

Tumefazioni linfonodali maligne primitive:

Ruolo e considerazioni dello specialista oncoematologo.

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Inquadramento iniziale

- Sintomatologia (calo ponderale, febbricola, sudorazioni notturne)
- Alterazioni ematochimiche (citopenia, LDH, VES, componente monoclonale, ipercalcemia)
- Modalità di presentazione (EO)
- Sierologia negativa

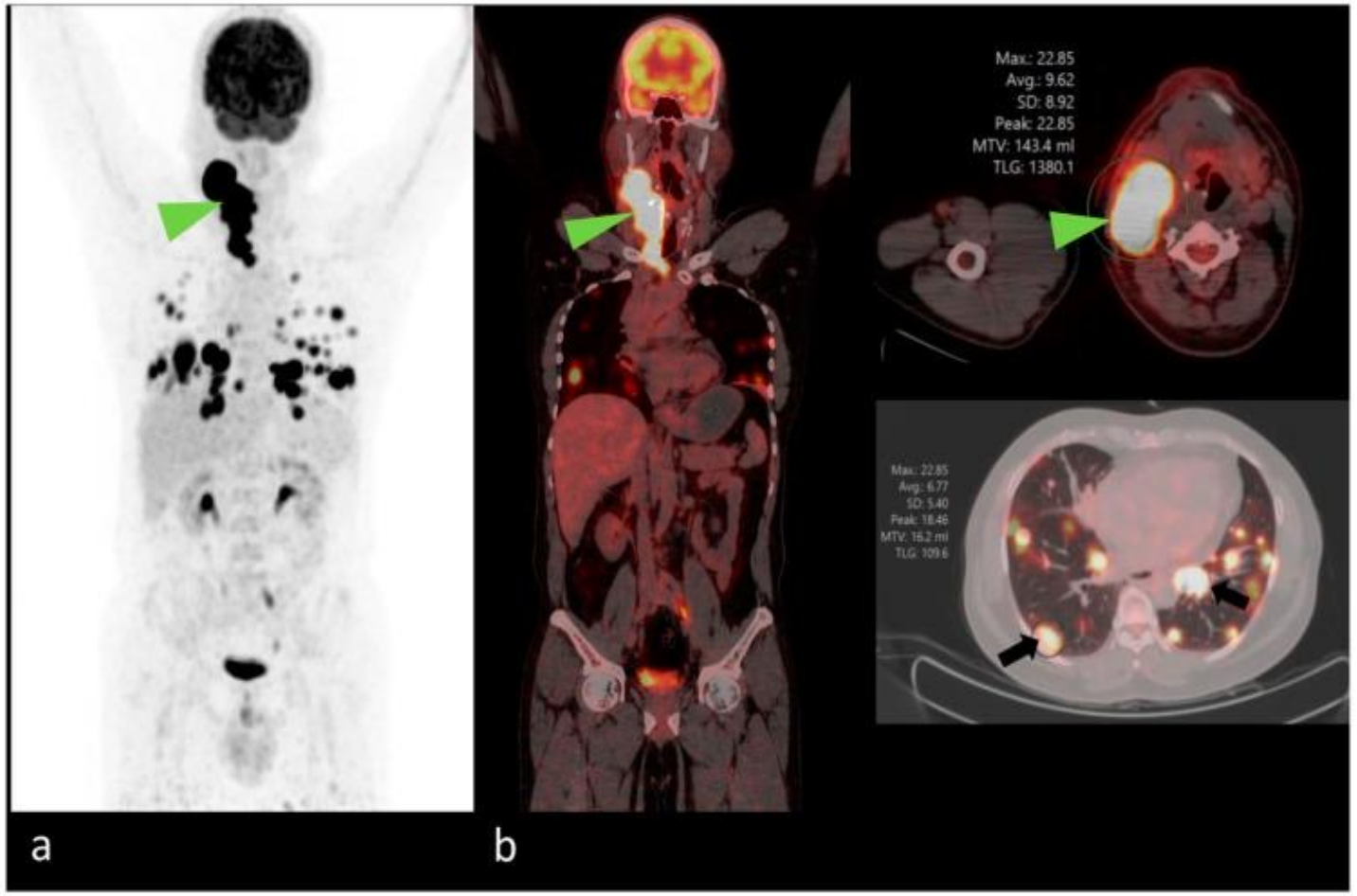


Indagini strumentali

- TCTB + PET FDG

- Campionamento lesione target

- Biopsia osteomidollare



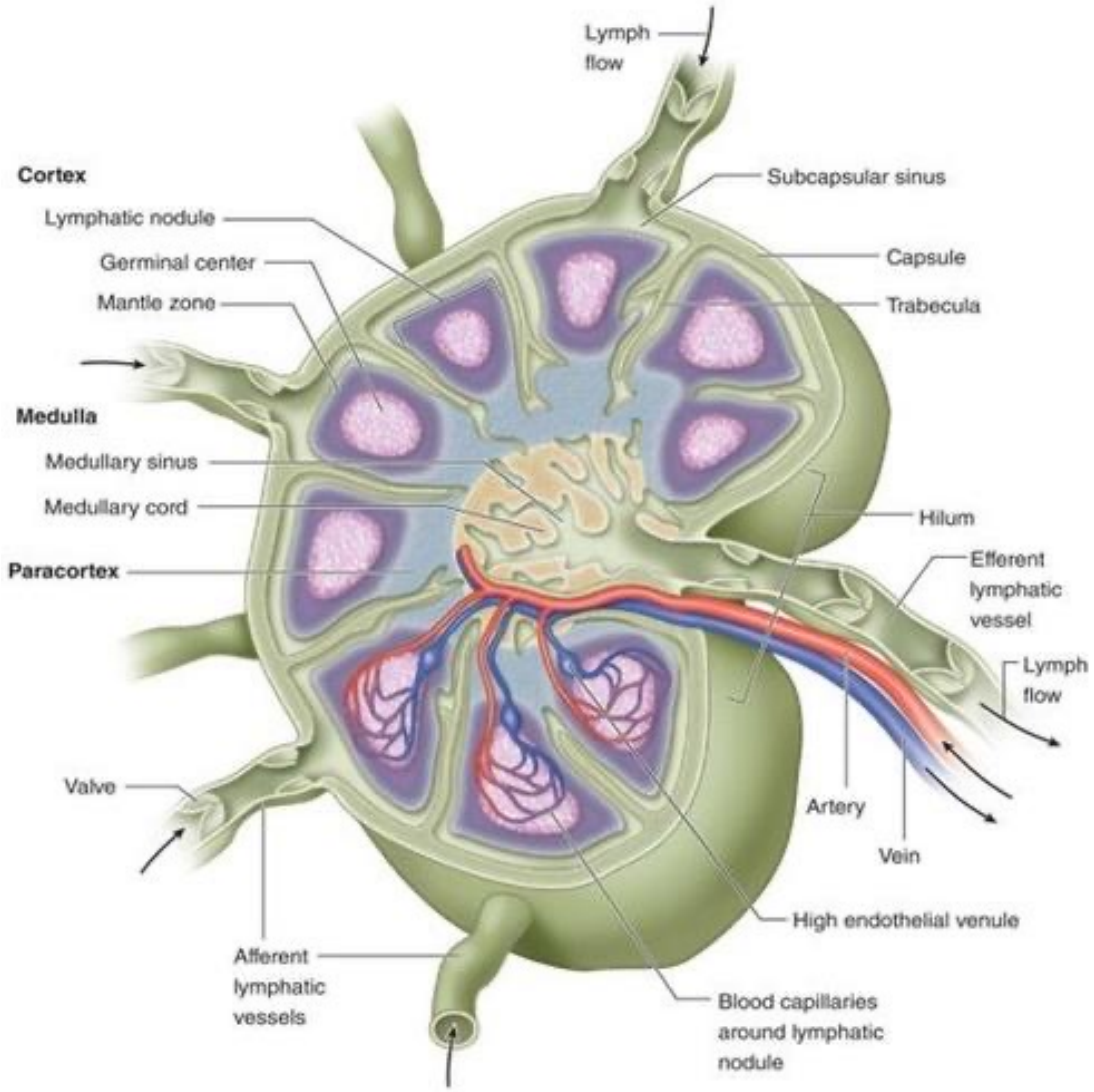
Classificazione WHO

WHO Classification, 5th edition	WHO Classification, revised 4th edition
Tumour-like lesions with B-cell predominance	
Reactive B-cell-rich lymphoid proliferations that can mimic lymphoma	*Not previously included*
IgG4-related disease	*Not previously included*
Unicentric Castleman disease	*Not previously included*
Idiopathic multicentric Castleman disease	*Not previously included*
KSHV/HHV8-associated multicentric Castleman disease	Multicentric Castleman disease
Precursor B-cell neoplasms	
B-cell lymphoblastic leukaemias/lymphomas	
B-lymphoblastic leukaemia/lymphoma, NOS	(Same)
B-lymphoblastic leukaemia/lymphoma with high hyperdiploidy	B-lymphoblastic leukaemia/lymphoma with hyperdiploidy
B-lymphoblastic leukaemia/lymphoma with hypodiploidy	(Same)
B-lymphoblastic leukaemia/lymphoma with iAMP21	(Same)
B-lymphoblastic leukaemia/lymphoma with *BCR::ABL1* fusion	B-lymphoblastic leukaemia/lymphoma with t(9;22)(q34;q11.2); *BCR-ABL1*
B-lymphoblastic leukaemia/lymphoma with *BCR::ABL1*-like features	B-lymphoblastic leukaemia/lymphoma, *BCR-ABL1*-like
B-lymphoblastic leukaemia/lymphoma with *KMT2A* rearrangement	B-lymphoblastic leukaemia/lymphoma with t(v;11q23.3); *KMT2A*-rearranged
B-lymphoblastic leukaemia/lymphoma with *ETV6::RUNX1* fusion	B-lymphoblastic leukaemia/lymphoma with t(12;21)(p13.2;q22.1); *ETV6-RUNX1*
B-lymphoblastic leukaemia/lymphoma with *ETV6::RUNX1*-like features	*Not previously included*
B-lymphoblastic leukaemia/lymphoma with *TCF3::PBX1* fusion	B-lymphoblastic leukaemia/lymphoma with t(1;19)(q23;p13.3); *TCF3-PBX1*
B-lymphoblastic leukaemia/lymphoma with *IGH::IL3 fusion*	B-lymphoblastic leukaemia/lymphoma with t(5;14)(q31.1;q32.1); *IGH/IL3*
B-lymphoblastic leukaemia/lymphoma with *TCF3::HLF* fusion	*Not previously included*
B-lymphoblastic leukaemia/lymphoma with other defined genetic abnormalities	(Same)
Mature B-cell neoplasms	
Pre-neoplastic and neoplastic small lymphocytic proliferations	
Monoclonal B-cell lymphocytosis	(Same)
Chronic lymphocytic leukaemia/small lymphocytic lymphoma	(Same)
(Entity deleted)	B-cell prolymphocytic leukaemia
Splenic B-cell lymphomas and leukaemias	
Hairy cell leukaemia	(Same)
Splenic marginal zone lymphoma	(Same)
Splenic diffuse red pulp small B-cell lymphoma	(Same)
Splenic B-cell lymphoma/leukaemia with prominent nucleoli	*Not previously included* (encompassing hairy cell leukaemia variant and some cases of B-cell prolymphocytic leukaemia)
Lymphoplasmacytic lymphoma	
Lymphoplasmacytic lymphoma	(Same)
Marginal zone lymphoma	
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue	(Same)
Primary cutaneous marginal zone lymphoma	*Not previously included* (originally included under "extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue")
Nodal marginal zone lymphoma	(Same)
Paediatric marginal zone lymphoma	(Same)
Follicular lymphoma	
In situ follicular B-cell neoplasm	In situ follicular neoplasia
Follicular lymphoma	(Same)
Paediatric-type follicular lymphoma	(Same)
Duodenal-type follicular lymphoma	(Same)

