Linfomi extra-nodali: biologia, quadro clinico e diagnosi

Dr. V. Pavone

U. O. EMATOLOGIA
AZ.OSP. TRICASE

LINFOMI

- Gruppo di neoplasie complesse che derivano dalla espansione clonale di una determinata popolazione di linfociti (T o B), cioè delle linee cellulari deputate nell' organismo alla difesa immunologica
- Espressività clinica dominante è l'aumento di volume degli organi linfoidi primari secondari e prevalentemente dei linfonodi superficiali, di quelli profondi e della milza
- I quadri clinici e la sintomatologia sono disparati e riflettono l'interessamento primitivo degli organi linfoidi secondari (gli organi interessati possono essere molteplici)

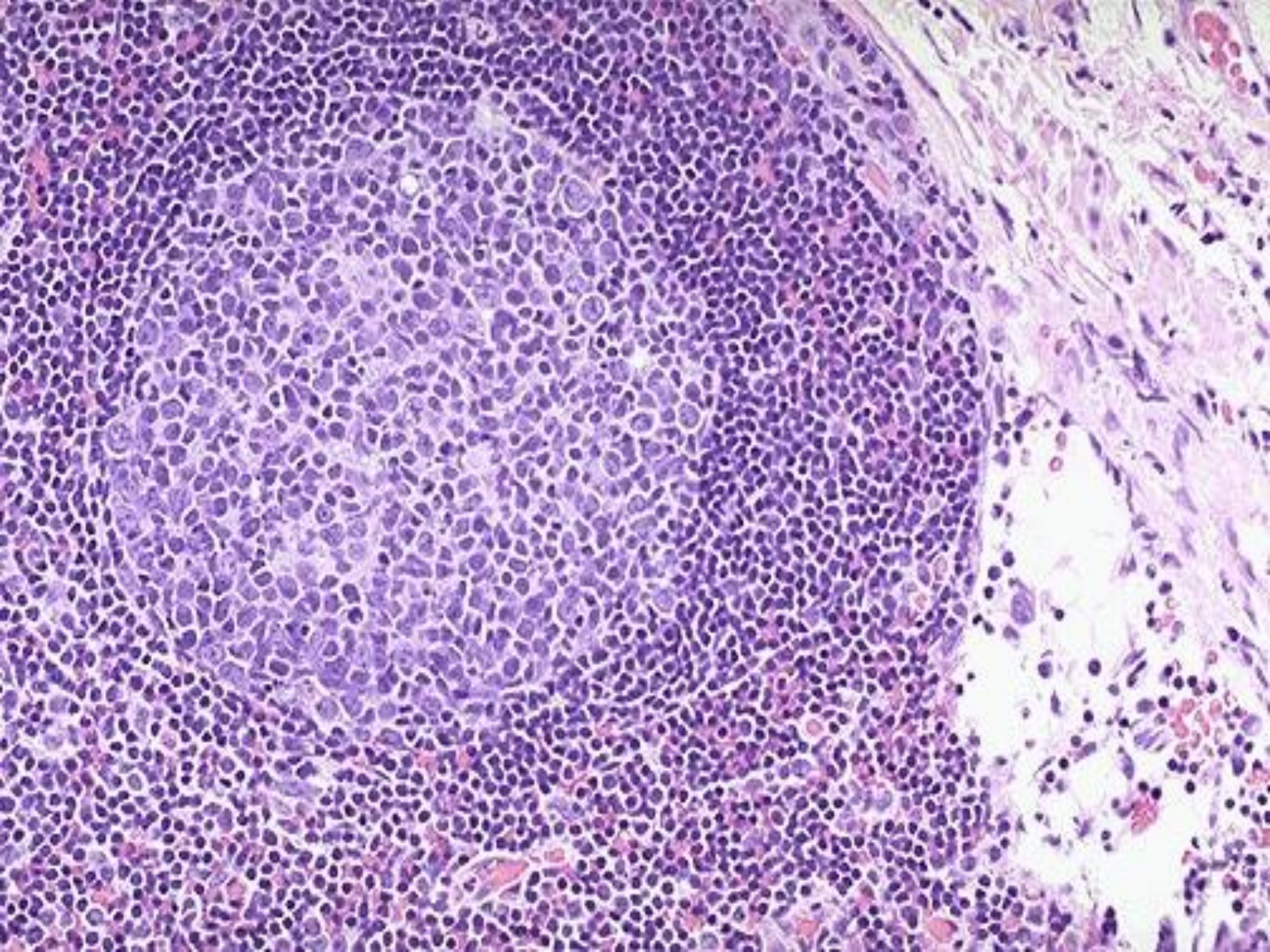
EPIDEMIOLOGIA

- **Incidenza**:
  - 100 casi / 100.000 abitanti / anno
  - aumenta con l' età
- **Causa Etiopatogenetica**:
  - nella maggior parte dei casi sconosciuta
  - difetti del sistema immunitario (AIDS, immunodeficienze ereditarie, trapianto d'organo)
  - Infezioni virali / batteriche:
    - EBV
    - HTLV1
    - HHV8
    - HCV
    - *H. pylori*

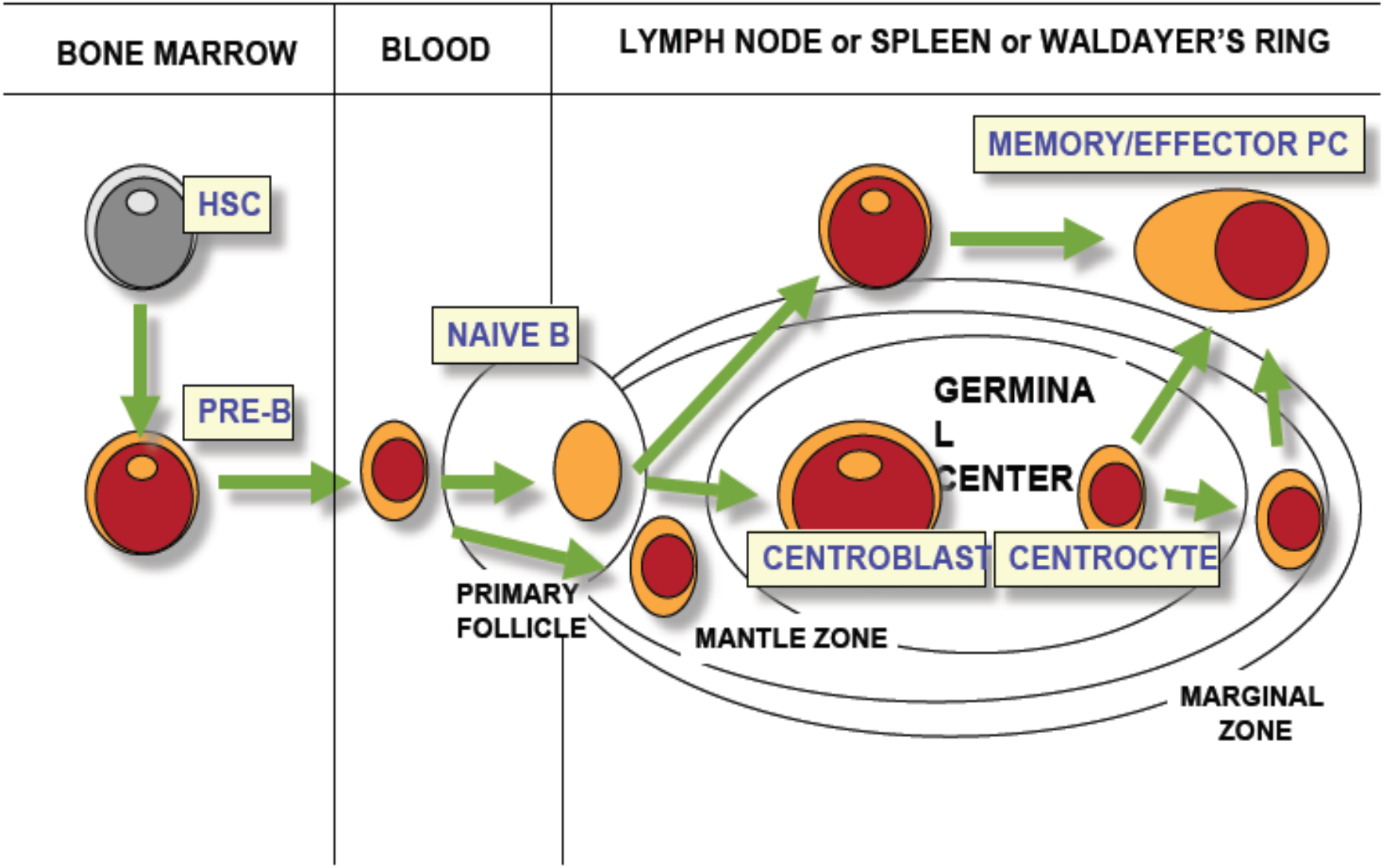
Incidenza delle principali neoplasie ematologiche

Patologia	*No/100.000/ per anno*
Linfomi (^)	**15-20**
Mielomi	**3-5**
Leucosi Acute	**8-10**
Leucosi Croniche (*)	**5-10**

(^) incremento del 150% dal 1950, con netto incremento per NHL rispetto ad HD
(*) notevole variabilità a seconda dell'età: 70 casi/100.000 adulti di oltre 80 anni

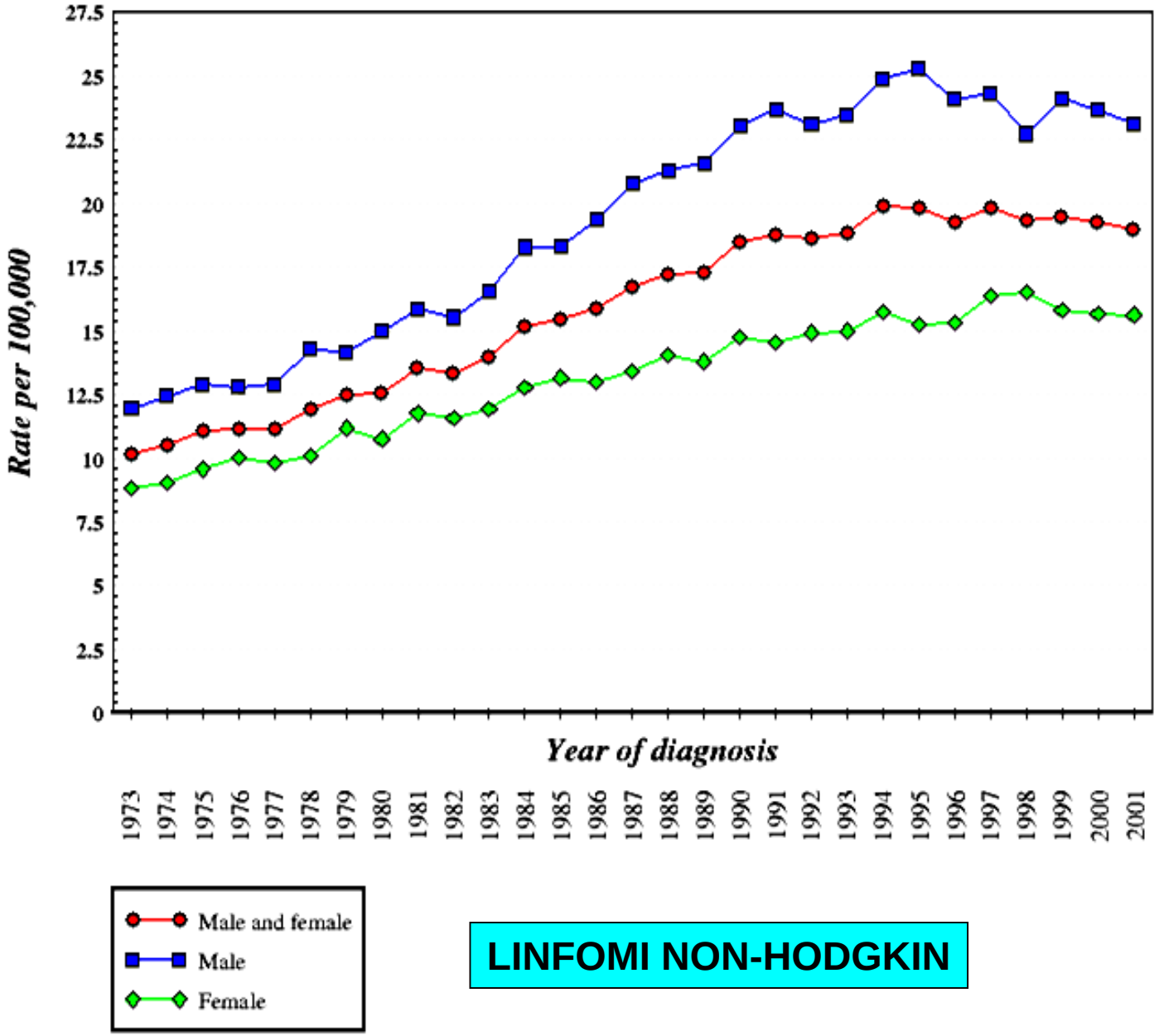


derivano dalle varie fasi differenziative dei linfociti B cui corrispondono funzioni, morfologia, fenotipo e genotipo diversi

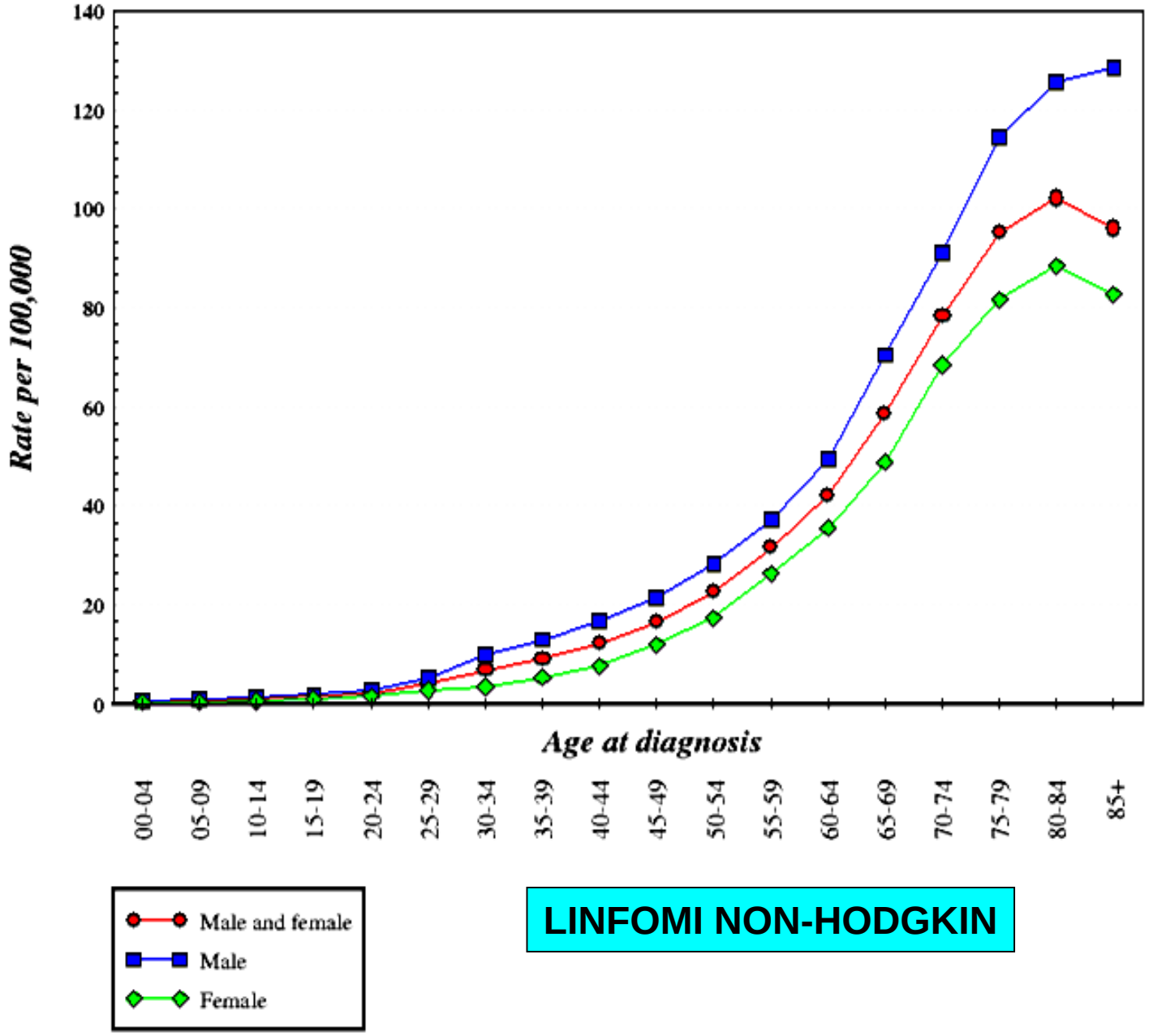


Lymphoid malignancies: the last 50 years

- **Incidence +150%**
- **Mortality + 90%**

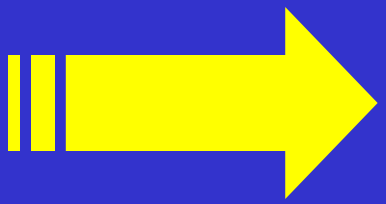


LINFOMI NON-HODGKIN

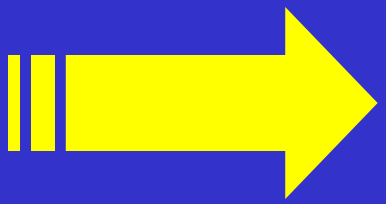


LINFOMI NON-HODGKIN

Several factors may explain the lower increase in mortality compared to incidence, in particular:



BETTER DIAGNOSIS



MORE EFFECTIVE THERAPY

Fattori associati ad aumentato rischio di insorgenza di linfoma non-Hodgkin (I)

Fattori generali di rischio aumentato

- Età avanzata
- Sesso maschile
- Razza bianca
- Stato socioeconomico avanzato

Stato di immunodepressione

- ***Congenita***
  - sindrome di Wiskott-Aldrich (WAS)
  - common variable immunodeficiency (CVID)
  - ataxia teleangectasia (AT)
  - severe combined immunodeficiency (SCID)
  - X-linked lymphoproliferative disorder (XLP)

- ***Acquisita***
  - trapianto d'organo (fegato, cuore, polmone, rene e midollo emopoietico)
  - terapie con immunosoppressori
  - AIDS

Fattori associati ad aumentato rischio di insorgenza di linfoma non-Hodgkin (II)

Cronica stimolazione antigenica

- Malattie autoimmuni
  - Sindrome di Sjögren
  - Tiroidite di Hashimoto
  - Artrite reumatoide
  - Lupus eritematoso sistemico
- Morbo celiaco
- Gastrite da Helicobacter pylori
- Flogosi croniche intestinali
- Dermatite erpetiforme

Virus

- EBV
- HTLV-I
- HTLV-II
- HHV-8
- HHV-6
- HIV
- HCV

Sostanze tossiche e farmaci

- Utilizzate per lo più in ambiente lavorativo
  - Erbicidi
  - Pesticidi
  - Solventi
- Tinture per capelli
- Fumo
- Difenilidantoina

Allergie?

APPROCCIO DIAGNOSTICO:

biopsia linfonodale

biopsia osteo-midollare

Biopsia di tessuto neoformato in organi fuori dal sistema linfatico nodale (cute ,stomaco ,intestino)

2ª DISTINZIONE

Classificazione WHO (OMS, 1994), sovrapponibile alla classificazione REAL.

È basata sulle caratteristiche della cellula neoplastica, a livello:

- Morfologico
- Immunofenotipico
- Molecolare

Tre categorie:

1) Neoplasie dai linfociti B

   Linfomi non Hodgkin di derivazione dai precursori o dai linfociti B periferici

2) Neoplasie a cellule T/NK

   Linfomi non Hodgkin di derivazione dai precursori o dai linfociti T periferici

3) Malattia/Linfoma di Hodgkin

APPROCCIO AL PAZIENTE CON SOSPETTO LINFOMA

INDAGINI DI LABORATORIO - 2

- Biopsia linfonodale ed osteomidollare utili per:
  - Studio di marcatori cellulari di membrana e citoplasmatici, mediante tecniche di immunocitochimica e immunoistochimica
  - Studi di biologia molecolare
    - t (11; 14) → bcl-1 LNH mantellare
    - t (14; 18) → bcl-2 LNH centrofollicolare
    - 3q27 → bcl-6 LNH a grandi cellule diffuso
    - t (2; 5) → ALK LNH a grandi cellule anaplastiche
    - c-myc LNH Burkitt
- Rachicentesi con esame citologico del liquor (LNH testicolari, LNH linfoblastici)

REAL CLASSIFICATION

B-cell neoplasms
Precursor B-cell neoplasms
- Precursor B-lymphoblastic leukaemia/lymphoma (precursor B-cell lymphoblastic leukaemia)

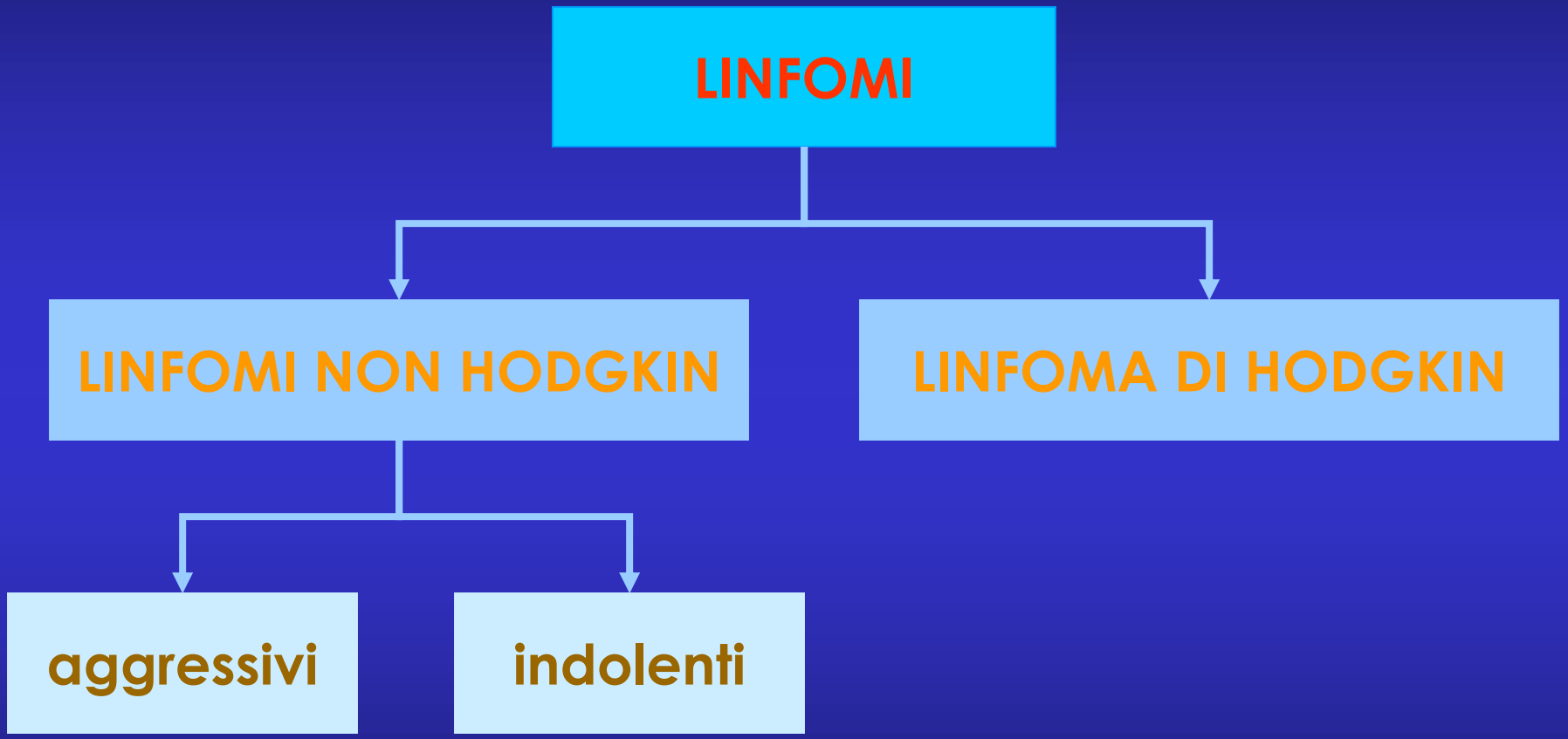
Mature (peripheral) B-cell neoplasms
- Chronic lymphocytic leukaemia/B-cell small lymphocytic lymphoma
- B-cell prolymphocytic leukaemia
- Lymphoplasmacytic lymphoma
- Splenic marginal zone B-cell lymphoma (splenic lymphoma with villous lymphocytes)
- Hairy cell leukaemia
- Plasma cell myeloma/plasmacytoma
- Extranodal marginal zone B-cell lymphoma (MALT lymphoma)
- Nodal marginal zone B-cell lymphoma
- Follicular lymphoma
- Mantle cell lymphoma
- Diffuse large B-cell lymphomas
- Burkitt's lymphoma/leukaemia

