at diagnosis (Lymphocare study)

- **Low albumin <3,6 gr/dl level**
- **Síntomas B + (GELL DATA)**
- **Indice NL > 2.6**



	RESULTADO	RANGO NORMAL ADUL
GLOBULOS ROJOS	4.760.000	4.0 - 5.5 mill / mm ³
HEMOGLOBINA	13.10	12 - 16 g / dL
HEMATOCRITO	40	40 - 54 / dL
VOL.CORP.MEDIO	81	85 - 95 %
GLOBULOS BLANCOS	7.400	5000 - 8500 / mm ³
PLAQUETAS	256.000	140.000 - 440.00 / mm
ACIDO URICO	3.76	2.5 -6.0 mg / dL
BILIRRUBINA TOTAL	1.34	0.3 - 1.5 mg /dL
CALCIO	9.50	8.5 - 10.0 mg / dL
COLESTEROL	227	150 - 239 mg / dL
CREATININA	0.95	0.5 - 1.5 mg / dL
FOSFATASA ALCALINA	75	30 - 130 U/L niños hast
GLICEMIA	122	70 - 110 mg / dL
PROTIDOS TOTALES	8.11	6.0 - 8.0 mg / dL
ALBUMINA	4.95	3.5 - 5.5 mg / dL
GLOBULINAS	3.16	2.5 - 4.0 mg / dL
TRANSAMINASA SGOT	36	8.0 - 40 U/L
TRANSAMINASA SGPT	29	6.0 - 36 U/L
TRIGLICERIDOS	69	35 - 150 mg / dL
UREA	35	18 - 40 mg / dL
FORMULA LEUCOCITARIA	SEG:84,LIN:11,MON: 5	

814 mm3

FLIPI Score 2 / FLIPPIscore 2 score: intermedio
GELF: Sintomas B +, Plastrón de 6 cm, más de 3 zonas ganglionares,

SUV max 8,6 retroperitoneo

<u>Indice N/L: 7,6 Linfopenia</u>

Radhika Takiar , Yasmin Karimi , Tycel J. Phillips ASH Education Program Dec 2022

Serum Albumin and Neutrophil-to-Lymphocyte Ratio, Two Independent Factor Predicting Survival in Patients with Follicular Lymphoma: A Multi-Institutional Retrospective Cohort of 741 FL, From the Latin American Lymphoproliferative Study Group (GELL)

María Alejandra Torres Viera, MD1,2; Luis Villela, MD5,6; Brady E. Beltrán, MD3,4; Denisse A. Castro, MD3,4; Myrna Candelaria, MD14; Henry Idrobo, MD10,11; Victoria Otero, MD7; Alana von Glasenapp, MD15; Sally Rose Paredes, MD3,4; Fabiola Valvert Gamboa, MD21; Ana Florencia Ramírez-Irbagüen MD14; Juan Carlos Barrios, MD21; Camila Peña, MD9; María Elena Cabrera, MD9; Claudia Gajardo, MD9; Macarena Roa, MD9; Catalina Diaz, MD9; Lorena Fiad, MD8; María Virginia Prates, MD8; Carlos Best, MD13; Juan A. Ospina, MD18,19; Laura Silva Idárraga, MD20; Humberto Martínez Cordero, MD19; Melani Otañez Arce, MD16; Maria Alejandra Luna Muñoz MD11; Carmen Lome MD14; Fernando Pérez-Jacobo, MD12; Rosio Baena Terán, MD22,23; José Macías Abasto, MD22; Nancy Cristaldo, MD7; Guilherme Fleury Perini, MD24; Larissa Lane Cardoso Teixeira, MD24,25; Rosa Rios Jimenez, MD26; Yusaima Rodriguez Fraga, MD26; Bryan Valcarcel, MD27; Jorge J. Castillo, MD28,29; Luis E. Malpica Castillo, MD30.

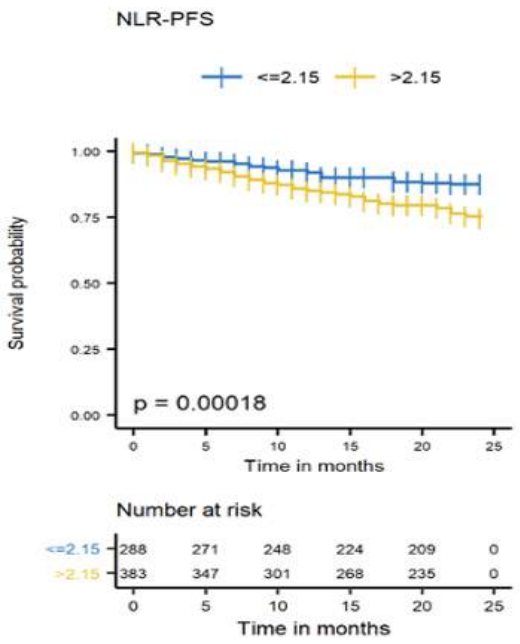
Blood Cancer J. 2019 Dec; 9(12): 104. PMCID: PMC6938796

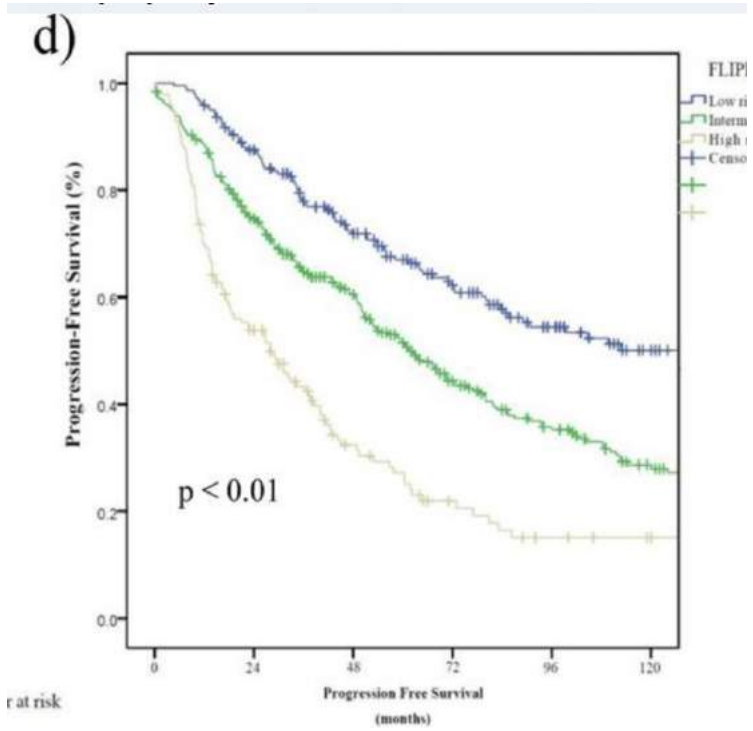
Published online 2020 Jan 2. doi: 10.1038/s41408-019-0269-6 PMID: 31894139

Several studies have demonstrated the association among high neutrophil-lymphocyte (NLR) and the increase in mortality in different populations with cancer. It's been speculated a relationship between increased intra tumoral lymphocytes with a better prognosis. On the contrary neutrophilia have been associated with NETosis programs, DNA exposition in tissues and ROS (Reactive oxygen species) and genetic B cell alterations. Neutrophils also suppress the cytolytic activity of immune cells such as lymphocytes. **Absolute lymphocyte count predicts overall survival in follicular lymphomas**.Serum leucocyte levels reflect tumor microenvironment, studies have been conducted, considering the relationship of absolute monocyte count (AMC) as well as absolute lymphocyte count (ALC) and FL patient's outcomes. Inflammation have been attributed as first tumorigenic mechanism in 20-50% cancer as an epigenetic condition. Epigenetic core carcinogenesis in FL, prognosis is not given by the tumor cell per se but by the composition of non-malignant cells. Albumin is a marker of inflammations.

Hemasphere. 2022 Jun; 6(Suppl): 1034-1035.

Enhancement of the Follicular Lymphoma International Prognostic Index (FLIPI) with lymphopenia (FLIPI-L): a predictor for overall survival and histologic transformation





Absolute lymphopenia was defined as $<1.0 \times 10^9/L$

Lymphopenia was an independent predictor of transformation on both univariate (odds ratio (OR) 2.53 95% CI 1.73–3.70, $p < 0.01$) and multivariate logistic-regression

Haematologica. 2020 Jul; 105(7): 1907–1913. PMCID: PMC7327641
Prepublished online 2019 Oct 10. doi: 10.3324/haematol.2019.230649 PMID: 31601688

Pre-treatment maximum standardized uptake value predicts outcome after frontline therapy in patients with advanced stage follicular lymphoma

The impact of pre-treatment maximum standardized uptake value (SUV_{max}) on the outcome of follicular lymphoma (FL) The impact of pre-treatment maximum standardized uptake value (SUV_{max}) on the outcome of follicular lymphoma (FL) The complete response rate was significantly lower among patients treated with non-anthracycline-based regimens if SUV_{max} was >18 (45% *vs*. 92%, $P<0.001$), but not among patients treated with R-CHOP ($P=1$). SUV_{max} >18 was associated with significantly shorter progression-free survival among patients treated with non-anthracycline-based regimens (77 months vs. not reached, $P=0.02$), but not among patients treated with R-CHOP ($P=0.73$). SUV_{max} >18 associated with shorter overall survival (OS) both in patients treated with R-CHOP (8-year OS 70% vs. 90%, $P=0.02$) and non-anthracycline-based frontline regimens (8-year OS 50% *vs*. 85%, $P=0.001$). In conclusion, pre-treatment PET scan has prognostic and predictive value in patients with advanced stage FL receiving frontline treatmen

Blood. 2020 Apr 9; 135(15): 1214–1218. PMCID: PMC7146018
Prepublished online 2020 Jan 21. doi: 10.1182/blood.2019001091 PMID: 31961926

Baseline SUVmax did not predict histological transformation in follicular lymphoma in the phase 3 GALLIUM study

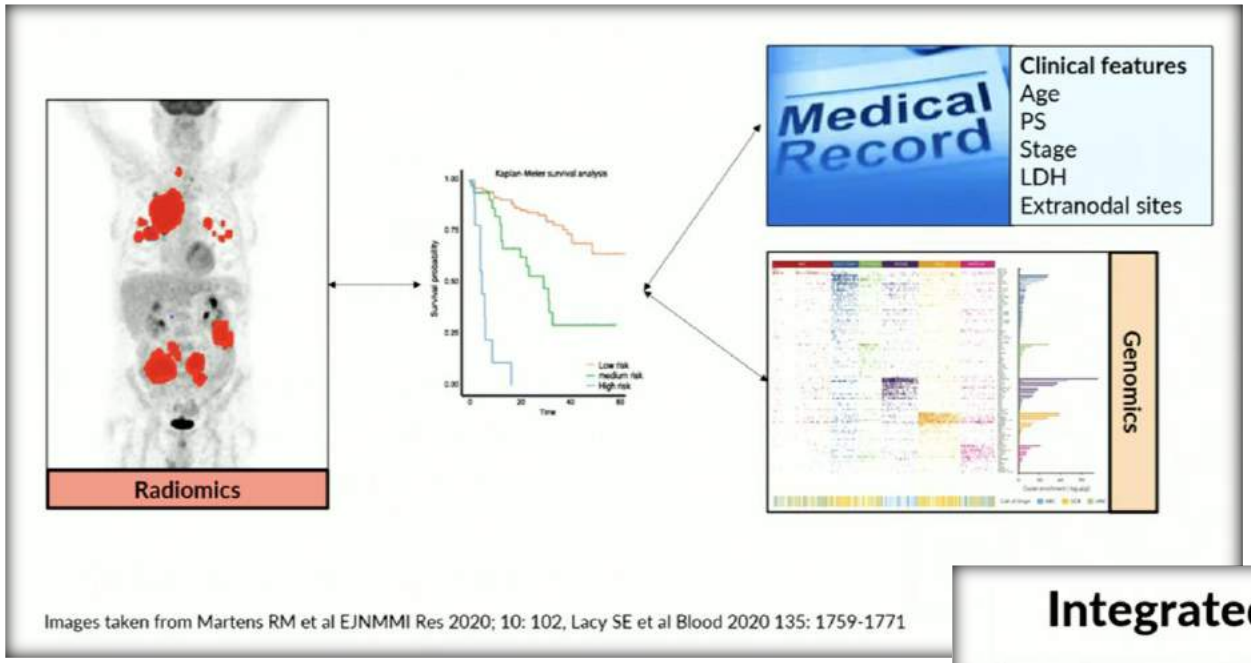
- SUVmax did not predict HT in patients in the GALLIUM study.

- Rebiopsy to exclude HT based on SUVmax alone may provide little benefit in de novo patients with high tumor burden FL.

Baseline SUV_{max} is related to tumor cell proliferation and patient outcome in follicular lymphoma

The PET results were investigated along with the tumor and immune microenvironment, which were determined by immunochemistry and transcriptome studies involving gene set enrichment analyses and immune cell deconvolution, together with the tumor mutation profile. **We report that baseline SUVmax >14.5 was associated with poorer PFS than baseline SUV_{max}≤14.5** (hazard ratio =0.28; P=0.00046). Neither immune T-cell infiltration nor immune checkpoint expression were associated with baseline PET metrics. By contrast, FL samples with Ki-67 staining ≥10% showed enrichment of cell cycle/DNA genes (P=0.013) and significantly higher SUVmax values (P=0.007). Despite similar oncogenic pathway alterations in both SUV_{max} groups of FL samples, four out of five cases harboring the infrequent *FOXO1* transcription factor mutation were seen in FL patients with SUV_{max}>14.5. Thus, high baseline SUV_{max} reflects FL tumor proliferation and, together with Ki-67 proliferative index, can be used to identify patients at risk of early relapse with rituximab

Sonali M. Smith Gilles Salles, Vol. 107 No. 1 (2022): January, 2022



Images taken from Martens RM et al EJNMMI Res 2020; 10: 102, Lacy SE et al Blood 2020 135: 1759-1771

REVIEW ARTICLE

WILEY

Advances in positron emission tomography and radiomics

Sally F. Barrington

S. Barrington, London, GB

Lugano 2023

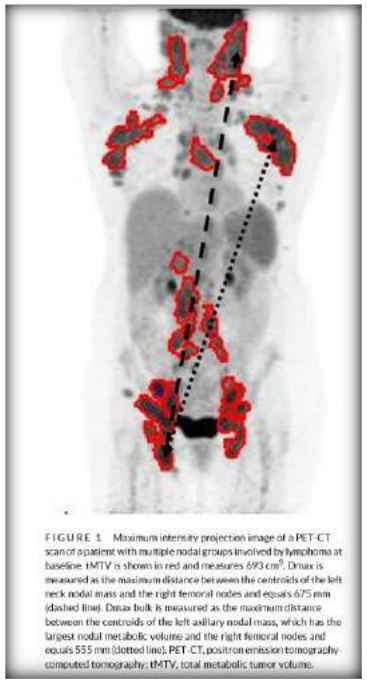


FIGURE 1 Maximum intensity projection image of a PET-CT scan of a patient with multiple nodal groups involved by lymphoma at baseline. tMTV is shown in red and measures 693 cm^3. Dmax is measured as the maximum distance between the centroids of the left neck nodal mass and the right femoral nodes and equals 675 mm (dashed line). Dmax bulk is measured as the maximum distance between the centroids of the left axillary nodal mass, which has the largest nodal metabolic volume and the right femoral nodes and equals 555 mm (dotted line). PET-CT, positron emission tomography-computed tomography; tMTV, total metabolic tumor volume.

Integrated models

Clinical	PET Radiomics	Clinical PET
Age PS Stage LDH Extranodal sites Bulk	MTV(SUV4 method) SUVpeak (hottest 1cm^3) Dmaxbulk	Age PS MTV SUVpeak (hottest 1cm^3) Dmaxbulk

Eertink JJ et al Eur J Nucl Med Mol Imaging 2022; 49: 932-942

NIHR | National Institute for Health and Care Research

• Discusión de la Mejor Inducción

- **R-B** mejor SLP. SLP a 3 a 90% Diferente perfil seguridad. NO≠ SG
  - Stil 39% reducción riesgo progresión respecto R-CHOP, media SLP 61,9m vs 31,2 m)
  - BRIGHT (no inferiority) Resp Global R-B 97% vs R-CHOP 90%
- **R-CHOP** SLP 3a: 87%
- R-CVP, SLP 3 a 76% (comorbilidades limitantes)

O-chemo[4]	88.5%	80% at 3y
R2[7]	84%	77% at 3y
O-Len[27]	94%	82% at 3y

Radhika Takiar , Yasmin Karimi , Tycel J. Phillips ASH Education Program Dec 2022

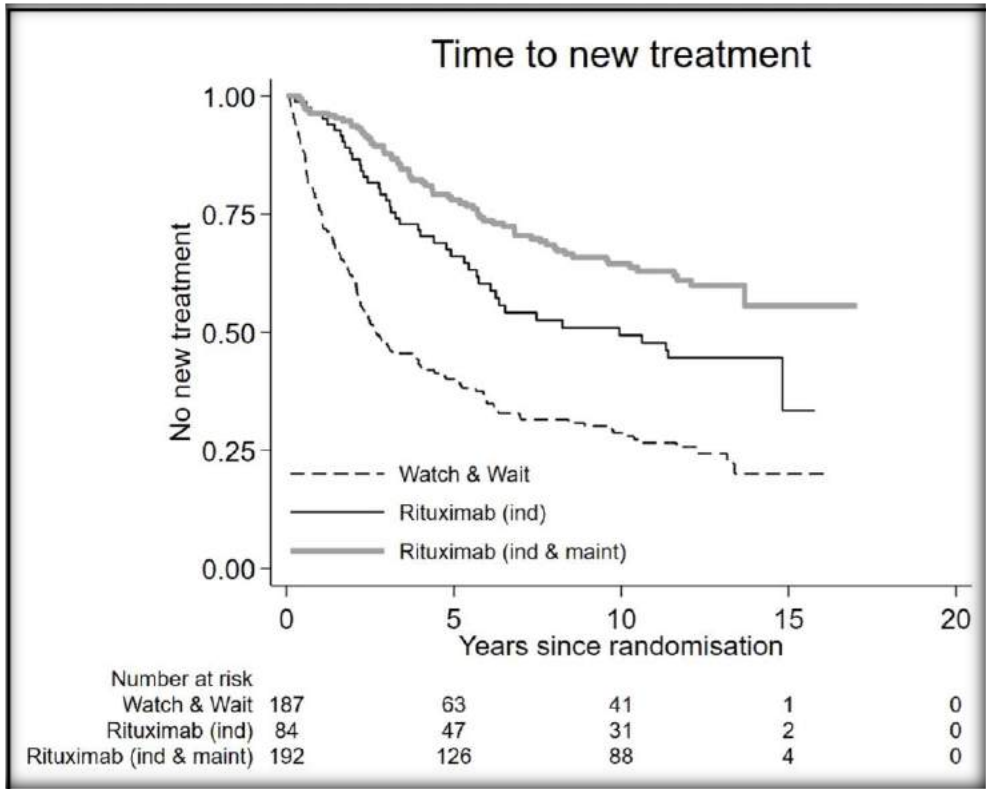
607 Long Term Follow-up of International Randomised Phase 3 Study of Rituximab Versus a Watch and Wait Approach for Patients with Asymptomatic, Low Tumour Burden Follicular Lymphoma Shows Rituximab Is Highly Effective at Delaying Time to New Treatment without Detrimental Impact Following Next Line of Therapy (oral presentation)