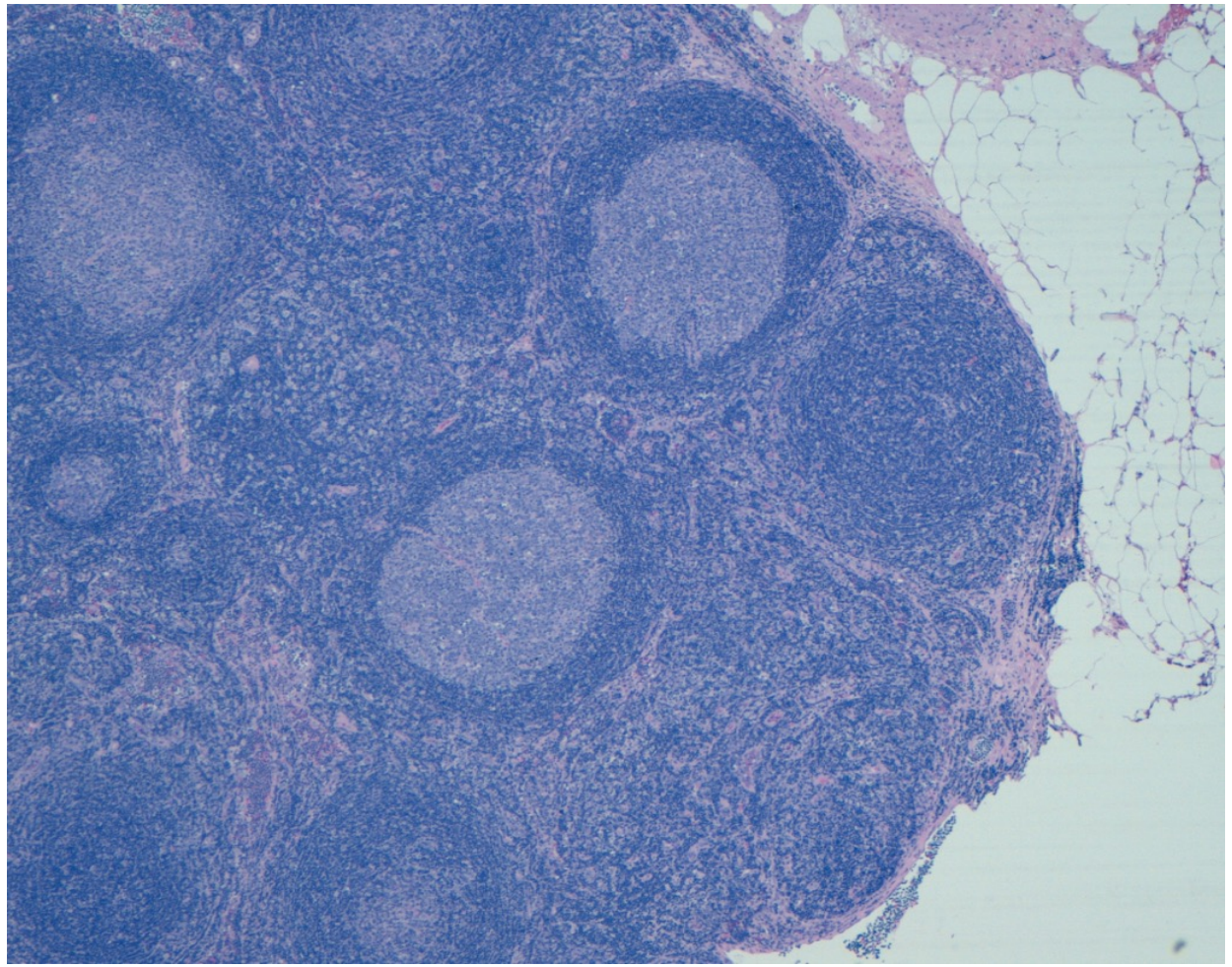
WHO Classification, 5th edition	WHO Classification, revised 4th edition
Cutaneous follicle centre lymphoma	
Primary cutaneous follicle centre lymphoma	(Same)
Mantle cell lymphoma	
In situ mantle cell neoplasm	In situ mantle cell neoplasia
Mantle cell lymphoma	(Same)
Leukaemic non-nodal mantle cell lymphoma	(Same)
Transformations of indolent B-cell lymphomas	
Transformations of indolent B-cell lymphomas	*Not previously included*
Large B-cell lymphomas	
Diffuse large B-cell lymphoma, NOS	(Same)
T-cell/histiocyte-rich large B-cell lymphoma	(Same)
Diffuse large B-cell lymphoma/ high grade B-cell lymphoma with *MYC* and *BCL2* rearrangements	High-grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* rearrangements
ALK-positive large B-cell lymphoma	(Same)
Large B-cell lymphoma with *IRF4* rearrangement	(Same)
High-grade B-cell lymphoma with 11q aberrations	Burkitt-like lymphoma with 11q aberration
Lymphomatoid granulomatosis	(Same)
EBV-positive diffuse large B-cell lymphoma	EBV-positive diffuse large B-cell lymphoma, NOS
Diffuse large B-cell lymphoma associated with chronic inflammation	(Same)
Fibrin-associated large B-cell lymphoma	*Not previously included* (Previously considered a subtype of diffuse large B-cell lymphoma associated with chronic inflammation)
Fluid overload-associated large B-cell lymphoma	*Not previously included*
Plasmablastic lymphoma	(Same)
Primary large B-cell lymphoma of immune-privileged sites	*Not previously included*, encompassing primary diffuse large B-cell lymphoma of the CNS in revised 4th edition (*plus primary large B-cell lymphoma of the vitreoretina and primary large B-cell lymphoma of the testis*)
Primary cutaneous diffuse large B-cell lymphoma, leg type	(Same)
Intravascular large B-cell lymphoma	(Same)
Primary mediastinal large B-cell lymphoma	(Same)
Mediastinal grey zone lymphoma	B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classic Hodgkin lymphoma
High-grade B-cell lymphoma, NOS	(Same)
Burkitt lymphoma	
Burkitt lymphoma	(Same)
KSHV/HHV8-associated B-cell lymphoid proliferations and lymphomas	
Primary effusion lymphoma	(Same)
KSHV/HHV8-positive diffuse large B-cell lymphoma	HHV8-positive diffuse large B-cell lymphoma, NOS
KSHV/HHV8-positive germinotropic lymphoproliferative disorder	HHV8-positive germinotropic lymphoproliferative disorder
Lymphoid proliferations and lymphomas associated with immune deficiency and dysregulation	
Hyperplasias arising in immune deficiency/dysregulation	*Not previously included*, encompassing non-destructive post-transplant lymphoproliferative disorders, among others
Polymorphic lymphoproliferative disorders arising in immune deficiency/dysregulation	*Not previously included*, encompassing polymorphic posttransplant lymphoproliferative disorders, other iatrogenic immunodeficiency-associated lymphoproliferative disorders, among others
EBV-positive mucocutaneous ulcer	(Same)
Lymphomas arising in immune deficiency / dysregulation	*Not previously included*, encompassing monomorphic posttransplant lymphoproliferative disorders, classic Hodgkin lymphoma posttransplant lymphoproliferative disorders, lymphomas associated with HIV infection, among others
Inborn error of immunity-associated lymphoid proliferations and lymphomas	Lymphoproliferative diseases associated with primary immune disorders

Table 1. continued

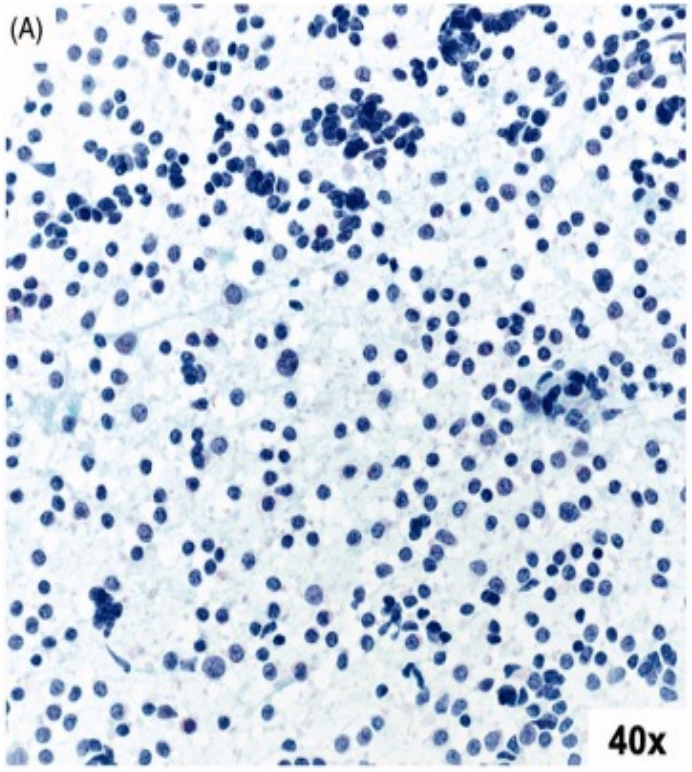
WHO Classification, 5th edition	
Hodgkin lymphoma	
Classic Hodgkin lymphoma	
Nodular lymphocyte predominant Hodgkin lymphoma	
Plasma cell neoplasms and other diseases with paraproteins	
Monoclonal gammopathies	
Cold agglutinin disease	
IgM monoclonal gammopathy of undetermined significance	
Non-IgM monoclonal gammopathy of undetermined significance	
Monoclonal gammopathy of renal significance	
Diseases with monoclonal immunoglobulin deposition	
Immunoglobulin-related (AL) amyloidosis	
Monoclonal immunoglobulin deposition disease	
Heavy chain diseases	
Mu heavy chain disease	
Gamma heavy chain disease	
Alpha heavy chain disease	
Plasma cell neoplasms	
Plasmacytoma	
Plasma cell myeloma	
Plasma cell neoplasms with associated paraneoplastic syndrome -POEMS syndrome -TEMPI syndrome -AESOP syndrome	