T-cell and NK-cell neoplasms
Precursor T-cell neoplasm
- Precursor T-lymphoblastic leukaemia/lymphoma (precursor T-cell acute lymphoblastic leukaemia)
- Blastoid NK-cell lymphoma

Mature (peripheral) T-cell neoplasms
- T-cell prolymphocytic leukaemia
- T-cell large granular lymphocytic leukaemia
- Aggressive NK-cell leukaemia
- Adult T-cell lymphoma/leukaemia (HTLV1+)
- Extranodal NK/T-cell lymphoma, nasal type
- Enteropathy-type T-cell lymphoma
- Subcutaneous panniculitis-like T-cell lymphoma
- Mycosis fungoides/Sezary syndrome
- Primary cutaneous anaplastic large cell lymphoma
- Peripheral T-cell lymphoma, not otherwise specified
- Angioimmunoblastic T-cell lymphoma
- Primary systemic anaplastic large cell lymphoma

Hodgkin's lymphoma

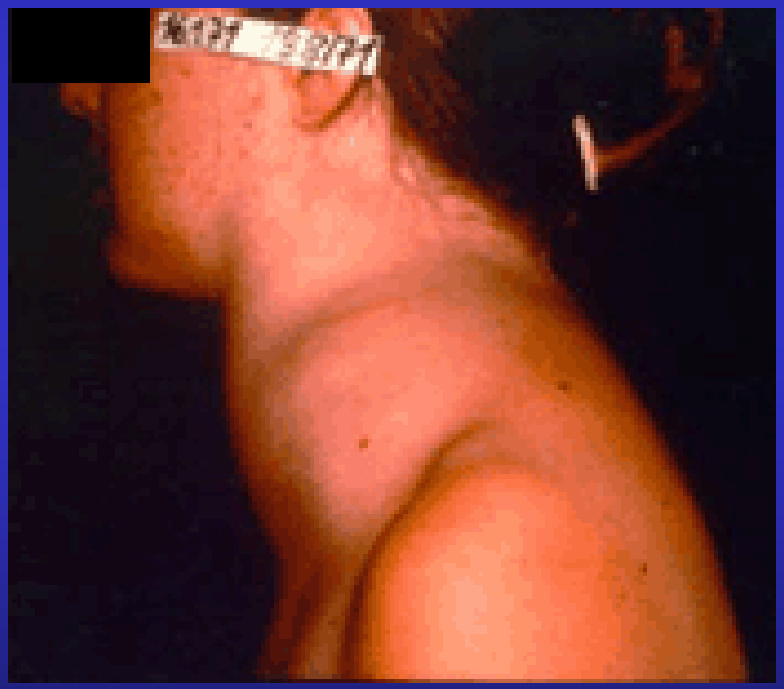
IN SINTESI

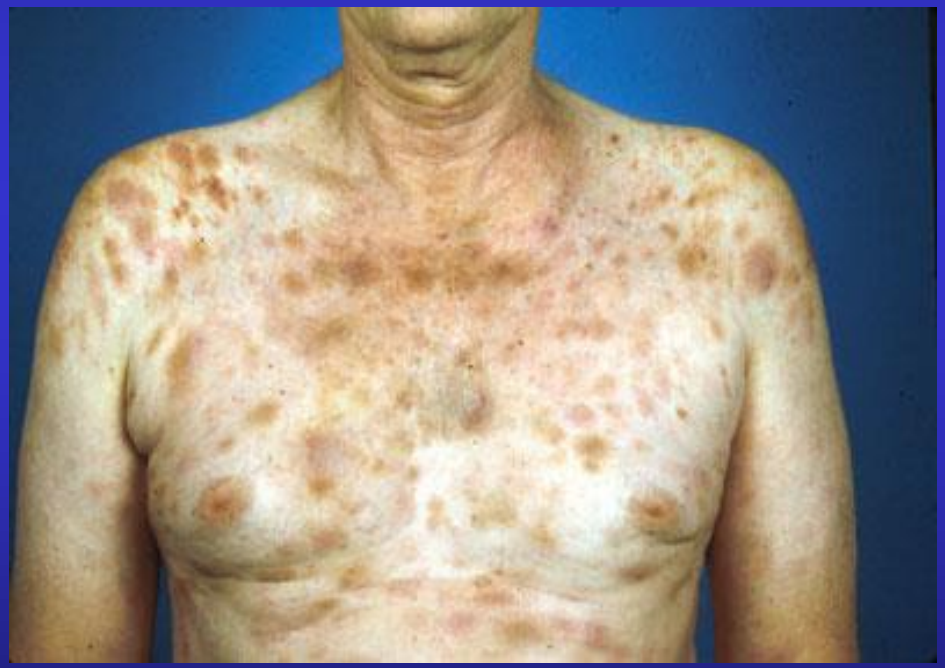

LINFOMI
LINFOMI NON HODGKIN
LINFOMA DI HODGKIN
aggressivi
indolenti

1ª DISTINZIONE

NODALI

EXTRANODALI





INDICE PROGNOSTICO PRE-TRATTAMENTO
IPI SCORE PER LNH AGGRESSIVI

Età < 60 anni:

- **Performance status**
- **Stadio della malattia all'esordio**
- **N° sedi extranodali interessate**
- **Valore di LDH**
- **Sintomi**

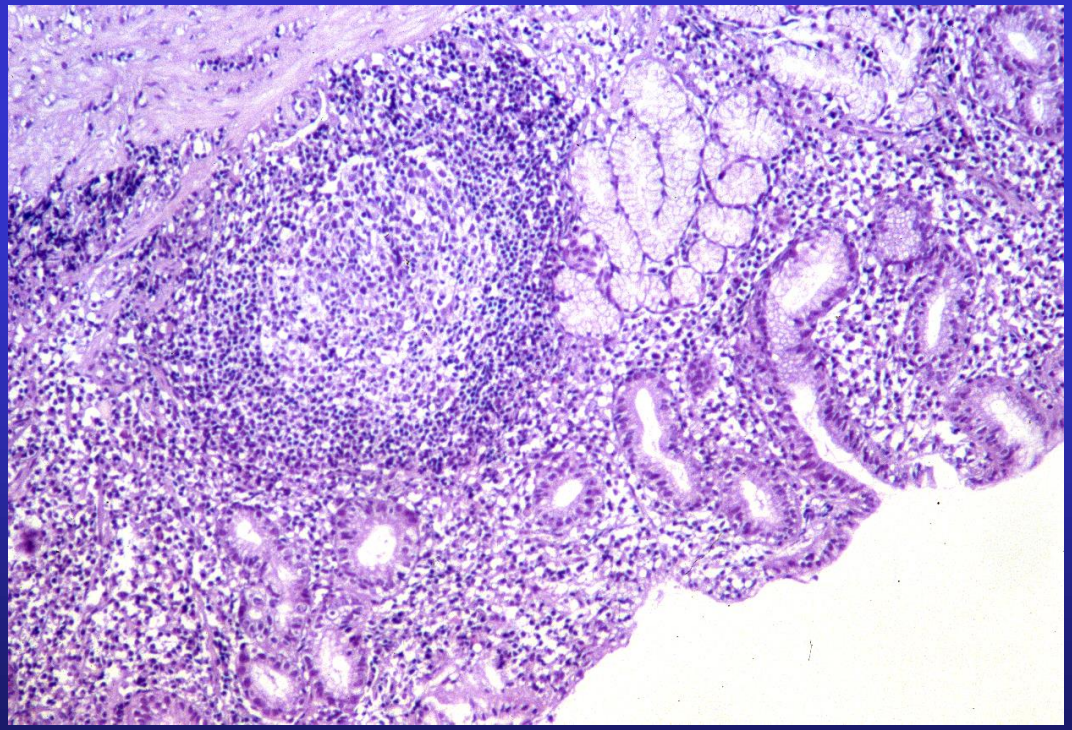
LINFOMI EXTRANODALI

Nel 20-30% dei casi la patologia neoplastica insorge in precursori della linfocitopoiesi che si trovano fuori dagli organi linfoidi secondari.

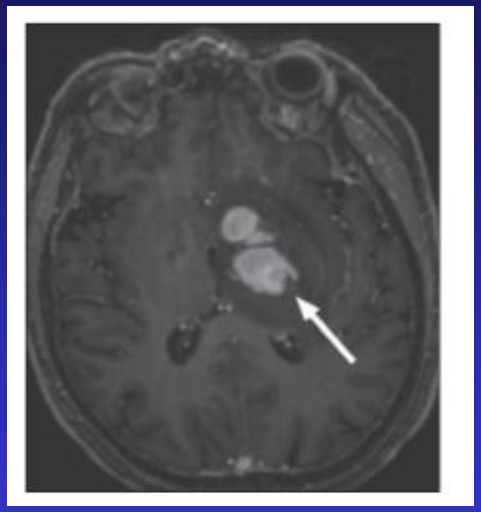
SEDI PIU' INTERESSATE:	•Tubo gastroenterico •Cute •SNC •Testicolo
LINFOMI DI DERIVAZIONE DAL TESSUTO LINFOIDE ASSOCIATO A MUCOSA (MALT)	•Stomaco (frequentemente associato ad un'infezione da *H. pylori*) •Intestino •Ghiandole salivari •Polmone •Tiroide •Cute

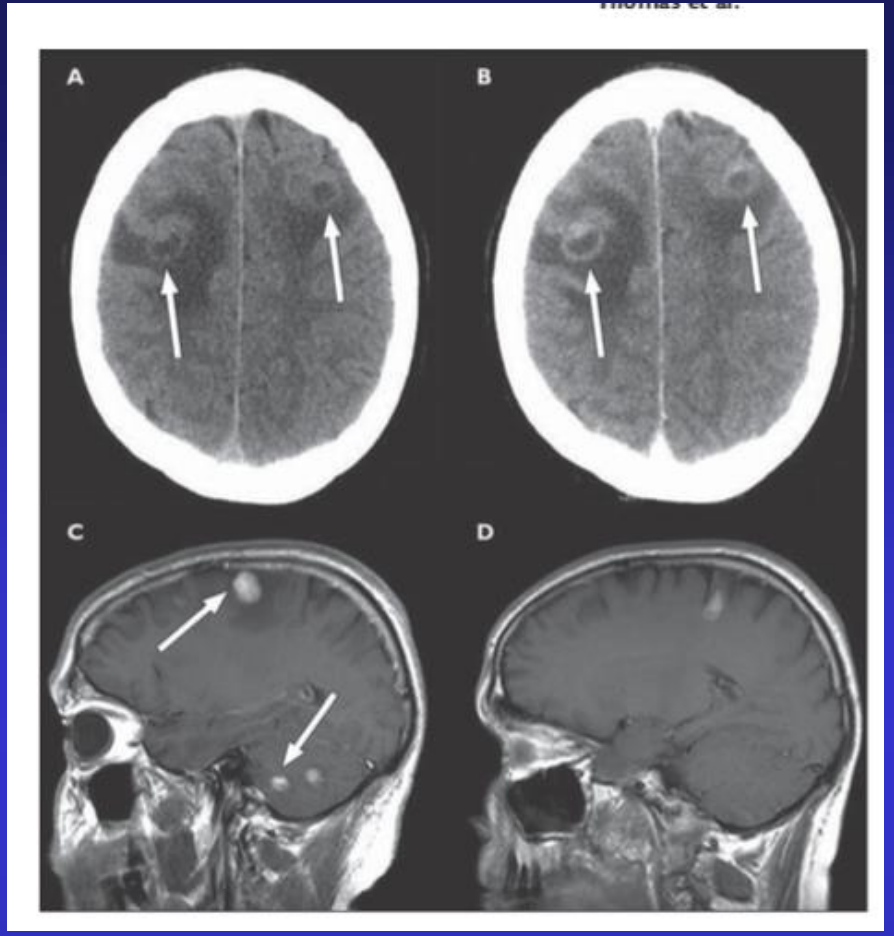
LINFOMI EXTRANODALI

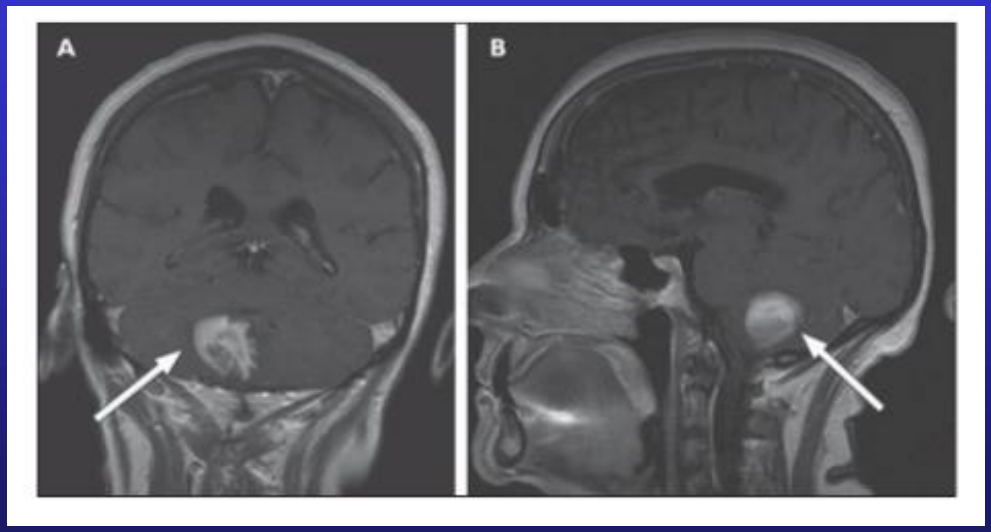
Fatta eccezione per l'intestino, nel quale il MALT è presente in forma nativa nelle placche del Peyer, in tutte le altre sedi anatomiche citate il sistema linfoide compare a seguito di ripetuti stimoli antigenici.

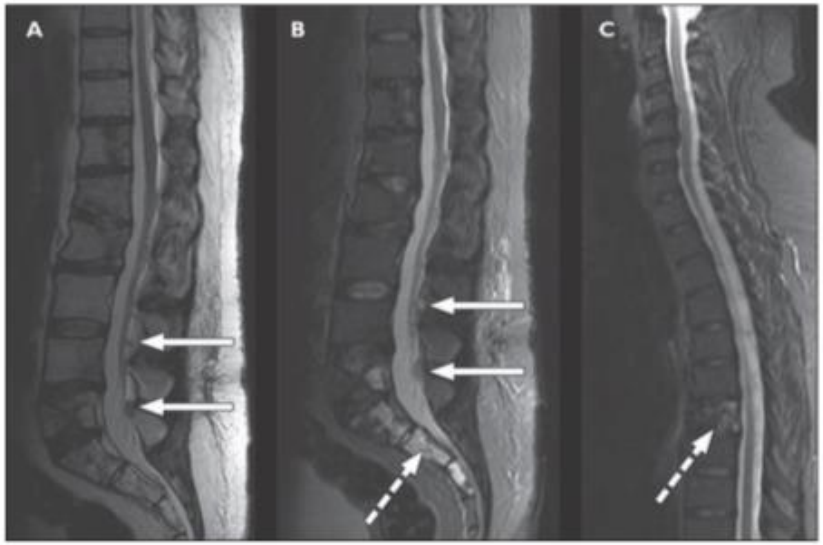


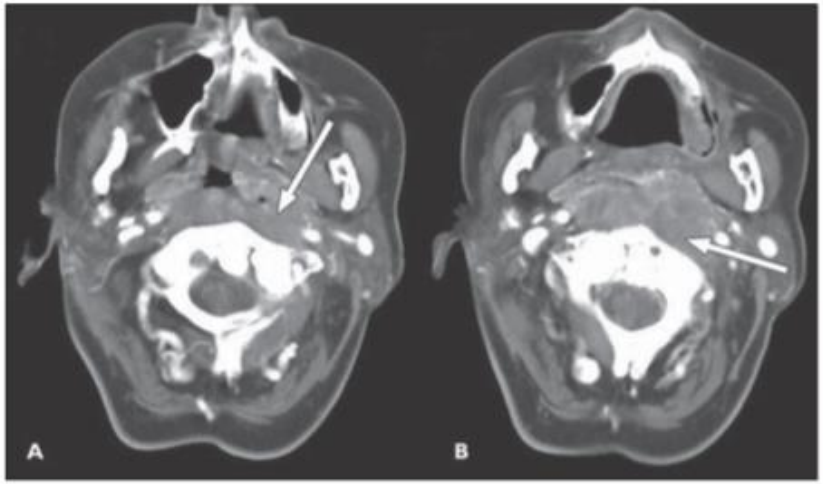
MALT gastrico

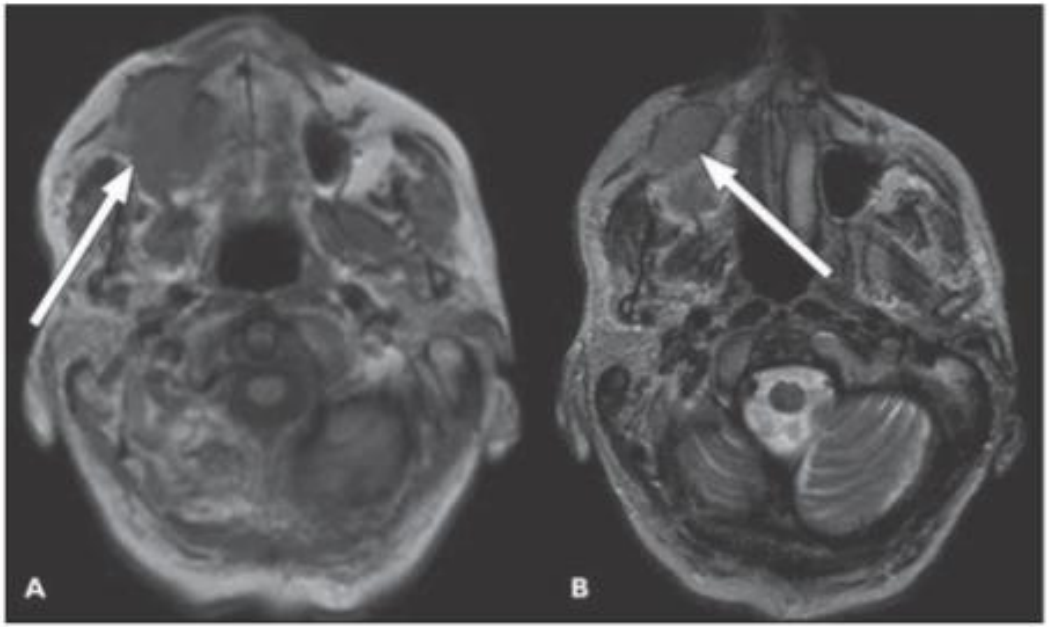


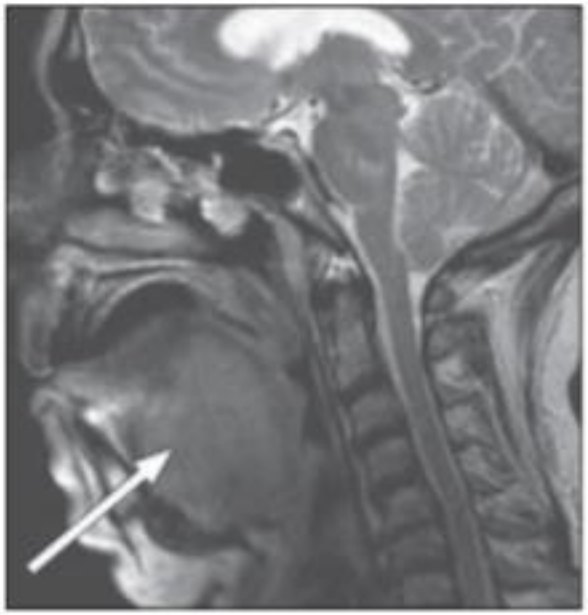

A
B
C
D

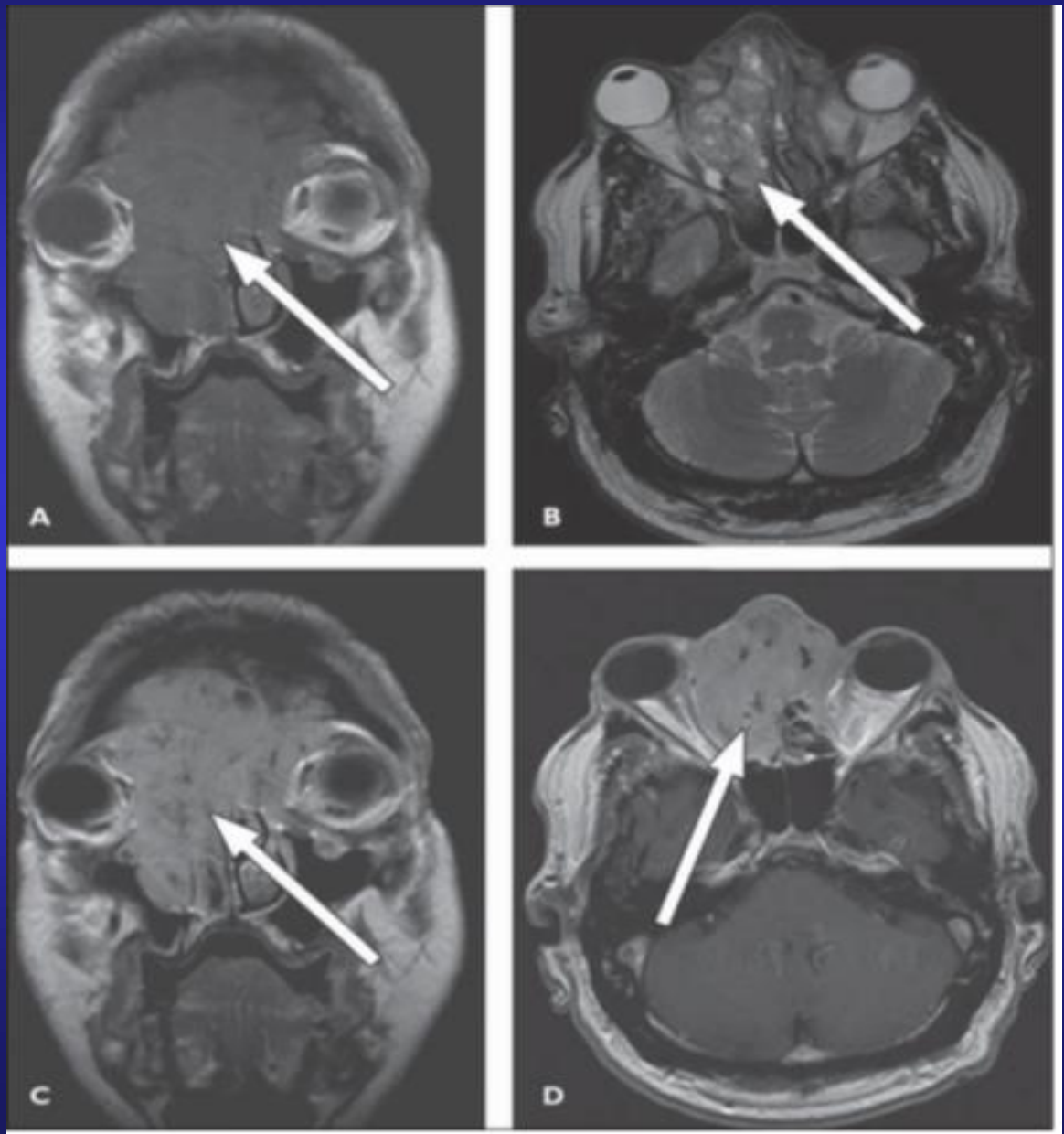

A
B


A
B
C


A
B


A
B




A
B
C
D

APPROCCIO AL PAZIENTE CON SOSPETTO LINFOMA

POSITRON EMISSION TOMOGRAPHY (^{18}F-FDG PET)

- Metodica di imaging funzionale che si basa sull'osservazione che le cellule neoplastiche sono caratterizzate da un elevato metabolismo glucidico (accentuazione dell'attività glicolitica per aumento del trasporto intracellulare di glucosio), ben differenziabile rispetto alle cellule normali.
- Il tessuto tumorale può essere caratterizzato funzionalmente indipendentemente dai parametri morfologici e/o dimensionali.