The phase 3 Watch & Wait vs Rituximab Low tumor bourden disease **12,3 y following**

463 patients with asymptomatic, low-tumor-burden FL.79% of patients had stage III-IV disease

Watch and wait (n=187) Vs induction with rituximab given at 375 mg/m2 weekly for 4 weeks (n=84), or the same rituximab induction followed by rituximab maintenance at 375 mg/m2, given every 2 months for 12 doses (n=192)

the median TTNT was 2.7 years in the watch-and-wait arm, 9.9 years in the rituximab induction arm, and was not reached in the rituximab maintenance arm. At 10 years, the proportion of patients who had not started a new treatment was 28.8% in the watch-and-wait arm, 49.4% in the rituximab induction arm, and 64.1% in the rituximab maintenance arm

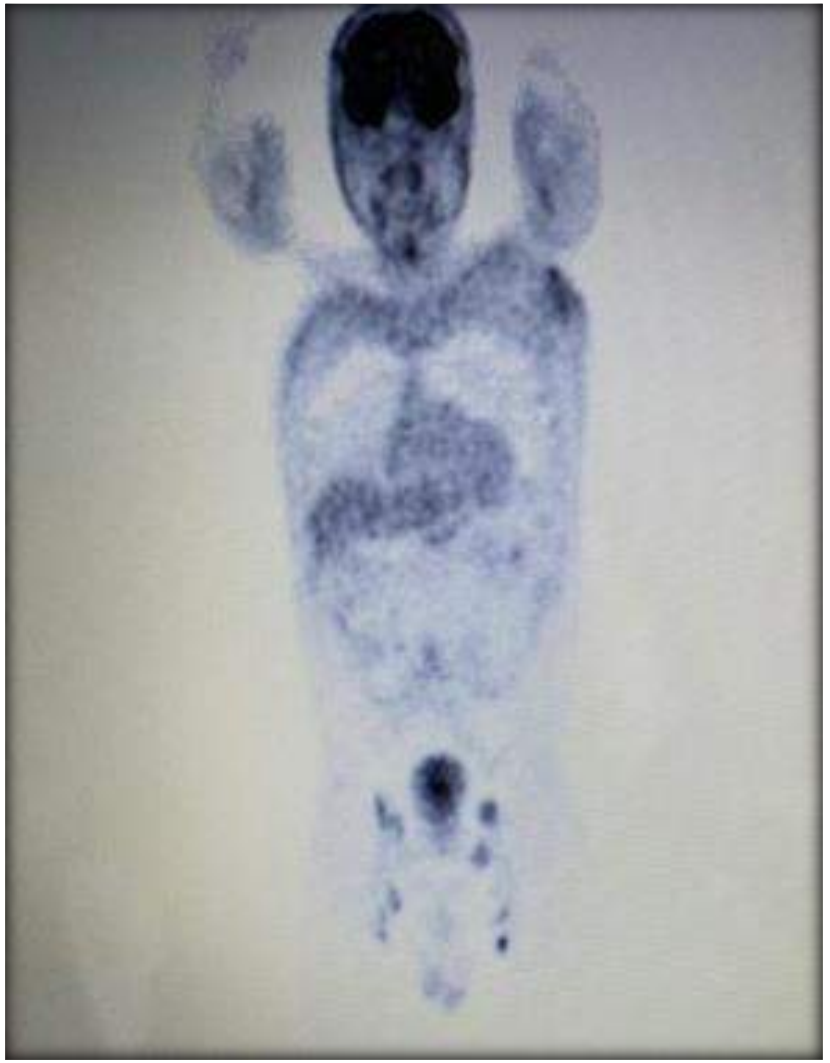


Conclusion:
After a long median follow-up of 12.3 years we **have shown that rituximab monotherapy is highly effective at deferring TTNT in patients with asymptomatic LTBFL, with RM being superior to RI. Initial treatment with rituximab did not result in inferior outcomes** following 1st new treatment compared with an initial period of observation. Upfront rituximab should therefore be considered an effective treatment option for patients who wish to delay chemoimmunotherapy.

Ardeshna, ASH 2022. December 10-13, 2022. Abstract 607.

Tratamiento

- Inducción rituximab semanal por 4 y luego rituximab cada dos meses <u>solo tres dosis</u>
- Junio 2020 suspendemos estrategia rituximab producto de la pandemia



COVID-19 in Patients with Lymphoma: A Grupo De Estudio Latinoamericano En Linfoproliferativos (GELL) Retrospective Study
Journal: Blood
Blood (2020) 136 (Supplement 1): 35–36.
DOI: https://doi.org/10.1182/blood-2020-142787

Recaida

Septiembre 2022

Intervalo Libre de enfermedad: 2ª 4 meses

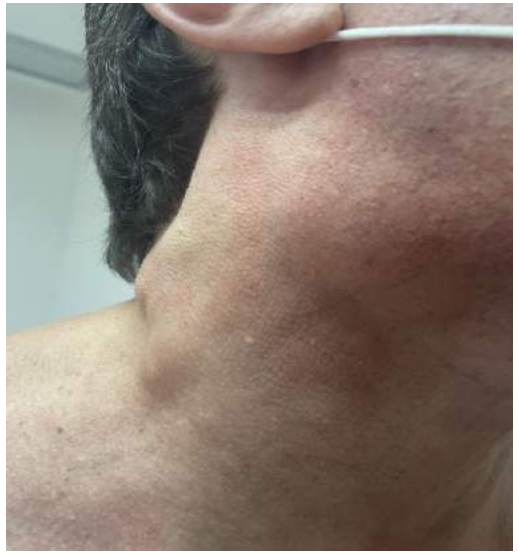
Sintomas B + (fiebre sudoración)

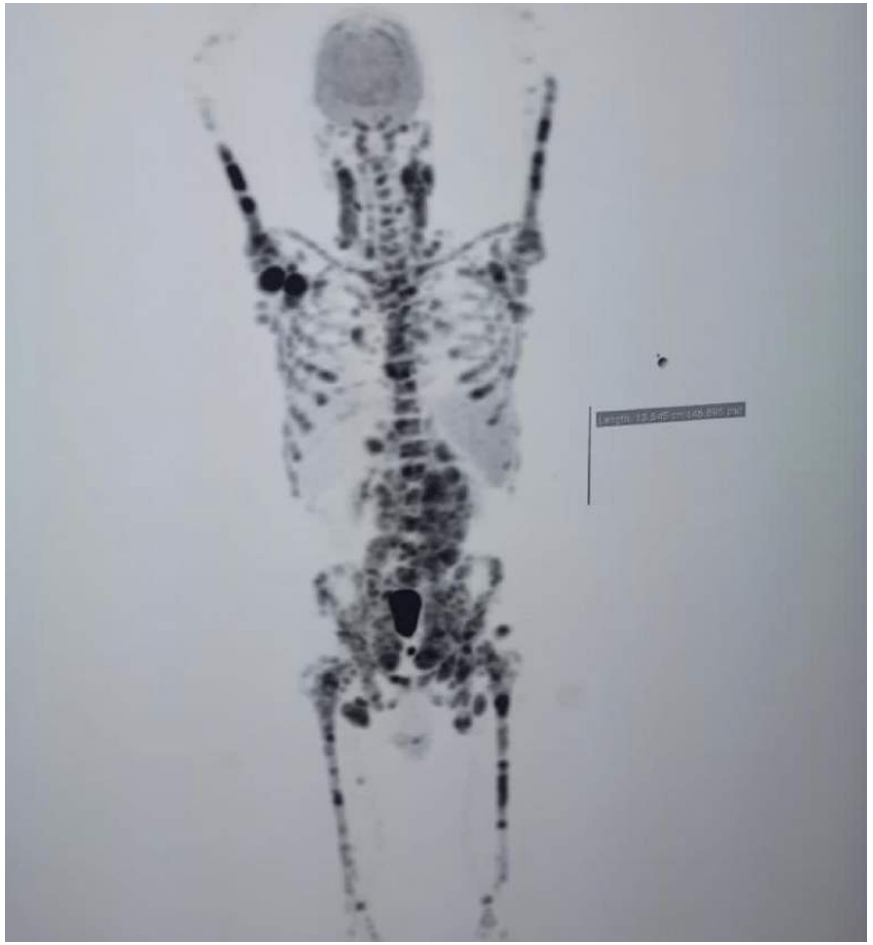
Crecimiento gangionar

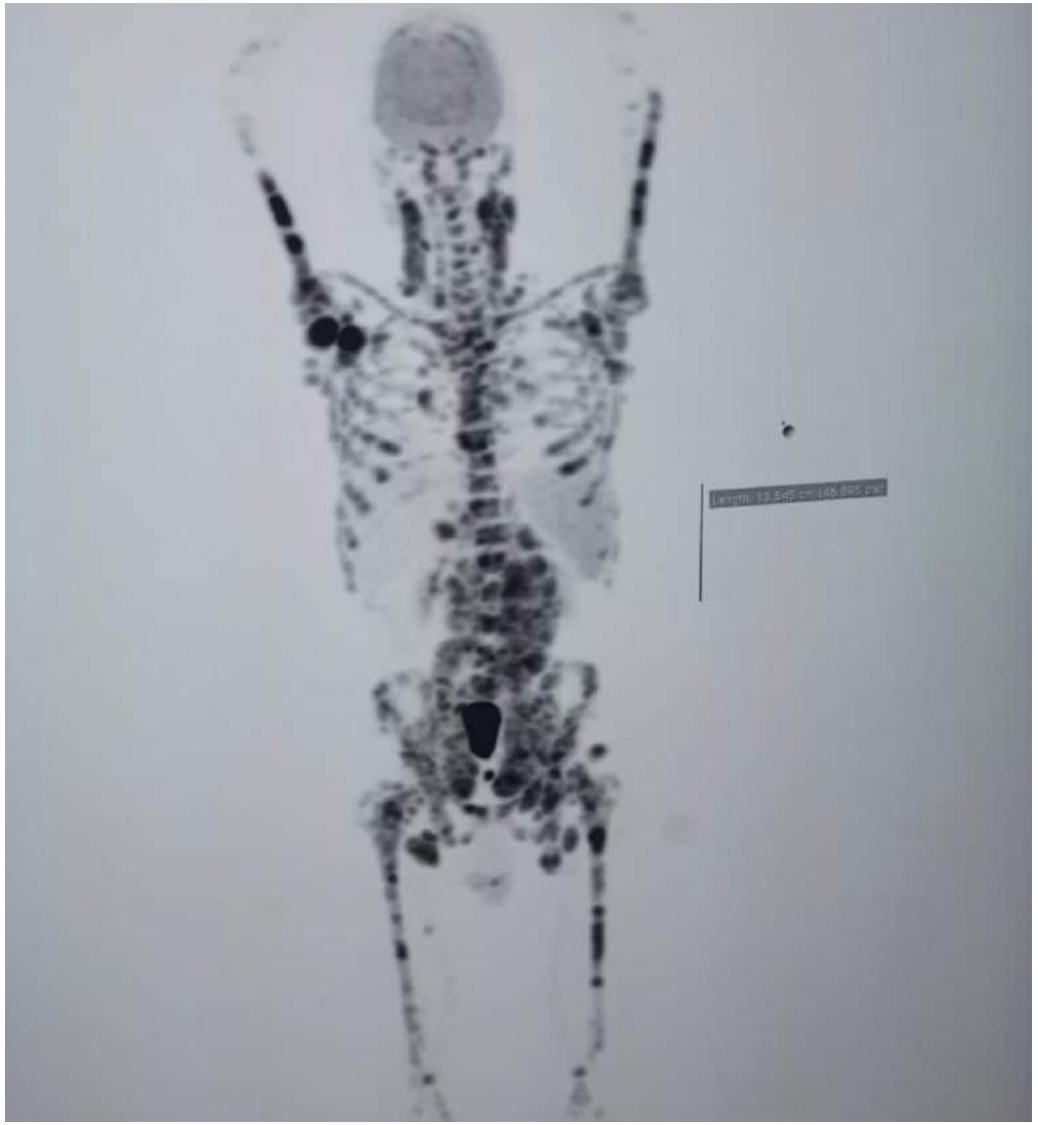
LDH alta

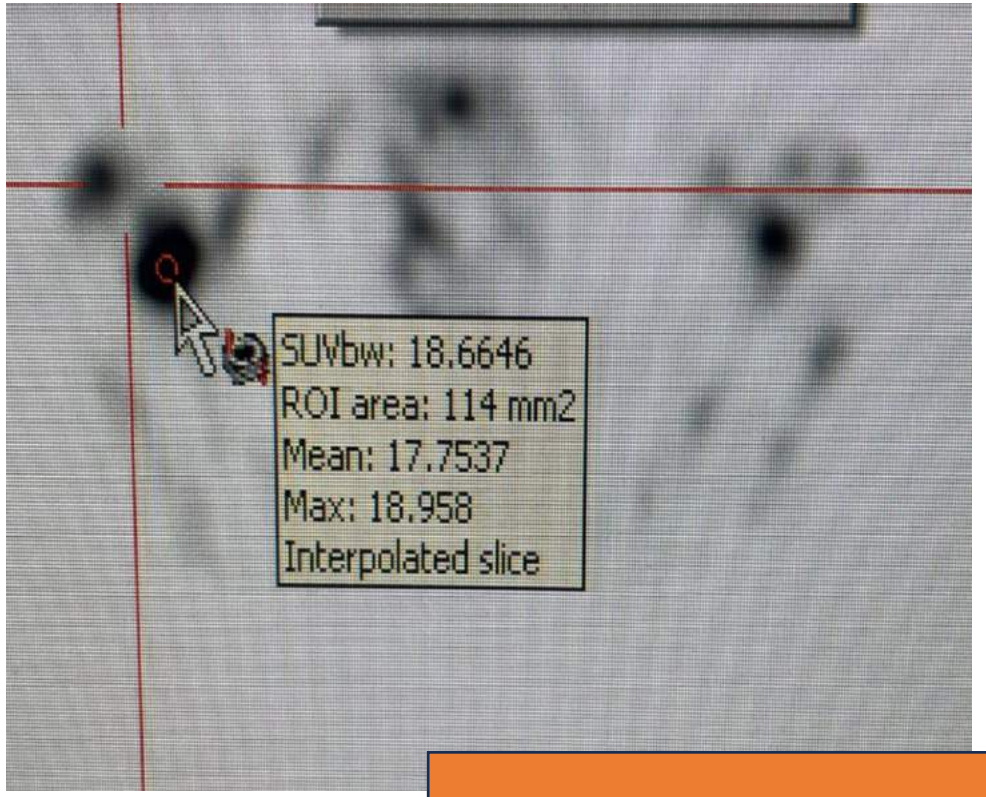
Beta dos 3.6 mg/dl

No linfocitos en sp








SUVbw: 18.6646
ROI area: 114 mm2
Mean: 17.7537
Max: 18.958
Interpolated slice

SUV max 18

Estudios Diagnósticos

Nombre: [redacted] **Céd. Ident:** 6130324

Muestra de: GANGLIO LINFATICO **Patología Nº:** MEB-53611

Méd. Solic: MARIA ALEJANDRA TORRES **Fecha:** 30/09/2022

INFORME ANATOMOPATOLOGICO

DESCRIPCION MACROSCOPICA:

Un fragmento irregular de 3,5 x 2,5 cm con tejido adiposo adherido en la superficie. Al corte aspecto homogéneo, de color pardo claro alternando con áreas pardo oscuras y de consistencia blanda. Se incluyen para estudio histológico

DIAGNOSTICO:

GANGLIO LINFATICO AXILAR DERECHO; BIOPSIA:

LINFOMA FOLICULAR GRADO 1-2, PREDOMINANTEMENTE FOLICULAR (MAYOR DEL 75% FOLICULAR)

NOTA: VER INFORME DE INMUNOHISTOQUIMICA NUMERO 204-22

JORGE ENRIQUE SANCHEZ LANDER CI: 6130324 Masculino 59.11 Años Ingreso: 10/0

Dir: Telf: 0212-9811109 03:34

Conv.: AMBULATORIO Ubic: Imp: 10/01/2023

Dr(a): MEDICO Enviar:

Hematología

Descripción del Exámen	Resultado	Unidades	Valores de Referencia
PERFIL HEMATOLOGICO			
LEUCOCITOS	6,17	10^3/uL	5,00 - 9,50
HEMATIES	3,99	10^6/uL	4,70 - 6,10
HEMOGLOBINA	10,0	g/dL	14,0 - 16,0
HEMATOCRITO	32,9	%	42,0 - 52,0
V.C.M.	82,5	fL	80,0 - 94,0
H.C.M.	25,1	pg	27,0 - 31,0
C.H.C.M.	30,4	g/dL	33,0 - 37,0
R.D.W.	14,8	%	11,5 - 15,5
NEUTROFILOS %	59,4	%	55,0 - 65,0
LINFOCITOS %	37,4	%	20,5 - 45,5
MONOCITOS %	2,3	%	5,5 - 11,7
EOSINOFILOS %	0	%	0 - 7
BASOFILOS %	0,7	%	0,2 - 1,0
NEUTROFILOS #	3,7	10^3/uL	2,2 - 4,8
LINFOCITOS #	2,3	10^3/uL	1,3 - 2,9
MONOCITOS #	0,1	10^3/uL	0,3 - 0,8
EOSINOFILOS #	0,0	10^3/uL	0,0 - 0,2
BASOFILOS #	0,0	10^3/uL	0,0 - 0,1
PLAQUETAS	193,0	10^3/uL	130,0 - 400,0
M.P.V.	7,8	fL	7,4 - 10,4