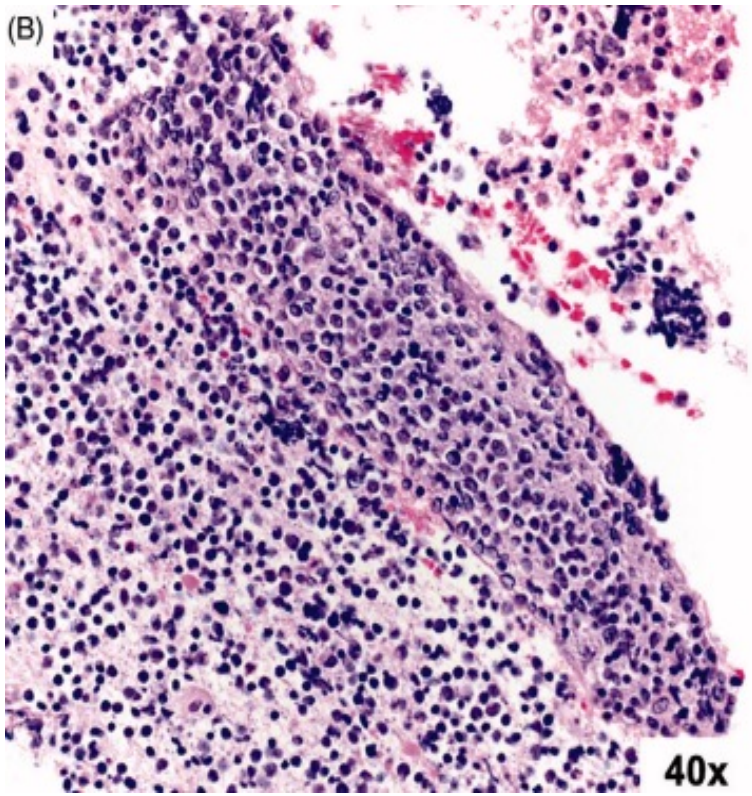
- CORTICALE: linfociti B
- PARACORTICALE: linfociti T
- MIDOLLARE



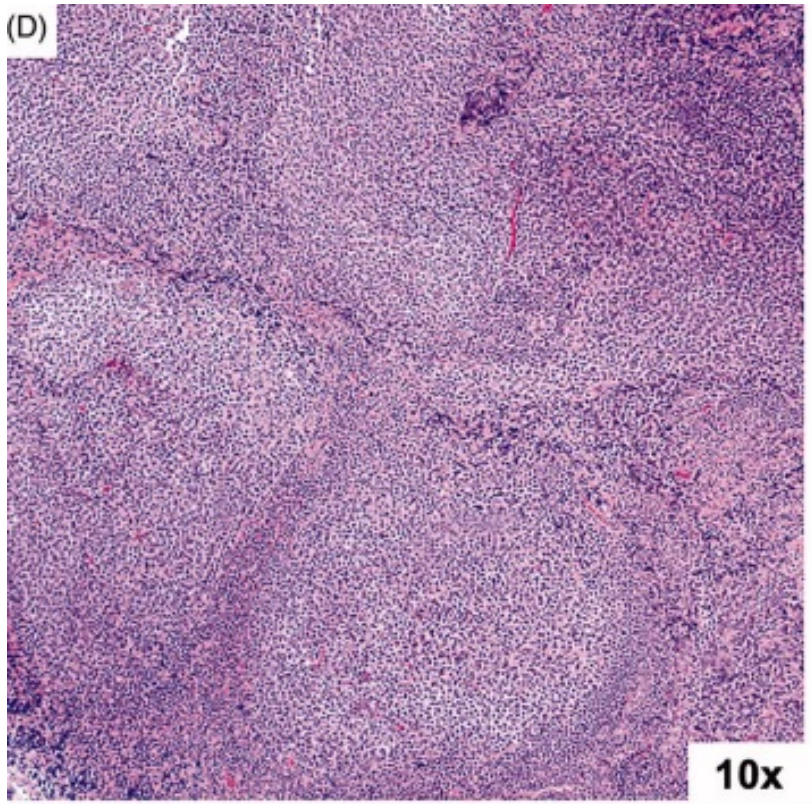
- LNH indolenti (LLC/FL/MZL/LPL/HCL) vs aggressivi (DLBCL/MCL/LNH T) o iLNH con di aree di trasformazione.