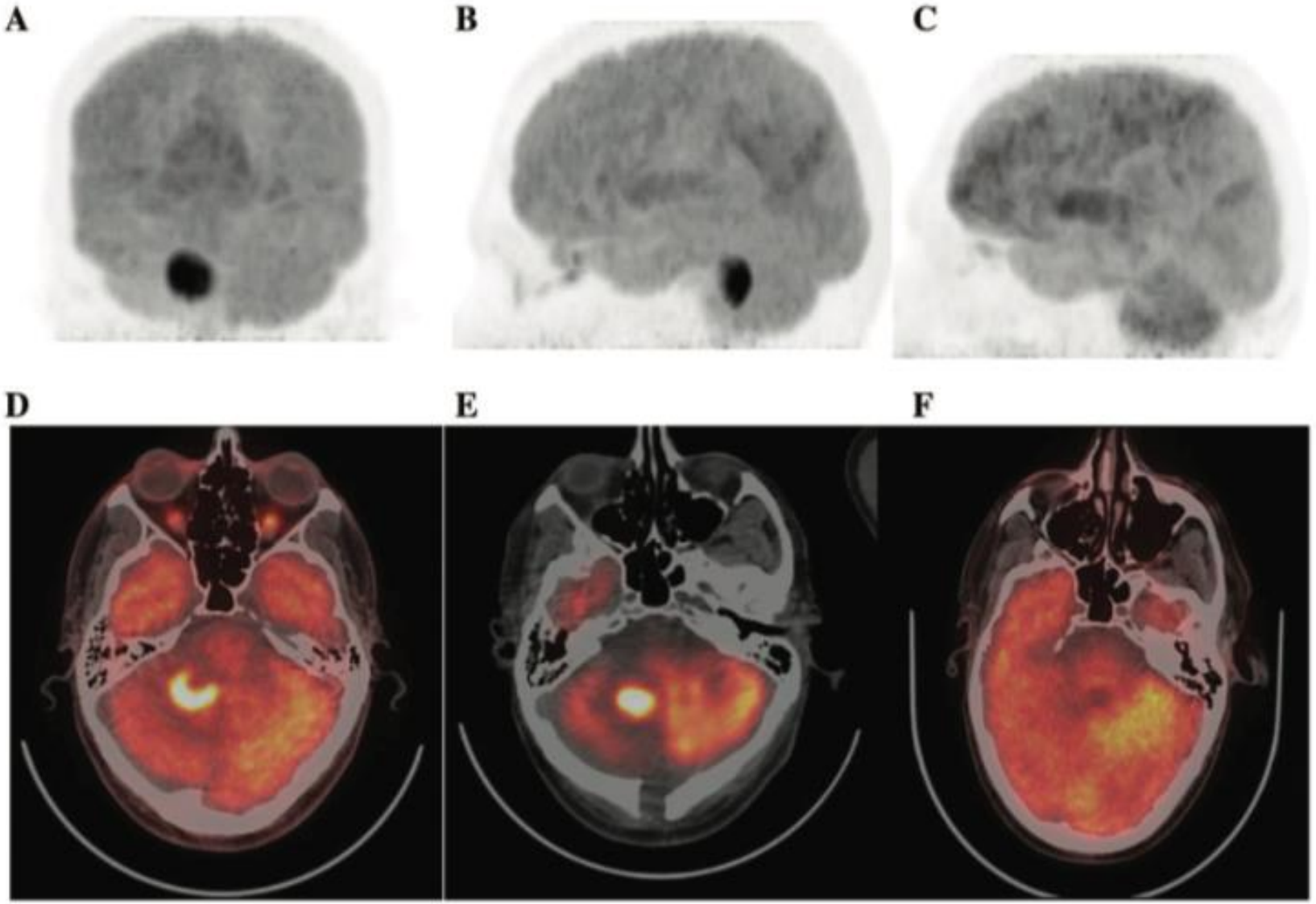


Figure 1 A 43-year-old man with a history of seizures. PET scan showed a hypermetabolic lesion in the cerebellum (A,D) which after craniotomy (B,E) and biopsy turned out to be primary CNS lymphoma involving the cerebellar region of diffuse large B cell subtype. Chemotherapy with methotrexate showed good response (C,F). PET scan in this case helped rule out demyelination, which was one of the differentials at the presentation, by showing the lesion to be intensely hypermetabolic.

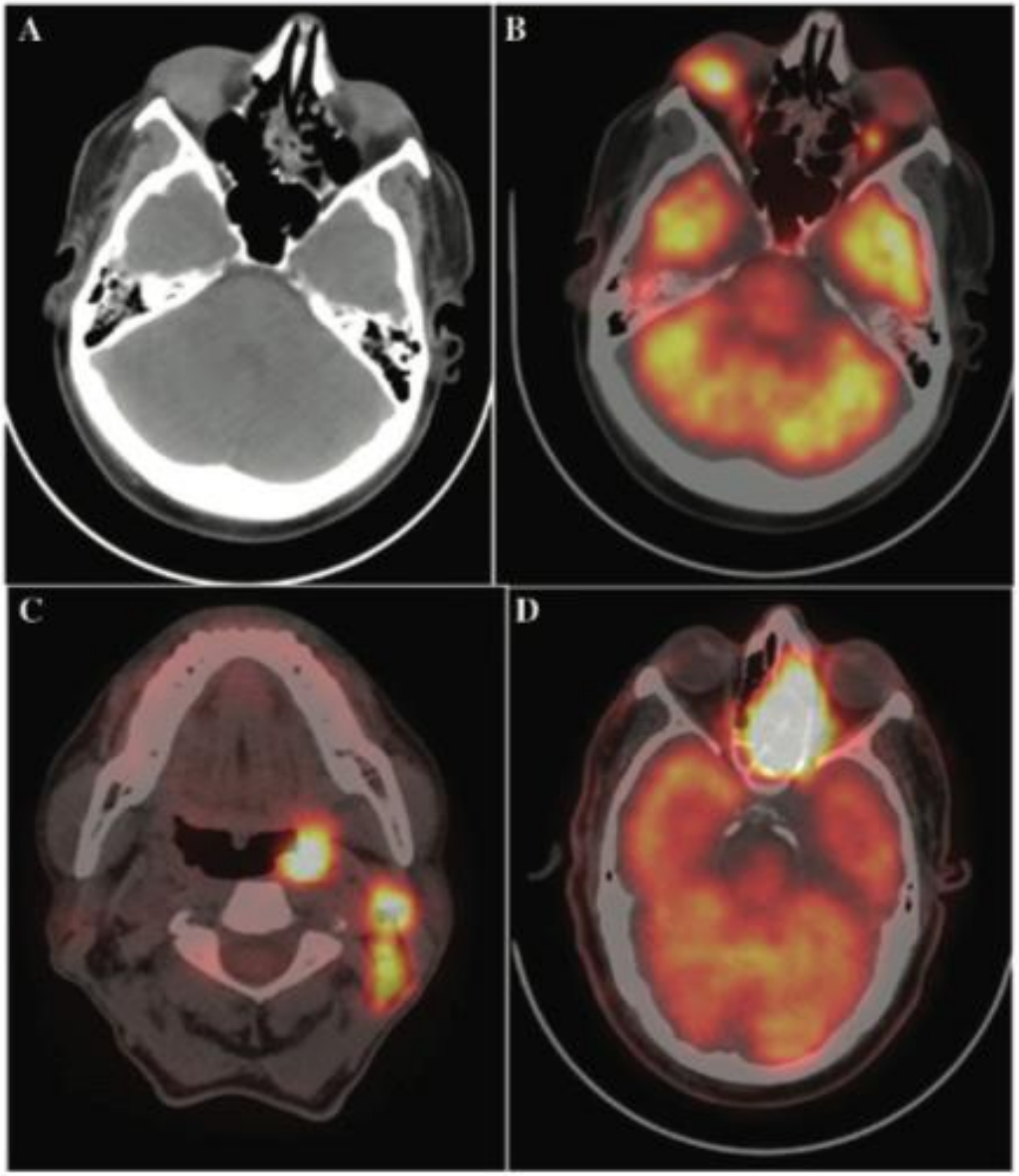
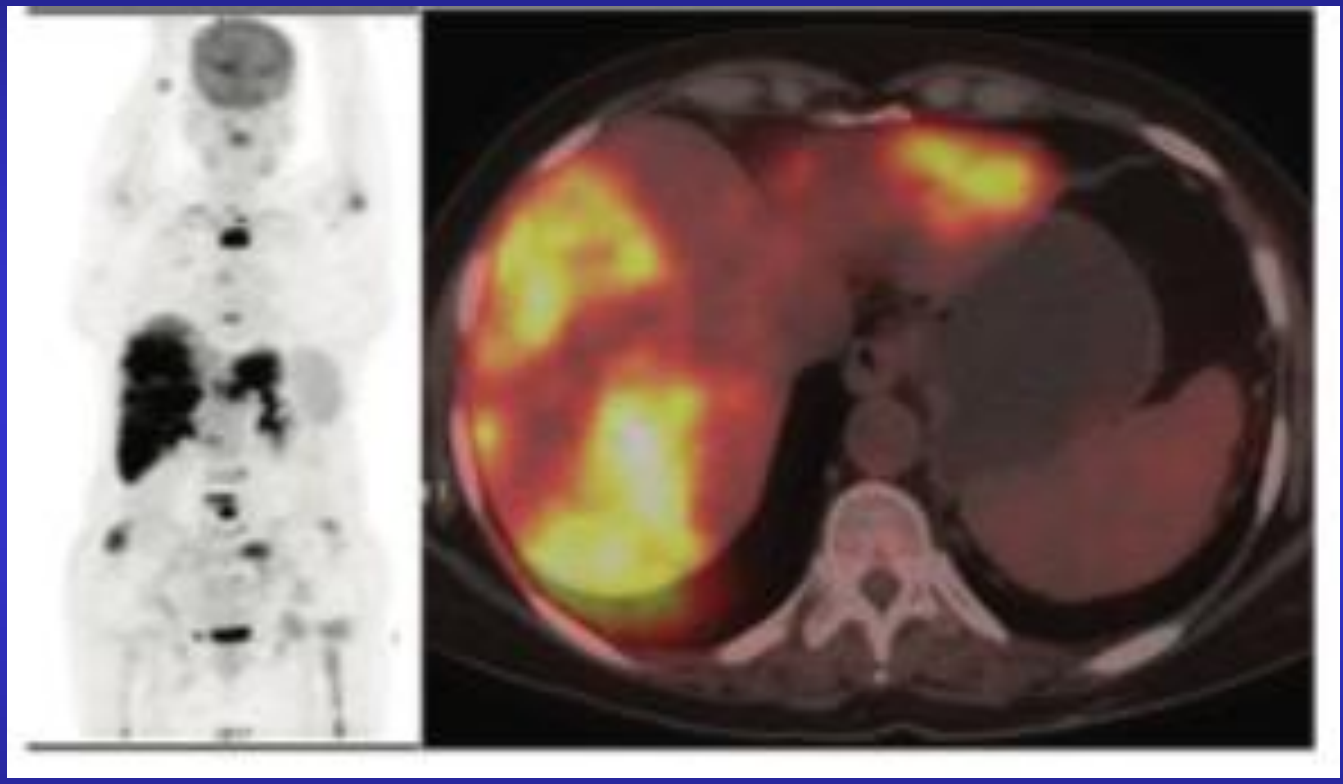


Figure 2 (A) CT of a 46-year-old man showing a homogeneous soft tissue lesion in the right orbit. (B) Intense FDG uptake is seen in the orbital lesion, which was proven to be diffuse large B cell lymphoma. (C) Tonsillar lymphoma in a 53-year-old man of T cell subtype. (D) Lymphoma of T cell subtype involving the ethmoid sinus on the left side in a 62-year-old male patient. All these lesions were found on PET/CT scans that were referred for staging purposes.



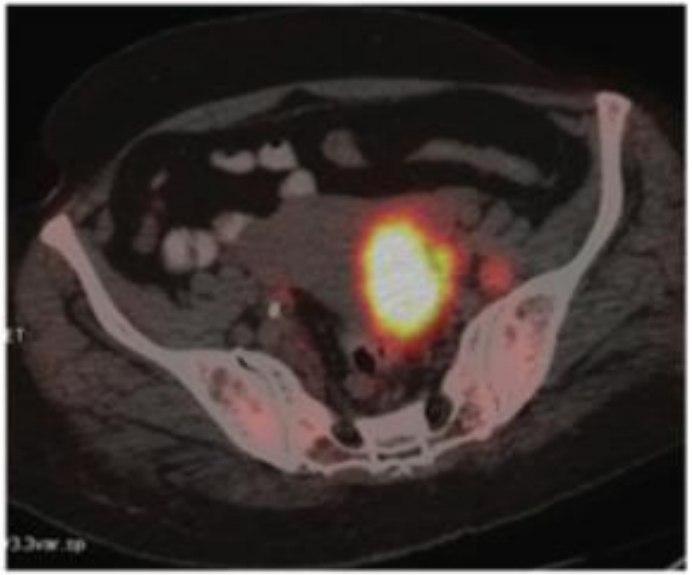


Figure 13 B cell NHL involving the body of the uterus in a 53-year-old woman.

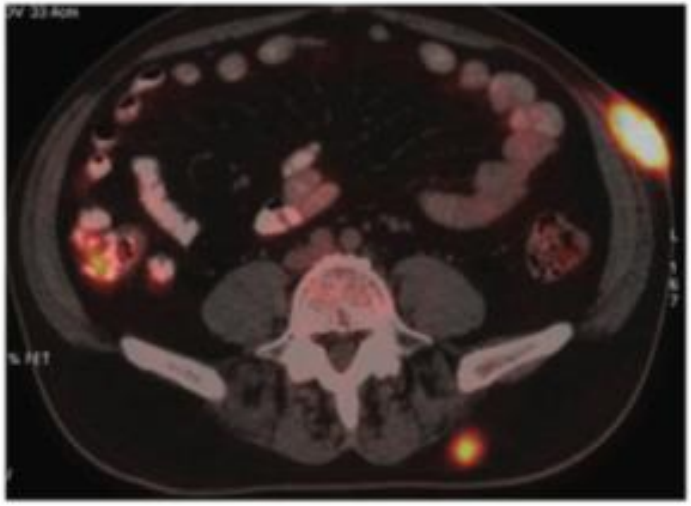


Figure 14 T cell cutaneous lymphoma showing intense FDG uptake in a skin lesion and subcutaneous nodules in a 62-year-old man.

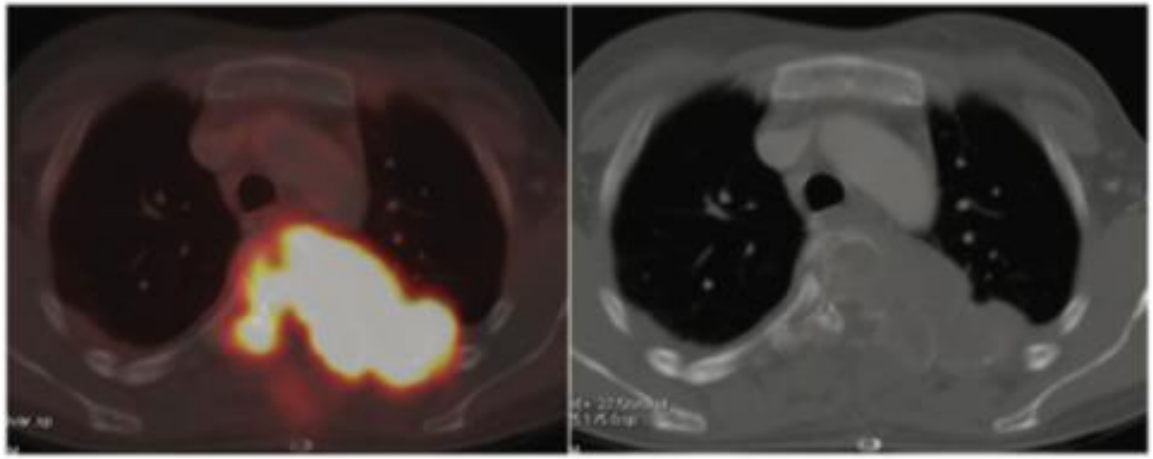


Figure 15 Diffuse large cell lymphoma involving the vertebra and adjacent rib causing expansile lytic destruction in a 40-year-old woman.

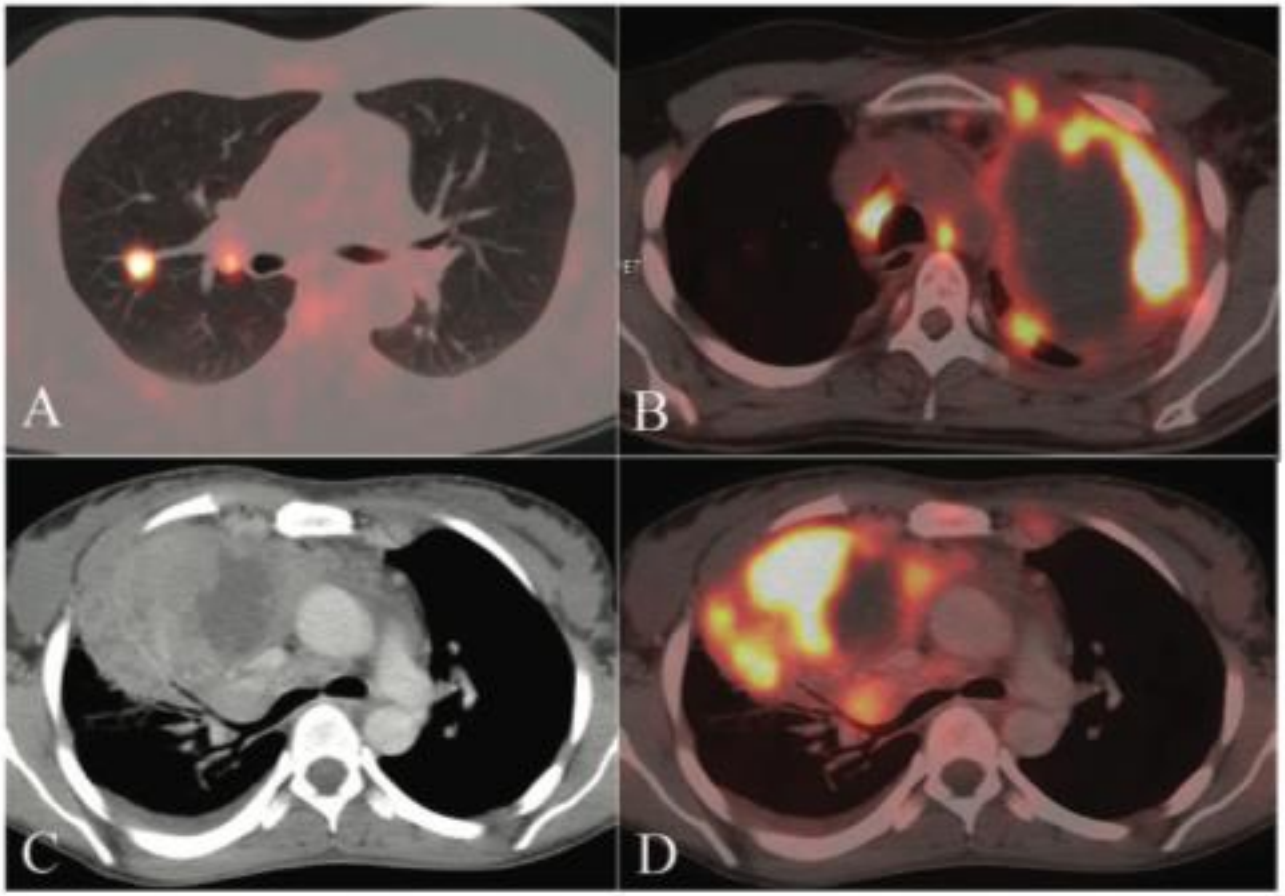


Figure 4 Various manifestations of lymphoma involving the lungs. (A) Nodular presentation of diffuse large B cell lymphoma in a 39-year-old man. (B) Hodgkin disease presenting as a mass lesion in a 24-year-old man. (C,D) NHL presenting as a mass-like consolidation in the right lung with intense uptake along with pleural effusion on the right side in a 28-year-old woman.

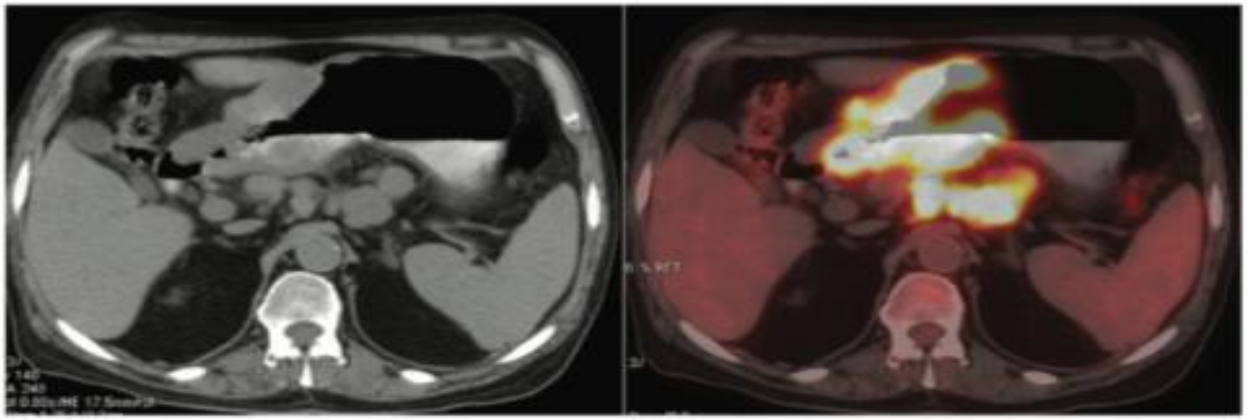


Figure 7 NHL showing intense FDG uptake in the anteropyloric region of the stomach along with perigastric lymph nodes in a 70-year-old man. Gastric lymphomas are usually associated with *H. pylori* gastritis.

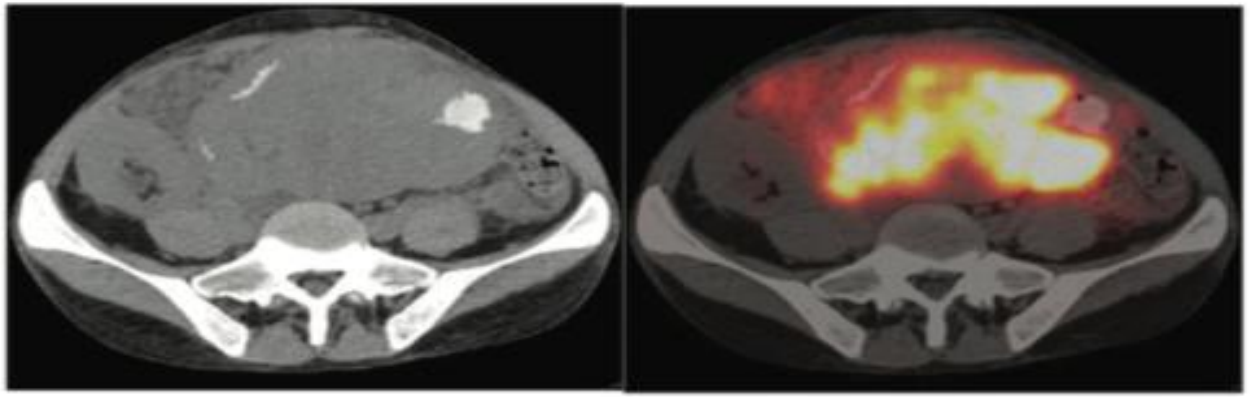
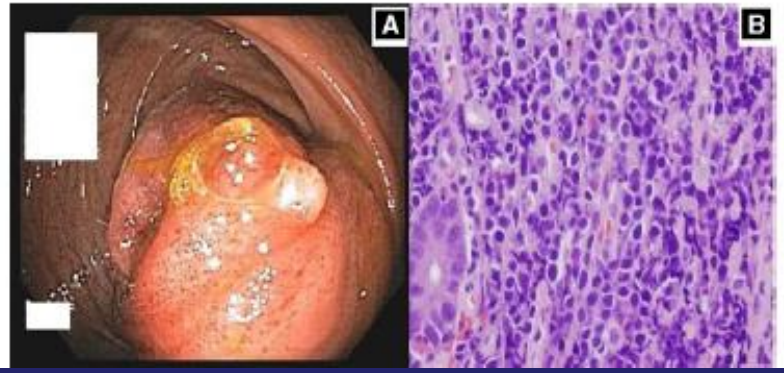


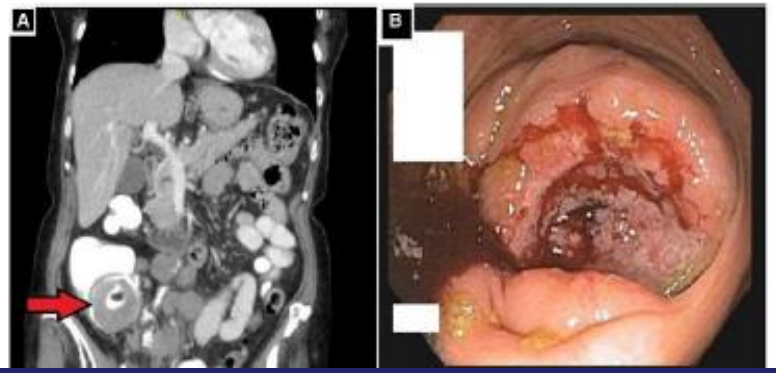
Figure 8 A 30-year-old male renal transplant patient (which is visible in the right iliac region). Intense FDG uptake is seen along the grossly thickened wall of a large segment of small bowel. This was confirmed to be plasmablastic variant of B cell lymphoma.