Marcador	Resultado %	Marcador	Resultado %
CD19	10	CD20	10
CD10	10	CD45	72
CD13	18	HLA-DR	10
CD7	15	CD5	15
CD3	15	CD4	7
CD8	8	CD14	15
KAPPA	CLONAL	LAMBDA	NEGATIVO
FMC7	NEGATIVO	CD23	NEGATIVO
CD25	NEGATIVO	CD38	NEGATIVO
CD200	5		

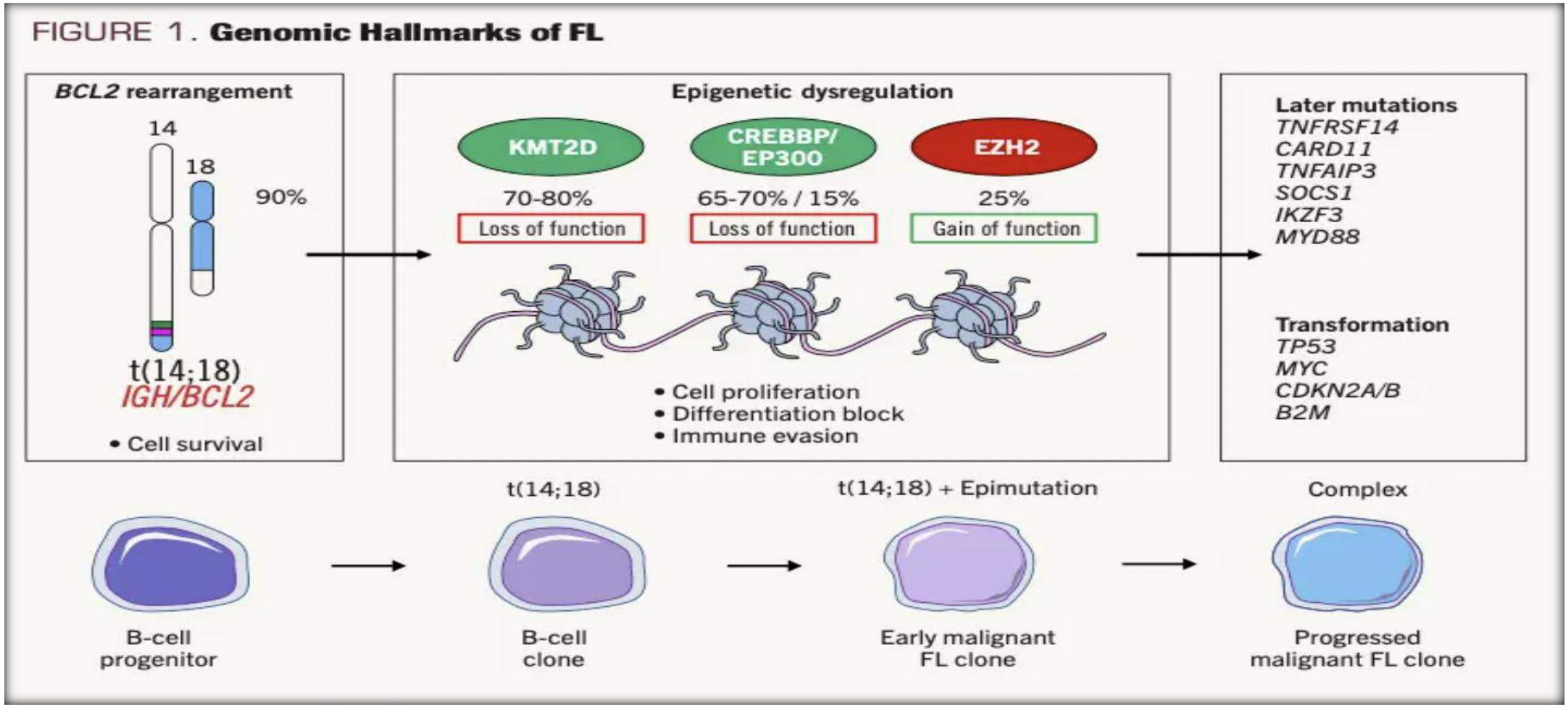
# EVENTOS	SENSIBILIDAD	RESULTADO
100.000	10-4	

EL ANÁLISIS DETECTÓ 10% DE CÉLULAS LINFOIDES B CLONALES KAPPA CON CARACTERÍSTICAS INMUNOFENOTÍPICAS DE LNH FOLICULAR.

LDH 442 U/L

MO albumina 3,2

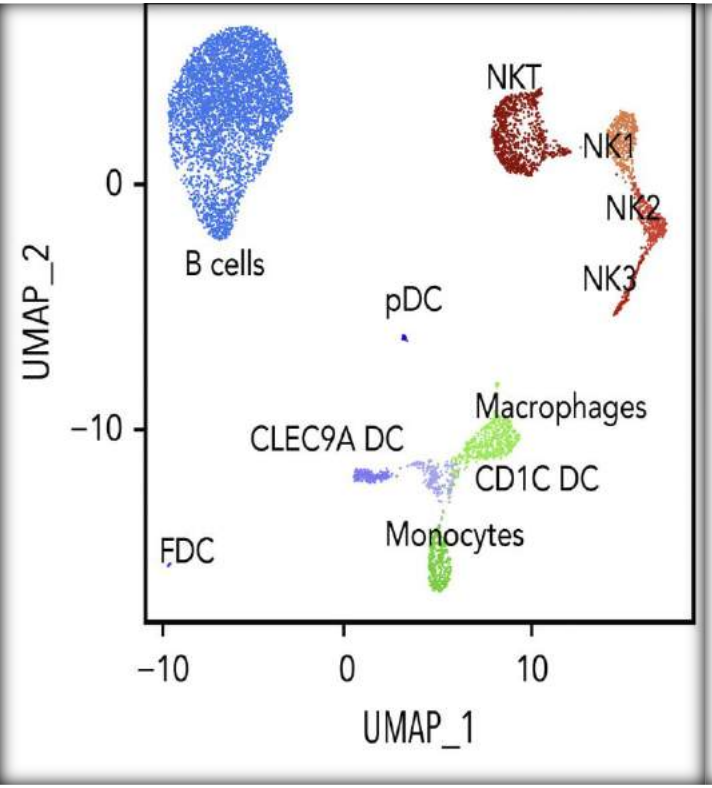
Follicular Lymphoma: Diagnosis Aspects

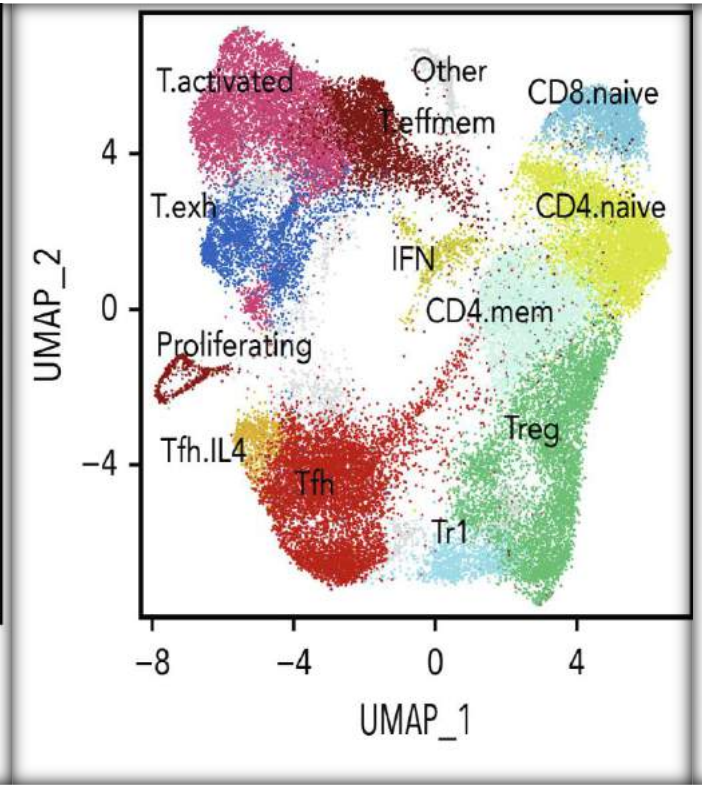


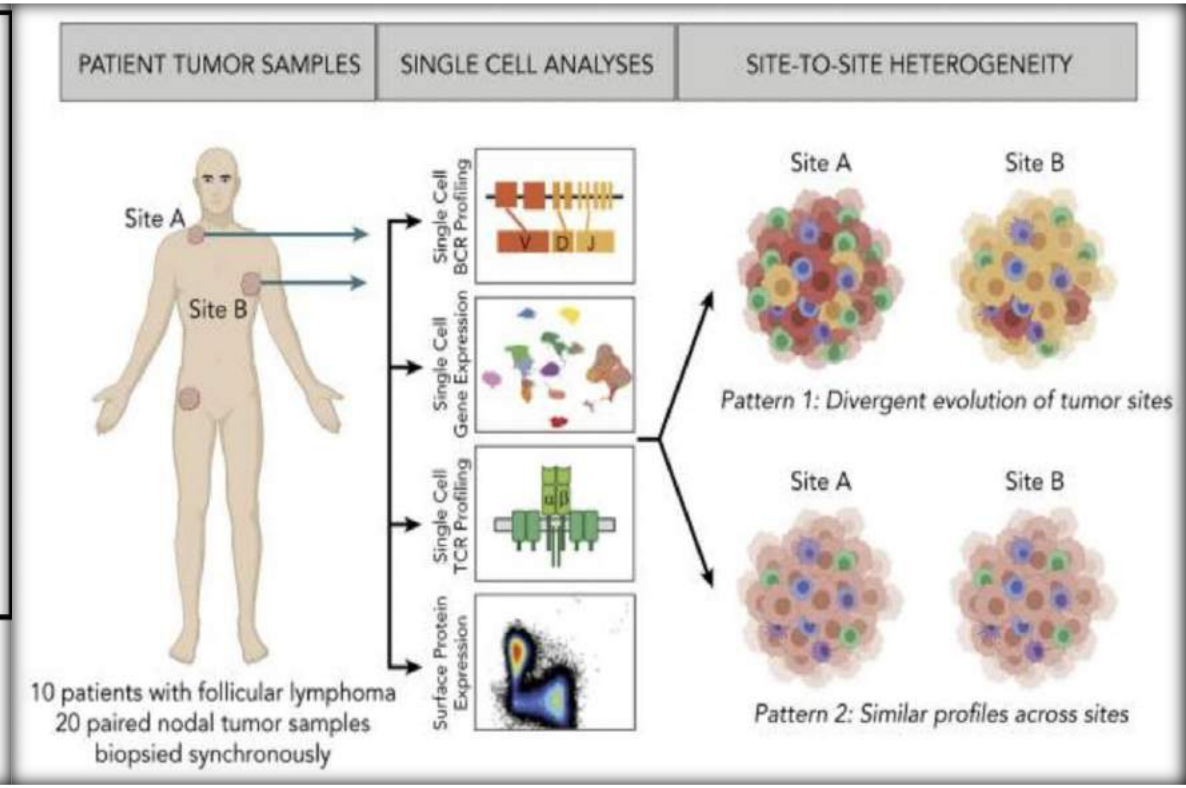
Kirk E. Cahill, MD, Sonali M. Smith, MDONCOLOGY Vol 36, Issue 2, Volume **36**Issue **2.** February 17, 2022

Single-cell analysis can define distinct evolution of tumor sites in follicular lymphoma

- FL can exhibit site-to-site genetic and phenotypic divergence as well as differential Tfh abundance and tumor-Tfh cross talk.
- **In FL, biopsy of a single anatomical site may not capture the full scope of a patient's disease**







Haebe S, Shree T, Sathe A, et al. *Blood*. 2021;137(21):2869-2880.

Tratamiento

Finales Octubre 2023
Inicia esquema RB

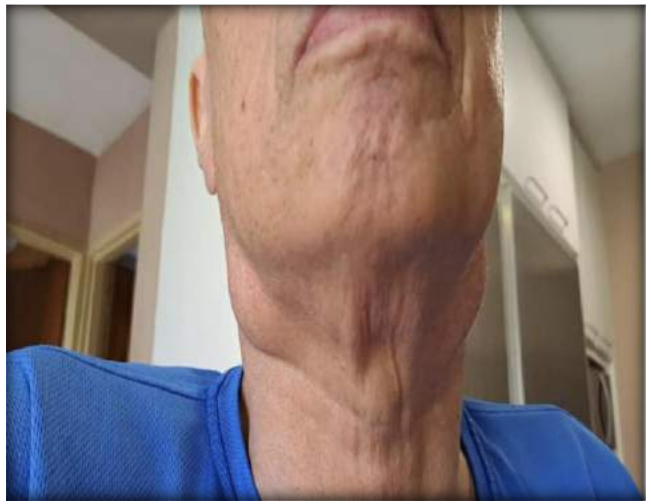
En segundo RB ciclo, reinicia fiebre y crecimiento ganglionar de nuevo

Incremento de LDH a 497 U/L

En Enero 2023
Nuevo crecimiento ganglionar
Fiebre vespertina. LDH alta 442 U/L

Serología hongos negativa, hemocultivos negativos, Urocultivo negativo Galactomanano negativo , gota gruesa negativa. Serologia viral negativa.

Cambio a R-CHOP (enero 2023)



CONTAJE DE RETICULOCITOS	0,90
GOTA GRUESA	NO SE OBSERVARON
VELOCIDAD DE SEDIMENTACION GLOBULAR*	89

* Valores Verificados

Química

Descripción del Exámen	Resultado
PROTEINA C REACTIVA	34,96

Serología

Descripción del Exámen	Resultado
ANTIGENOS FEBRILES (WIDAL)	
SALMONELLA TYPHI O	NEGATIVO
SALMONELLA H PARATYPHI A	NEGATIVO
SALMONELLA H PARATYPHI B	NEGATIVO
SALMONELLA TYPHI H	NEGATIVO
BRUCELLA ABORTUS	NEGATIVO
PROTEUS OX19	NEGATIVO

M0060 - P62572

[redacted] Masculino 56.11 Años Ingreso: 20/01/2020
Telf: 10:47:58 a.m.
Conv.: AMBULATORIO Ubic: Imp: 31/01/2020 03:04pm
Dr(a): SANCHEZ LANDER JORGE ENRI Enviar:

Pruebas Especiales

Descripción del Exámen	Resultado	Unidades	Valores de Referencia
CITOMEGALOVIRUS IgG	240.8	U/ml	NEGATIVO: 0.0 - 6.0 INDETERMINADO: 6.0 - 15.0 POSITIVO: MAYOR de 15.0
CITOMEGALOVIRUS IgM	0.6	U/ml	INDEX NEGATIVO: MENOR DE 9 INDETERMINADO: 9 - 11 POSITIVO: MAYOR DE 11

Referencias

Descripción del Exámen	Resultado	Unidades	Valores de Referencia
EPSTEIN BARR IgG ANTI-EBV(VCA)IgG	1.124		NEGATIVO: MENOR DE 9 INTERMEDIO: 9-11 POSITIVO: MAYOR DE 11
EPSTEIN BARR IgM ANTI-EBV(VCA)IgM	0.294	Indice Cut-off	NEGATIVO: MENOS DE 0.900 INTERMEDIO: 0.900 - 1.100 POSITIVO: MAYOR DE 1.100

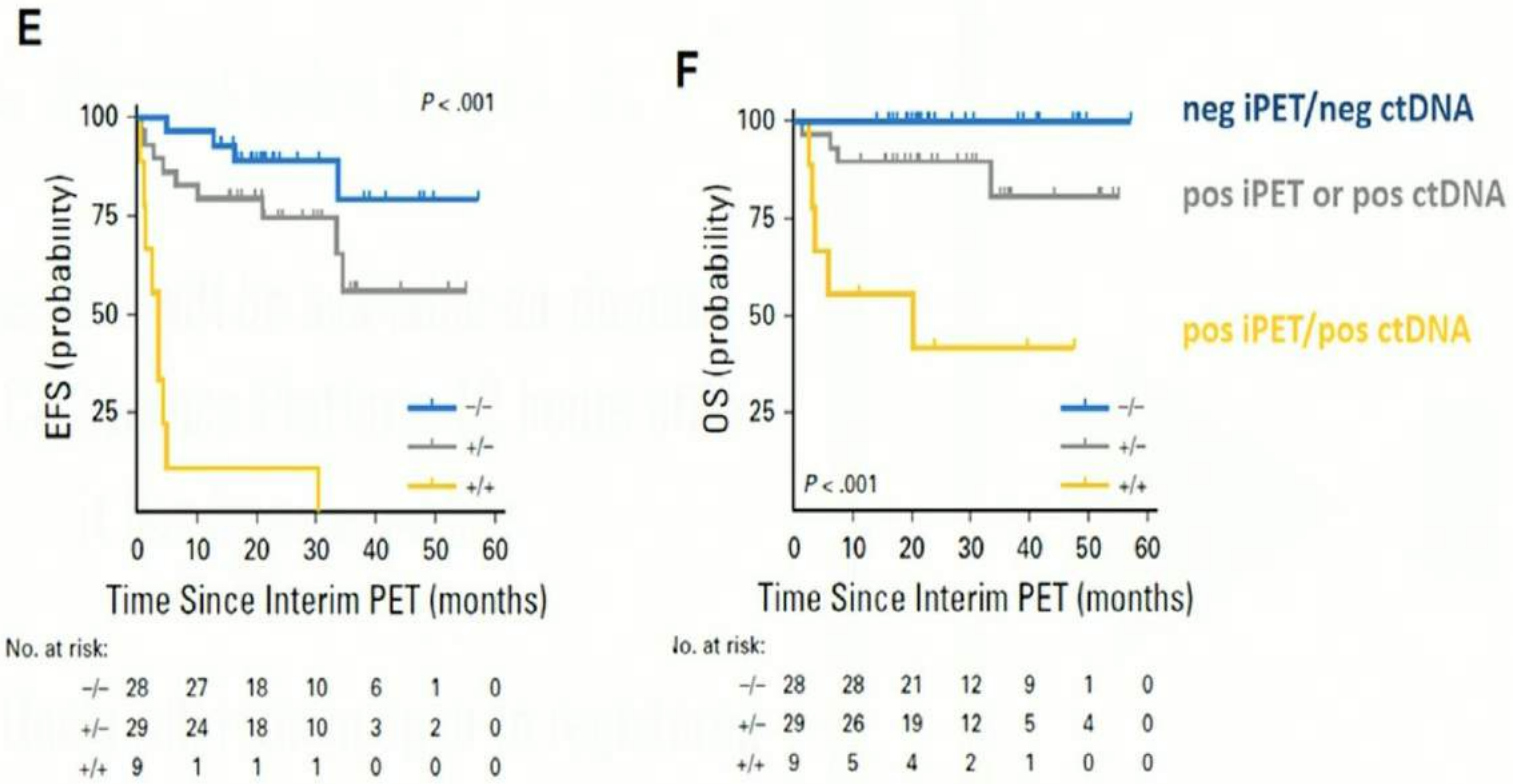
[redacted] Masculino 59.11 Años Ingreso: 12/01/2023
Dir: Telf: 0212-9811109 11:51:16 a. m
Conv.: AMBULATORIO Ubic: Imp: 12/01/2023 04:14pm
Dr(a): TORRES VIERA MARIA ALEJAN **Enviar:**

Micología

Descripción del Exámen	Resultado	Unidades	Valores de Referencia	
GALACTOMANANO	0,70 (Suero)		NEGATIVO: < 0,5 POSITIVO: > o igual a 0,5	MDF

MÉTODO: INMUNOCROMATOGRAFÍA (LFA)

iPET and change in ctDNA at c1 or c2



n = 217 ct DNA ; n = 66 iPET

Kurtz D et al J Clin Onc 2018; 36: 2845-53

NIHR | National Institute for Health and Care Research

Liquid biopsies hold great promise for achieving precision medicine. Indeed, in FL mutations detected within circulating tumor DNA may be a better reflection of the inherent intratumoral heterogeneity than the biopsy of a single site.