FNAC

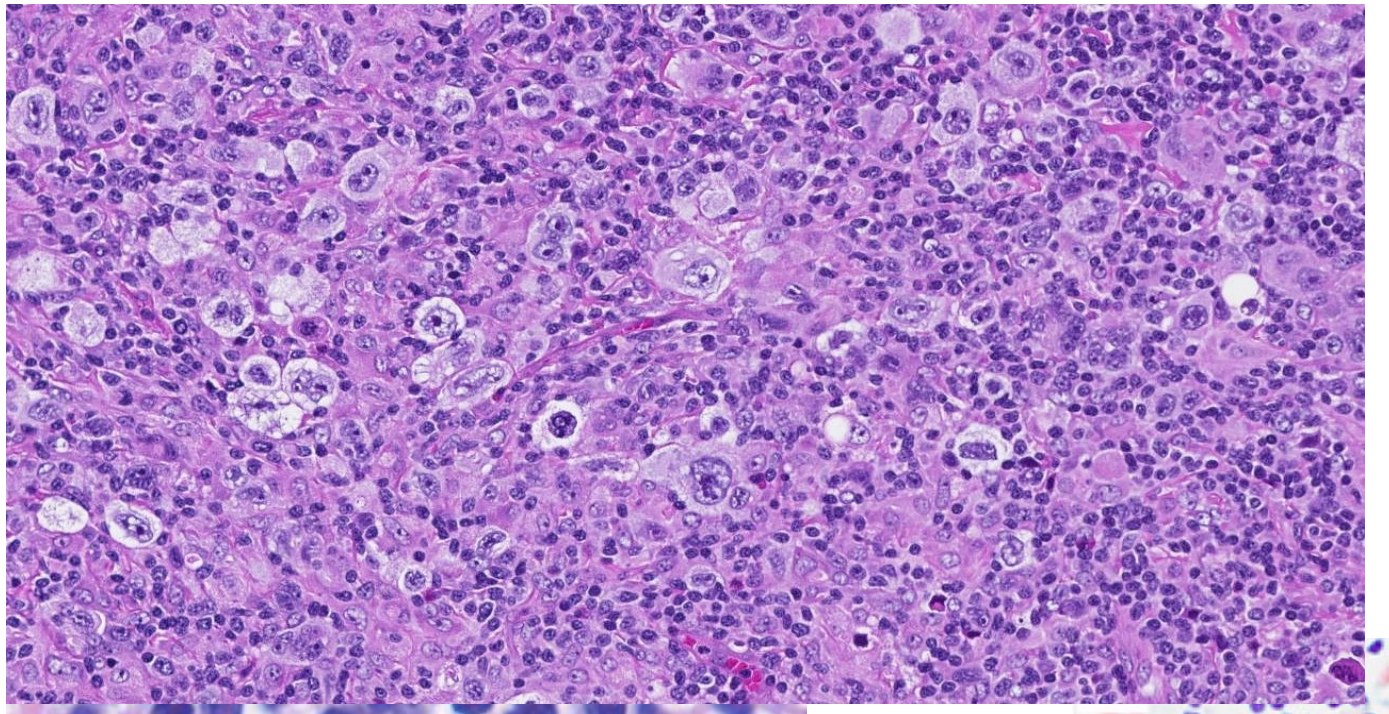


FNAB

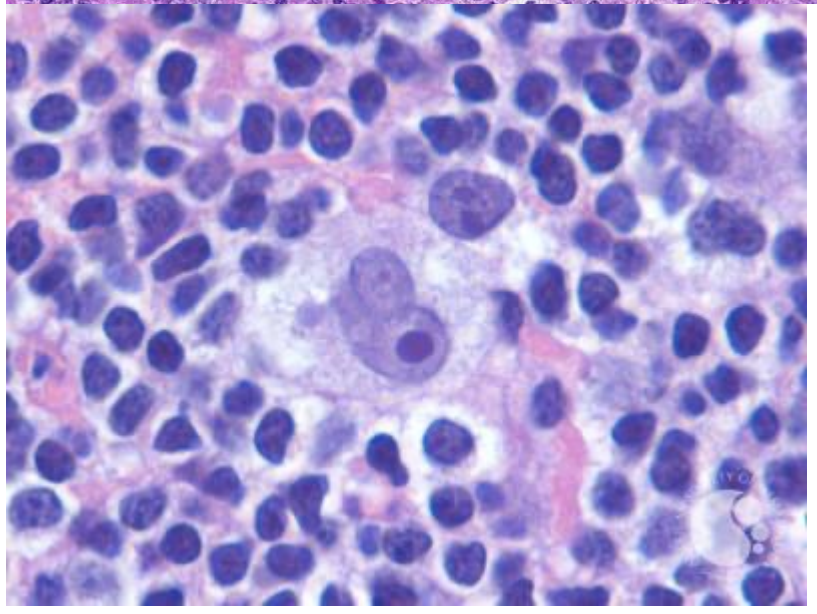


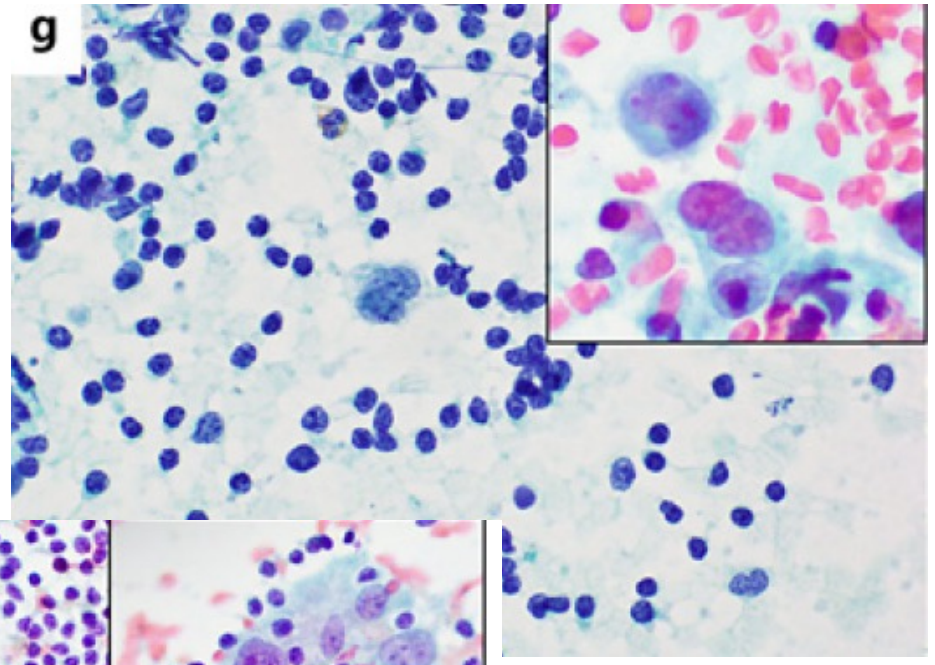
BIOPSIA

- Linfoma di hodgkin vs Linfomi non hodgkin T e B

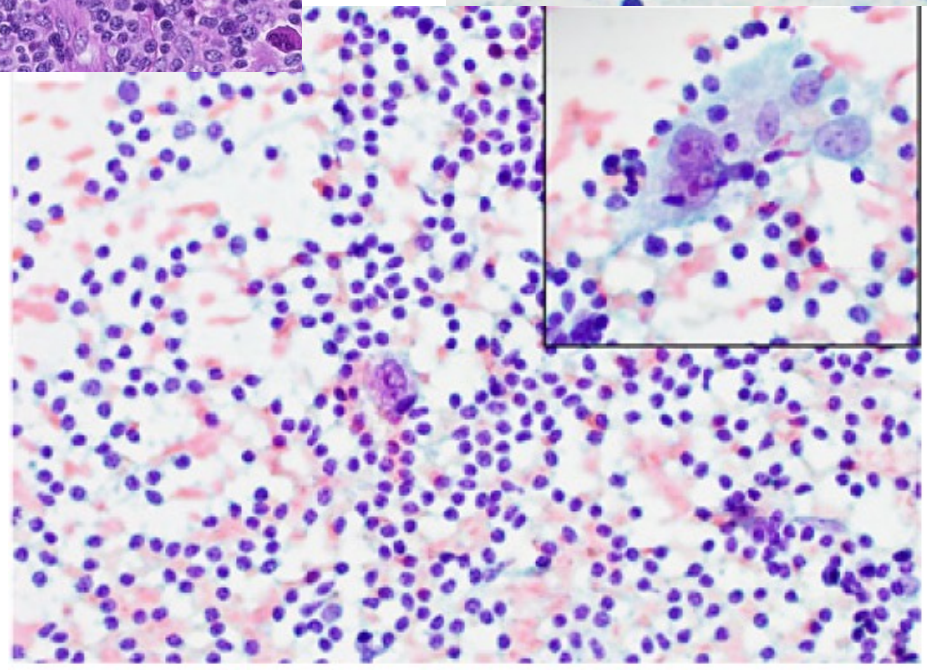


HD Classico