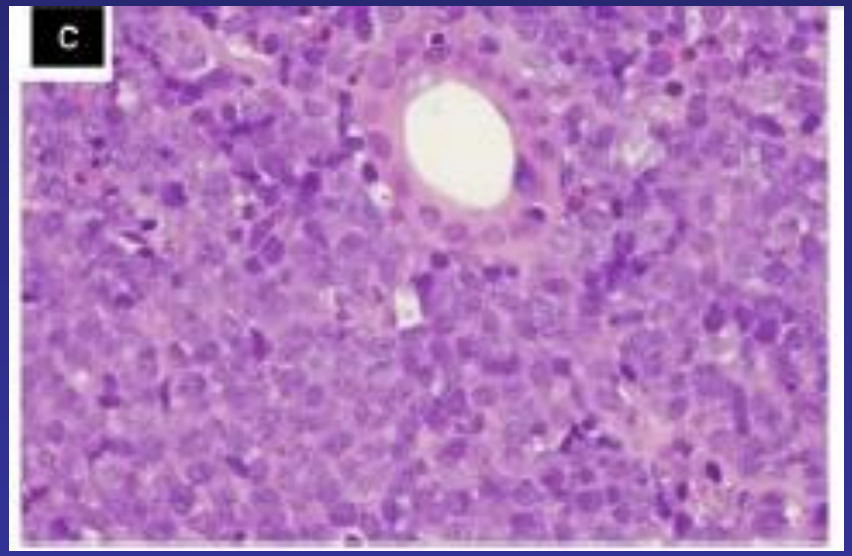
Table 1 Demographics, presenting features and clinical findings in 16 consecutive cases of gastrointestinal lymphoma

Case	Gender	Clinical presentation	Endoscopy
1	Female	Dyspepsia	Antral 'gastritis', duodenitis
2	Male	Chronic diarrhoea	Multiple colonic polyps
3	Male	Positive stool DNA testing	Ulcerated mass at splenic flexure and ascending colon
4	Male	Food impaction, dysphagia	Clean-based gastric ulcers
5	Male	Melena	Fungating, ulcerated circumferential mass in the gastric fundus
6	Male	Gastric outlet obstruction	Fungating, infiltrative, ulcerated circumferential mass in gastric body
7	Female	Haematemesis	Large cratered necrotic duodenal ulcer
8	Male	Intussusception at terminal ileum (TI)	Partially obstructing mass at the ileocaecal valve
9	Male	Abdominal pain	Fungating, partially obstructing mass in ascending colon and caecum
10	Female	Epigastric pain	Patchy mild erythema in duodenum
11	Male	Haematochezia	3 cm ulcerated non-obstructing polypoid mass in the terminal ileum
12	Female	Abdominal pain	Partially obstructing tumour in the caecum
13	Male	Abnormal abdominal imaging, anaemia	Partially obstructing mass at the ileocaecal valve
14	Female	Profound hypoalbuminaemia (malnutrition), anasarca	Mucosal changes in jejunum
15	Male	Severe anaemia, abdominal pain	Non-obstructing, circumferential, polypoid mass in the terminal ileum
16	Female	Iron deficiency anaemia	Large, ulcerated, non-obstructing mass at ileocaecal valve

Shirwaikar Thomas A, et al. BMJ Open Gastro 2019;6:e000320. doi:10.1136/bmjgast-2019-000320 1







Shirwaikar Thomas A, et al. BMJ Open Gastro 2019;6:e000320. doi:10.1136/bmjgast-2019-000320 1

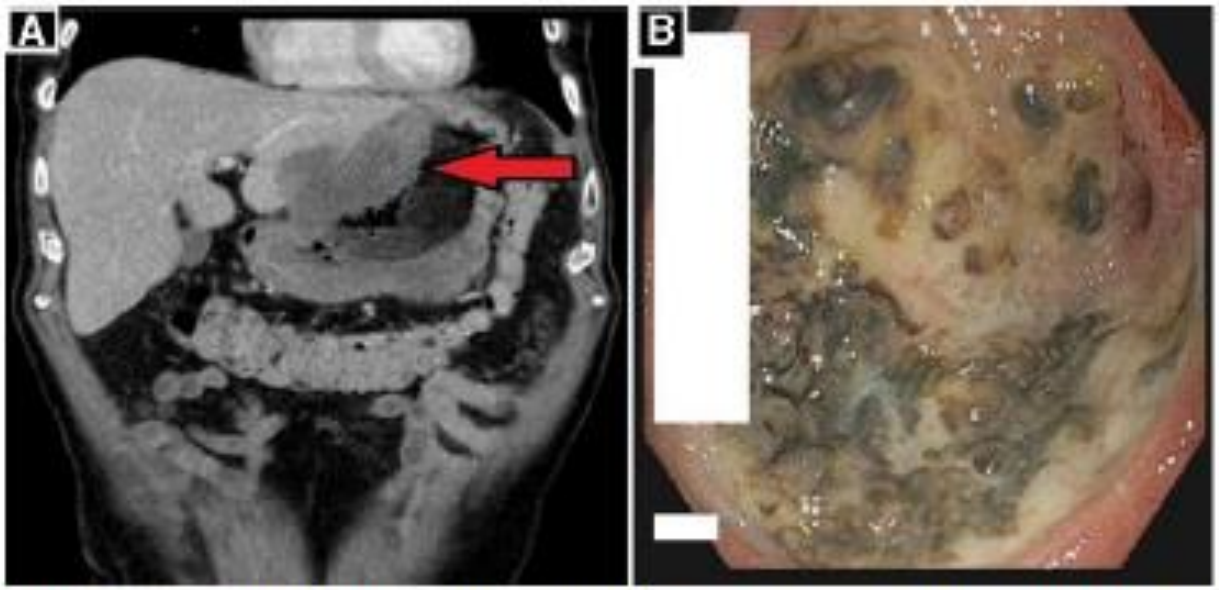


Figure 8 (A) Large gastric mass with direct invasion into left lobe of liver on contrasted abdominal imaging. (B) Fungating, ulcerated mass in gastric body. (C) Diffuse large B cell lymphoma.

Shirwaikar Thomas A, et al. BMJ Open Gastro 2019;6:e000320. doi:10.1136/bmjgast-2019-000320 1

APPROCCIO AL PAZIENTE CON SOSPETTO LINFOMA

del tratto gastroenterico

INDAGINI ENDOSCOPICHE

- **Esofago-gastro-duodenoscopia** (EGDS), con biopsie e valutazione della positività per infezione da *Helicobacter pylori* (LNH-MALT).
- **Pancolonscopia** (PCS) con biopsie multiple.

Original Article

A Study of Clinical Profile of Primary Extranodal Lymphomas in a Tertiary Care Institute in South India

Abstract

Context: Primary extranodal lymphoma (pENL) refers to group of disorders arising from tissues other than lymph nodes. The incidence of pENL is increasing and is probably due to better diagnostic immunophenotyping and imaging modalities. Hence, this study was undertaken to ascertain the incidence, distribution, and histological subtypes of extranodal non-Hodgkin lymphoma (NHL) in a tertiary care institute in South India. **Subjects and Methods:** This was a retrospective study of patients diagnosed to have histologically proven NHL. The demographic and clinical features, laboratory parameters, imaging findings, histopathology, and immunophenotyping were documented. The lymphomas were grouped as extranodal and nodal. The data were tabulated in a Microsoft Excel sheet, and descriptive analysis was done. **Results:** Primary extranodal NHLs constituted 35.96% (41/114) of all NHLs. The B symptoms were less common in pENL compared to nodal NHL. Gastrointestinal tract (GIT) constituted the most common extranodal site (19/41, 46.34%), and diffuse large B-cell lymphoma (DLBCL) was the most common histological subtype. Majority (40/41, 97%) of the patients with pENL were immunocompetent. 31/41 (75%) patients were in Stage I–II compared to 58/73 (79.4%) patients in Stage III–IV in nodal NHL. **Conclusions:** Primary extranodal NHL constituted about one-third of patients diagnosed to have NHL at our center with the GIT being the most common site of presentation and DLBCL being the most common histology. A strong suspicion of NHL at an extranodal site with appropriate pathological and immunophenotyping evidence is needed to establish the diagnosis of a pENL.

Keywords: *Diffuse large B cell, extranodal, lymphoma, Non-Hodgkin*

Ananth Pai, Thiruvengadasamy Kannan, RG Balambika, Vindhya Vasini

Department of Medical Oncology, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, Ind

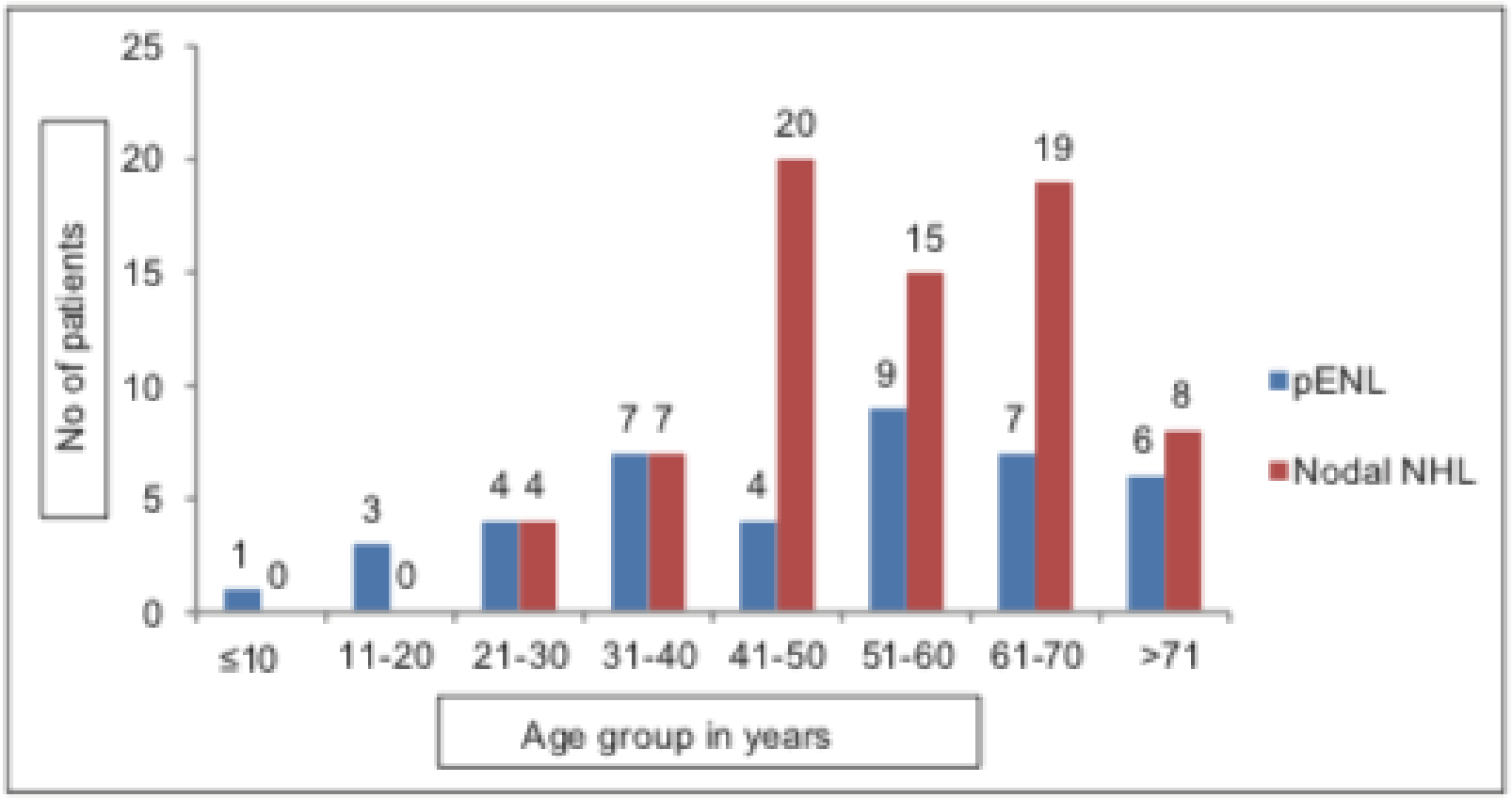


Figure 1: Age group distribution

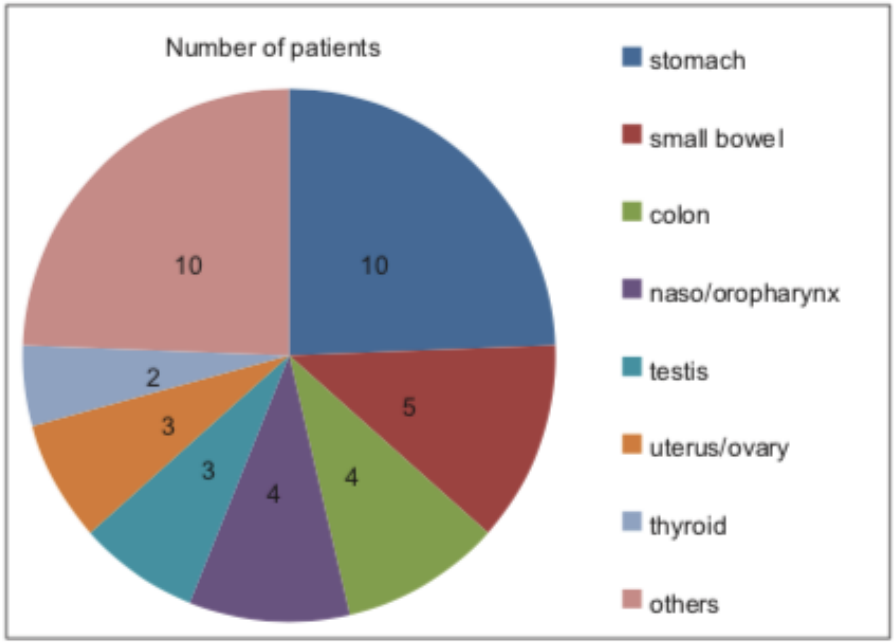


Figure 2: Site wise distribution

Table 2: Histology of the lymphomas

Histology	pENL	Nodal NHL
DLBCL	19	24
BL, unclassified	14	25
T-cell lymphoma	6	9
FL	0	9
SLL	0	3
Mantle cell lymphoma	0	2
MALToma	2	0
ALCL	0	1

pENL – Primary extranodal lymphoma; NHL – Non-Hodgkin lymphoma; DLBCL – Diffuse large B-cell lymphoma; FL – Follicular lymphoma; SLL – Small lymphocytic lymphoma; ALCL – Anaplastic large cell lymphoma; BL – B-cell lymphoma; MALToma – Mucosa-associated lymphoid tissue lymphoma

Primary extranodal B-cell lymphoma: current concepts and treatment strategies

Barbara Vannata, Emanuele Zucca

Oncology Institute of Southern Switzerland, Ospedale San Giovanni, Bellinzona, Switzerland

Correspondence to: Emanuele Zucca, MD. Oncology Institute of Southern Switzerland, Ospedale San Giovanni, CH-6500 Bellinzona, Switzerland. Email: ielsg@ticino.com.

Abstract: Around 30% of all non-Hodgkin lymphoma (NHL) cases arise from extranodal sites. Often the primary extranodal presentation requires site-specific strategies either for diagnosis or therapy. However, several issues remain controversial such as the definition itself of primary extranodal lymphoma, and the most appropriate staging system to characterize the disease extent. Moreover, the specific presenting sites may have *per se* prognostic implications. The vast majority of the published reports on primary extranodal lymphomas are represented by single-institution retrospective studies. In most clinical trials the primary extranodal lymphomas are often included together with the nodal ones and only a few studies have investigated the peculiarity of extranodal lymphomas. This review summarizes the recent advances in B-cell extranodal lymphomas, addressing the critical points in the management of the more frequently involved sites.

Table 1 Site-specific work-up procedures for primary extranodal B-cell NHL

Site	Procedure
CNS	MRI of the brain with gadolinium (spinal MRI if indicated)
	Stereotaxic biopsy
	Lumbar puncture with CSF examination
	Ophthalmologic examination
Ocular adnexa	MRI (or CT scan)
	Ophthalmologic examination
	Chlamydophila psittaci in the tumor biopsy and PBMNCs by PCR
Waldeyer's ring	Gastro-duodenal endoscopy with gastric biopsies
Salivary glands	ENT examination and echography
Thyroid	Echography +/– CT scan of the neck
	Thyroid function tests
Stomach	Gastro-duodenal endoscopy and endoscopic ultrasound
	Helicobacter pylori status (by IHC)
	FISH or molecular assay for the t(11;18) translocation
	Waldeyer's ring examination
Intestine, small	Endoscopy with multiple biopsies
	Campylobacter Jejuni search in IPSID (by PCR, IHC or in situ hybridization in tumor biopsy)
Intestine, large	Colonoscopy with multiple biopsies
Breast	Bilateral Mammography and MRI (or CT scan)
Testis	Ultrasonography of the scrotum
	Lumbar puncture with CSF examination
Skin	*Borrelia Burgdorferi* in the tumor biopsy by PCR in PCMZL
Bone	MRI

CNS, central nervous system; MRI, magnetic resonance imaging; CSF, cerebrospinal fluid; PBMNCs, peripheral blood mononuclear cells; CT, computed tomography scan; PCR, polymerase chain reaction; IHC, immunohistochemistry; FISH, fluorescence in situ hybridization; ENT, Ear Nose Throat; PCMZL, primary cutaneous marginal zone lymphomas.

Clinical features and outcomes of diffuse large B-cell lymphoma based on nodal or extranodal primary sites of origin: Analysis of 1,085 WHO classified cases in a single institution in China

Yuankai Shi[1], Ying Han[1], Jianliang Yang[1], Peng Liu[1], Xiaohui He[1], Changgong Zhang[1], Shengyu Zhou[1], Liqiang Zhou[1], Yan Qin[1], Yongwen Song[2], Yueping Liu[2], Shulian Wang[2], Jing Jin[2], Lin Gui[1], Yan Sun[1]

[1]Department of Medical Oncology, Beijing Key Laboratory of Clinical Study on Anticancer Molecular Targeted Drugs, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China; [2]Department of Radiation Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China

Correspondence to: Yuankai Shi. Department of Medical Oncology, Beijing Key Laboratory of Clinical Study on Anticancer Molecular Targeted Drugs, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, No. 17 Panjiayuan Nanli, Chaoyang District, Beijing 100021, China. Email: syuankai@cicams.ac.cn.

Abstract

Objective: To explore the clinicobiologic features and outcomes of diffuse large B-cell lymphoma (DLBCL) patients in China according to the primary site.

Methods: A total of 1,085 patients diagnosed with DLBCL in National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College during a 6-year period were enrolled. Their clinical characteristics and outcomes were analyzed according to the primary site.

Results: In the 1,085 patients, 679 (62.6%) cases were nodal DLBCL (N-DLBCL) and 406 cases (37.4%) were extranodal DLBCL (EN-DLBCL). The most common sites of N-DLBCL were lymphonodus (64.8%), Waldeyer's ring (19.7%), mediastinum (12.8%) and spleen (2.7%), while in EN-DLBCL, stomach (22.4%), intestine (16.0%), nose and sinuses (8.9%), testis (8.4%), skin (7.9%), thyroid (6.9%), central nervous system (CNS) (6.4%), breast (5.7%), bone (3.4%), and salivary gland (2.7%) were most common. N-DLBCL patients tend to present B symptoms, bulky disease, and elevated LDH more often, while age >60 years, extranodal sites >1, Ann Arbor stage I or II, bone marrow involvement, and Ki-67 index >90% were usually seen in EN-DLBCL. The 5-year overall survival (OS) rate and progression-free survival (PFS) rate for all patients were 62.5% and 54.2%. The 5-year OS rate for patients with N-DLBCL and EN-DLBCL were 65.5% and 56.9% (P=0.008), and the 5-year PFS were 57.0% and 49.0% (P=0.020). Waldeyer's ring originated DLBCL possessed the highest 5-year OS rate (83.6%) and PFS rate (76.9%) in N-DLBCL. The top five EN-DLBCL subtypes with favorable prognosis were stomach, breast, nose and sinuses, lung, salivary gland, with 5-year OS rate: 70.3%, 69.6%, 69.4%, 66.7% and 63.6%, respectively. While CNS, testis, oral cavity and kidney originated EN-DLBCL faced miserable prognosis, with 5-year OS rate of 26.9%, 38.2%, and 42.9%.

Conclusions: In our study, primary sites were associated with clinical characteristics and outcomes. Compared with EN-DLBCL, N-DLBCL had better prognosis.

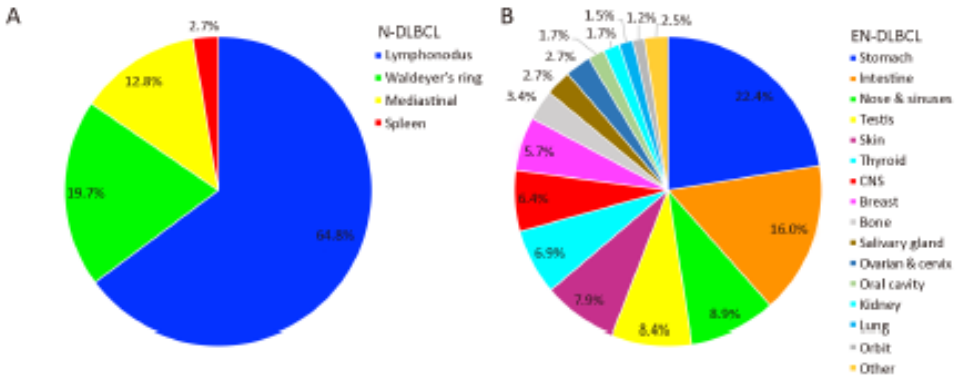
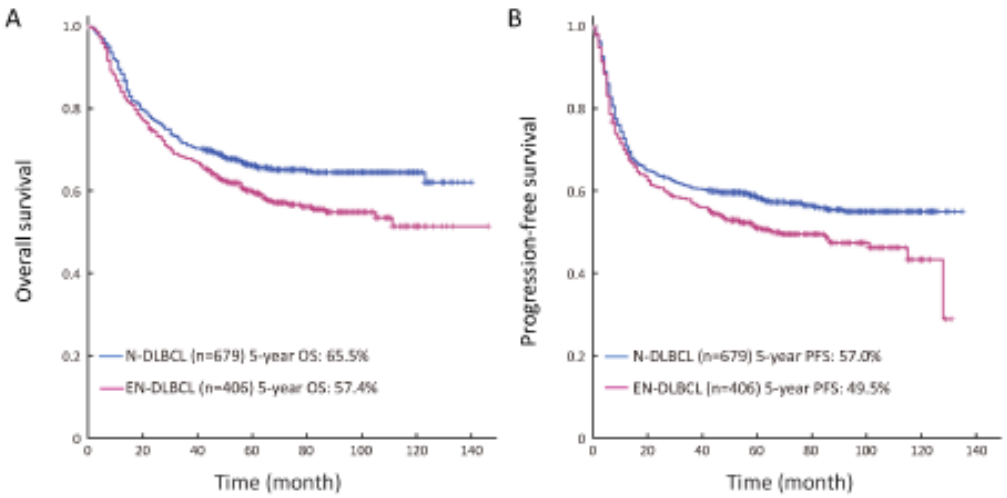


Figure 2 Distribution of primary sites in nodal diffuse large B-cell lymphoma (N-DLBCL) (A) and extranodal diffuse large B-cell lymphoma (EN-DLBCL) (B). CNS, central nervous system.



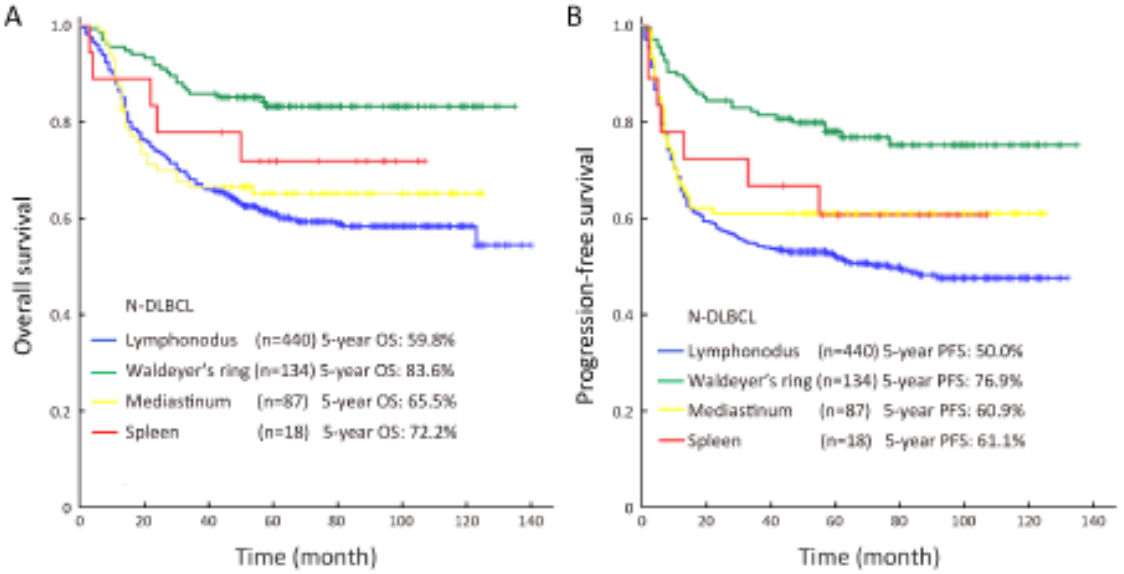
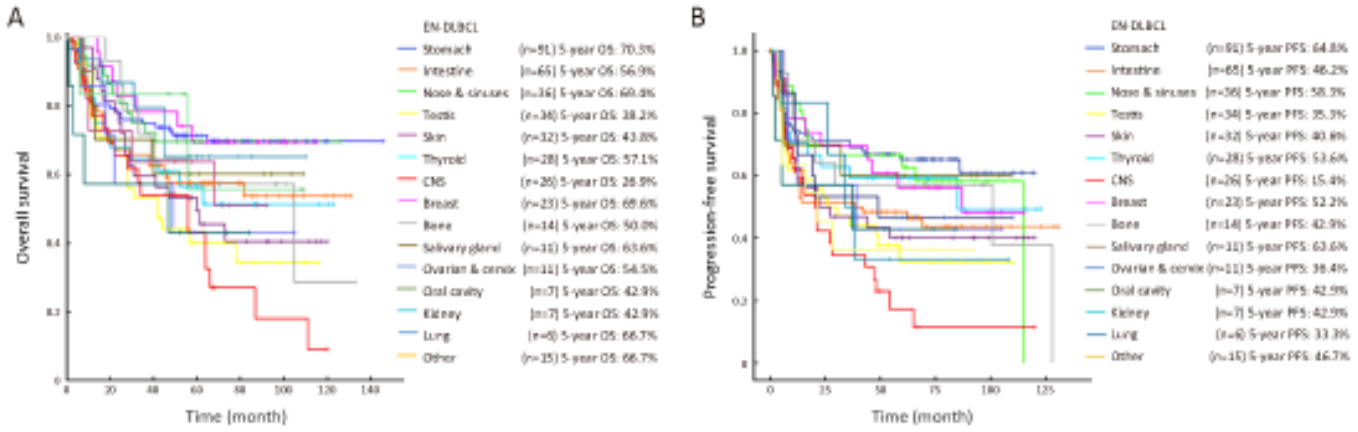


Figure 4 Overall survival (OS) (A) and progression-free survival (PFS) (B) for patients with nodal diffuse large B-cell lymphoma (N-DLBCL) according to the primary site of the lymphoma. (A) P<0.001; (B) P<0.001.