Evolución

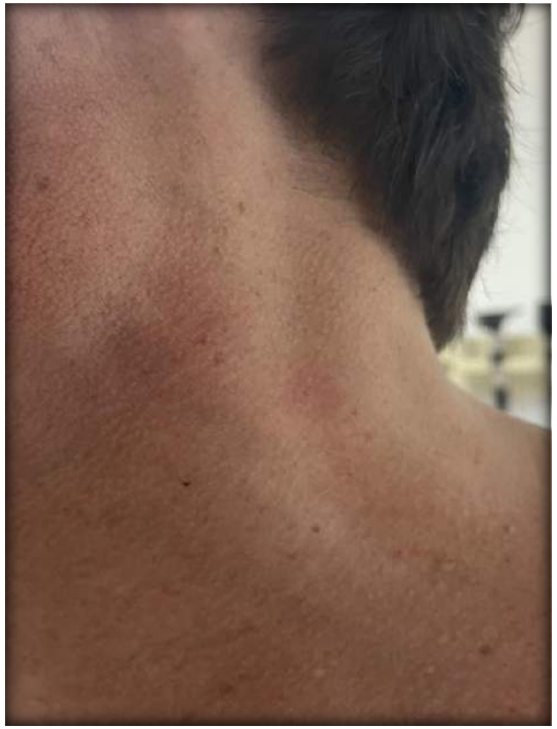
Evolución Tórpida

Febril

Proteína C reactiva 36

LDH 796 U/L

Inicia Somnolencia



CONTAJE DE RETICULOCITOS	0,90
GOTA GRUESA	NO SE OBSERVARON
VELOCIDAD DE SEDIMENTACION GLOBULAR*	**89**

* Valores Verificados

Química

Descripción del Exámen	Resultado
PROTEINA C REACTIVA	34,96

Serología

Descripción del Exámen	Resultado
ANTIGENOS FEBRILES (WIDAL)	
SALMONELLA TYPHI O	NEGATIVO
SALMONELLA H PARATYPHI A	NEGATIVO
SALMONELLA H PARATYPHI B	NEGATIVO
SALMONELLA TYPHI H	NEGATIVO
BRUCELLA ABORTUS	NEGATIVO
PROTEUS OX19	NEGATIVO

M0051 - P62572

JORGE ENRIQUE SANCHEZ LANDER CI: 6130324 — Masculino 59.11 Años — Ingreso: 12/01/2023
Dir: — Telf: 0212-9811109 — 11:51:16 a. m
Conv.: AMBULATORIO — Ubic: — Imp: 12/01/2023 04:14pm
Dr(a): TORRES VIERA MARIA ALEJAN — Enviar:

Micología

Descripción del Exámen	Resultado	Unidades	Valores de Referencia	
GALACTOMANANO	0,70 (Suero)		NEGATIVO: < 0,5 POSITIVO: > o igual a 0,5	MDF

MÉTODO: INMUNOCROMATOGRAFÍA (LFA)

INVESTIGACION DE BK

COLORACIONES

ZIEHL NEELSEN DIRECTO: NO SE OBSERVARON BACILOS ACIDO RESISTENTES

Patient ID	Patient Name		Birth Date	Sex	Age
SJ130324	S, J130324		1963-01-20	M	60
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
ML09964993	23-121016	CLEANT CLEANT	SANCHEZ JORGE		
Account Information		**Collected**			
C7033264 Laboratorios Inmunofuturo XXI C.A.		21 Jan 2023 15:02			

QuantiFERON-Tb Gold Plus, B

QuantiFERON-Tb Gold Plus Result — SDL
Indeterminate — Reference Value: Negative
Abn
Indeterminate due to a low interferon-gamma level in the mitogen (positive control) tube. This may occur due to a low lymphocyte count, reduced lymphocyte activity or inability of the patient's lymphocytes to generate interferon-gamma.

The reference range for the 'Mitogen minus Nil Result' is ≥0.5 IU/mL.

TB1 Ag minus Nil Result — SDL
-0.03 IU/mL

TB2 Ag minus Nil Result — SDL
0.03 IU/mL

Mitogen minus Nil Result — SDL
0.06 IU/mL

Nil Result — SDL
0.05 IU/mL

Received: 26 Jan 2023 12:01 — Reported: 26 Jan 2023 15:12

Clínic Barcelona

SERVICIO DE ANATOMÍA PATOLÓGICA

SANCHEZ LANDER, JORGE

Estado:	DEFINITIVO	Ref. externa:		Centro solicitante:	ALTRES PROCEDENCIES
F. petición:	06/02/2023 16:31	Estudio:	B23-003867	Dirección:	
F. rec. muestra:	06/02/2023 16:33	Sexo:	Hombre		
F. último doc.:	17/02/2023 22:26	Edad:	0 años	Localidad:	
F. nacimiento:		NHC:	-992359233	Remitir A:	

INFORME DE BIOPSIA

DESCRIPCIÓN MACROSCOPICA

B23-003867-A CONSULTA DIAGNÒSTICA

Motivo: revisión diagnóstica
Número de bloques de parafina:1 Identificados con el número:53611 Color de bloque: BLANCO
Correspondientes a: GANGLIO LINFATICO AXILAR DERECHO
Procedencia del material biológico:INSTITUTO MÉDICO LA FLORESTA Dr/a:MARIA ESTHER GUEVARA
Informe anatomopatológico adjuntado: Sí

DESCRIPCIÓN MICROSCOPICA

Ganglio linfático con arquitectura alterada a expensas de una proliferación linfoide de patrón nodular, con nódulos homogéneos compuestos predominantemente por centrocitos, con focal extensión extracapsular. No se observan macrófagos de cuerpo tingible en el interior de los nódulos ni mantos aparentes alrededor de los mismos. Se contabilizan menos de 15 centroblastos por campo de gran aumento, aunque llama la atención la presencia de centrocitos de tamaño aumentado.

Al estudio inmunohistoquímico, la celularidad neoplásica es positiva para los marcadores B CD20 y CD79a, así como para los marcadores de centro germinal CD10 y BCL6. Dichas células se localizan tanto en los nódulos como por fuera de ellos. BCL2 es positivo en las células neoplásicas tanto de dentro como de fuera de los nódulos. CD3 y CD5 realzan el componente T acompañante entre los nódulos. La celularidad neoplásica es negativa para ciclina D1. IgD resalta la ausencia de mantos. Los nódulos están sustentados por tramas de células foliculares dendríticas positivas para CD21 y CD23. p53 es intensamente positiva en alrededor del 10-20% de las células neoplásicas. El índice proliferativo Ki67 es alto, de alrededor del 30-40% fuera de los nódulos y del 60-70% dentro de los nódulos.

DIAGNÓSTICO

ADENOPATÍA AXILAR DERECHA, ESCISIÓN (CASO CONSULTA REF. 2022000204; MEB 53611-22):

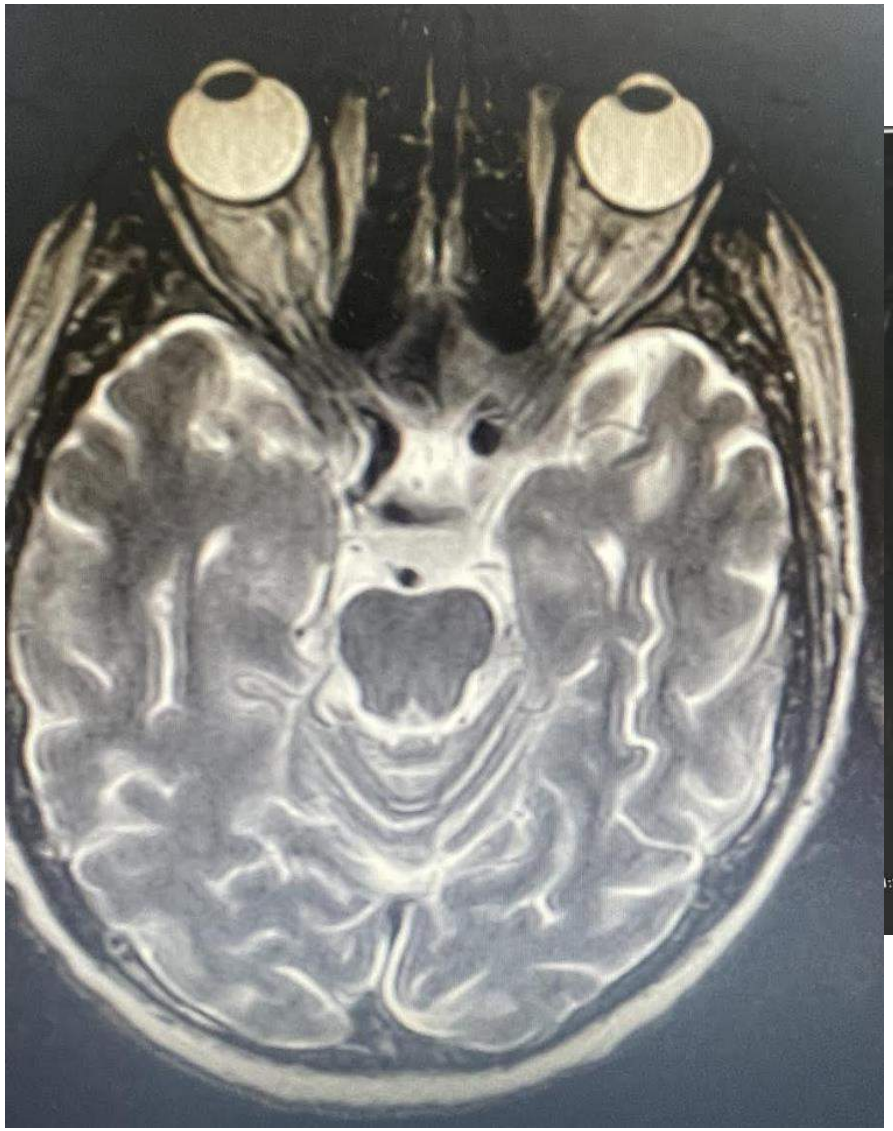
- LINFOMA FOLICULAR DE GRADO 2 CON ALTO ÍNDICE PROLIFERATIVO

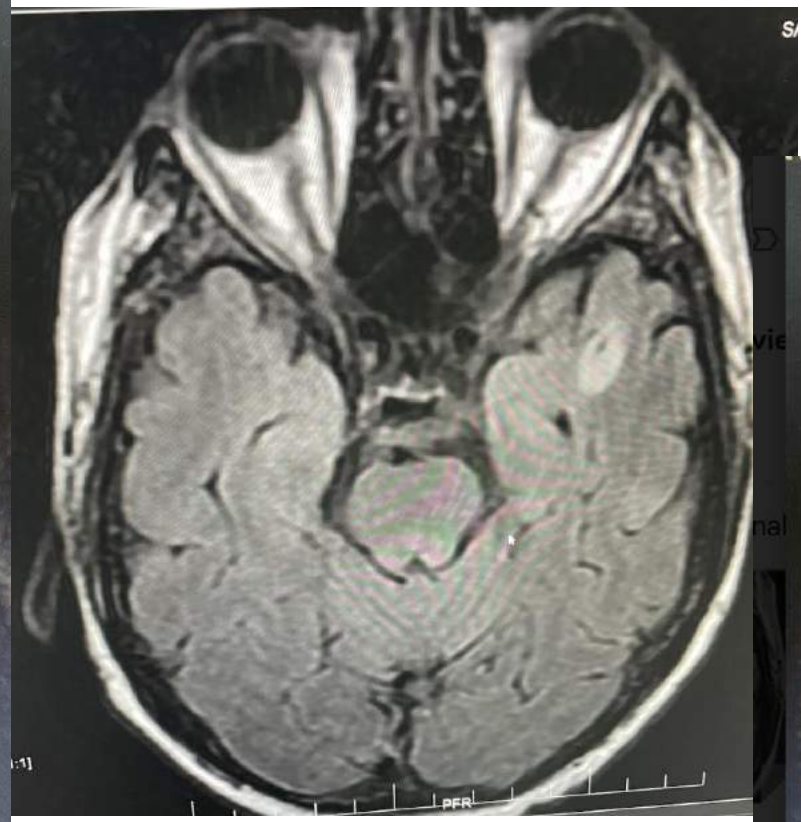
NOTAS

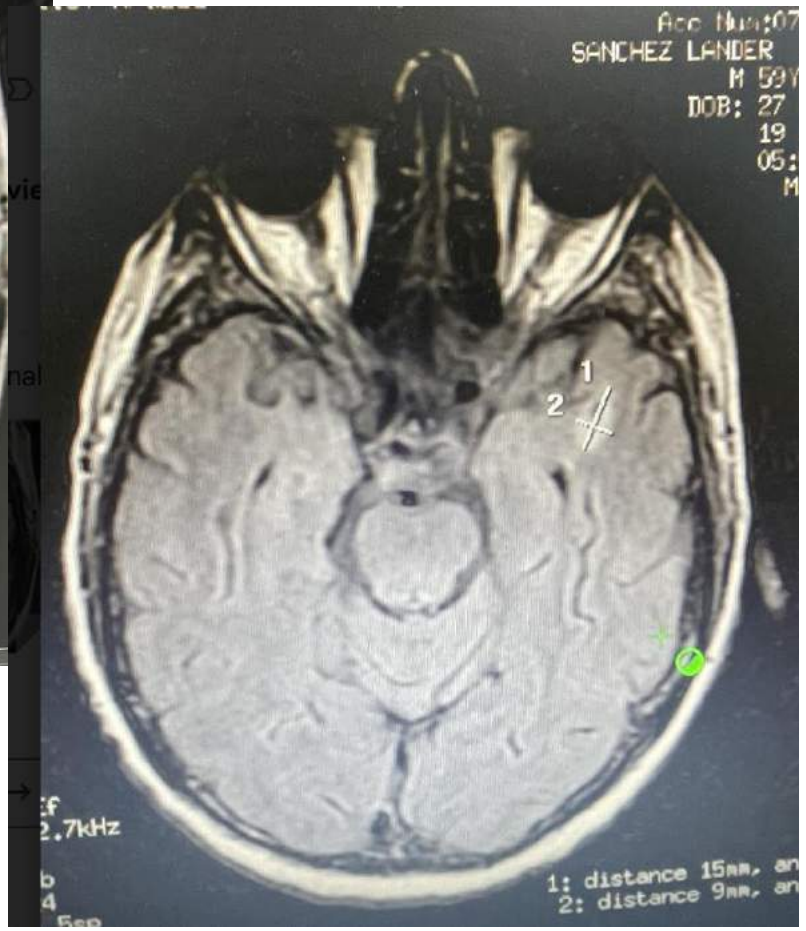
Se ha descrito que los linfomas foliculares de bajo grado con alto índice proliferativo pueden tener un comportamiento clínico más parecido a los linfomas foliculares de grado 3. Llama la atención en este caso la repsencia de células intensamente positivas para p53 que sugiere que pueda estar mutada, aunque el % de estas células no es muy alto. Estos dos aspectos pueden estar relacionados con la evolución clínica que se nos indica.

Wang SA, Wang L, Hochberg EP, Muzikansky A, Harris NL, Hasserjian RP. Low histologic grade follicular lymphoma with high proliferation index: morphologic and clinical features. Am J Surg Pathol. 2005;29(11):1490-6. doi: 10.1097/01.pas.0000172191.87176.3b

Colocamos 2do
R-CHOP, febrero 2023






SANCHEZ LANDER
DOB: 27
19
05:
1
2
2.7kHz
1: distance 15mm, an
2: distance 9mm, an

Review > Surg Neurol. 2006 Jun;65(6):590-4. doi: 10.1016/j.surneu.2005.08.027.