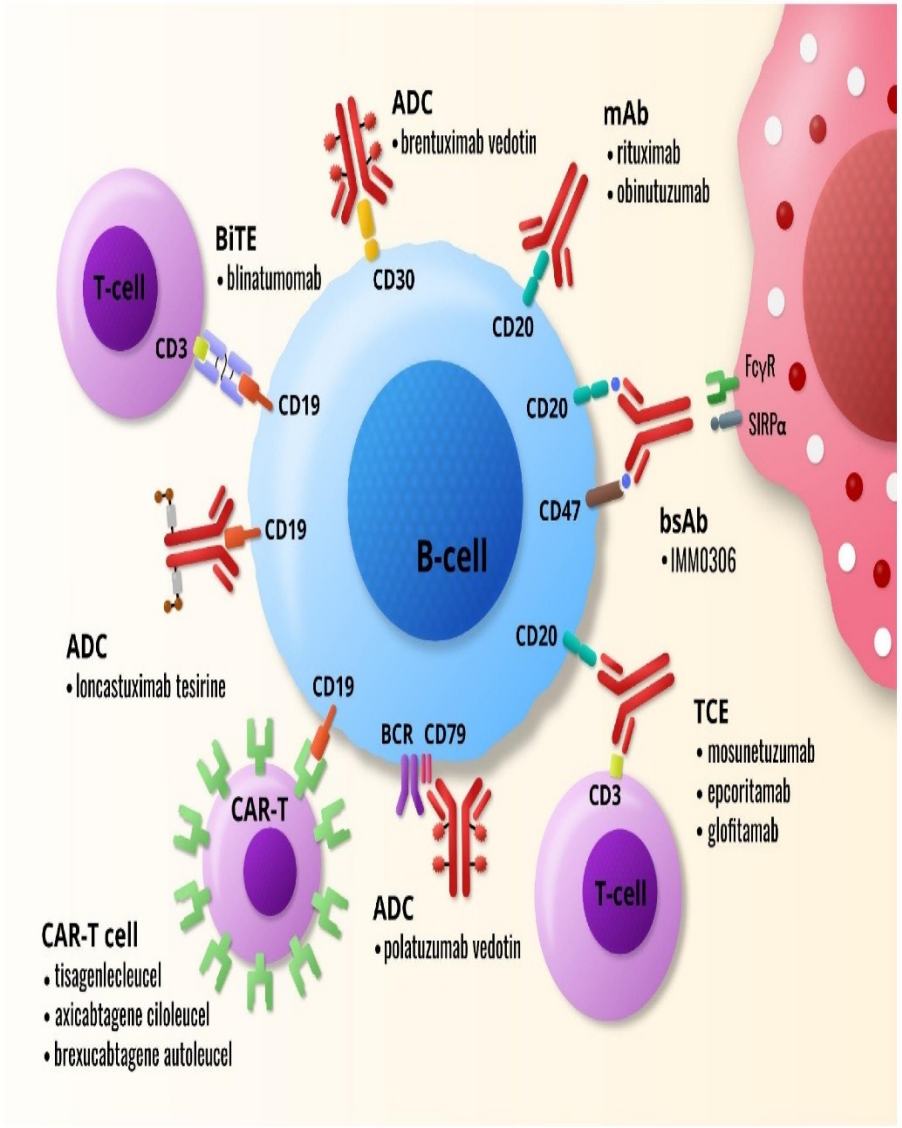


g ALCL
with HRS-like cells on a background of small lymphocytes; inset shows binucleated RS-like cells



h AITL showing
scattered large HRS-like cells on a background of smaller lymphocytes, mimicking HL; inset shows a binucleated RS-like cell