Chin J Cancer Res 2019;31(1):152-161

Robert Bosch Stiftung

RBK

Robert-Bosch-Krankenhaus

IKP

STUTTGART

Challenging Extranodal Lymphomas

ECP Nice, September 9th, 2019

German Ott

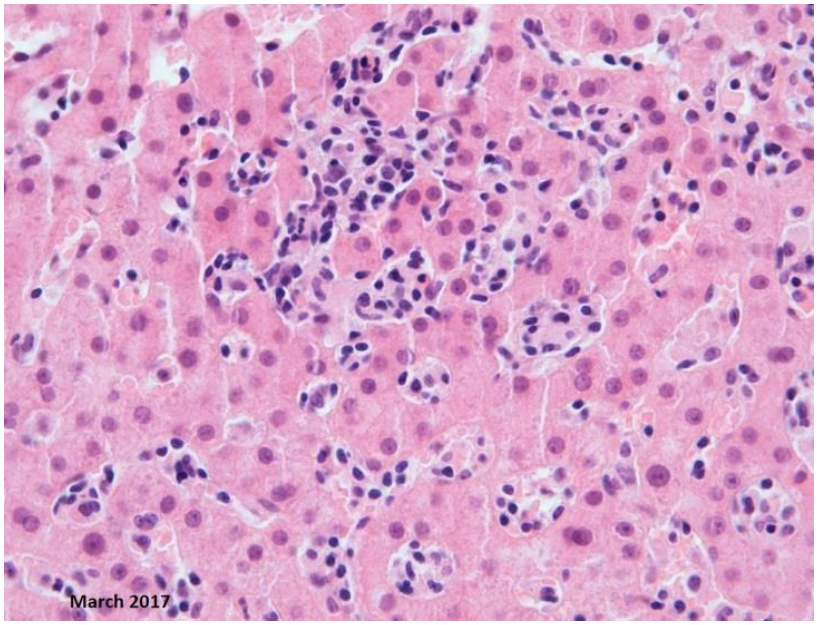
Department of Clinical Pathology, Robert-Bosch-Krankenhaus and

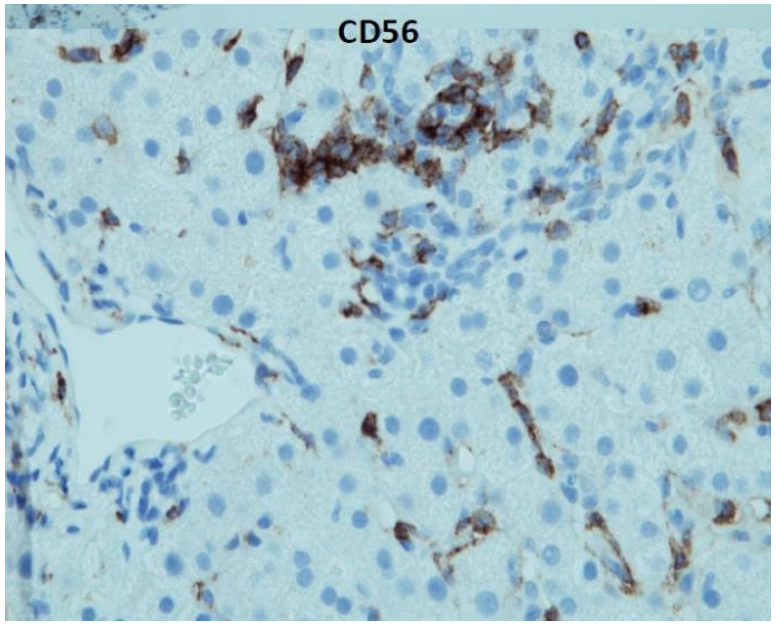
Dr. Margarete Fischer-Bosch Institute of Clinical Pharmacology, Stuttgart

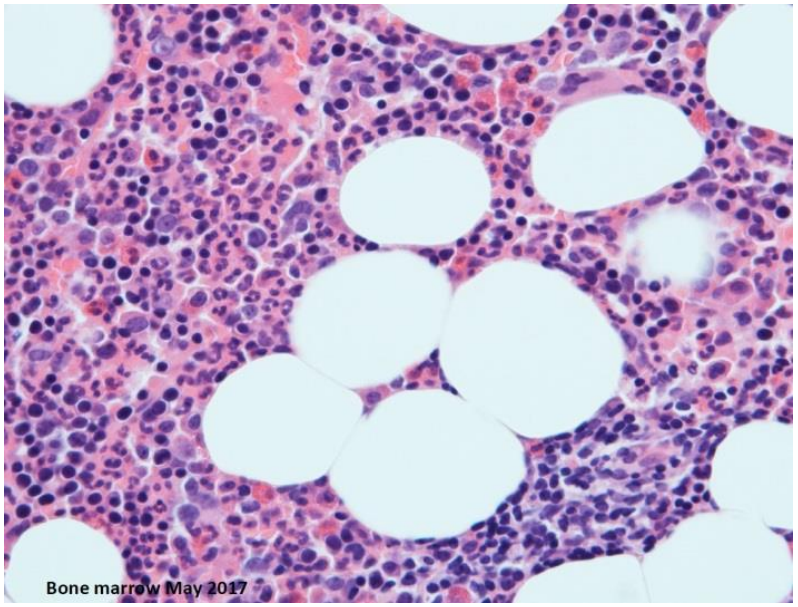
Reactive lesions mimicking lymphomas and borderline neoplasia

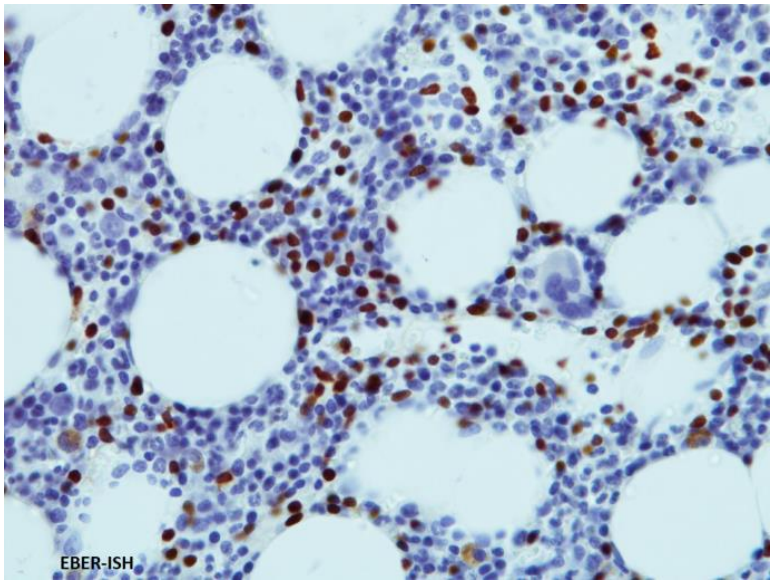
Number	Submitter	Panel Diagnosis
140	Dr. Venkatraman	Chronic active EBV infection, NK cell type
182	Dr. Ng	IgG4-related disease (bilateral mastitis and dacryoadenitis)
190	Dr. Lorenzi	Monotypic IgG4+ lambda+ MZL of the orbit
202	Dr. Ben-Ezra	Reactive lymphatic hyperplasia
245	Dr. Chen	Mucous membrane plasmacytosis
268	Dr. Ashton-Key	Atypical lymphoproliferative disorder in the setting of activated phosphoinositide 3-kinase delta syndrome (APDS)
285	Dr. Soma	Atypical polyclonal T cell lymphoproliferative disorder in the setting of myasthenia gravis
324	Dr. Sadigh	Rectal tonsil
473	Dr. Ma	Atypical (reactive) T-cell lymphoproliferation in the skin

LYWS140 Chronic active EBV infection, NK cell-type

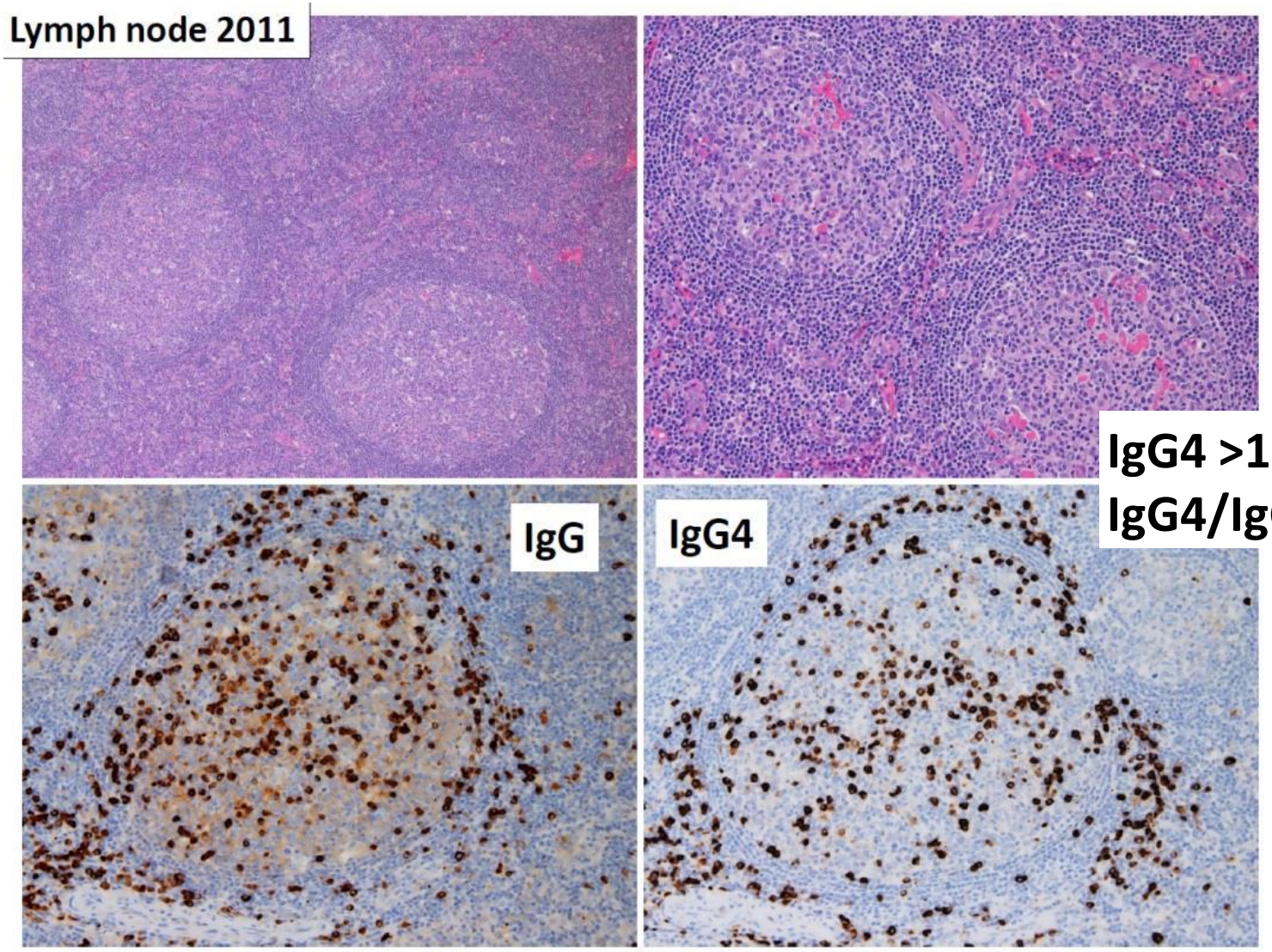




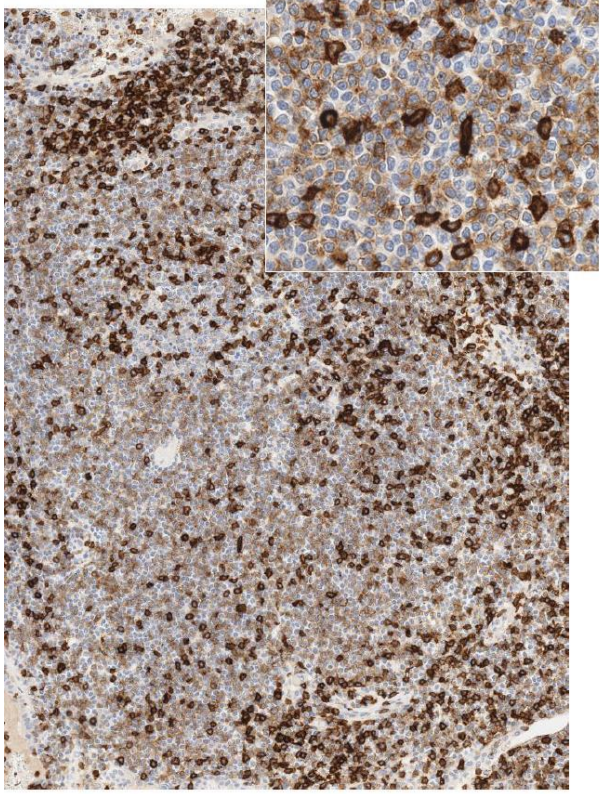




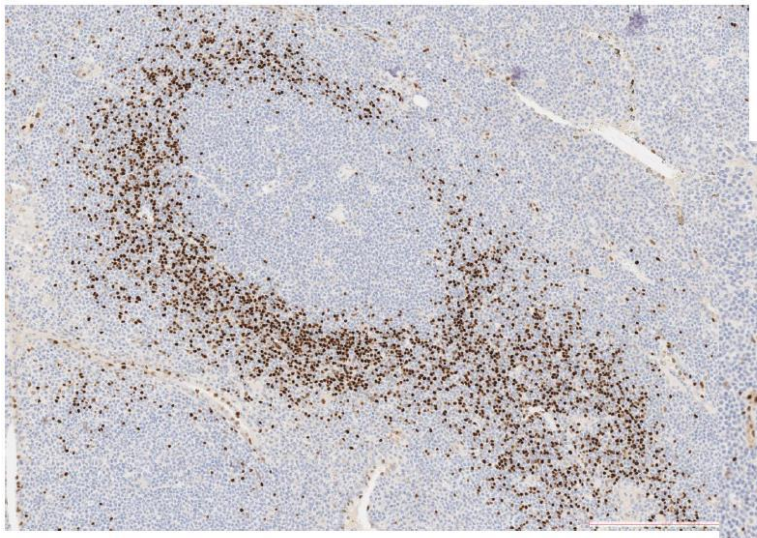
LYWS190 Monotypic IgG4+ lambda+ plasma cell proliferation of the orbit

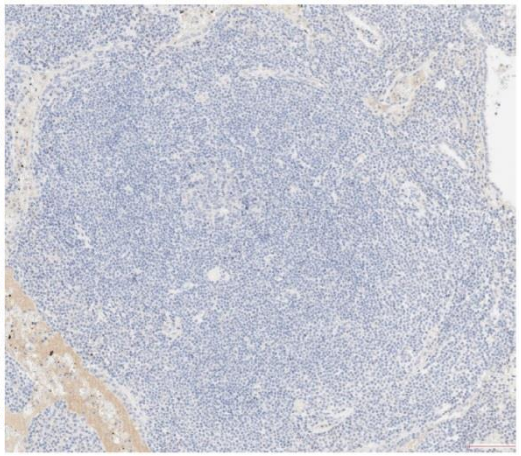


IgG4 >100/field
IgG4/IgG>40%

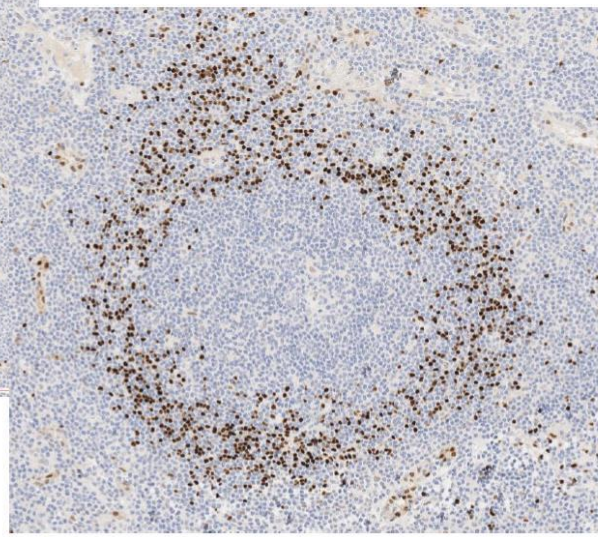


CD5





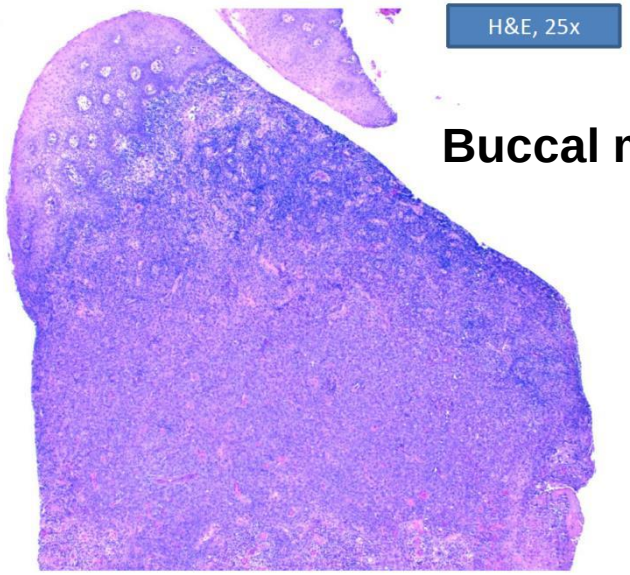
SOX11



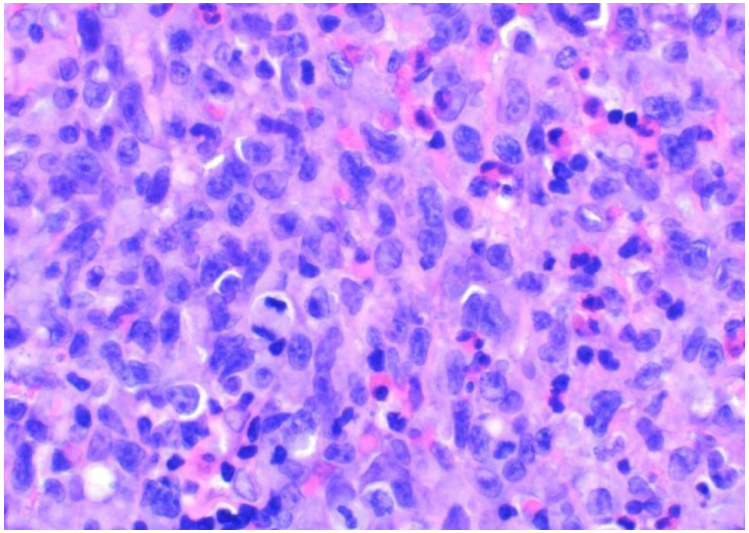
CyclinD1

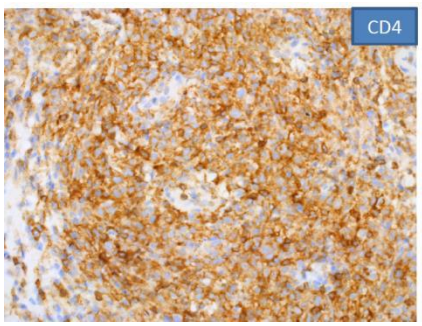
Dx: Composite lymphoma: Extranodal MZL (MALT lymphoma) and early MCL SOX11-

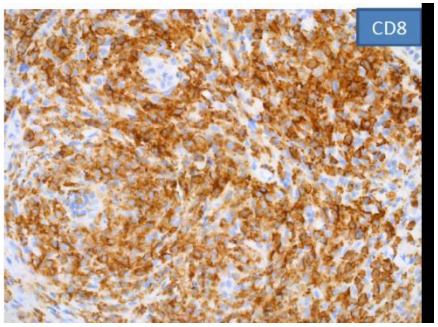
LYWS335 Anaplastic large cell lymphoma ALK-

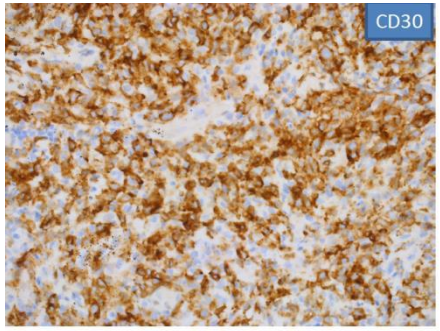


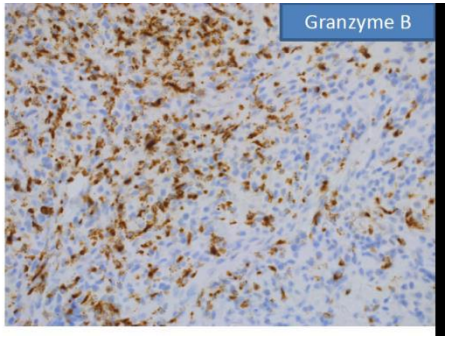
Buccal mucosa







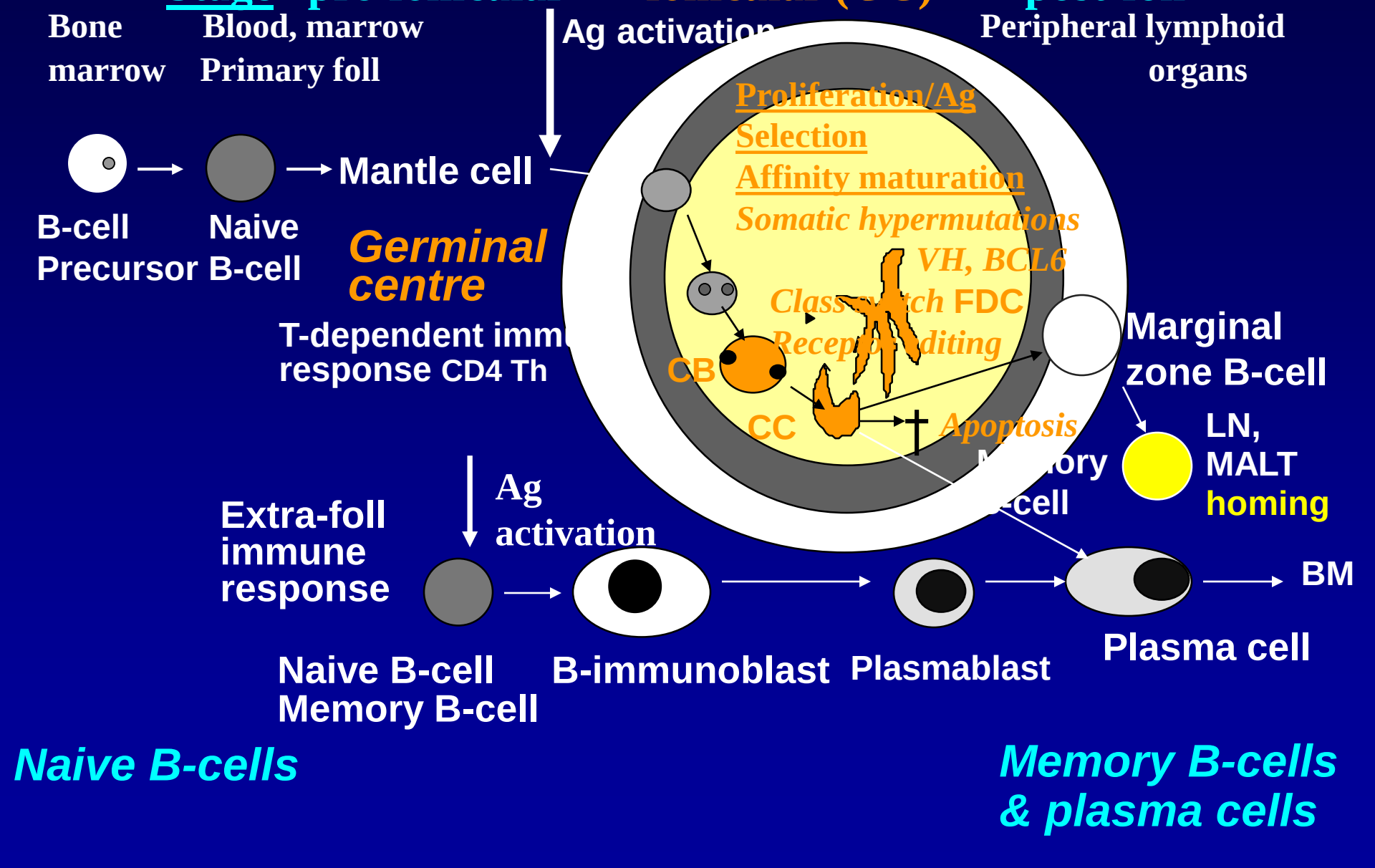




Mucosal Type: A distinct category?

