Reappraisal of Primary Epstein-Barr Virus (EBV)-positive Diffuse Large B-Cell Lymphoma of the Gastrointestinal Tract

Comparative Analysis Among Immunosuppressed and Nonimmunosuppressed Stage I and II-IV Patients

汇报人： 李超

指导老师：郭双平教授

EB病毒阳性的弥漫大B细胞淋巴瘤，非特指 EBV(+)DLBCL （NOS）

是EBV阳性的B淋巴细胞克隆性增生性疾病，不包括淋巴瘤样肉芽肿病，有急性或近期EBV感染迹象的病例，其他可能是EBV阳性的明确淋巴瘤和EBV阳性的粘膜皮肤溃疡。

临床特征

超过一半的患者具有较高或高的国际预后指数（IPI）评分。

EBV(+)DLBCL （NOS）

流行病学

EB病毒阳性DLBCL在亚洲和拉丁美洲人中占比<5%-15%，在西方患者这占比<5%，无易感性免疫缺陷记录；大多数患者年龄超过50岁，患病率在80岁达高峰，偶发于年轻患者，在30岁出现第二个小高峰，男女患病率1.2-3.6:1

老年患者中EBV阳性DLBCL的发生率增加被认为与免疫衰老有关。免疫微环境的改变可能在任何患者年龄都起作用。

结内和结外均可发生，结外最常好发于肺和胃肠道；

EBV(+)DLBCL （NOS）

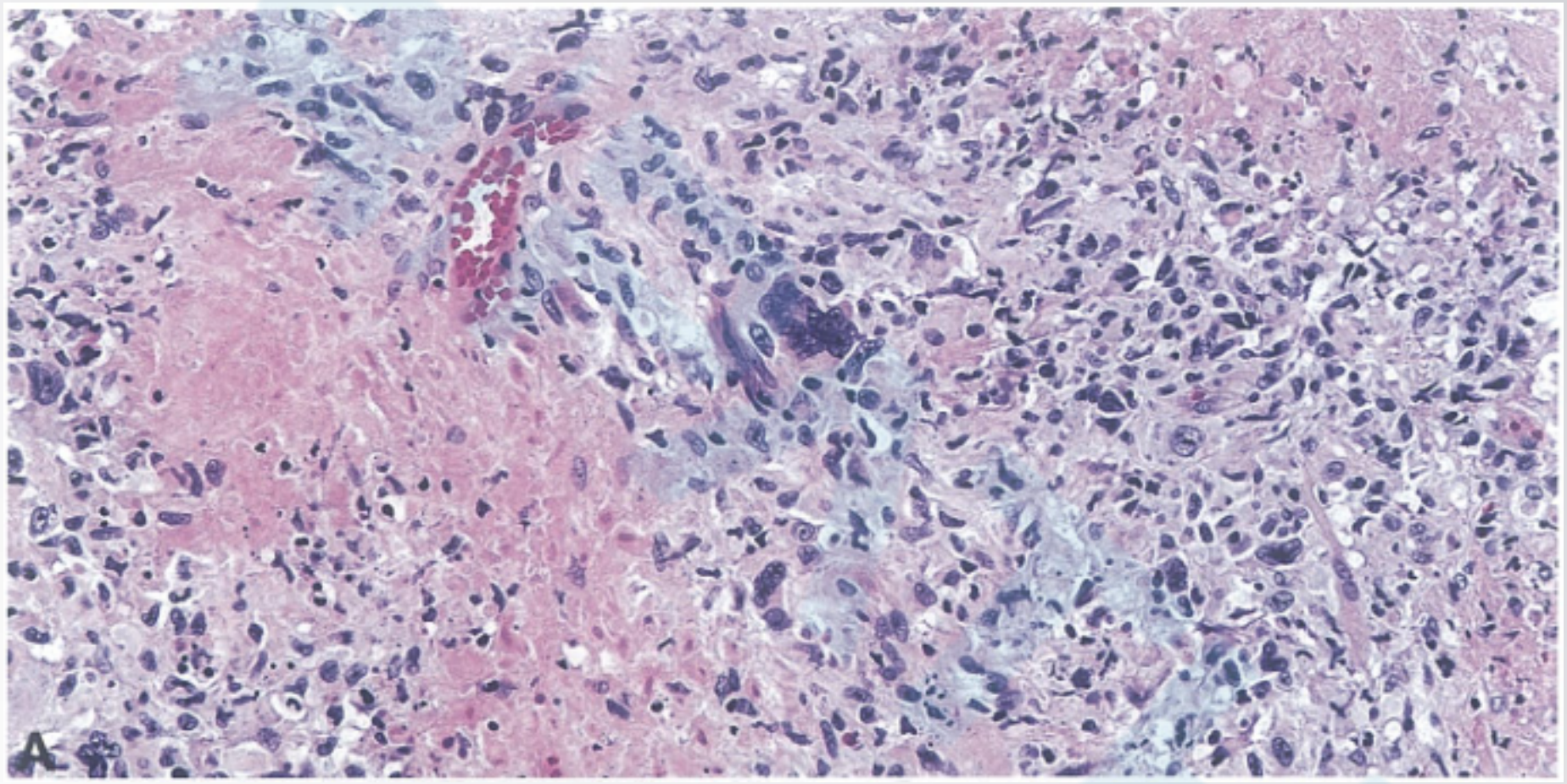
组织学特征

与其他EBV相关淋巴样增生性疾病（包括EBV阳性经典霍奇金淋巴瘤）重叠。
肿瘤成分通常由大量的转化细胞/免疫母细胞和霍奇金/R-S样细胞组成。
大面积坏死和血管浸润是其特征性发现，但并不总是存在。