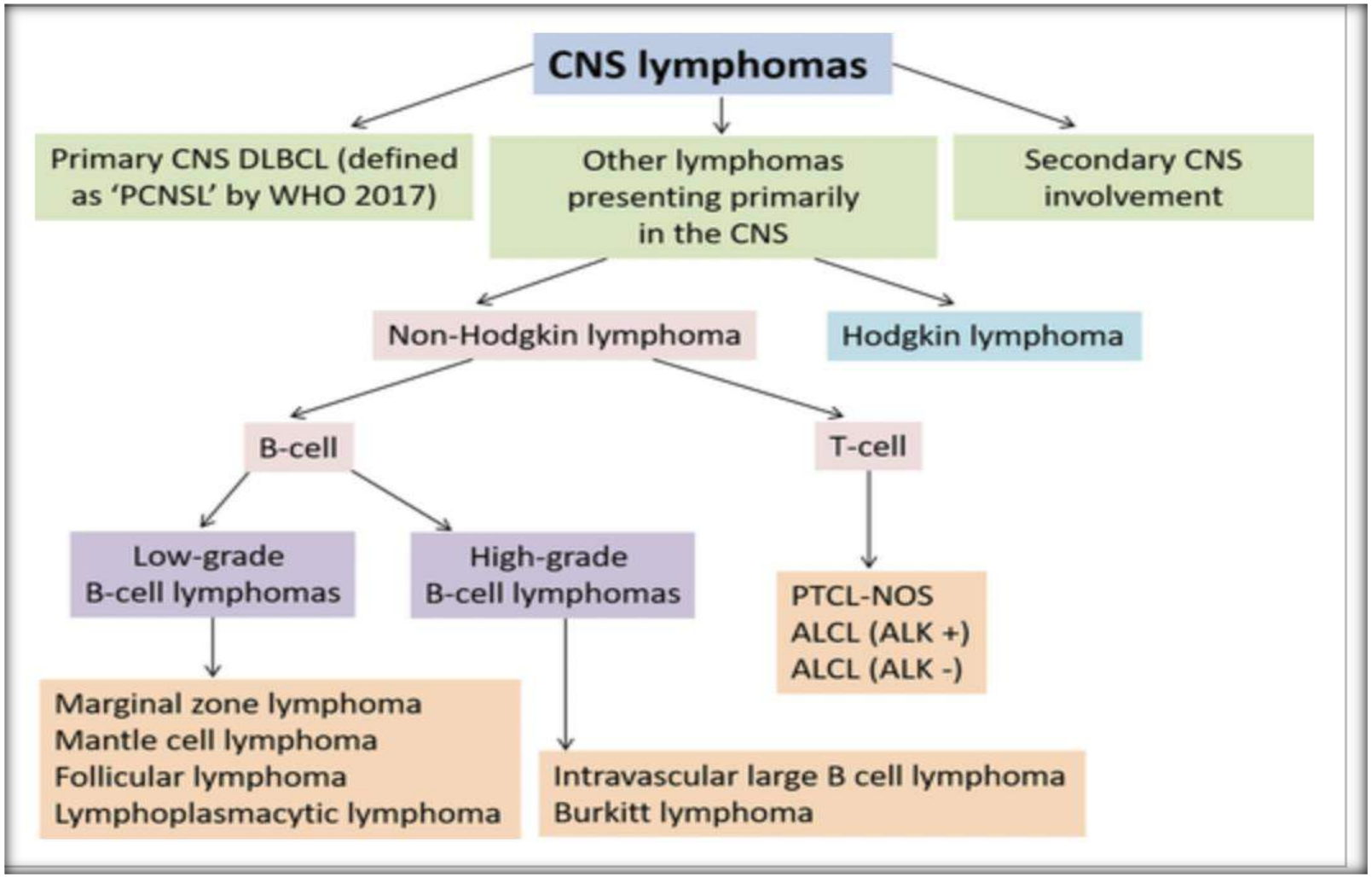
Secondary central nervous system involvement by follicular lymphoma: case report and review of the literature

N L Grupka [1], J Seinfeld, J Ryder, K O Lillehei, B K Kleinschmidt-Demasters

Parenchymal brain involvement, as opposed to dural or leptomeningeal, is a relatively uncommon pattern of spread to the CNS for systemic lymphomas. More significantly, follicular lymphomas are one of the least frequent types of indolent lymphomas to develop clinically apparent, secondary CNS spread.

Rare central nervous system lymphomas

Furqaan Ahmed Kaji, Nicolás Martinez-Calle, Vishakha Sovani, Christopher Paul Fox



Br J Haematol. 2022;197:662–678.

Received: 29 November 2021 | Accepted: 23 February 2022
DOI: 10.1111/bjh.18128

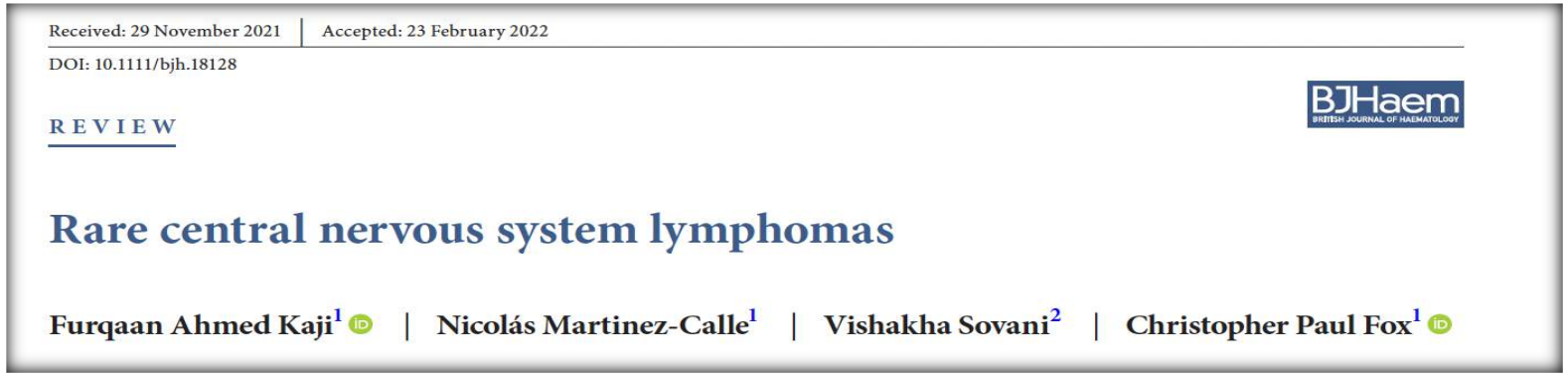
REVIEW

Rare central nervous system lymphomas

Furqaan Ahmed Kaji[1] | Nicolás Martinez-Calle[1] | Vishakha Sovani[2] | Christopher Paul Fox[1]

Marginal zone lymphoma

- By contrast to CNS-DLBCL, a recent systematic review of the literature found **that 77% of reported cases of CNS-Mage at diagnosis was 55 years ZL affect female patients**.
- The estimated median (range: 18–78), considerably younger compared to patients with CNS-DLBCL
- often associated with chronic infectious or inflammatory processes (e.g. *Helicobacter pylori* infection in the stomach, Hashimoto's thyroiditis, and Sjögren's syndrome).
- Extra-nodal MZLs of the CNS predominantly present as **dural-based lesions commonly mistaken for meningiomas on initial diagnostic imaging**
- Marginal zone B cells express pan B-cell markers (CD20, CD79A, CD19, CD22 and paired box 5 [PAX5]) and are typically CD5 and CD10 negative, and trisomy 3 as a common genetic abnormality in primary CNS-MZL rather than IGH translocation



Received: 29 November 2021 | Accepted: 23 February 2022
DOI: 10.1111/bjh.18128

REVIEW

Rare central nervous system lymphomas

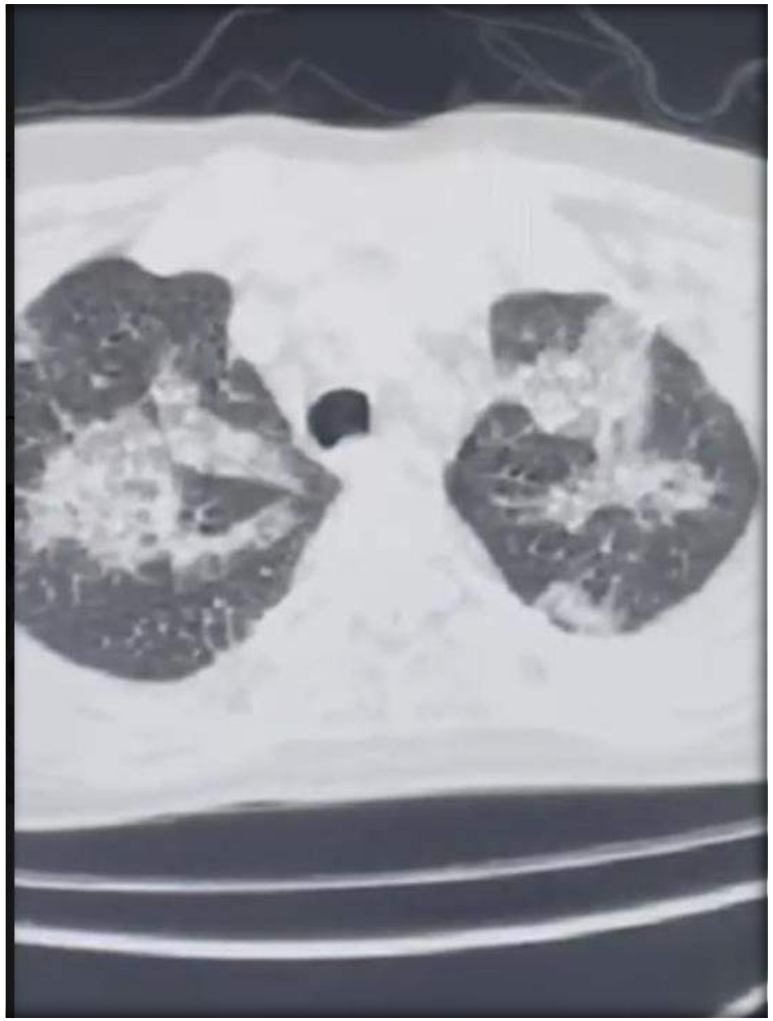
Furqaan Ahmed Kaji[1] | Nicolás Martinez-Calle[1] | Vishakha Sovani[2] | Christopher Paul Fox[1]

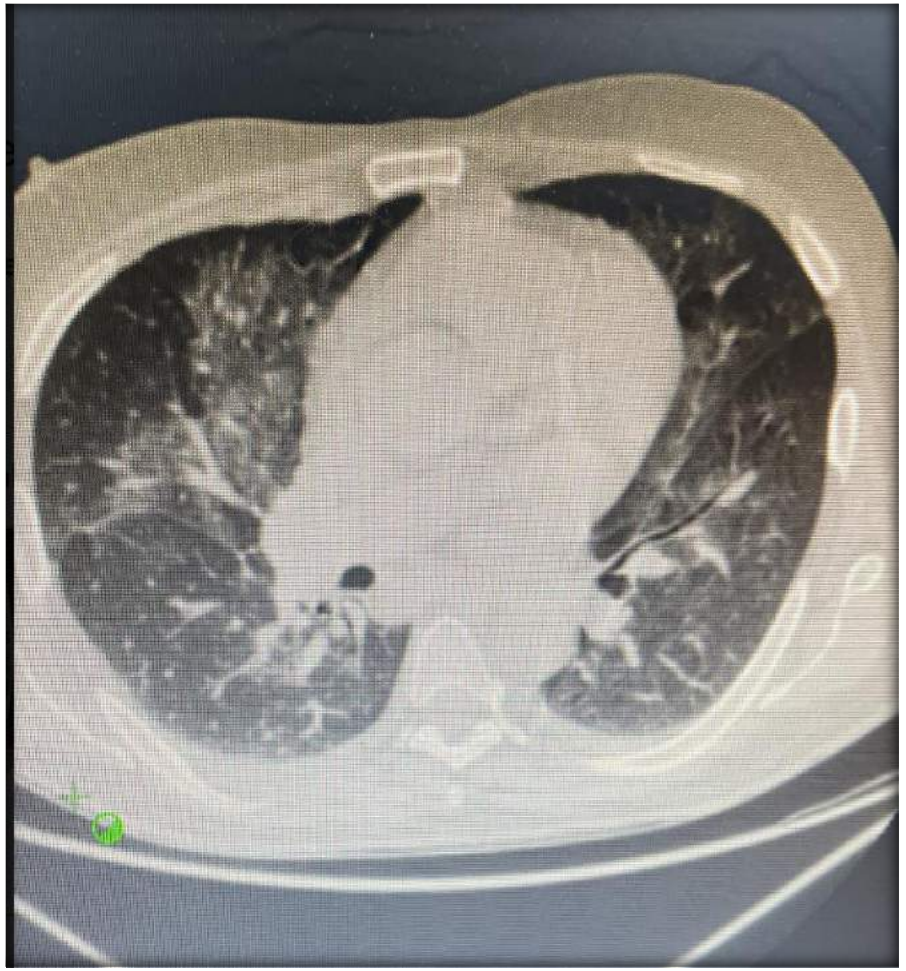
Mantle cell lymphoma

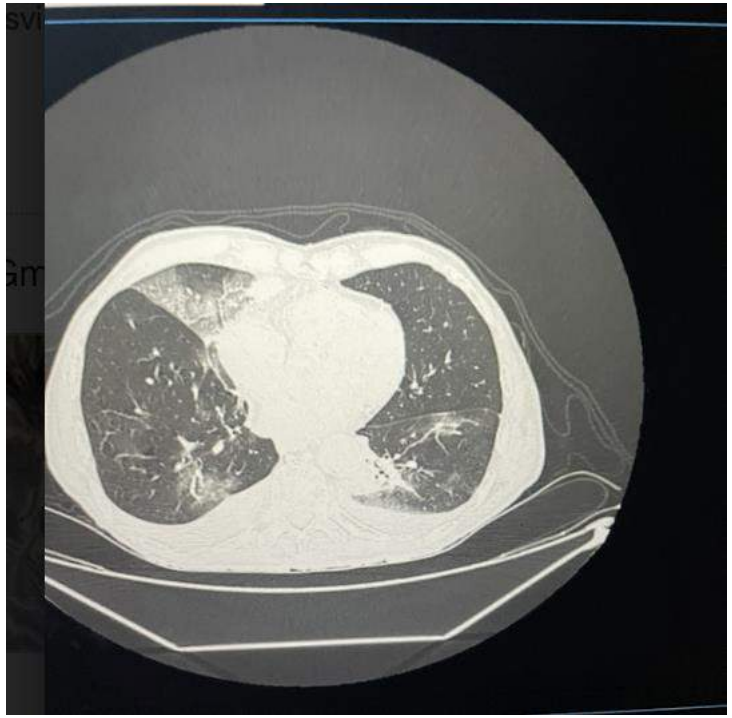
- Most cases of CNS disease involving MCL occur **in the context of relapsed** disease with an estimated reported frequency at relapse of 4.1%–7.8%
- Late event following initial therapy
- **Both parenchymal and leptomeningeal CN**S-MCL have been reported.
- Risk factors for developing CNS relapse include blastoid histology, raised serum LDH and high proliferative index

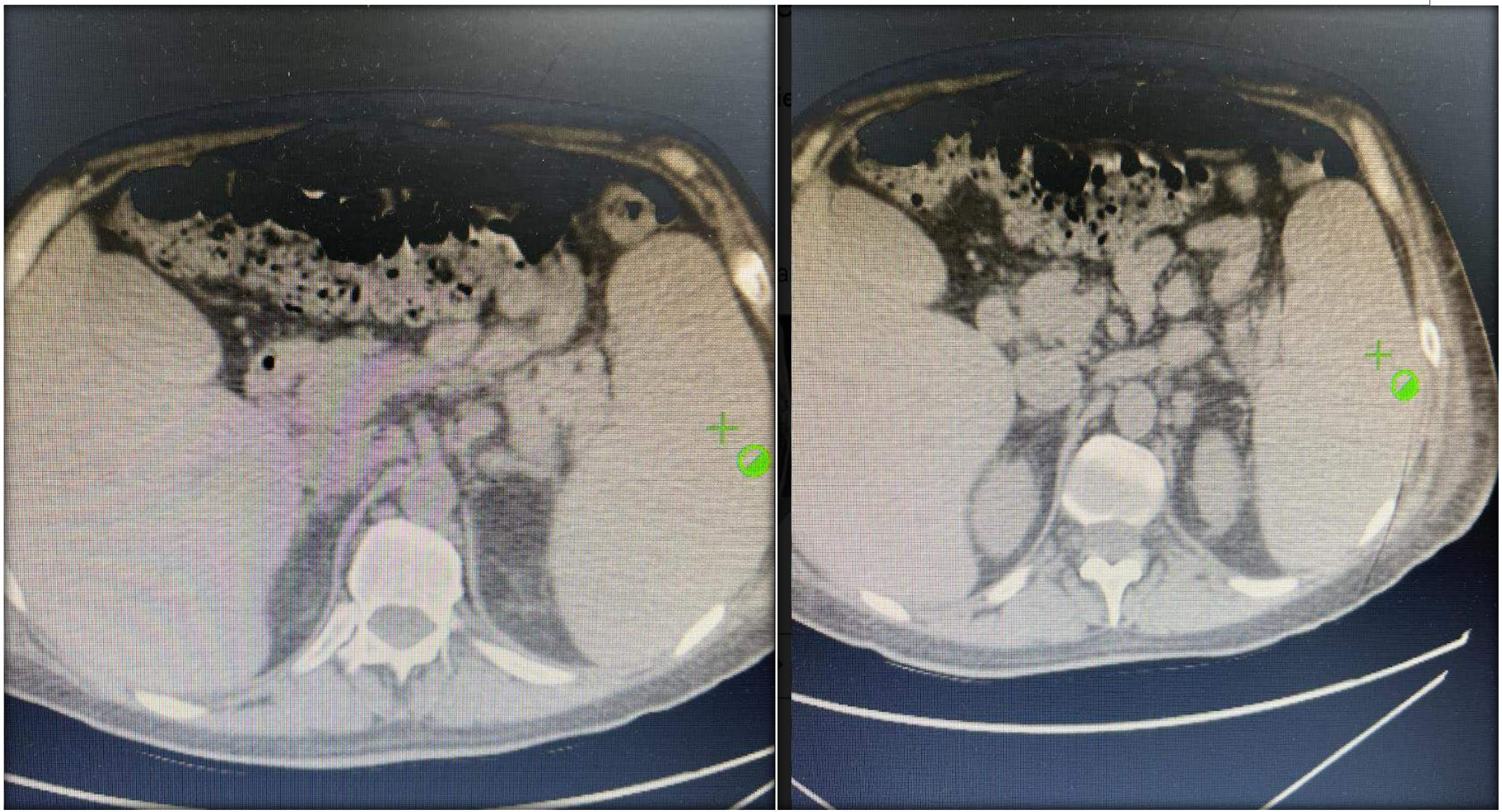
Follicular lymphoma

- Case reports dominate the literature on CNS-FL.
- Both primary and secondary CNS-FL have been described, although **transformation into high-grade B-cell non-Hodgkin lymphoma (B-NHL) must always be considered in the context of secondary CNS disease**
- Histopathologically, CNS-FL can manifest as a nodular or diffuse pattern and show a mixed population of centrocytes and centroblasts that typically co-express CD10 and BCL6. BCL2 overexpression, the hallmark of FL, is seen commonly in low-grade disease or can at times be negative