Terapia



Chemioterapia

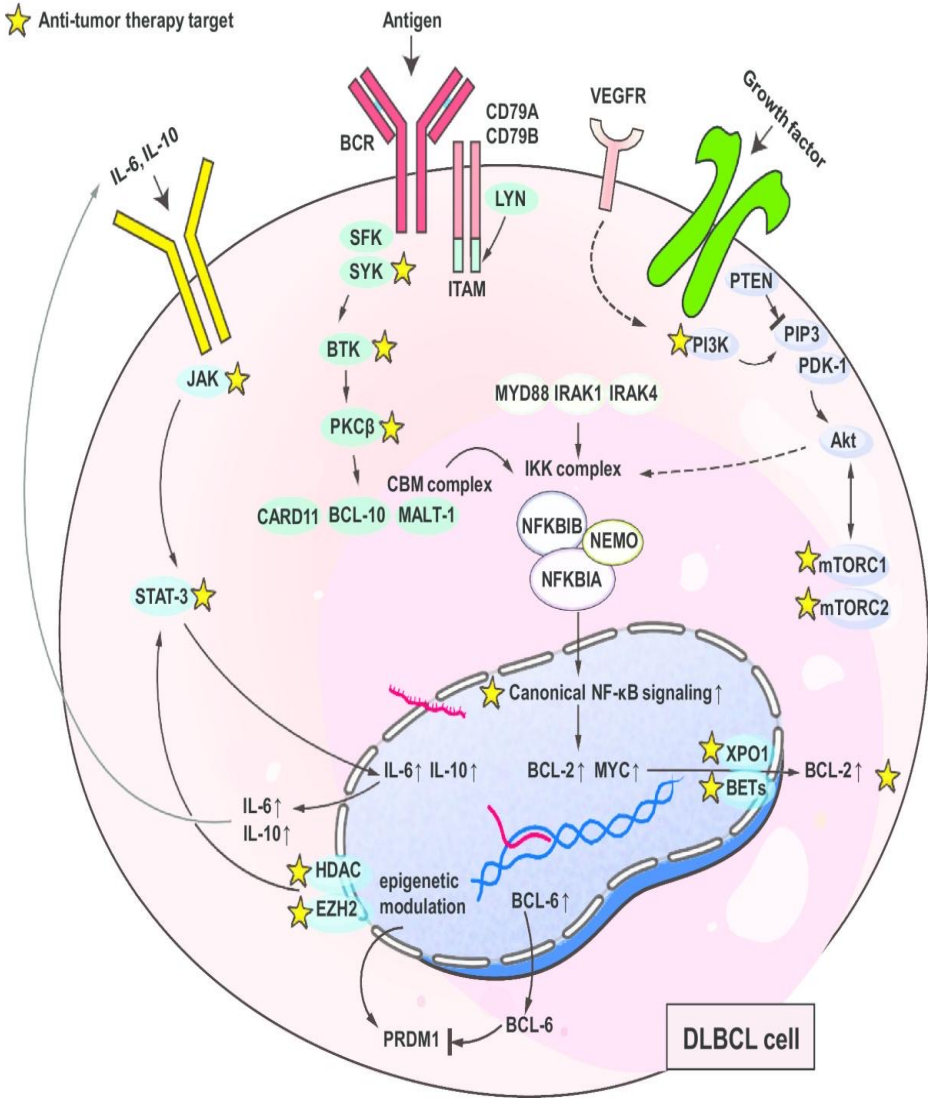
Anticorpi Monoclonali

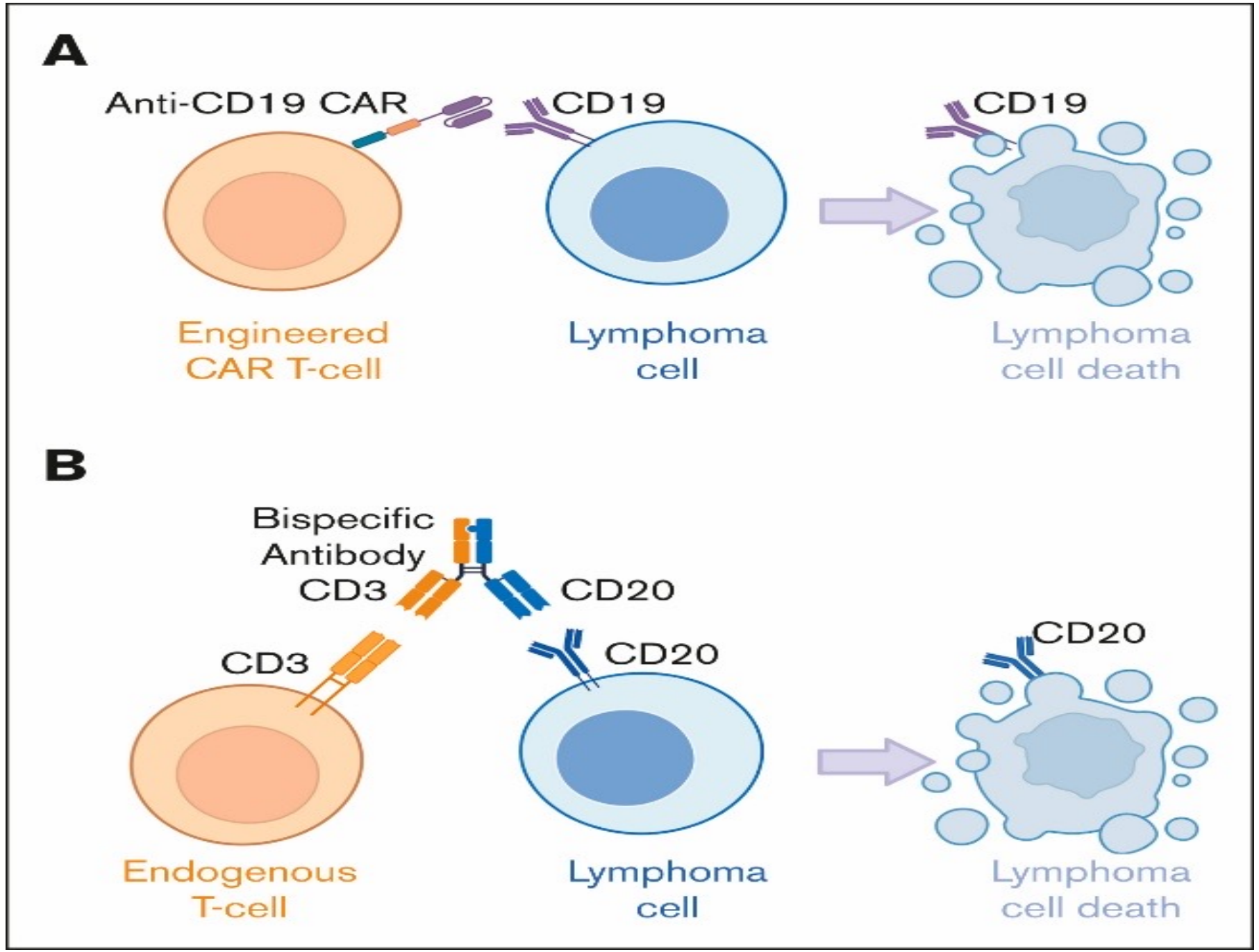
Immunomodulanti

Inibitori BTK – BCL2

CAR-T

Anticorpi bispecifici




A
Anti-CD19 CAR
CD19
CD19
Engineered
CAR T-cell
Lymphoma
cell
Lymphoma
cell death
B
Bispecific
Antibody
CD3
CD20
CD3
CD20
CD20
Endogenous
T-cell
Lymphoma
cell
Lymphoma
cell death

Caso clinico 1

N.C. Uomo di 73aa

NIDDM - Ipertensione arteriosa - Dislipidemia

Sintomi B: calo ponderale astenia e febbricola

EE: lievi citopenie Hb 11,5 g/dl – plt 120000 – GB nn

09/2023 TCTB: numerose tumefazioni LN in sede laterocerv. e sovraclaveare bilaterali (diam. max 26x15), LN confluenti omogenee al mediastino; splenomegalia 15cm omogenea. Piccoli LN perigastrici, a ridosso del tripode celiaco, all'ilo epatico e lungo i grossi vasi retroperitoneali con LN tendenti a confluire in pacchetti in sede lateroaortica ed all'ilo renale sin.