Marginal Zone Lymphomas

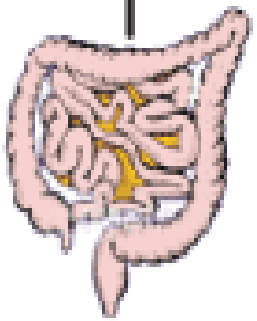
Normal cell counterparts in B-cell differentiation



MALT

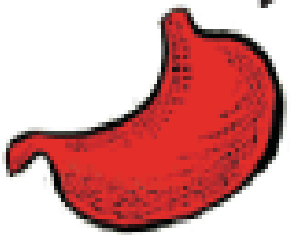
tessuto linfoide associato alle mucose

nativo



acquisito

infiammazione cronica

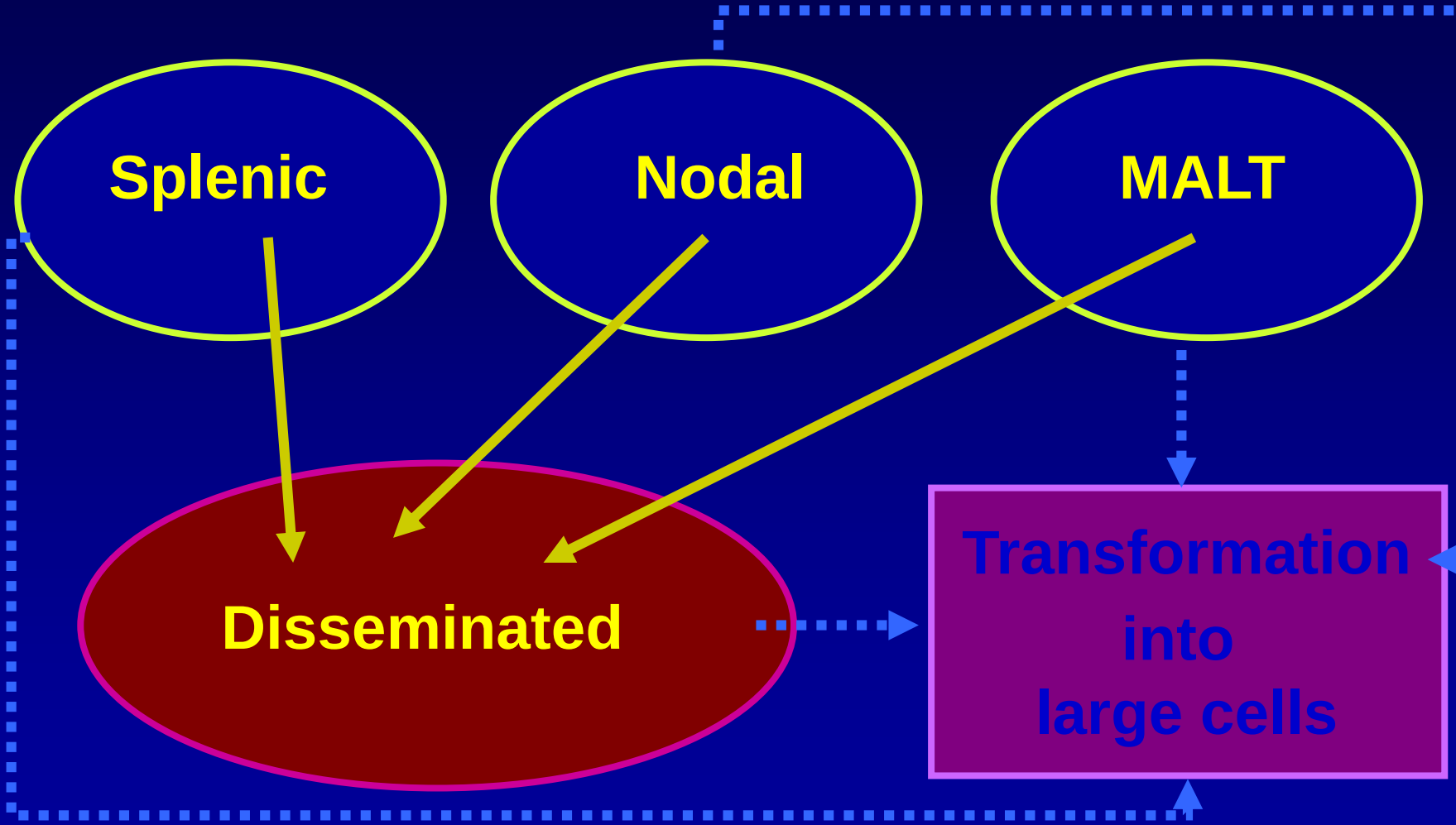


MALT

Il MALT, presente fisiologicamente in alcuni organi, può svilupparsi in ogni organo come risposta a stimoli flogistici cronici

Da questo tessuto, nativo o acquisito, può generare un linfoma della zona marginale (Linfoma MALT o MALTomi)

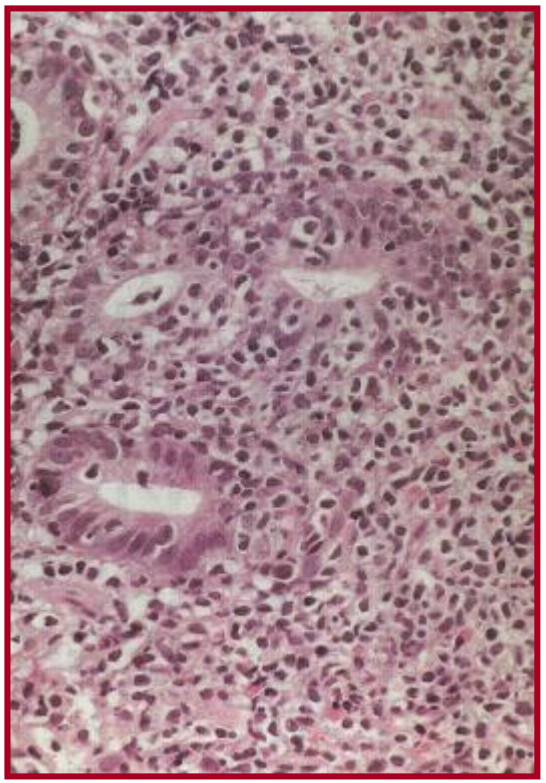
An Intricate Disease



MALT lymphoma

(Extranodal Marginal Zone B-Cell Lymphoma of MALT)

- **Histological features seem to suggest that the tumor cells have taken or are taking part into an immune reaction …**
  - Centrocyte-like cells (usually)
  - Lymphoepithelial lesions
  - Plasma cell differentiation
  - Scattered transformed blasts
  - Admixed non-neoplastic T-cell
  - Follicular colonisation



The Third Lymphoma

Series	No. of patients	MZL
REAL	1 378	6.7%
EORTC	522	5.0%
UK	441	6.0%
Japan	4 312	11.5%
Korea	1 466	17.3%
India	2 773	8.2%
CHLS	3 230	17.0%
	14 392	10.2%

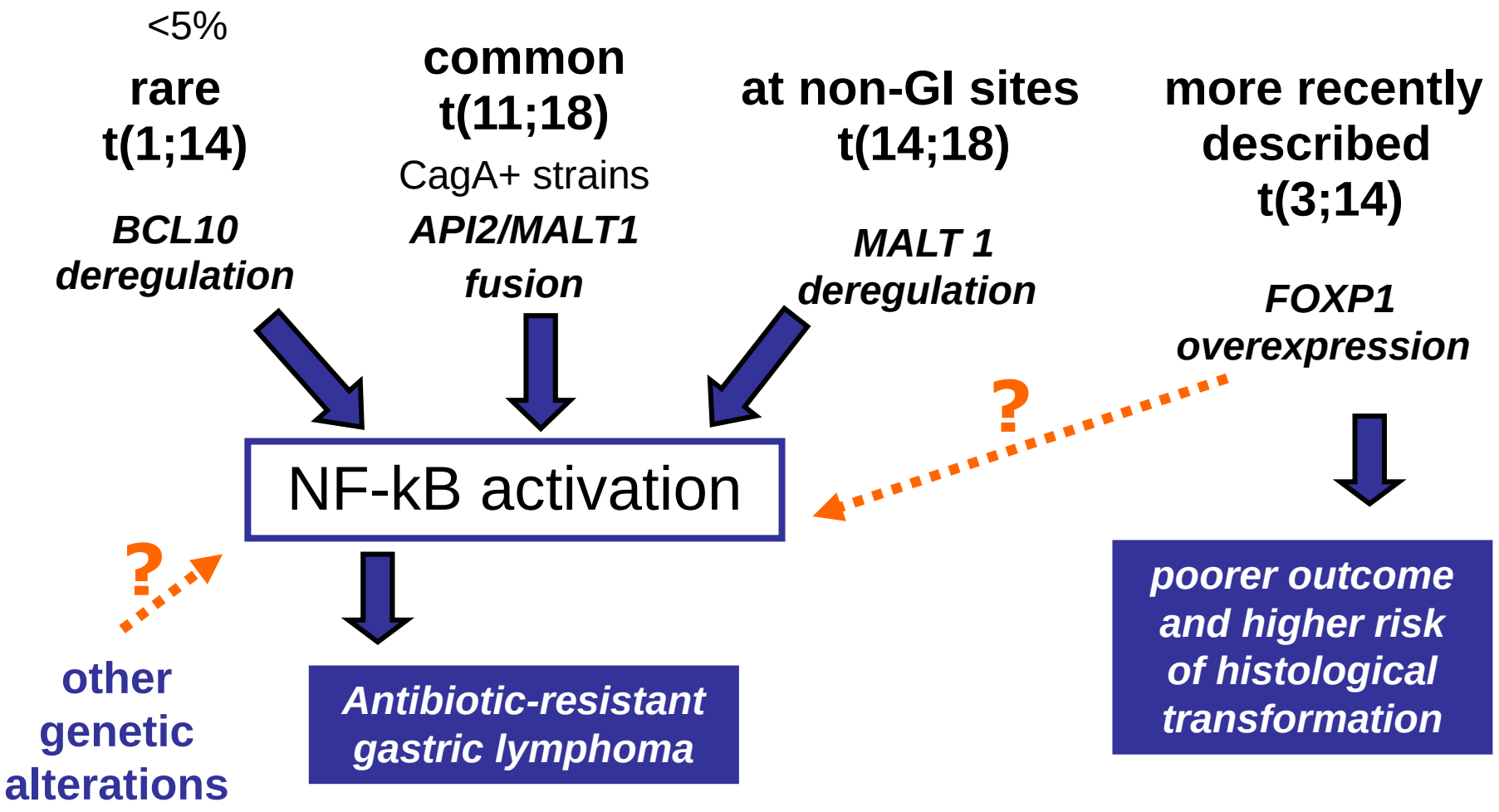
50% to 70% of the cases being MALT L.

A Similar Immunophenotype

- **Typically:**
  - **Presence of SIg, frequently IgM, IgD variable**
  - **Pan-B cell +: CD20+, CD19+, CD79a+**
  - **No expression of CD5, CD23, CD10**
  - **Variable expression of CD43**
  - **No expression of cyclin D1**
  - **Bcl-2 protein is expressed in most cases**
- **Atypical phenotype**
  - **Expression of CD5 or CD23**
  - **Expression of cyclin D1**

Different chromosomal translocations

affecting the same signalling pathway in MALT lymphoma



Constitutive activation of NF-κB in MZL via recurrent translocations or A20 inactivation

(A20 is a negative regulator of BCL10- mediated activation of NF-kappaB)

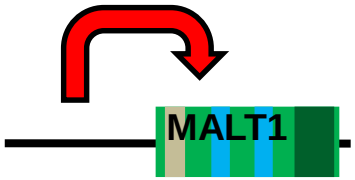
1. Deregulated MALT1

t(11;18)

up to 35 %

t(14;18)

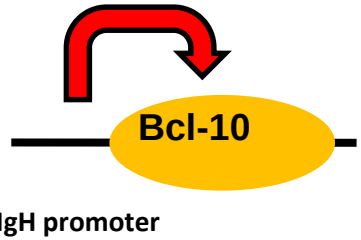
15 - 20 %

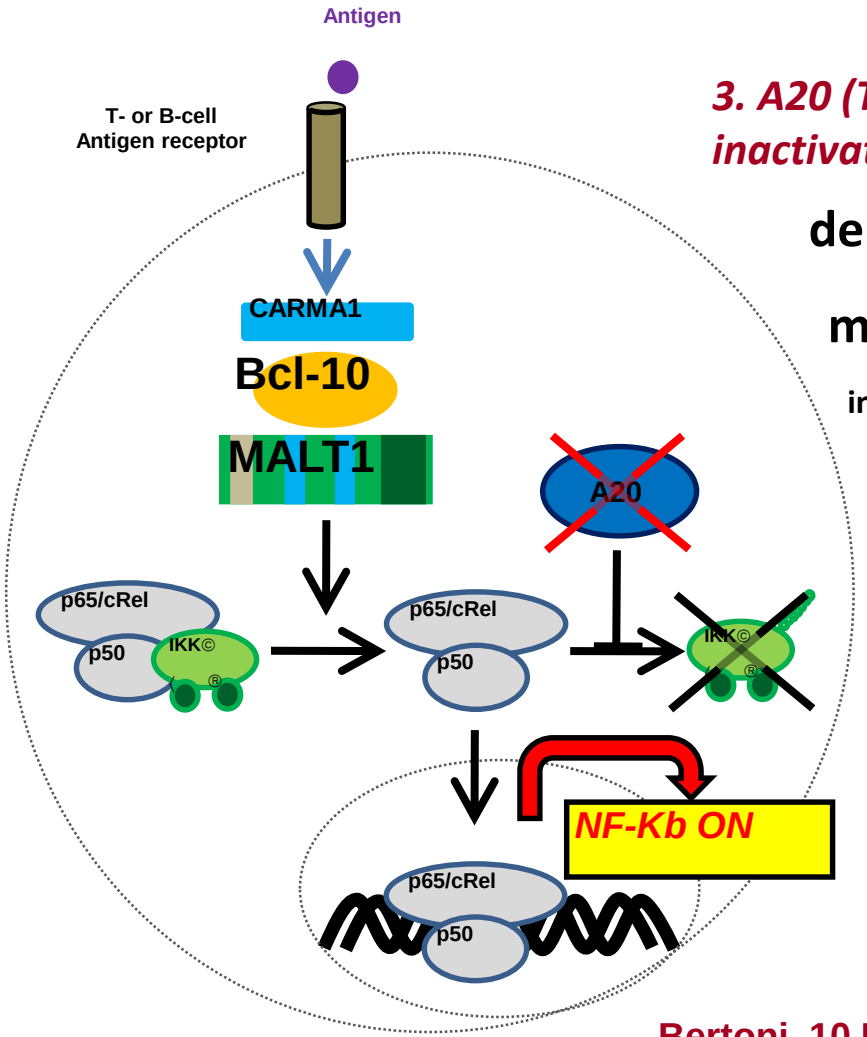


2. Deregulated Bcl-10

t(1;14)

Rare





3. A20 (TNFAIP3) inactivations

deletions or

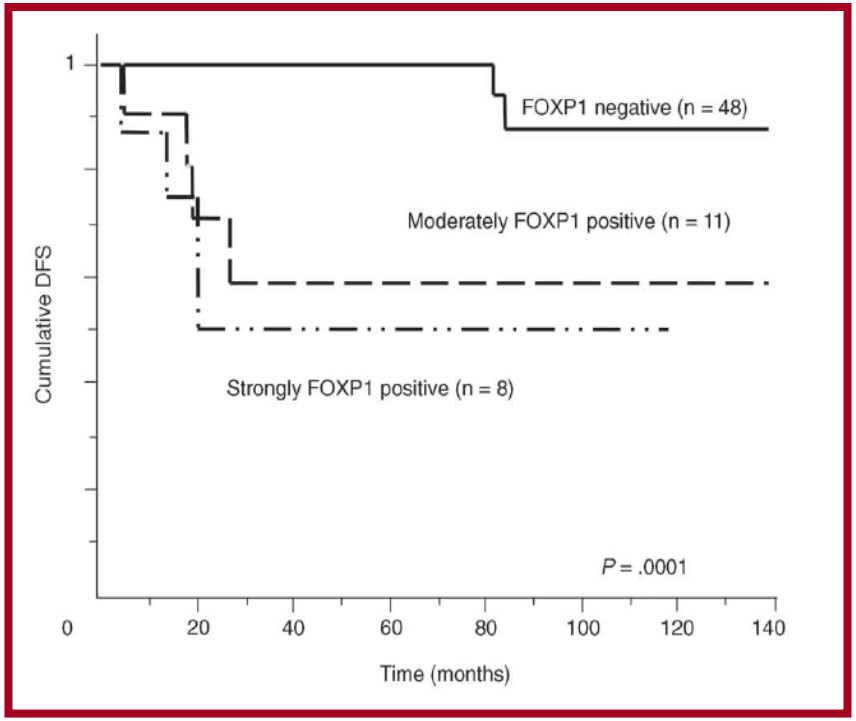
mutations

in up to 40 %

Bertoni, 10 ICML, abs.#O61

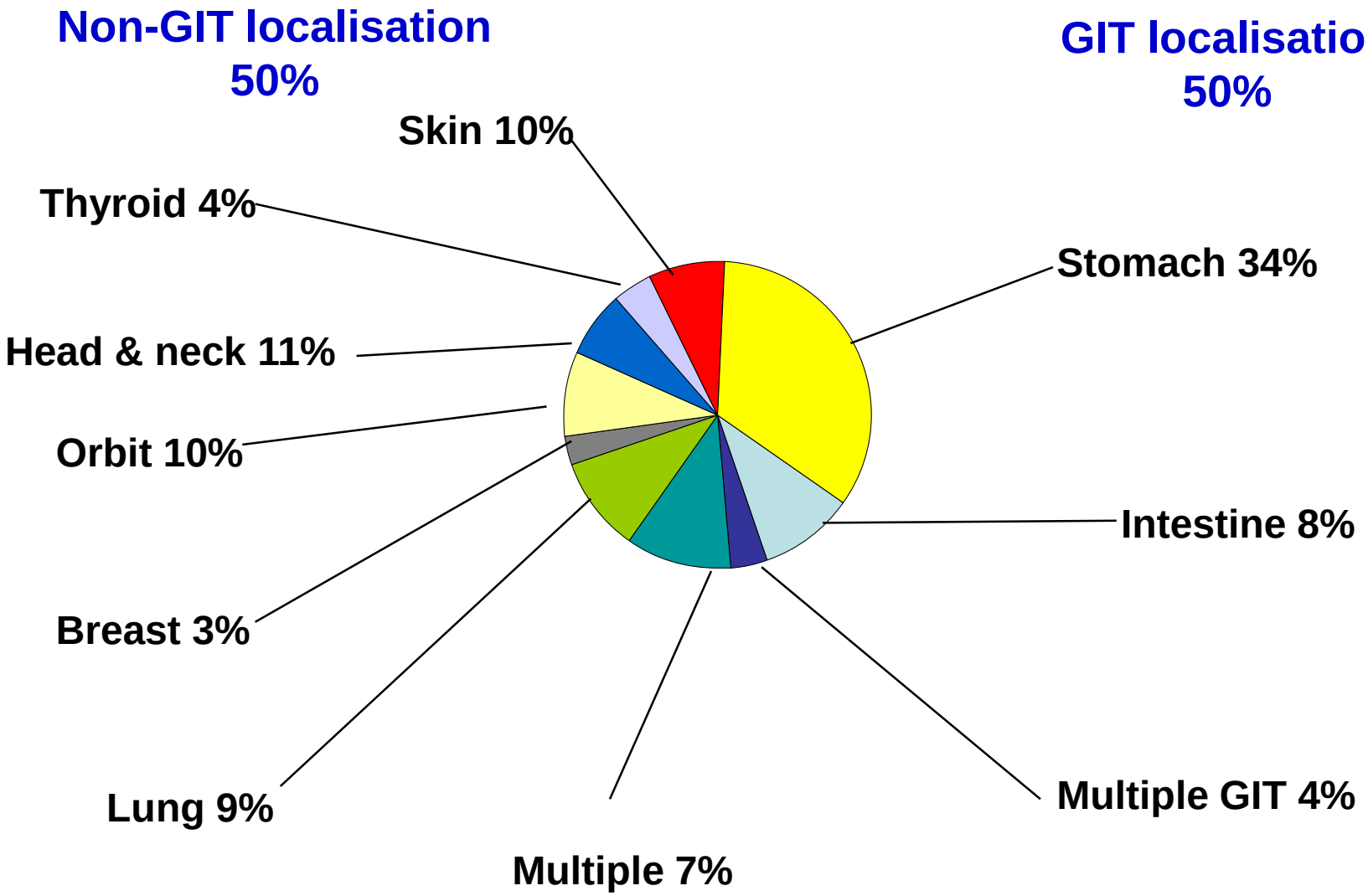
FOXP1 expression is an independent prognostic factor in MALT lymphomas

- Nuclear FOXP1 expression in 30% of MALTomas
- FOXP1 positivity associated with poor outcome
- MALT lymphomas with strong FOXP1 expression are at risk of transforming into an aggressive DLBCL of non-germinal center phenotype if they feature, in addition, a polymorphic histology and the presence of trisomy 3 and 18.