Estudios Complementarios

CD4 < 200 (SP 134 mm3)

DESCRIPCIÓN

ESTUDIO SOLICITADO:

DETECCIÓN DE CITOMEGALOVIRUS Y EPSTEIN BARR POR REACCIÓN EN CADENA DE LA POLIMERASA (PCR)

TIPO DE MUESTRA: SANGRE TOTAL

RESULTADO:

• EPSTEIN BARR **POSITIVO** Y CITOMEGALOVIRUS NEGATIVO

DESCRIPTION

REQUESTED STUDY:

DETECTION OF CYTOMEGALOVIRUS AND EPSTEIN BARR BY POLYMERASE CHAIN REACTION (PCR)

SAMPLE TYPE: TOTAL BLOOD

RESULTS:

• EPSTEIN BARR **POSITIVE** AND CYTOMEGALOVIRUS NEGATIVE

REQUESTED STUDY:

DETECTION OF CYTOMEGALOVIRUS AND EPSTEIN BARR BY POLYMERASE CHAIN REACTION (PCR)

SAMPLE TYPE: LAVADO BRONCO ALVEOLAR

RESULTS:

• THE SAMPLE TESTED IS **POSITIVE** FOR CYTOMEGALOVIRUS AND EPSTEIN BARR

DESCRIPTION

REQUESTED STUDY:

QUANTIFICATION OF CYTOMEGALOVIRUS (CMV) DNA BY REAL-TIME POLYMERASE CHAIN REACTION (PCR)

QUANTIFICATION OF A HUMAN CMV PP65 PHOSPHORYLATED MATRIX PROTEIN GENE FRAGMENT BY REAL-TIME POLYMERASE CHAIN REACTION (PCR) USING SPECIFIC PRIMERS AND A TAQMAN PROBE.
IT IS RECOMMENDED THAT ABSOLUTE VIRAL LOAD VALUES OBTAINED BY GENOMIC AMPLIFICATION PROCEDURES BE INTERPRETED AS ANY VALUE WITHIN 0.5 LOG (± 300 TIMES) OF THE VALUE OBTAINED.

SAMPLE TYPE: LAVADO BRONCO ALVEOLAR

RESULTS:

• CMV DNA DETECTED, 942 Copies/ml

• LOG: 2,97

TEST DETECTION LIMIT 100 Copies/ml

GELL
Grupo de Estudio Latinoamericano de Linfoproliferativos

DESCRIPTION

REQUESTED STUDY:
DETECTION OF HISTOPLASMA CAPSULATUM BY POLYMERASE CHAIN REACTION (PCR)

SAMPLE TYPE: LCR

RESULTS:

• THE TESTED SAMPLE IS NEGATIVE

DESCRIPTION

REQUESTED STUDY:
DETECTION OF TOXOPLASMA DNA BY POLYMERASE CHAIN REACTION (PCR)

SAMPLE TYPE: LCR

RESULTS:

• THE SAMPLE ANALYZED IS **NEGATIVE**

DESCRIPTION

REQUESTED STUDY:
MULTIPLEX VIII FOR THE DETECTION OF CMV, EBV, HERPES SIMPLE TYPE 1 AND 2, VARICELA ZOSTER, HERPES VIRUS 6. BY POLYMERASE CHAIN REACTION (PCR)

SAMPLE TYPE: LCR

• EPSTEIN BARR DNA DETECTION: **POSITIVE**
• CYTOMEGALOVIRUS DNA DETECTION: **NEGATIVE**
• VARICELLA ZOSTER DNA DETECTION: **NEGATIVE**
• HERPES SIMPLEX 1 DNA DETECTION: **NEGATIVE**
• HERPES SIMPLEX 2 DNA DETECTION: **NEGATIVE**
• HERPES VIRUS 6 DNA DETECTION: **NEGATIVE**

DESCRIPTION

REQUESTED STUDY:
DETECTION OF MYCOBACTERIUM TUBERCULOSIS BY REAL-TIME POLYMERASE CHAIN REACTION (PCR)

SAMPLE TYPE: LCR

RESULTS:

• THE ANALYZED SAMPLE IS **NEGATIVE**. NO AMPLIFICATION OF DNA WAS OBSERVED IN THE SAMPLE ANALYZED.

ESTUDIO INMUNOFENOTÍPICO DEL LÍQUIDO CEFALORRAQUÍDEO (LCR) POR CITOMETRÍA DE FLUJO

0076/ ID 424303
Fecha del Examen: 17/01/2023

DATOS DEL PACIENTE
NOMBRE/APELLIDO: JORGE SÁNCHEZ LANDER
Género: M
C. I. Nº: V.- 6.130.324
Fecha Nacimiento: 27/01/1963
Edad: 59.11 AÑOS
Ciudad / Población de Residencia: SANTA SOFIA
Estado: MIRANDA

DATOS DE LA REFERENCIA
Médico que refiere: MARÍA ALEJANDRA TORRES
Nº M.P.P.S.: 30.846
Especialidad: HEMATOLOGÍA
Hospital/Clínica/Centro de Salud: CLÍNICA SANTA SOFÍA
Ciudad: EL CAFETAL
Estado: MIRANDA
Diagnóstico Presuntivo: LNH-B FOLICULAR INFILTRANDO SNC
Muestra remitida: LCR
Fecha de la muestra: 17/01/2023

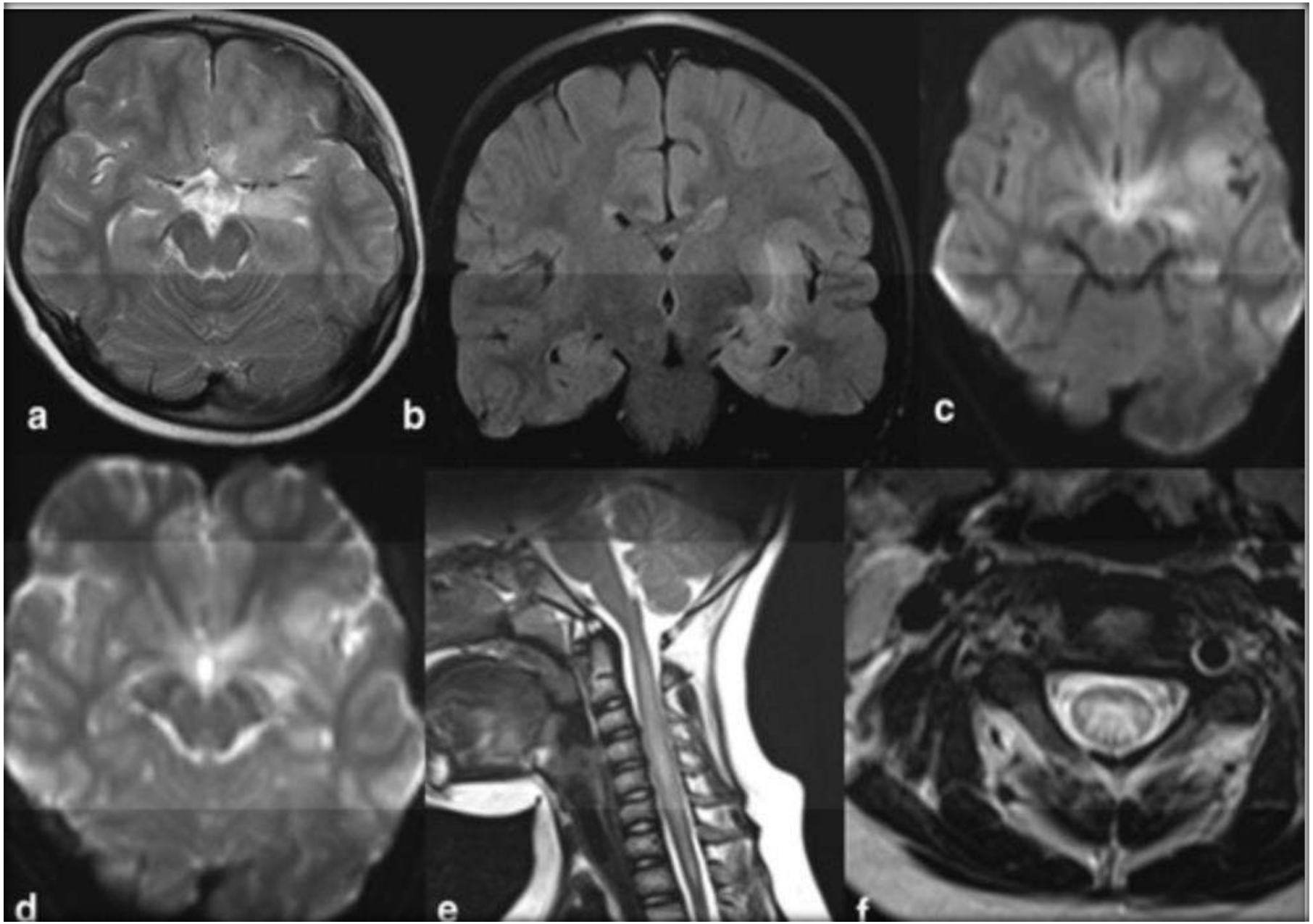
ANTECEDENTES: estudio realizado en muestra de ganglio el 11/02/2020: detectó un 45% de células linfoides B monoclonales Lambda, cuyo fenotipo está asociado a LNH-B, expresando CD45(+)HT, CD19(+)HT, CD20(+)HT , CD22(+)DIM, CD79b(+)HT, CD38(+)HT, suplgM(+)HT, suplgLambda(+), suplgKappa(-), CD200(-) CD25(-), CD11c(-), CD103(-), CD123( ), CD30(-) , CD5(-), CD2(-), CD3(-), CD4( ), CD8(-) y CD10(-).
Estudio realizado en muestra de ganglio el 30/09/20222: detectó un 3.41% de células linfoides B monotípicas Lambda, cuyo fenotipo es CD45(+)HT, CD19(+)DIM CD20(+)DIM , CD22(+)DIM, CD79b(+)DIM, CD38(+)HT, suplgM(+)HT, suplgLambda(+), suplgKappa(-), CD200(-) CD25(-), CD11c(-), CD103(-), CD123(-), CD30(-) , CD5(-), CD2(-), CD3(-), CD4(-), CD8(-) y CD10(-).
Estudio realizado en muestra de sp, realizado el 16/01/2023: detectó un 51.50% de células linfoides B monotípicas kappa, expresando el fenotipo CD45(+)HT, CD19(+)DIM, CD20(+)HT , CD22(+)DIM, CD79b(+)HT, CD10(+)DIM, CD38(+)HT, CD81(+)HT, CD200PE(50%)DIM, CD25PE(50%)DIM, suplgKappa(+), suplgLambda(-), suplgM(-), CD11c(-), CD103(-), CD123(-), CD30(-) , CD5(-), y CD3(-) .

COMENTARIOS: se recibe 1mL de muestra de LCR incoloro de aspecto límpido, donde el 35.20% de los eventos corresponden a células evaluables. Eventos adquiridos evaluables: 19.000

POBLACIONES CELULARES IDENTIFICADAS EN LA MUESTRA (datos referidos a la celularidad total):
Linfocitos T: 2.10% **Linfocitos B**: 0.50%

CONCLUSIÓN Y OBSERVACIONES:
El estudio no detectó células linfoides B monotípicas. Correlacionar con datos citomorfológicos y clínicos.

GELL
Grupo de Estudio Latinoamericano de Linfoproliferativos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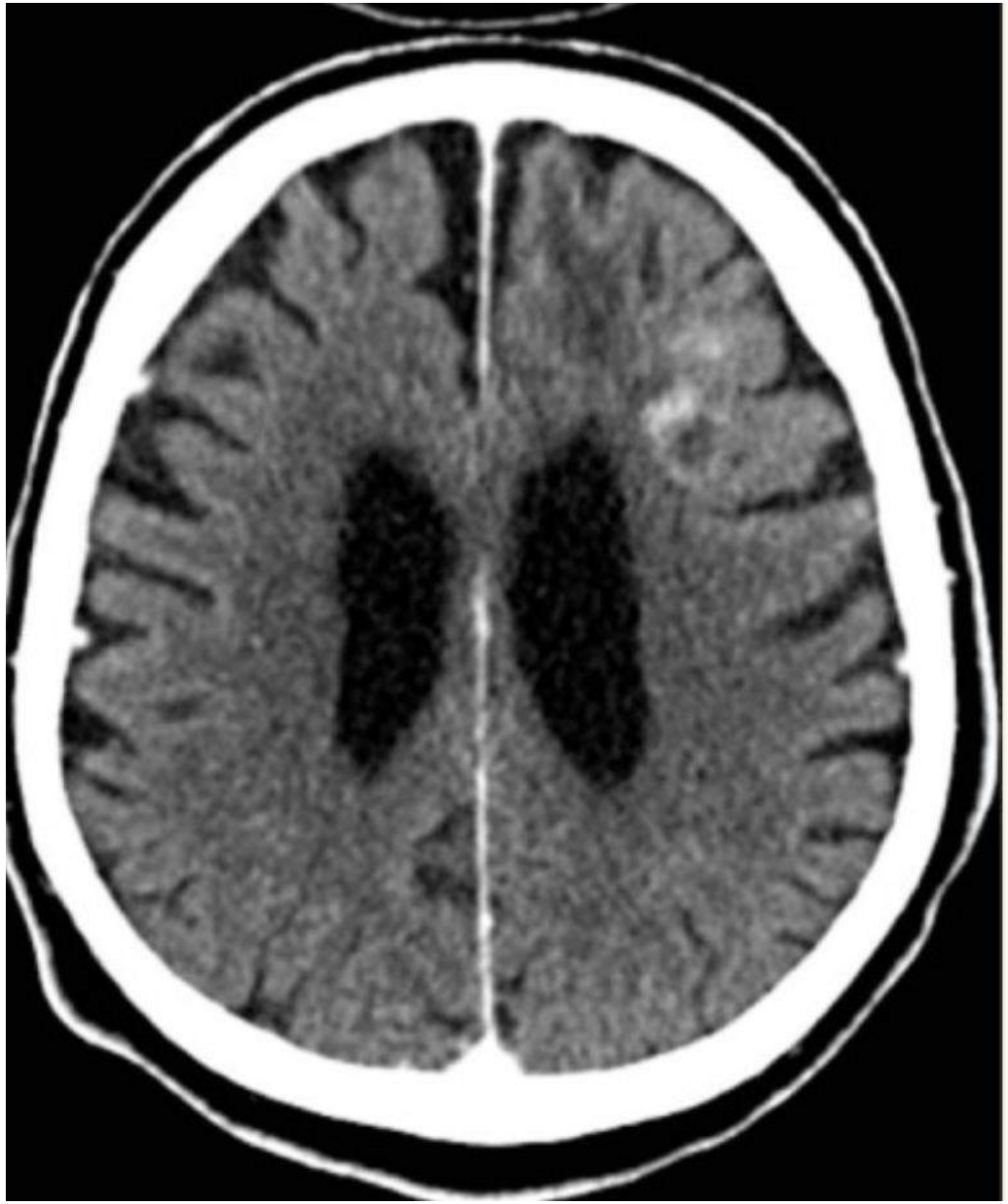
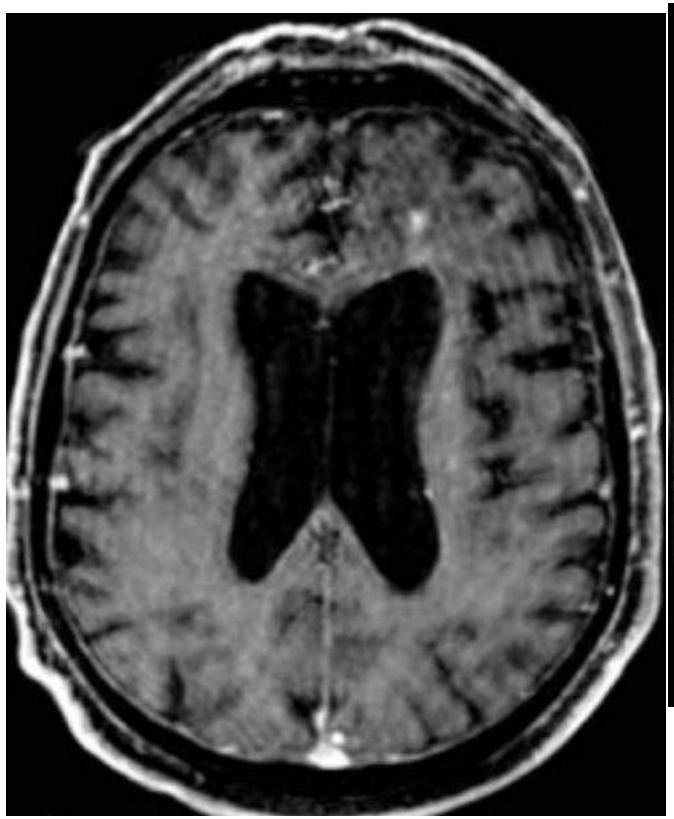
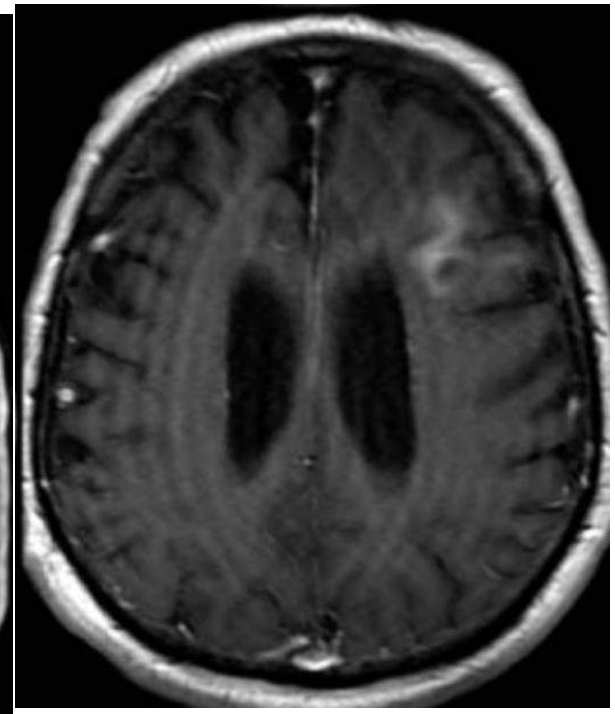






Axial computed tomography (CT) images show left frontal lobe heterogeneus hypodensity in the white matter with areas of abnormal contrast enhancement.