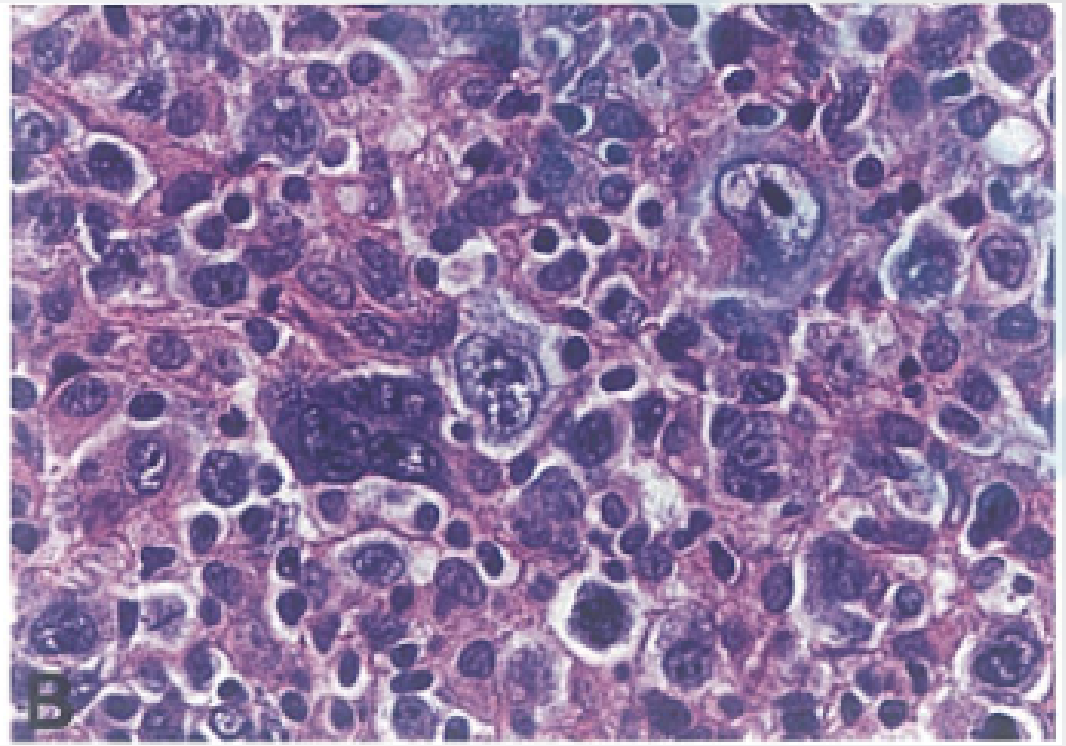
IHC

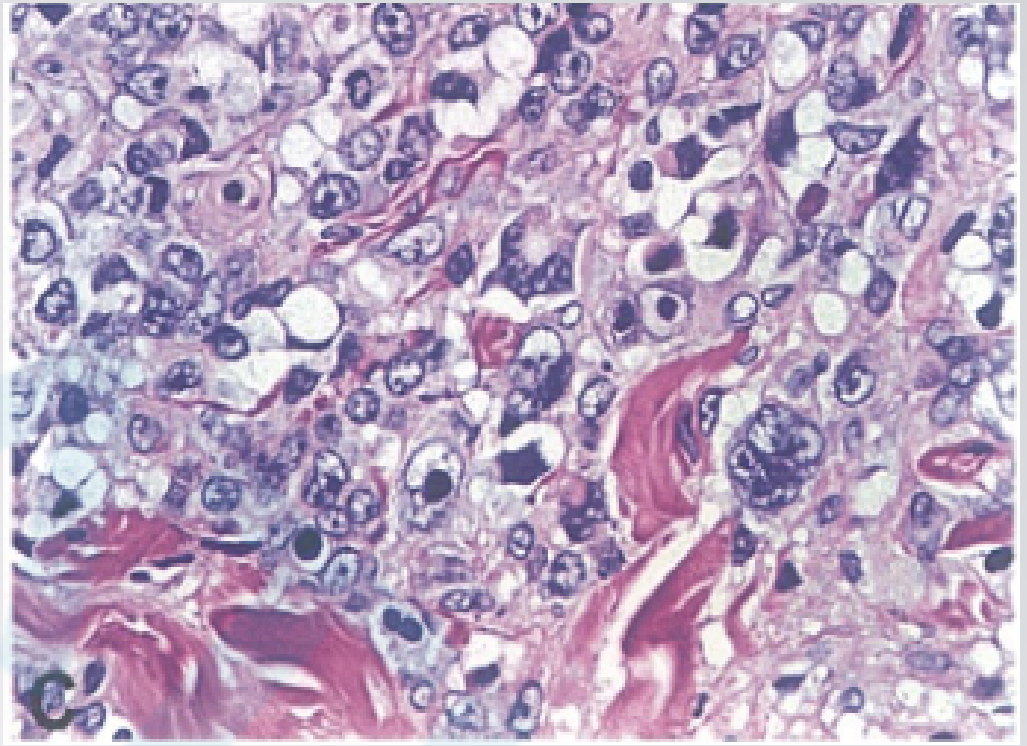
CD19、CD20、CD22、CD79、PAX5、IRF4/MUM1、CD30（+）
CD10、BCL6(-)

EBEN2(EBV核心抗原2)和LMP1（潜伏膜蛋白）分别在7-36％和＞90％的病例中表达。



REevised 4th Edition WHO Classification of Tumour of Heamatopietic and Lymphoid Tissues