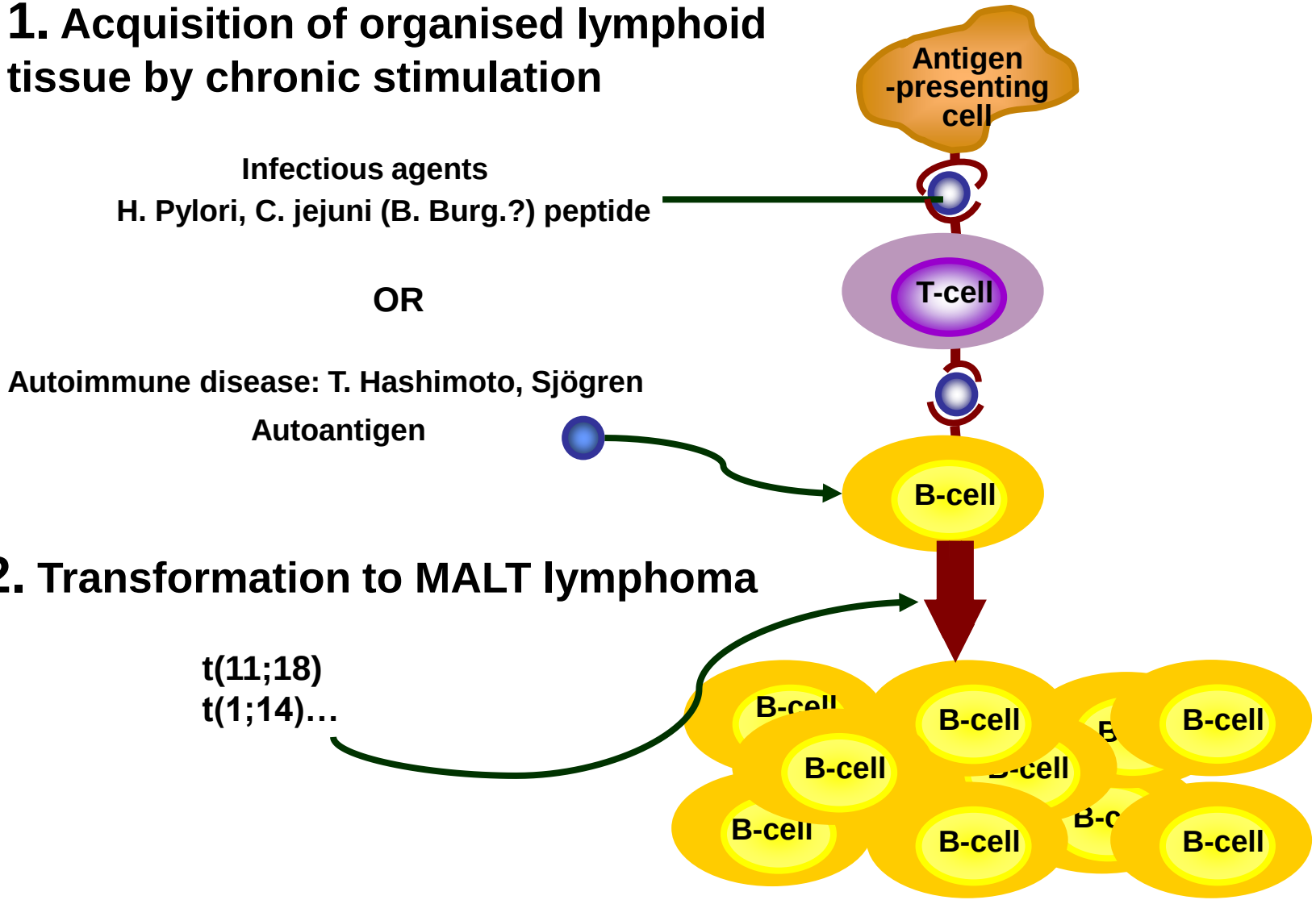
Sagaert et al. JCO 2006

Sites of presentation



MALT lymphomas: Physiopathology

1. Acquisition of organised lymphoid tissue by chronic stimulation



Involved Pathogens

• Helicobacter pylori	Stomach
• Borrelia burgdorferi	Skin
• Campylobacter jejuni	Intestine
• Chlamydia psittaci	Orbit
• Hepatitis C virus	Spleen/node
• Paludism	Spleen

Autoantigens

- Thyroid

  Hashimoto's thyroiditis
- Salivary glands

  Myoepithelial sialoadenitis

  +/- Sjögren's syndrome
- Lung

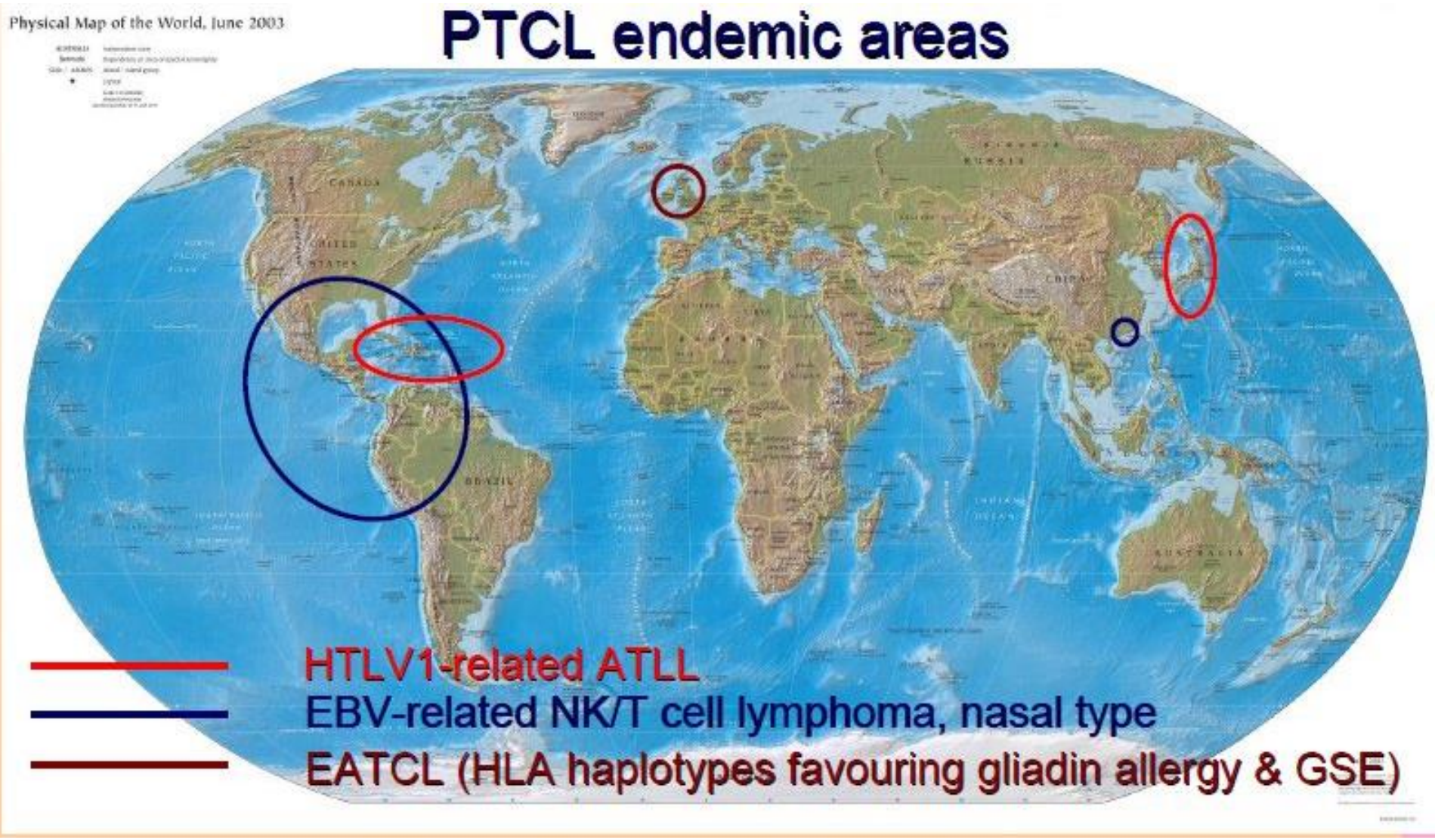
  Lymphoid interstitial pneumopathy

MALT lymphomas: Treatment

- **Treatment of the pathogen**
  - **H pylori in gastric location**
  - **other?**
- **Classic**
  - **Localised: surgery or RT**
  - **Disseminated: chemotherapy**
    Chlorambucil, fludarabine
    Multidrug regimen
- **Anti- CD20**

  alone or in combination with chemotherapy?

PTCL endemic areas



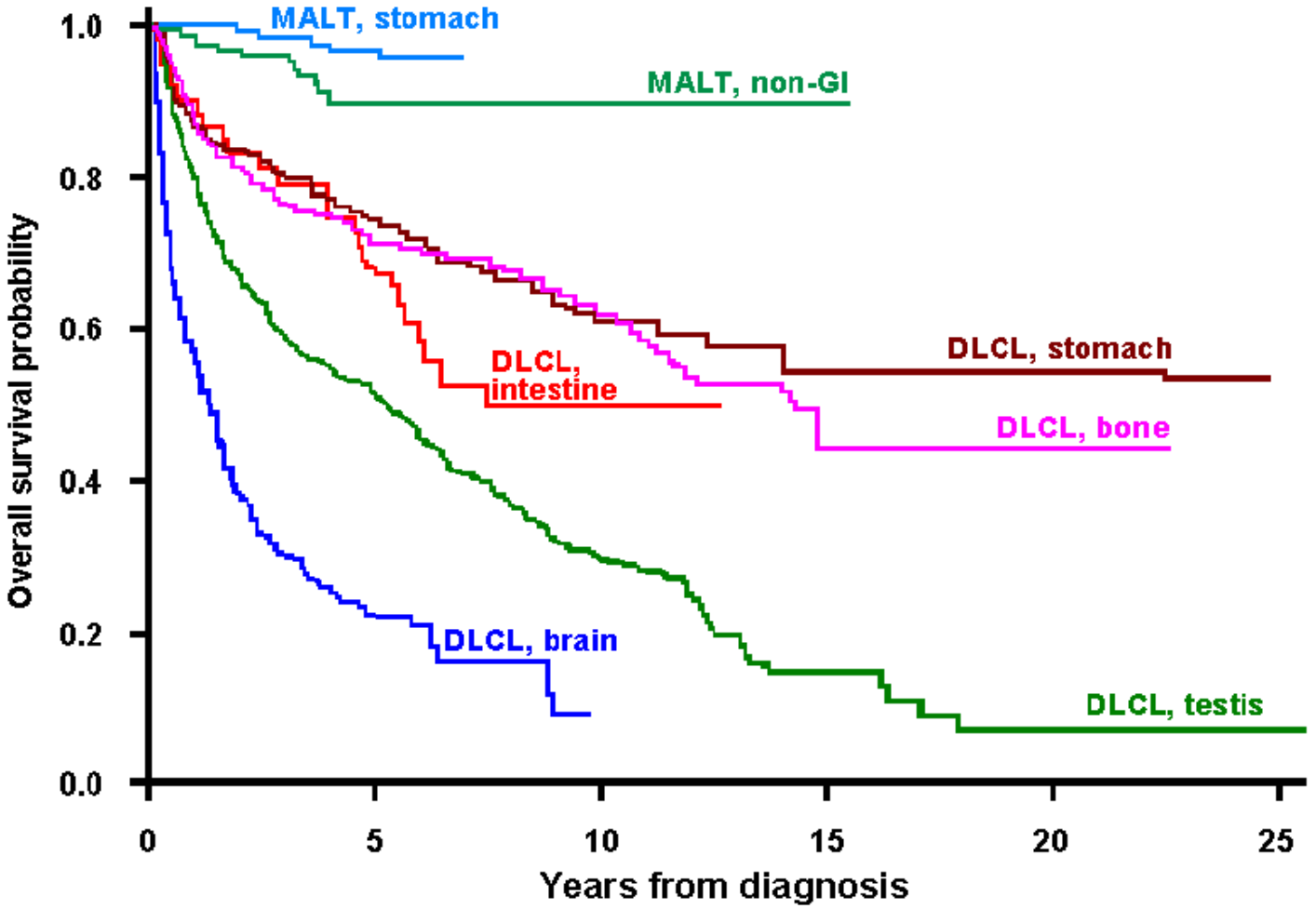
LINFOMI MALT

INCIDENZA

Istotipi per sede dei linfomi primitivi extranodali

	a grandi cellule B	MALT	a cellule T
Stomaco	+	+++	/
Intestino	+++	+	+
Waldeyer	+++	/	+
Annessi oculari	/	+++	/
Tiroide	++	++	/
Gh. Salivari	++	++	/
Ossa	+++	/	/
Polmone	+	+++	/
Cervello	+++	/	/
Testicolo	+++	/	/
Fegato	++	++	+
Cute	+	++	+++

Extranodal NHL, survival by histology and site in the IELSG series



LINFOMI MALT

OUTCOME

Overall Survival a 5 anni: 86-95%

(indipendente dalla sede e dallo stadio)

Time-to-progression: 8,9 anni

per le localizzazioni gastrointestinali

4,9 anni

per le localizzazioni non gastrointestinali

Case Report

Complete Response to R-EPOCH in Primary Cardiac Lymphoma

Kartik Anand,[1] **Sai Ravi Pingali**,[1] **Barry Trachtenberg**,[2] **and Swaminathan Padmanabhan Iyer**[1,3]

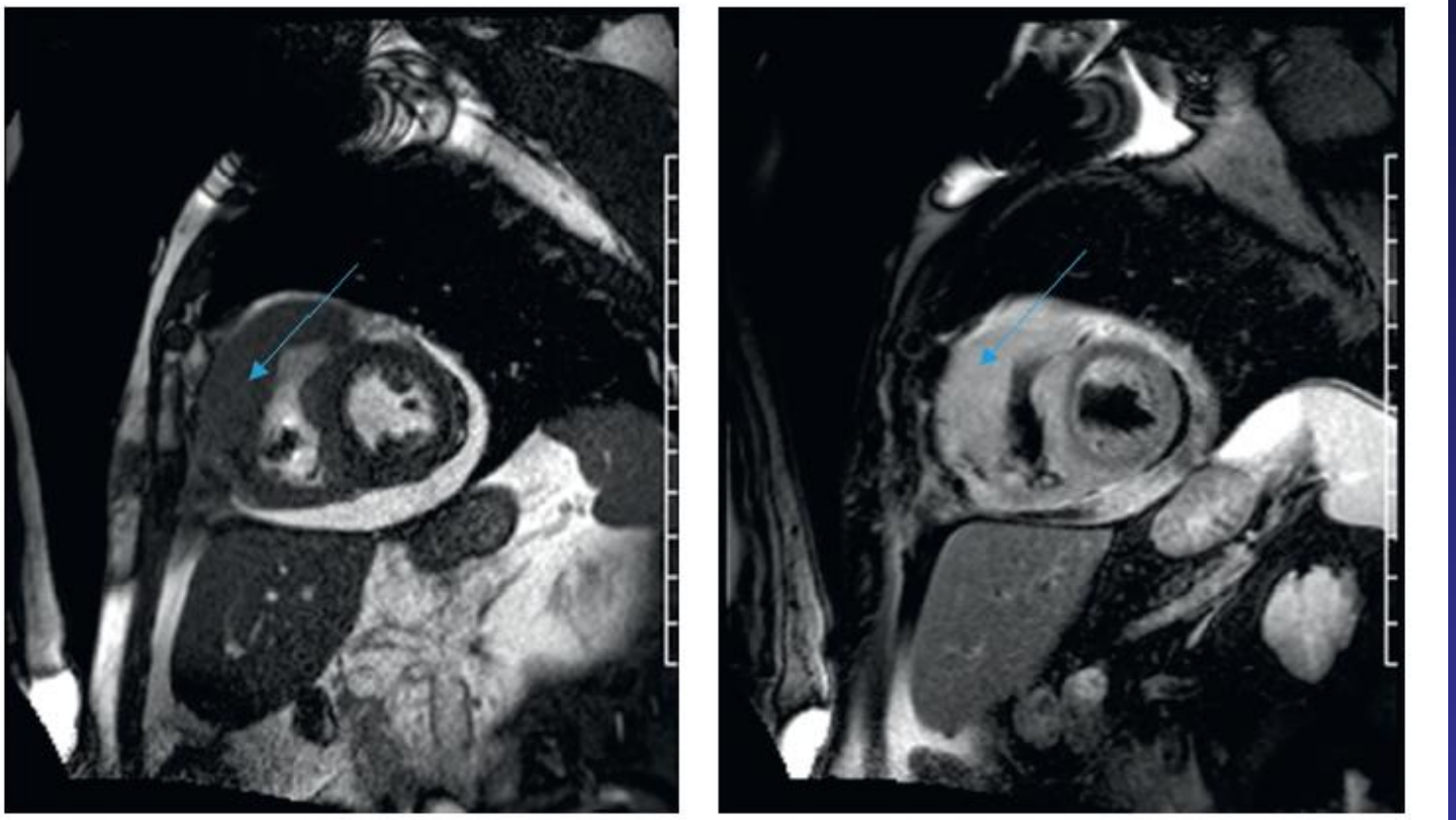
[1]*Houston Methodist Cancer Center, Weill Cornell Medicine, Houston, TX, USA*
[2]*Division of Cardiology, DeBakey Heart & Vascular Institute, Houston Methodist Hospital, Houston, TX, USA*
[3]*Department of Lymphoma/Myeloma, UT MD Anderson Cancer Center, Houston, TX, USA*

Correspondence should be addressed to Kartik Anand; kartikanand88@gmail.com

Received 10 December 2018; Accepted 21 February 2019; Published 10 April 2019

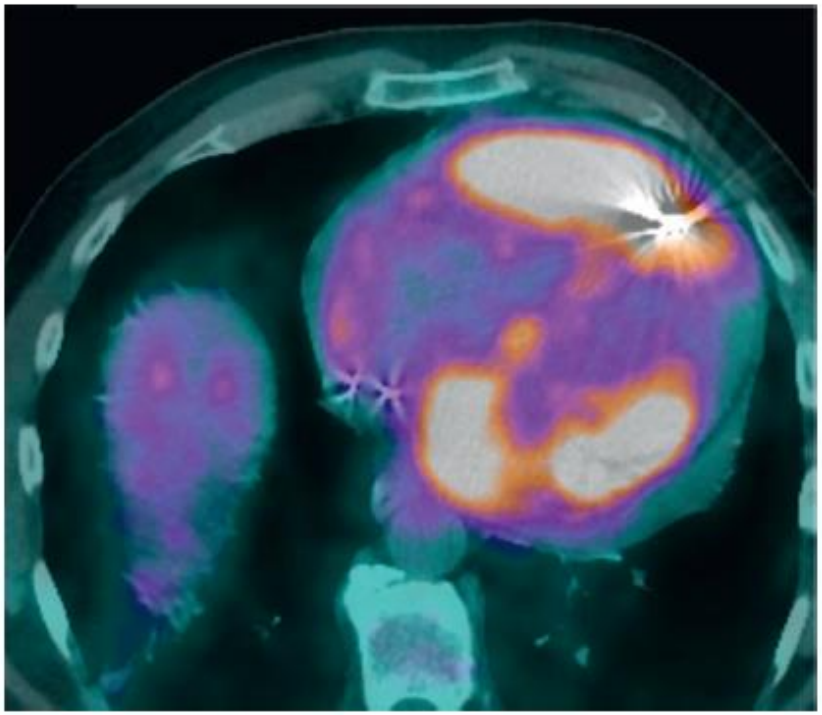
Academic Editor: Sylvain Choquet

Primary cardiac lymphoma (PCL) is a rare extranodal lymphoma involving only the heart and/or the pericardium. Most common presenting signs and symptoms are nonspecific including dyspnea, pericardial effusion, and arrhythmia. Prognosis of PCL patients remain poor compared to non-cardiac lymphoma patients. Since most of the information about PCL comes from case reports or case series, there is no treatment consensus. Anthracycline containing chemotherapy remains main treatment modality which is potentially cardiotoxic. We present a case of PCL that achieved complete remission using R-EPOCH (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin). We also used dexrazoxane in an effort to reduce cardiotoxicity of chemotherapy.

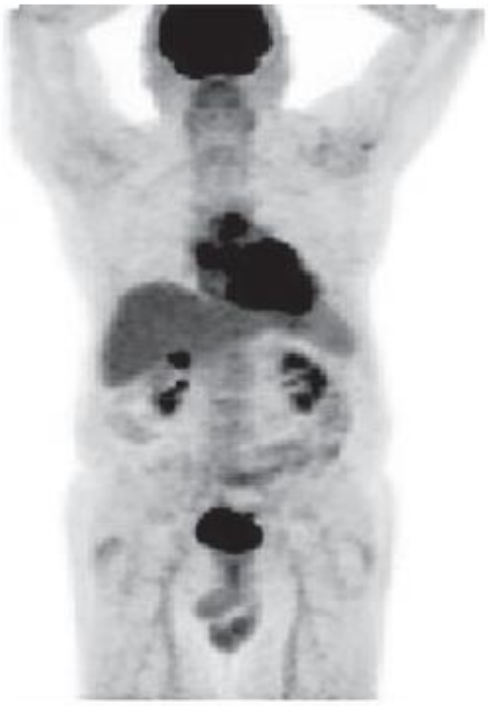


(a) (b)

Case Reports in Hematology Volume 2019, Article ID 7690430



(a)



(b)

Case Reports in Hematology Volume 2019, Article ID 7690430

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Case Series

Extranodal lymphoma of the tongue, a very rare entity-report of two cases with literature review

J. Clarke[a,c], S. Medford[a,c], S. Islam[b,c,*], C. Ramsingh[a,c], M. Christopher[a,c]

[a] Department of Otorhinolaryngology and Head and Neck Surgery, San Fernando Teaching Hospital, Trinidad and Tobago
[b] Department of General Surgery, San Fernando Teaching Hospital, Trinidad and Tobago
[c] Department of Clinical Surgical Science, University of the West Indies, St. Augustine, Trinidad and Tobago

ARTICLE INFO

Article history:
Received 7 September 2018
Accepted 30 September 2018
Available online 30 November 2018

Keywords:
Base of tongue lymphoma
High grade T cell lymphoma
DBCL
Extranodal lymphoma
Waldeyer's ring

ABSTRACT

BACKGROUND: Lymphomas are malignant neoplasms of the lymphocyte cell lines affecting the lymph nodes, spleen and other nonhemopoietic tissues. Of the extranodal lymphomas found in the head and neck region, 3–5% of malignant lymphomas arise in the oral and paraoral region, mainly from Waldeyer's ring. The involvement of the base of the tongue is extremely rare.

SUMMARISED CASE: Case 1: 64 year old female who presented initially with an enlarged occipital lymph node which gradually became generalized cervical lymphadenopathy with initial histology confirmed reactive lymphoid hyperplasia. Biopsy of left postero-lateral tongue lesion eventually showed high grade T cell lymphoma.

Case 2: 85 year old male presented with history of dysphagia for one year who was found to have a lesion extending from his base of tongue into the nasopharynx. Histology showed a diffuse B cell lymphoma.

DISCUSSION: Both patients were noted to have lesion of the tongue, but tongue lesions are noted in the literature to be extremely rare. When tongue lymphomas do occur, most are of B-cell origin; the diffuse large-cell variety is the most common. Extranodal lymphomas of the T cell phenotype tend more to be sinonasal in origin than of the tongue, with T cell lymphomas of the tongue being even rarer than B cell lymphomas.

CONCLUSION: With regards to tumours arising in the tongue, squamous cell carcinomas are still classified as the most common. Lymphomas however, should still be kept in consideration as a differential diagnosis with regards to lesions arising from this site.

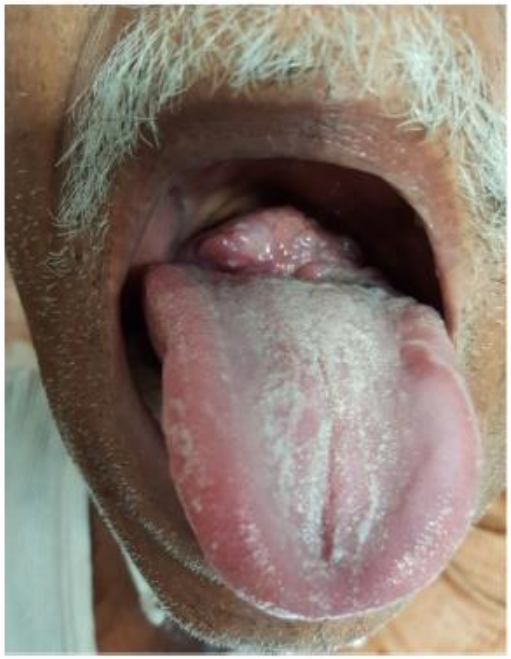


Fig. 3. Showing the mass at the base of tongue as indicated by the black arrow.

a centroblastic appearance. The cells had a diffuse strong expression of both CD 10 and Bcl-2 and expressed the B-cell marker CD 20 but were negative for CD 3. A diagnosis of diffuse large B-Cell Lymphoma (DLBCL) was thus made. The patient was then referred to Haematology where he underwent treatment of his condition.

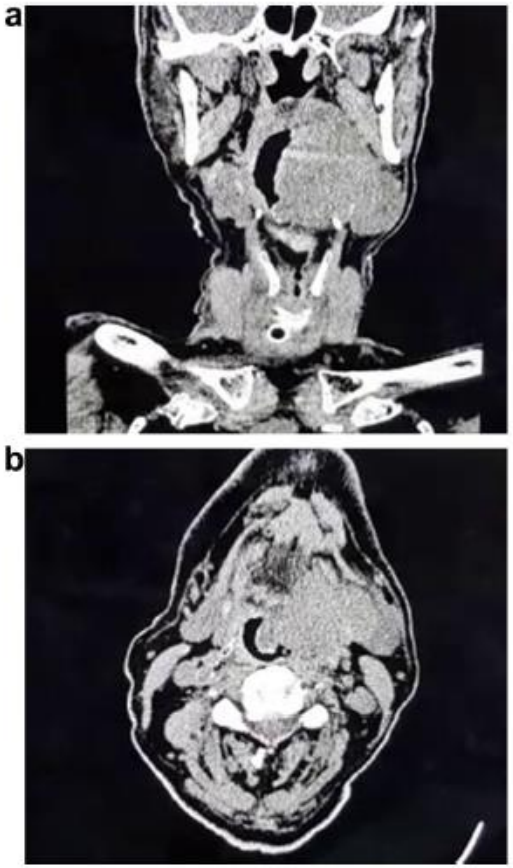


Fig. 4. (a) CT scan of the face and Neck (Coronal view); (b): CT scan of the face and Neck (Axial view)- showing 7.4 cm x 6.9 cm x 4.6 cm solid mass at the base of the tongue as denoted by the white arrows.