PET: iperaccumulo in sede retrofaringea (SUV 6), laterocervicale ds ai livelli II, III, IV e V (SUV 12), laterocervicale sin al livello II, sovraclaveare bilaterale, epiaortica (SUV 4), paratracheale, precarenale (SUV 10), ilare polmonare ds, periceliaca, paraortica (SUV 7) ed interaortocavale; iperfissazione alla tonsilla faringea (SUV 5); disomogenea captazione alla milza.

10/2023 BOM: infiltrato che non consente di porre dg. di interessamento da parte di malattia linfoproliferativa ed è compatibile con infiltrato di significato reattivo. Non evidenzia di neoplasia.

Valutazione ORL:
In Lista per biopsia linfonodale.

Biopsia Rinofaringe:
MACROSCOPIA:Tre irregolari frammenti biancastri in aggregato di cm 1.
DIAGNOSI:reperto morfofenotipico orientativo nel senso di proliferazione linfomatosa di piccoli linfociti di derivazione B a tipo linfoma linfocitico/LLC sec WHO. Reperto da inquadrare nel contesto clinico-strumentale-laboratoristico.

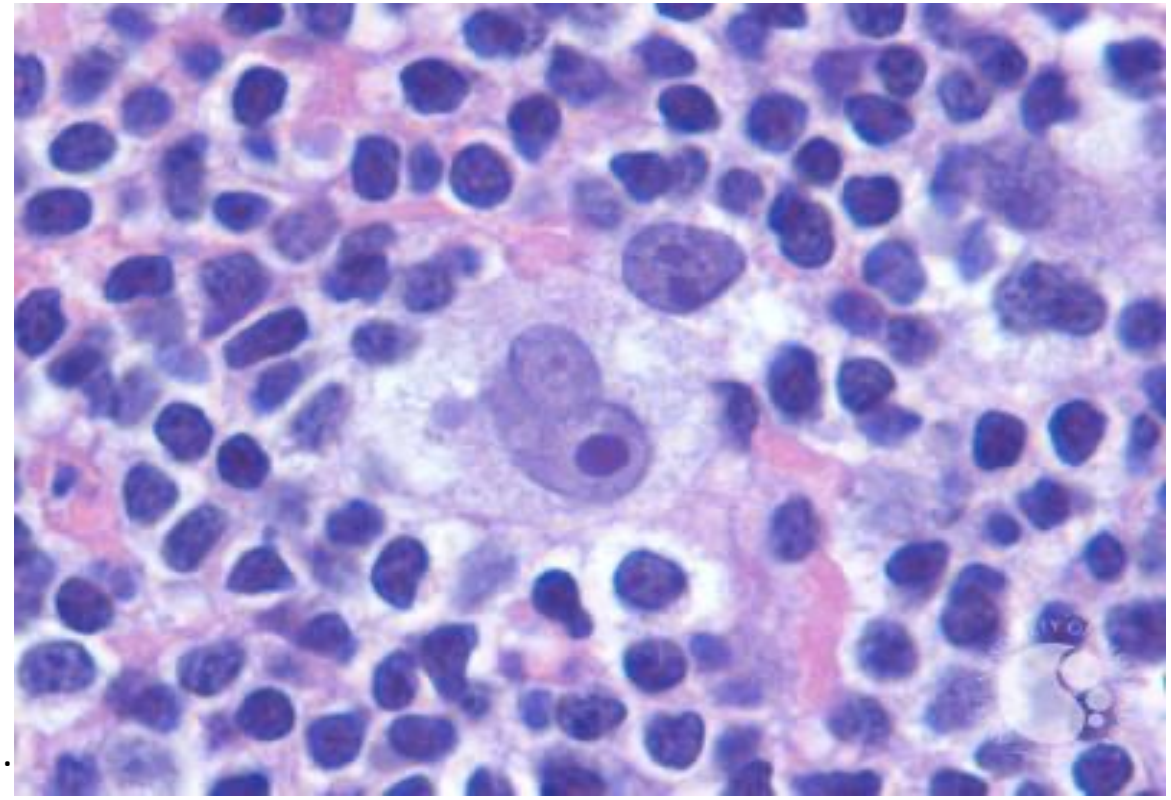
Ricovero per peggioramento clinico con insorgenza di severa piastrinopenia autoimmune con conta < 10000 mm3 e sanguinamento gastrointestinale.