Bendamustine Reactivates Latent Epstein-Barr Virus

Samantha G. Fernandez[a] and JJ L. Miranda[a,b,#]

Because bendamustine plus rituximab, an anti-CD20 monoclonal antibody, effectively treats indolent non-Hodgkin lymphoma, we investigated this combination's interaction with latent EBV. 100 μg/mL rituximab and 10 μM bendamustine independently induce EBV reactivation after 2 days, but combination generates even more Rituximab similarly enhances reactivation induced by dexamethasone. CD20 engagement combined with other latency disruptors may be a general means of enhancing induction.

The ability of bendamustine to reactivate latent EBV informs future clinical strategies. Taken pessimistically, our work warns that drug treatment may exacerbate risk of adverse effects caused by viremia in an already weakened immune system. Impairment of lymphocyte recovery by bendamustine [14] particularly warrants heightened precautions. Personalised medicine that tailors chemotheraphy regimens to EBV status of the tumor may suggest the preferred treatment

Leuk Lymphoma. 2016 May; 57(5): 1208–1210.

GENOMIK
J-30636863-9
LABORATORIO GENOMIK C.A.

# DE PACIENTE:	C-70881
NOMBRE Y APELLIDO:	JORGE ENRIQUE SANCHEZ LANDER
# CEDULA:	V-6130324
EDAD:	60 Años
FECHA DE TOMA DE MUESTRA:	06-03-2023 16:30
MÉDICO TRATANTE:	MARIA TORRES

DESCRIPCIÓN

ESTUDIO SOLICITADO:
DETECCIÓN DE CITOMEGALOVIRUS Y EPSTEIN BARR POR REACCIÓN EN CADENA DE LA POLIMERASA (PCR)

TIPO DE MUESTRA: SANGRE TOTAL

RESULTADO:

• LA MUESTRA ANALIZADA ES NEGATIVA PARA CITOMEGALOVIRUS Y EPSTEIN BARR

DESCRIPTION

REQUESTED STUDY:
DETECTION OF CYTOMEGALOVIRUS AND EPSTEIN BARR BY POLYMERASE CHAIN REACTION (PCR)

SAMPLE TYPE: TOTAL BLOOD

RESULTS:

• SAMPLE TESTED NEGATIVE FOR CYTOMEGALOVIRUS AND EPSTEIN BARR

Nombre: Jorge Sanchez **Céd. Ident:** 6130324
Muestra de: MEDULA OSEA **Patología Nº:** MEB-53776
Méd. Solic: MARIA ALEJANDRA TORRES **Fecha:** 23/03/2023

INFORME ANATOMOPATOLOGICO

DESCRIPCION MACROSCOPICA:
Tres fragmentos cilíndricos el mayor de 1 x 0,2 cm y el menor de 0,4 x 0,2 cm de color pardo oscuro y de consistencia firme. Se incluyen para estudio histológico

DIAGNOSTICO:
MEDULA OSEA; BIOPSIA:
HIPERCELULAR
PANHIPERPLASIA MODERADA
SERIE ERITROIDE PRESENTE CON MADURACION NORMOBLASTICA
SERIE GRANULOCITICA PRESENTE CON ARRESTO PARCIAL DE LA MADURACION
SERIE MEGACARIOCITICA PRESENTE CON ALGUNAS FORMAS HIPOLOBULADAS
HEMOSIDEROSIS MARCADA (GRADO 4)
FIBROSIS MODERADA
EDEMA Y HEMORRAGIA RECIENTE
NO SE OBSERVA INFILTRACION POR LINFOMA

JORGE ENRIQUE SANCHEZ LANDER **C.I.: 6.130.324** FEMENINO Ingreso:23/3/2023 10:58 a. m.
Edad: 60 Años **ID: 13936** Impreso:24/3/2023 12:55 p. m.
Dirección: AV. PPAL. SAN MARINO RESD. DORAVILA
Convenio: AMBULATORIO

MARCADORES MONOCLONALES

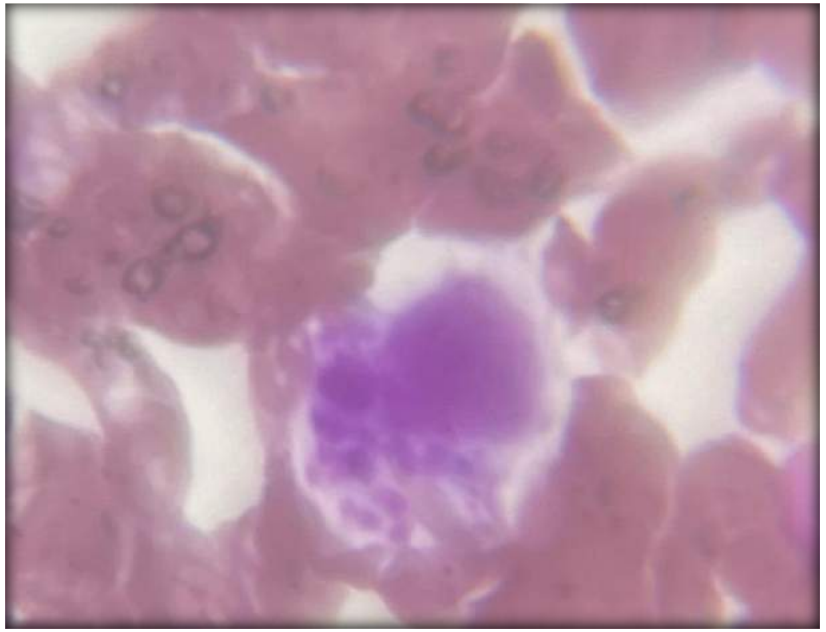
IDX: LNH FOLICULAR
DRA. MARÍA ALEJANDRA TORRES
HEMATOLOGÍA ONCOLOGÍA 360, C.A.
EL CAFETAL - CARACAS
Tipo de Muestra MO
CELULARIDAD: MODERADA
ESPÍCULAS: MODERADAS
Fecha de la Toma: 23/03/2023
Fecha Recepción: 23/03/2023

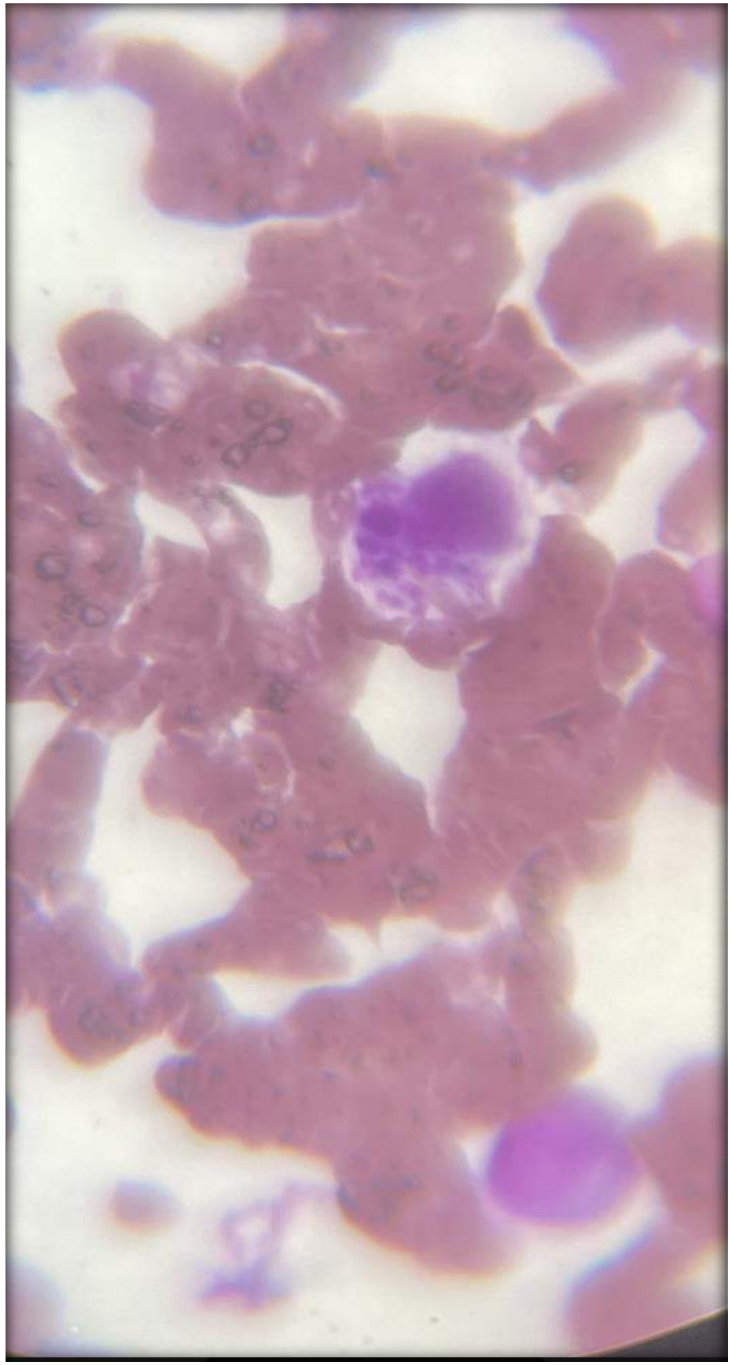
Marcador	Resultado %
CD19	10
CD10	10
CD13	18
CD7	15
CD3	15
CD8	8
KAPPA	CLONAL
FMC7	NEGATIVO
CD25	NEGATIVO
CD200	5

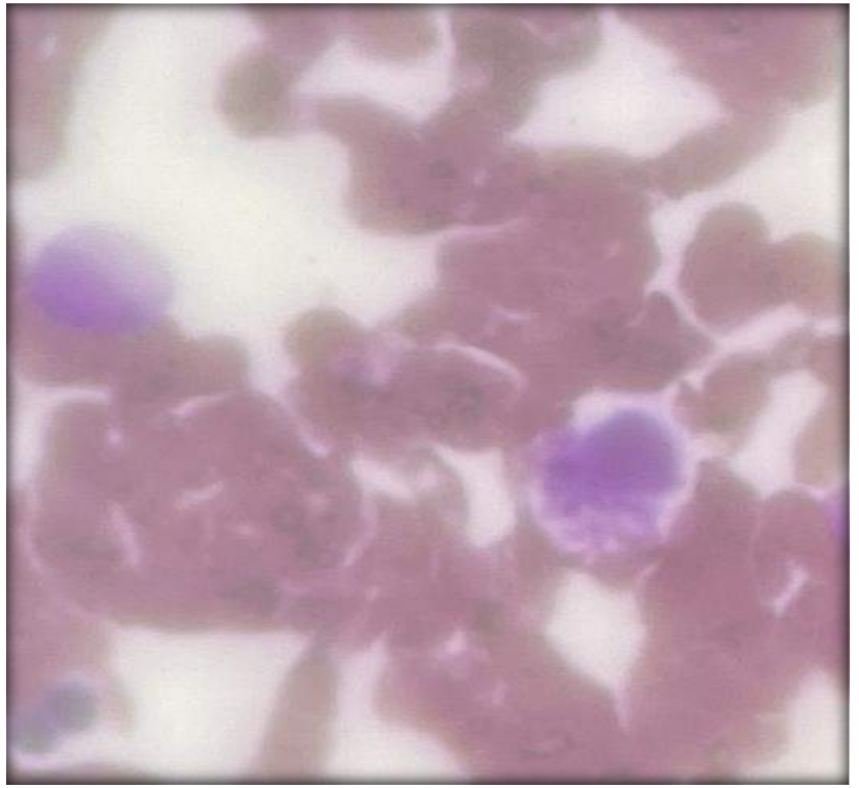
Marcador	Resultado %
CD20	10
CD45	72
HLA-DR	10
CD5	15
CD4	7
CD14	15
LAMBDA	NEGATIVO
CD23	NEGATIVO
CD38	NEGATIVO

# EVENTOS	SENSIBILIDAD	RESULTADO
100.000	10-4	

EL ANÁLISIS DETECTÓ 10% DE CÉLULAS LINFOIDES B CLONALES KAPPA CON CARACTERÍSTICAS INMUNOFENOTÍPICAS DE LNH FOLICULAR.







Pancitopenia
Hepato esplenomegalia leve
LDH 798 U/L
Ferritina 18.300 mg/dl
Proteina C reactiva 49
VSG 129
Triglicéridos 520 mg/dl

Epstein-Barr Virus-Associated Hemophagocytic Lymphohistiocytosis Resembling Recurrent Follicular Lymphoma: A Case Report

Clin Pediatr Hematol Oncol 2022;29:79-83.

EBV is a common pathogen causing HLH During an EBV infection, the virus immortalizes B lymphocytes, and cytotoxic T lymphocytes are directed toward both latent and lytic viral antigens expressed on EBV-infected B-cells HLH is characterized by persistent fever, cytopenia, liver dysfunction, hepatosplenomegaly, and hemophagocytosis in the bone marrow, lymph nodes, liver, and spleen.

Secondary Hemophagocytic Lymphohistiocytosis With Epstein–Barr Virus-Associated Transformed Follicular Lymphoma: A Case Report and Literature Review

Huan Xu[1], Xia Xu[2], Guohui Cui[3], Jun Fang[3], Wanxin Chen[3], Mei Xue[3], Runming Jin[1], Hongbo Chen[1], Lu Zhang[3] and Yu Hu[3*]*

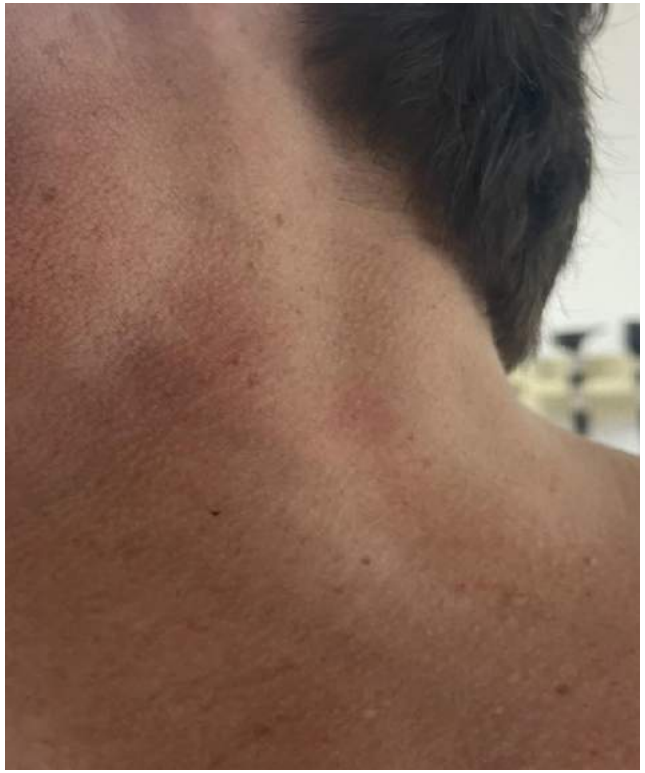
Secondary Hemophagocytic Lymphohistiocytosis With Epstein–Barr Virus-Associated Transformed Follicular Lymphoma: A Case Report and Literature Review

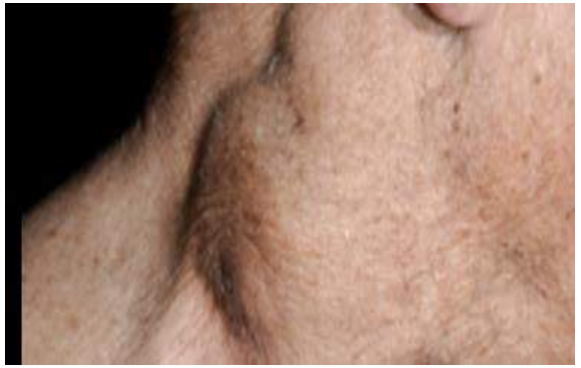
Front. Oncol., 25 June 2021
Sec. Hematologic Malignancies
Volume 11 - 2021 |
https://doi.org/10.3389/fonc.2021.681432

EBV is also the most common infection highly associated with HLH, which is a rare syndrome of severe, life-threatening hyperinflammation. The underlying pathophysiology of HLH is the impaired activity of cytotoxic T lymphocytes and natural killer (NK) cells, leading to uncontrolled immune activation, hypercytokinemia, and macrophage proliferation.

The main pathophysiology of HLH is the impaired activity of cytotoxic T lymphocytes and NK cells, leading to uncontrolled immune activation, hypercytokinemia, macrophage proliferation, and immune-mediated injury of multiple organ systems HLH comprises primary (genetic) and secondary (infection, malignancy, and autoimmune disease-associated) forms. **Viral infection is the most frequent immunologic trigge**r. Approximately half of all infection-associated HLH cases involve EBV

Presence of Epstein–Barr virus infection in patients with follicular lymphoma is associated with more aggressive clinical course and increased risk of high-grade transformation. Hemophagocytic lymphohistiocytosis in response to Epstein–Barr virus infection or lymphoma remains fatal.