Journal of
Clinical Medicine

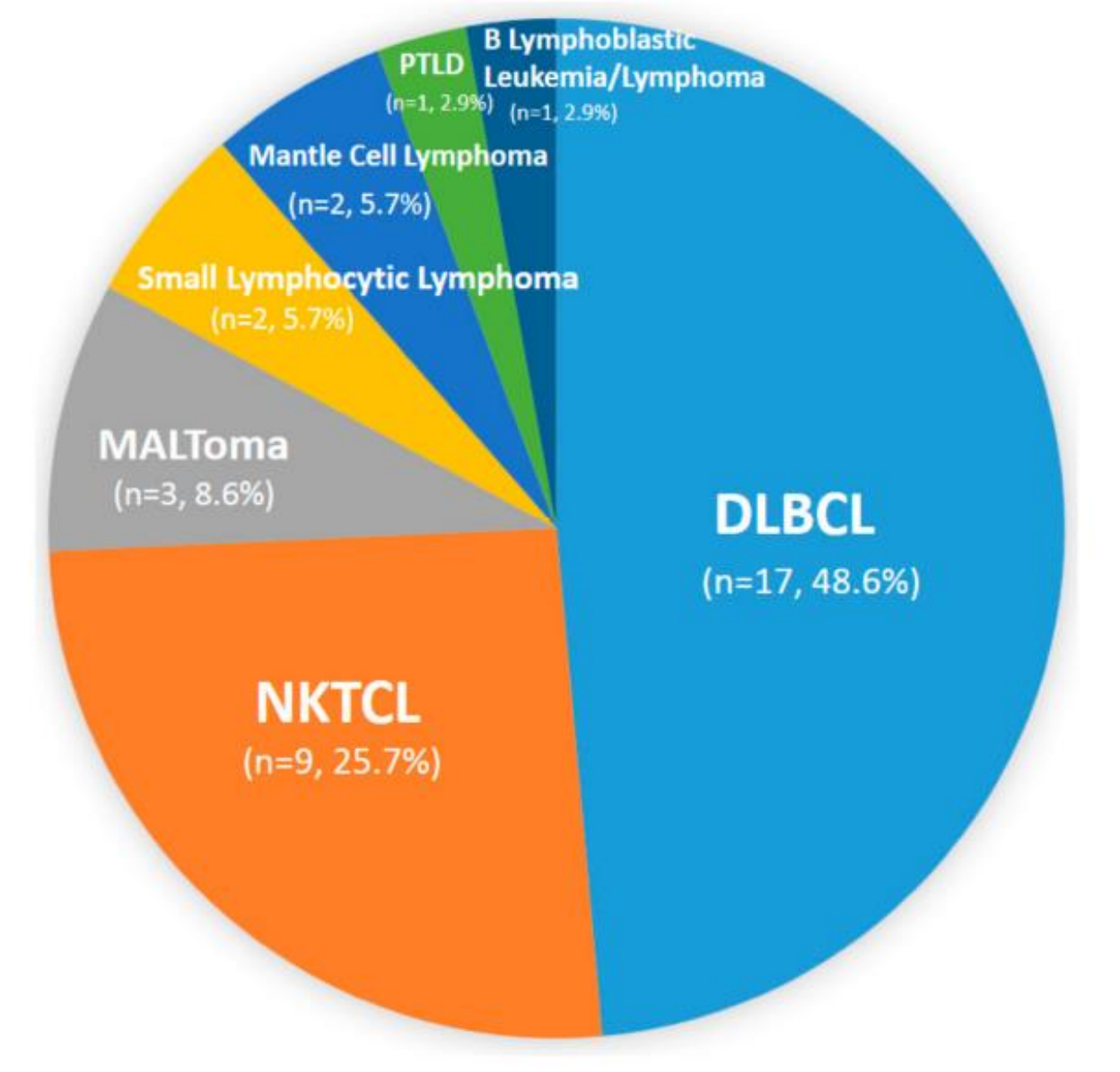
MDPI

Article

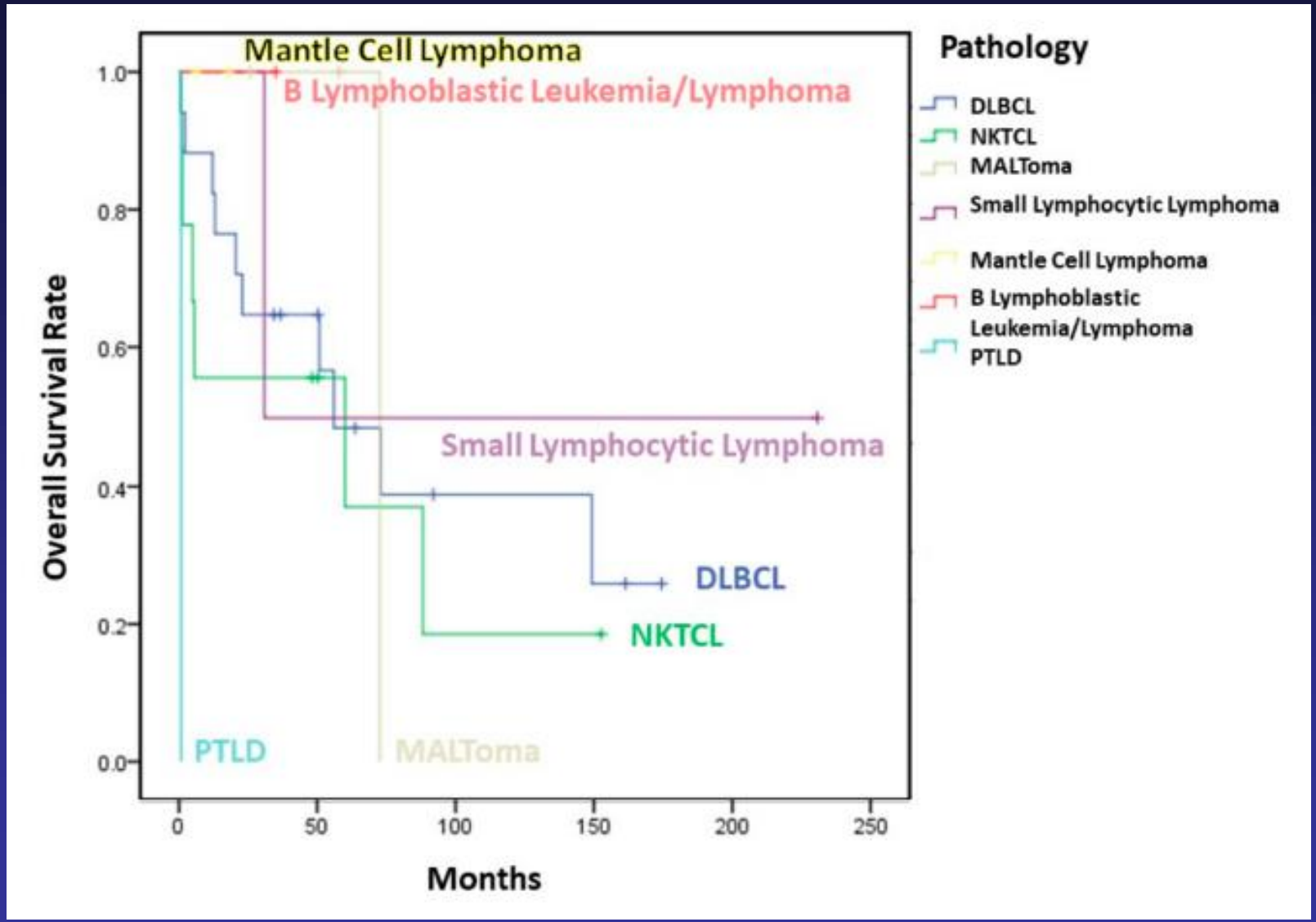
Nasopharyngeal Lymphoma: A 22-Year Review of 35 Cases

Chien-Yu Hsueh [1,2], Ching-Fen Yang [2,3], Jyh-Pyng Gau [2,4], Edward C. Kuan [5], Ching-Yin Ho [2,6], Tzeon-Jye Chiou [2,7], Liang-Tsai Hsiao [2,4], Ting-An Lin [2,4] and Ming-Ying Lan [1,2,*]

Abstract: Nasopharyngeal (NP) lymphoma is a rare primary malignancy of the head and neck and represents a minority of malignancies originating from the nasopharynx. For this reason, there are limited data regarding epidemiologic and treatment outcomes. This is a retrospective review of patients diagnosed with NP lymphoma from 1995 to 2017 at a tertiary medical center. The patients' demographic data, clinical presentations, treatment modalities, Epstein–Barr virus (EBV)-encoded small RNA (EBER) staining, and outcomes were investigated. We considered a total of 35 patients, including 20 males and 15 females, diagnosed with NP lymphoma. The age ranged from 17 to 88 years (mean = 59.6). The common presentations were nasal obstruction, epistaxis, and neck mass. In our study, the most common pathological diagnosis of NP lymphoma was diffuse large B cell lymphoma (DLBCL) (n = 17), followed by NK/T cell lymphoma (NKTCL) (n = 9). Other pathologic diagnoses included extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALToma), small lymphocytic lymphoma, mantle cell lymphoma. There were 13 cases showing EBER positivity, including 7 cases of NKTCL, 5 cases of DLBCL, and 1 case of post-transplant lymphoproliferative disorder (PTLD). Most patients received chemotherapy alone, while some patients received both chemotherapy and radiotherapy. Seven patients had local recurrence, and fewer than half of the patients (n = 16) were alive at the time of the study (mean follow-up duration: 54.4 months). The five-year overall survival was 50.4%. NP lymphoma is very rare, and the most common pathologic type is DLBCL. EBER positivity is found in both NKTCL and DLBCL. Identifying more effective therapeutic agents is extremely important to improve patients' survival.



J. Clin. Med. 2019, 8, 1604; doi:10.3390/jcm8101604



J. Clin. Med. 2019, 8, 1604; doi:10.3390/jcm8101604

Cancer, Renal Lymphoma

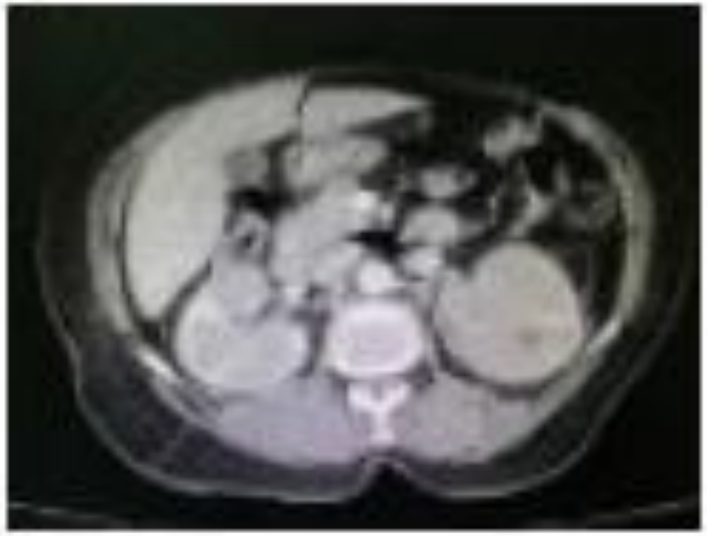
Maria R. Bokhari; Syed Rizwan A. Bokhari.

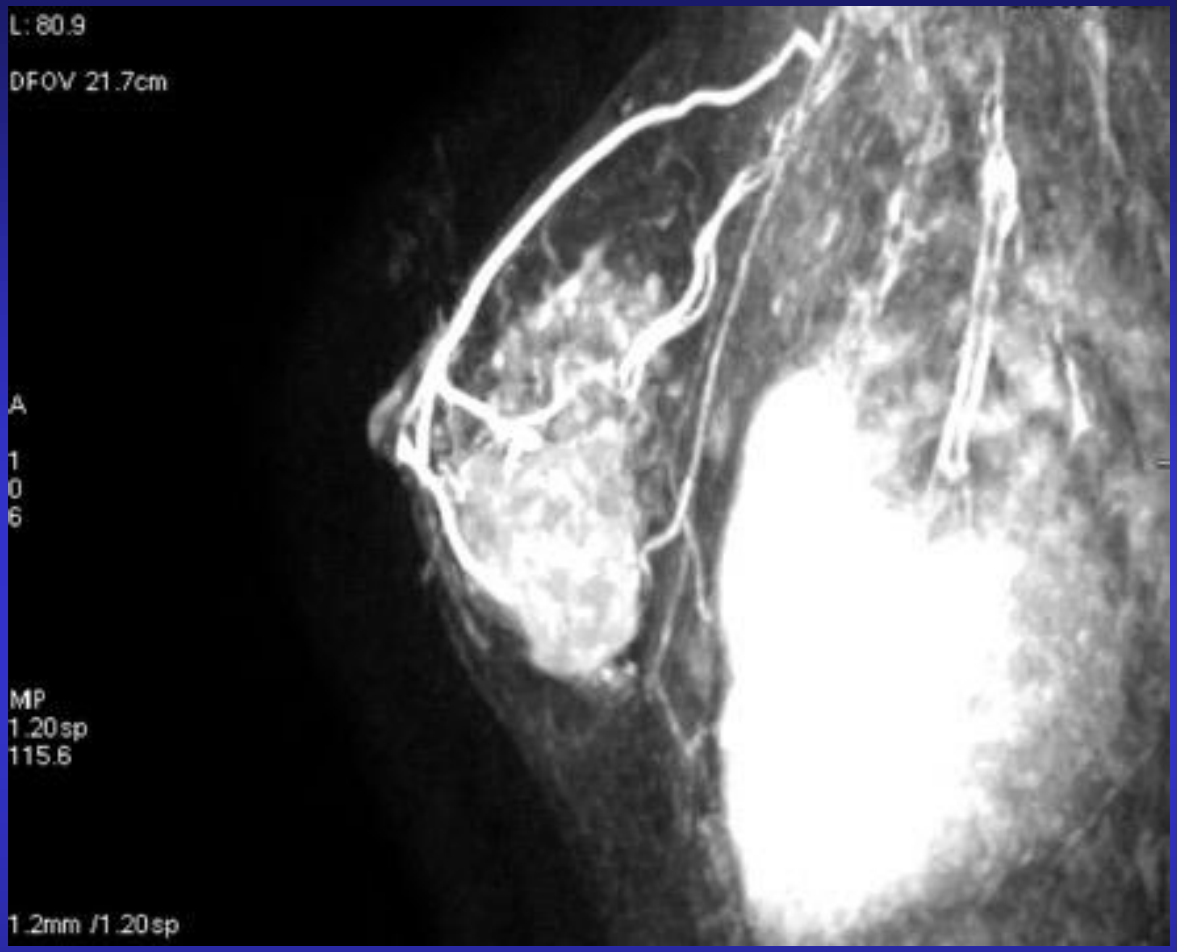
Author Information

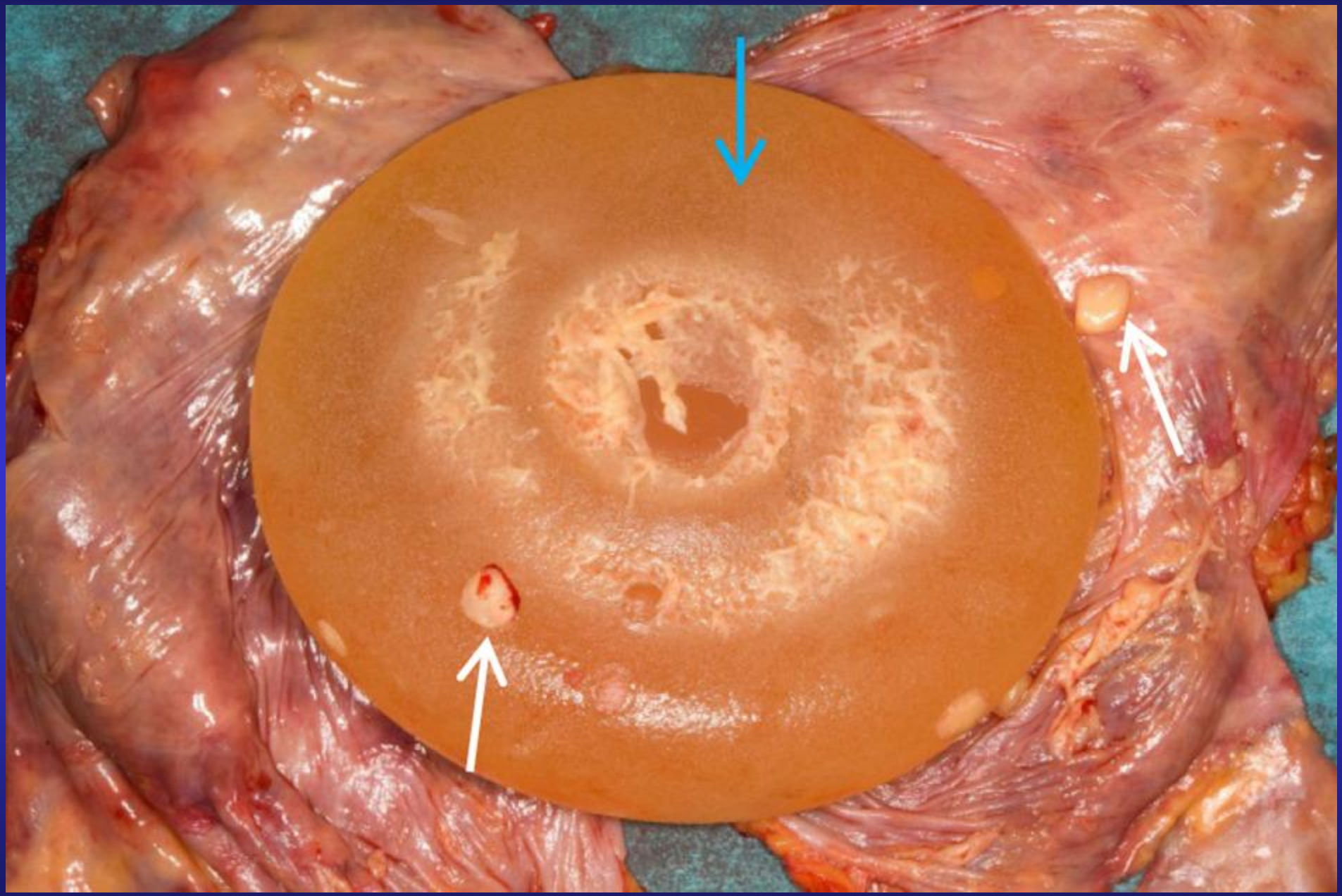
Last Update: April 23, 2019.

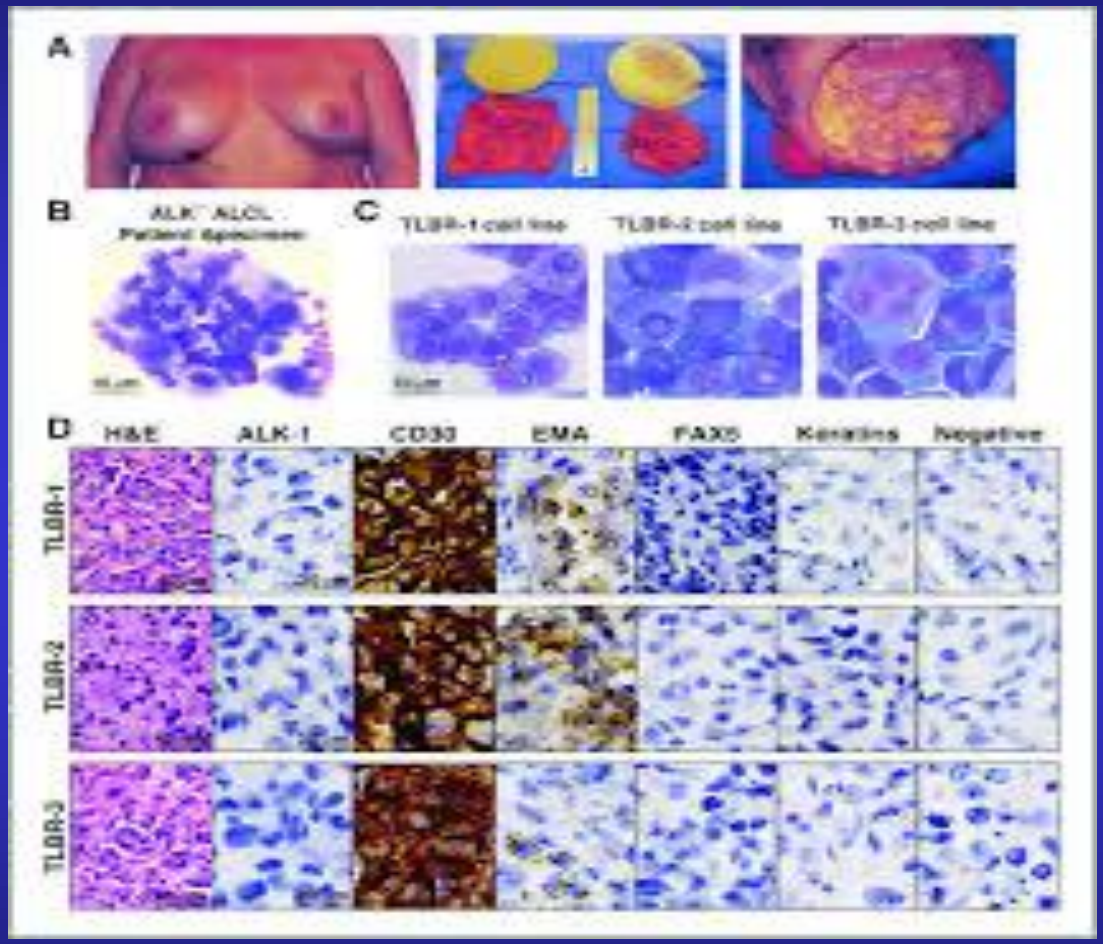
Introduction

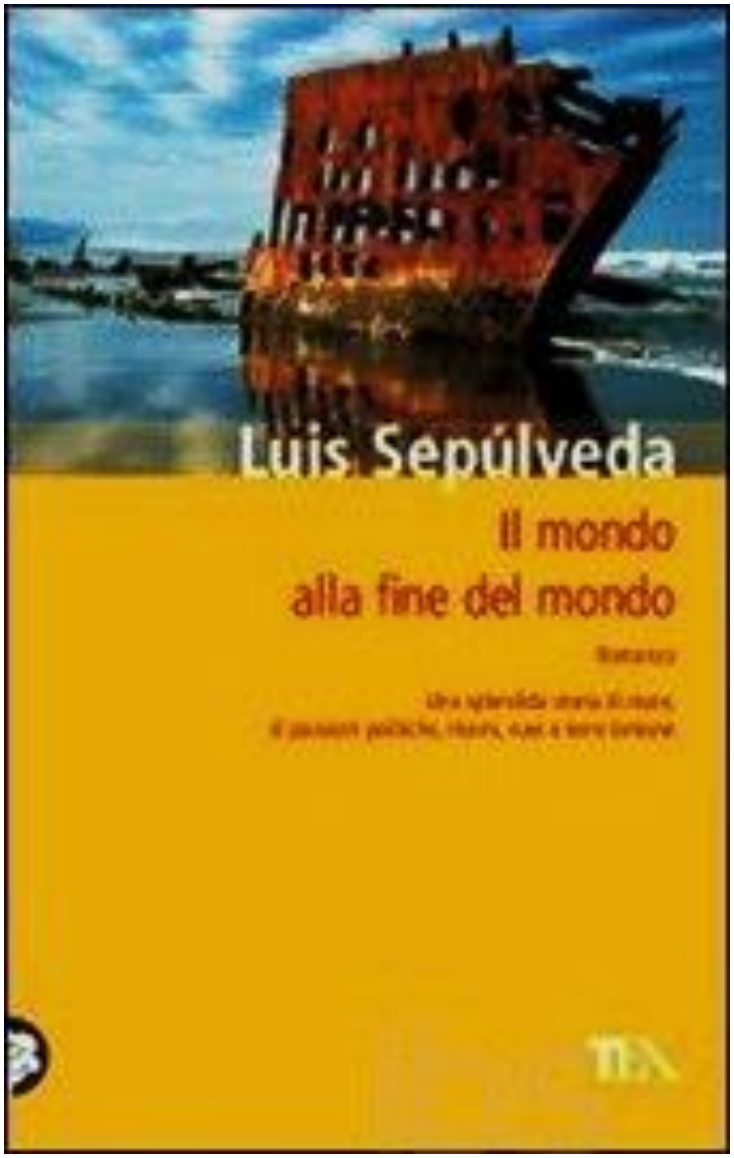
Renal involvement in lymphoma is commonly in the presence of widespread nodal or extranodal lymphoma. This is classified as secondary renal lymphoma (SRL). Rarely, lymphoma may involve the kidneys alone without evidence of disease elsewhere; this presentation is termed *primary renal lymphoma* (PRL). Although the diagnosis of renal lymphoma can be challenging, an awareness of the spectrum of imaging findings can help to differentiate lymphoma from other renal malignancies, such as renal cell carcinoma (RCC), and can lead to appropriate recommendations for biopsy. An accurate diagnosis is critical because renal lymphoma is treated by chemotherapy whereas RCC is typically managed by surgery or ablation.[1][2][3]Renal lymphoma is commonly secondary to lymphomatous infiltration of the kidneys in systemic disseminated lymphoma and advanced stage IV disease while renal lymphoma arising primarily in the renal parenchyma is a rarely described entity. Primary renal lymphoma comprises only 0.7% of extranodal lymphomas.[4][5]




L: 80.9
DFOV 21.7cm
A
1
0
6
MP
1.20sp
115.6
1.2mm /1.20sp




A
B
ALK+ ALCL
Patient specimen
C
TLBR-1 cell line
TLBR-2 cell line
TLBR-3 cell line
D
H&E
ALK-1
CD30
EMA
FAS5
Keratins
Negative
TLBR-1
TLBR-2
TLBR-3


Luis Sepúlveda
Il mondo
alla fine del mondo
Romanzo
TEA