Biopsia ritenuta non praticabile.

Avvio terapia con Inibitore BTK Acalabrutinib + revisione istologico .

Revisione biopsia rinofaringe :
REPERTI COMPATIBILI CON LOCALIZZAZIONE DI LINFOMA DI HODGKIN CLASSICO

Chemioterapia secondo schema ABVD → 07/2024 remissione completa.



Caso clinico 2

M.B. donna 70aa

Nessuna comorbidità, asintomatica

8/2022
TC TB: lesione ovalare 24x35 mm tonsilla dx, plurime adenopatie patologiche in tutte le stazioni del collo a dx in parte confluenti max 3 cm,non linfoadenomegalie mediastiniche, cisti spleniche.

PET: iperaccumulo tonsilla dx (suv 17), plurime laterocervicale dx (suv 14), ilare splenica (suv 9), ingunale sx (suv 9), parenchima splenico (suv 11)

Valutazione ORL:
biopsia tonsilla dx: LNH diffuso a grandi cellule B (DLBCL) BCL2 e cMYC negativo – Ki 67 80%

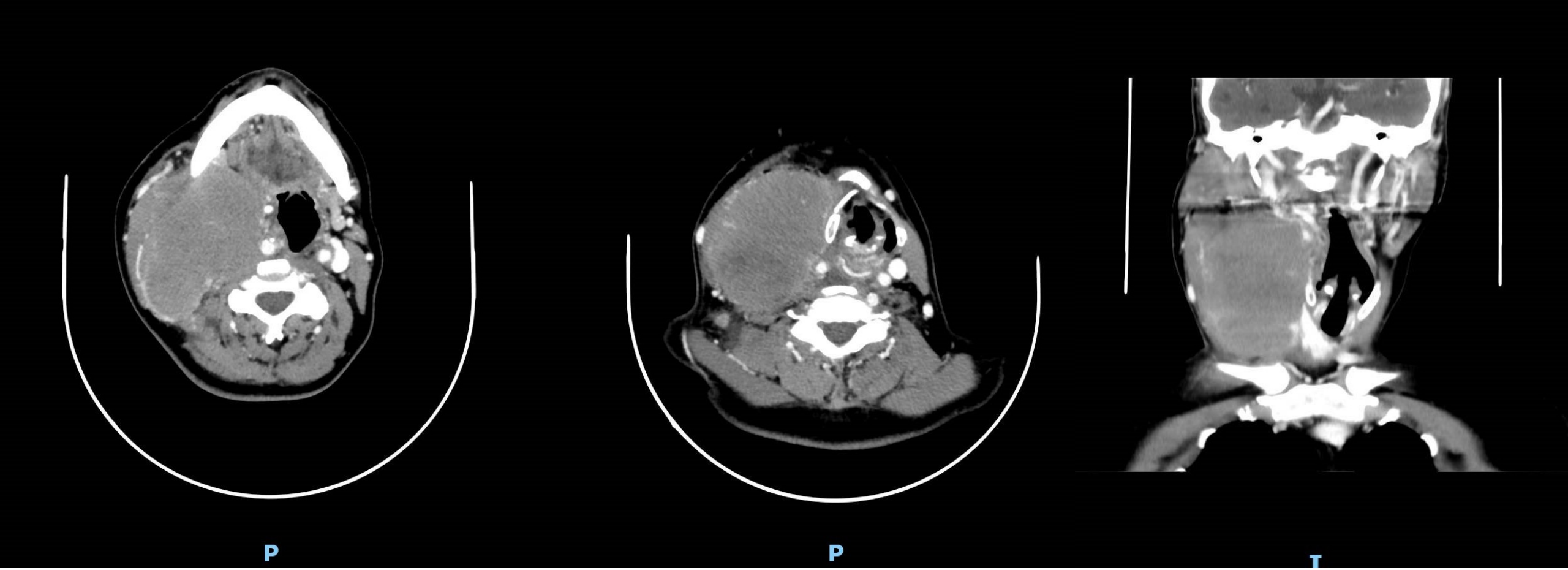
BOM: popolazione B linfoide con fenotipo maturo irregolare (cd19+ cd20+ cd5- cd200- cd23- cd38- cd43- cd45+ restrizione IgM kappa) pari a 2,6% degli elementi nucleari.

1 linea R-CHOP da 10/2022 a 12/2022 x 3 cicli – progressione clinica

Agobiopsia LN: localizzazione di LNH di derivazione dai linfonodi periferici con caratteristiche di tipo aggressivo. Linfociti di medie-grandi dimensioni ad habitus blastico CD 20 parziale, CD79a, cMyc (diffusa) CD21 , CD5 debole; CD3-, Bcl-2-, CD10-, Bcl-6-, IRF/MUM1-, TdT-, Ciclina-D1-, Ki-67 80-90% (High grade B-cell lymphoma NOS WHO 2017).

2 linea R-DHAOX: progressione, complicata da ricovero per neutropenia febbrile

TC collo: netto incremento dimensionale del conglomerato linfonodale patologico occupante tutte le stazioni lc a dx esteso sino a cavo sovraclaveare dx 105x65x77 mm con iniziale colliquazione. Deviazione verso sin di faringe e laringe e compresione strutture vascolari con giugulare e succlavia dx collabite; formazione aggettante a partenza loggia tonsillare dx.



Indicazione a CAR-T terapia ponte con Polatuzumab (antiCd79) + Radioterapia → ulteriore incremento volumetrico della lesione peggioramento disfagia ed iniziale dispnea.

Rivalutazione ORL: tracheotomia 27/3/23 → CAR T maggio 2023 → progressione e decesso.

Conclusioni

- Una migliore definizione diagnostica aumenta la possibilità di cura dei pazienti con patologia oncoematologica.

- Terapia mirata e personalizzata.