JORGE ENRIQUE SANCHEZ LANDER **C.I.: 6.130.324** FEMENINO Ingreso: 10/4/2023 11:36 a. m.
Edad: 60 Años **ID: 13936** Impreso: 12/4/2023 12:17 p. m.
Dirección: AV. PPAL. SAN MARINO RESD. DORAVILA
Convenio: AMBULATORIO

MARCADORES MONOCLONALES

IDX: LNH
DRA. MARIA ALEJANDRA TORRES
HEMATOLOGIA ONCOLOGIA 360 C.A.
Tipo de Muestra SP
CELULARIDAD:ABUNDANTE
Fecha de la Toma: 10/04/2023
Fecha Recepción: 10/04/2023

Marcador	Resultado %
CD19	POSITIVO 90
CD10	POSITIVO 90
HLA-DR	POSITIVO 90
CD5	2
CD4	1
CD14	NEGATIVO
LAMBDA	NEGATIVO
CD23	NEGATIVO
CD38	POSITIVO 90

Marcador	Resultado %
CD20	POSITIVO 90
CD45	98
CD7	2
CD3	2
CD8	1
KAPPA	CLONAL
FMC7	POSITIVO 60
CD25	NEGATIVO
CD200	POSITIVO 90

# EVENTOS	SENSIBILIDAD	RESULTADO
100.000	10-4	POSITIVO

EL ANÁLISIS DETECTÓ 90% DE CELULAS B CLONALES KAPPA TIPO LNH DE ALTO GRADO DE PROLIFERACION.

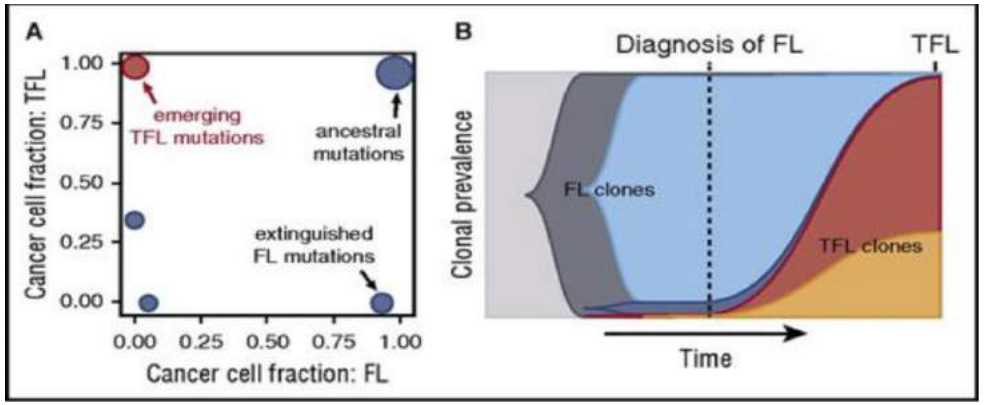
Role of Epstein-Barr virus in transformation of follicular lymphoma to diffuse large B-cell lymphoma: a case report and review of the literature

Massimo Granai,[1] Maria Raffaella Ambrosio,[1] Ayse Akarca,[2] Lucia Mundo,[1] Federica Vergoni,[3] Raffaella Santi,[3] Virginia Mancini,[1] Gioia di Stefano,[3] Teresa Amato,[1] Cristiana Bellan,[1] Benedetta Puccini,[3] Ester Sorrentino,[1] Kikkeri N. Naresh,[4] Lorenzo Leoncini,[1] Teresa Marafioti,[2] and Stefano Lazzi[1]

El proceso de transformación

- El impacto de la quimioterapia en el microambiente inmunitario; el papel del sistema inmunitario; la ventaja proliferativa proporcionada por el VEB;
- **Nuestro caso favorece la hipótesis de que el VEB fue el desencadenante responsable de la transformación de FL en DLBCL, en condiciones inmunológicas permisivas**.

- Convencionalmente, se piensa que la linfomagénesis impulsada por el VEB implica principalmente el ciclo latente, pero cada vez hay más pruebas de que los productos génicos líticos contribuyen al desarrollo y mantenimiento de las neoplasias malignas mediante la inducción de factores de crecimiento, la producción de citocinas oncogénicas como la interleucina-10, el factor de crecimiento transformante-β9-11 y la evasión de la respuesta inflamatoria mediante la atenuación del interferón-γ



Can histologic transformation of follicular lymphoma be predicted and prevented?

On the molecular level, transformed FL (TFL) differs from preceding indolent FL by higher numbers of single-nucleotide mutations, small insertions and deletions, copy-number changes, and structural rearrangements. Transformation occurs via the activation of known or putative oncogenes (*MYC, CCND3*) and inactivation of known or putative tumor suppressor genes (*TP53, CDKN2A/B*, *B2M*

In this regard, *TP53* is one of the genes that is most strongly associated with transformation, mutations being rare in diagnostic samples (~5%) but common in TFL (25%-30%). Whereas *TP53* mutations typically occur in the absence of deletion of the other allele in untransformed FL, biallelic hits through deletion, loss of heterozygosity, or further mutation are common in TFL

Moreover, it is unclear, at present, whether transformation occurs by determined sequences of successive genetic hits and/or whether certain alterations need to co-occur in order to confer an aggressive phenotype.

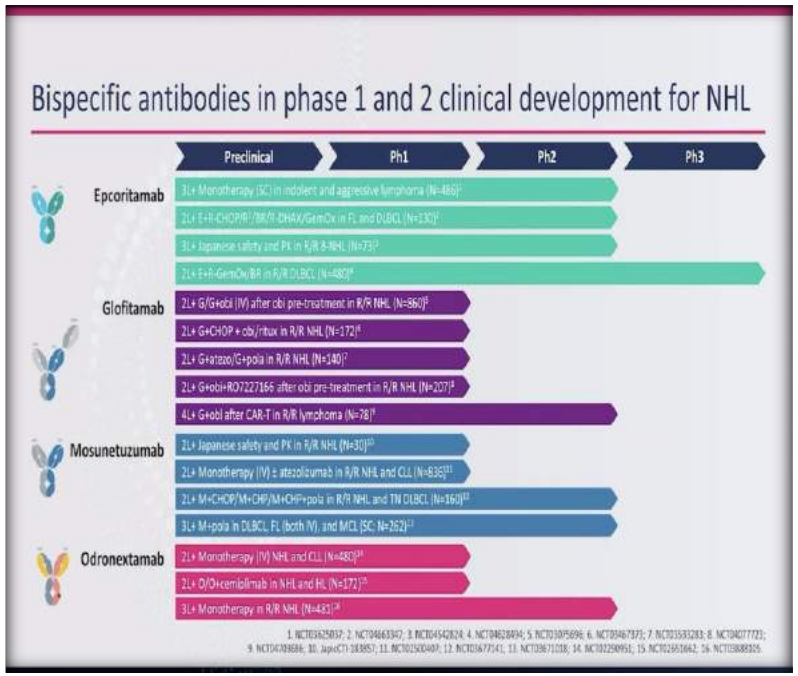
Tumor-specific ctDNA may originate from multiple clones and ctDNA is thus often considered as an integrator of the intrapatient mutational heterogeneity

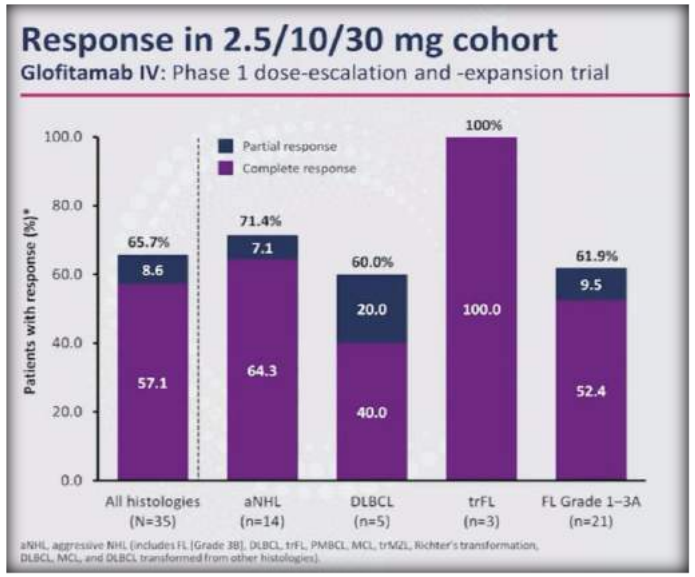
Robert Kridel, Laurie H. Sehn, Randy D. Gascoyne . *Blood* (2017) 130 (3): 258–266.

En la circunstancia de No limitacioón para nuevos tratamientos

- Qué hubiesen hecho diferente? En el mejor escenario teórico
- Monclonales?
- Biespecificos?
- Car -T cell?

- Cómo sería su secuenciación

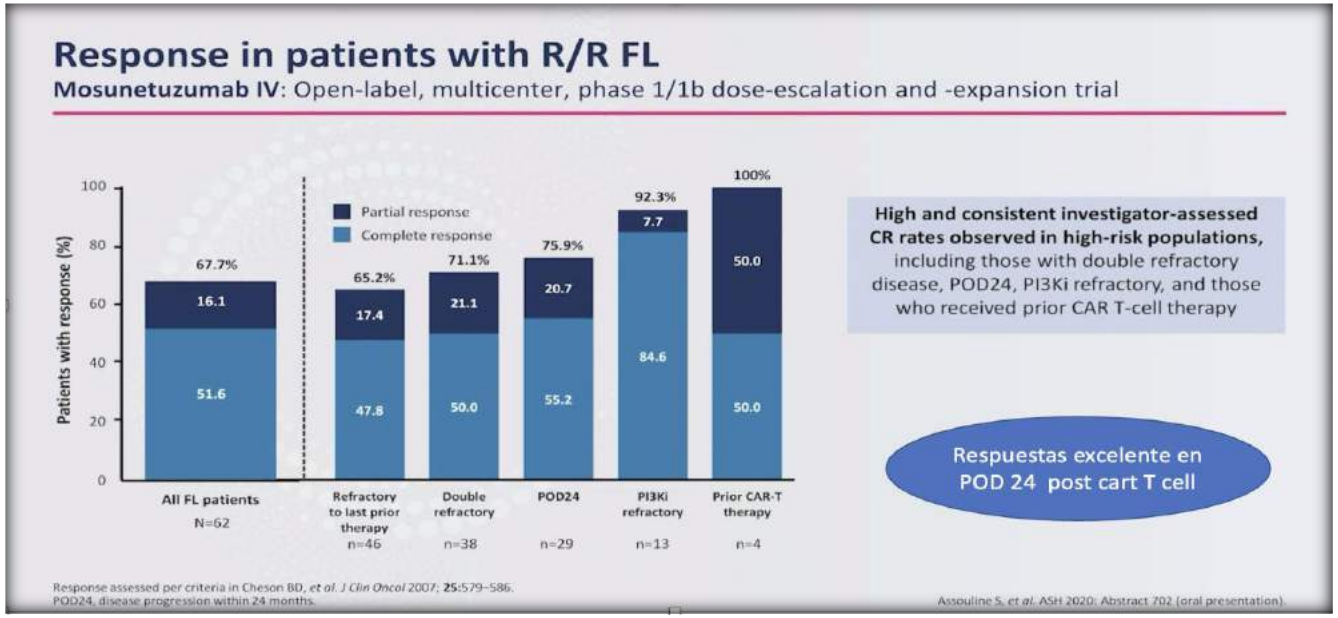




Neurologic AEs in ≥5%, n (%)	2.5/10/30 mg cohort (n=35)
Any neurologic AEs	11 (31.4)
Grade ≥3	
Headache	0
Dizziness	0

Other common (≥5% of patients) Grade ≥3 AEs, n (%)	2.5/10/30 mg cohort (n=35)
Thrombocytopenia	3 (8.6)
Neutropenia	9 (25.7)
Cytokine release syndrome	2 (5.7)

Biespecificos

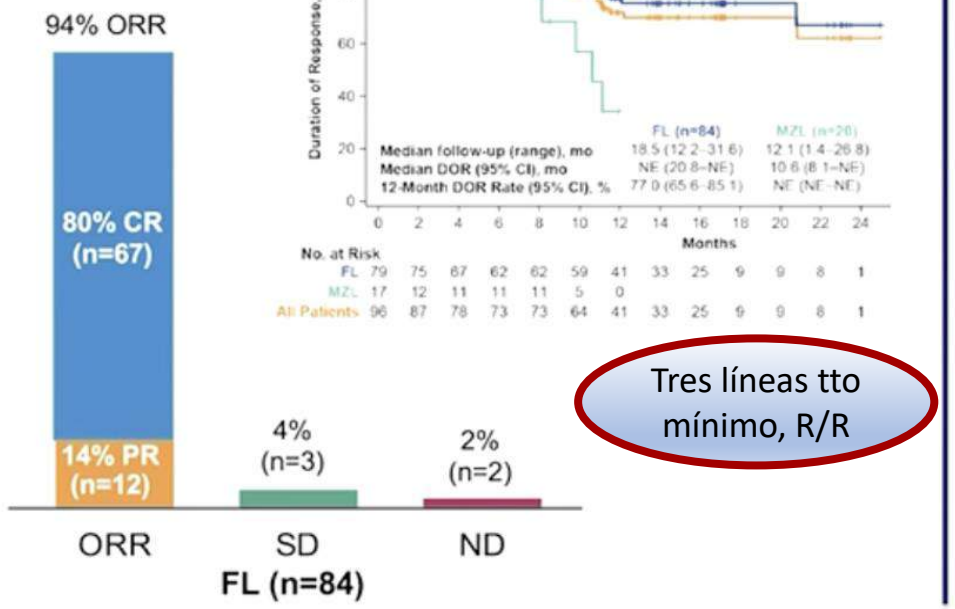


Linfomas Folicular CAR T Cell

CAR is a synthetic receptor comprising an extra-cellular tumor antigen recognition domain (CD1,-CD20), which is fused to the CD3ζ chain for intracellular signaling The binding triggers the T-cell receptor (TCR) intracellular domain and leads to T-cell responses against antigen-expressing cells.

Selected AEs ≤8 Weeks of Infusion	Treated Patients N=124 All Grades, %	Grade ≥3, %
CRS[b]	78	6
Neurological event	56	15

ZUMA-5



Tres líneas tto mínimo, R/R

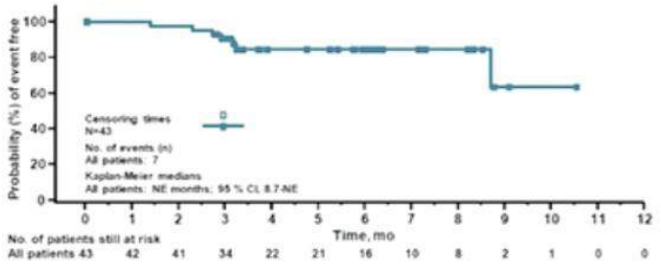
Jacobson et al. EBMT 2021

Elara

Best Overall Response Rate

Response Rate, %	Patients Evaluable for Efficacy[a] (n=52)
CR	65.4[a]
PR	17.3
ORR (CR + PR)	82.7

At 10 Months Median Follow-up for Efficacy, Median DOR Not Reached



Selected AEs ≤8 Weeks of Infusion	Treated Patients N=97 All Grades, %	Grade ≥3, %
CRS[b]	48.5	0
Neurological event	9	1

4 líneas tto mínimo, R/R

Fowler NH et al. ASH 2020.

Traslating Novel Biological Insights Into Clinics

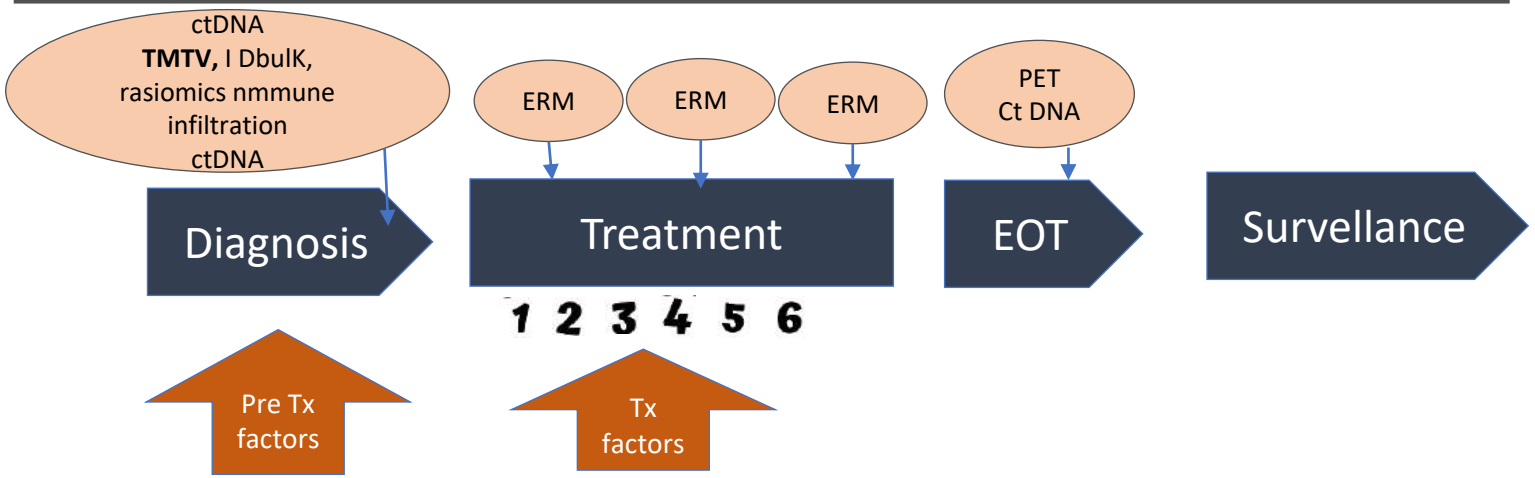
New: TP53, EZH2
EOT PET, MRD, ct(DNA)

¨ **in evaluation** ¨
23-GEPscore
TMTV

Perspective: from risk-adapted therapy towards **Biological-Guide Therapies**

In development
Molecular FL subtypes?

Dynamic Risk Profiling (Continuous Individualized Risk Index)



GELL
Grupo de Estudio Latinoamericano de Linfoproliferativos

Muchas Gracias por su Atención

Valle de la Ciudad de Caracas-Venezuela