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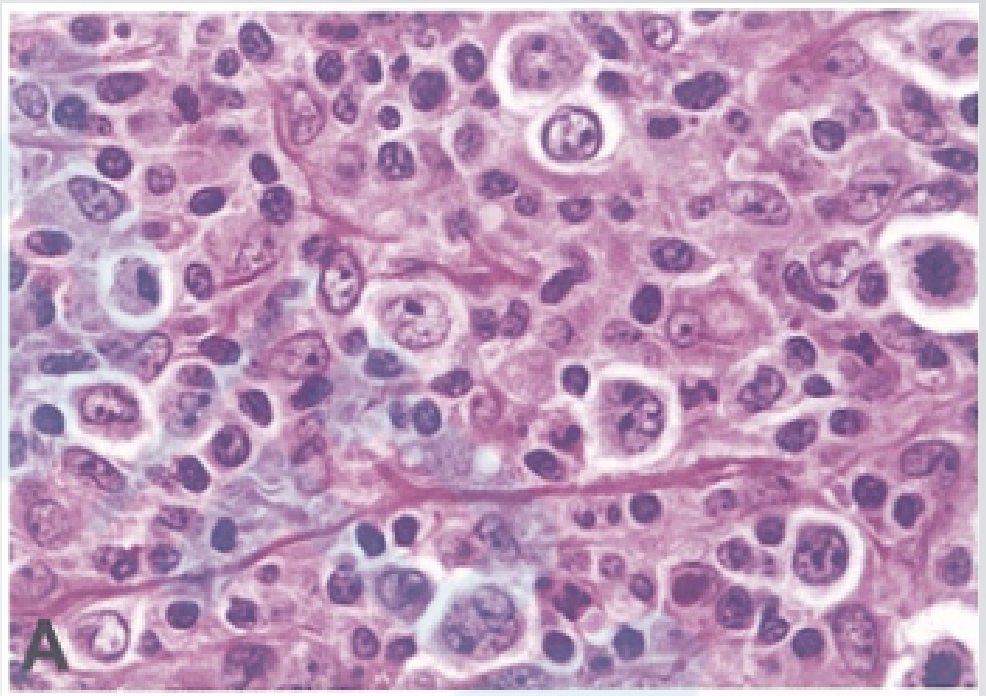
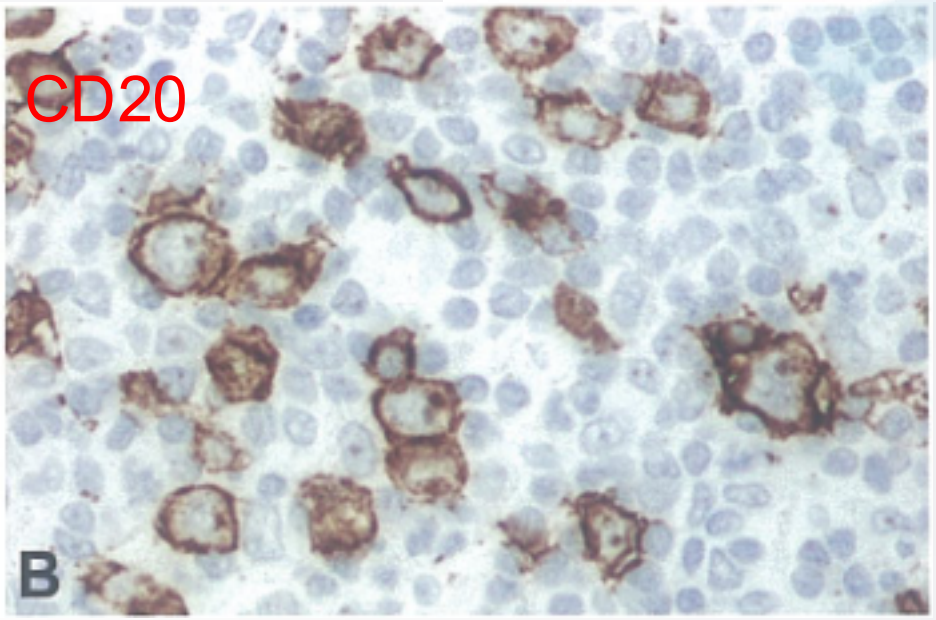
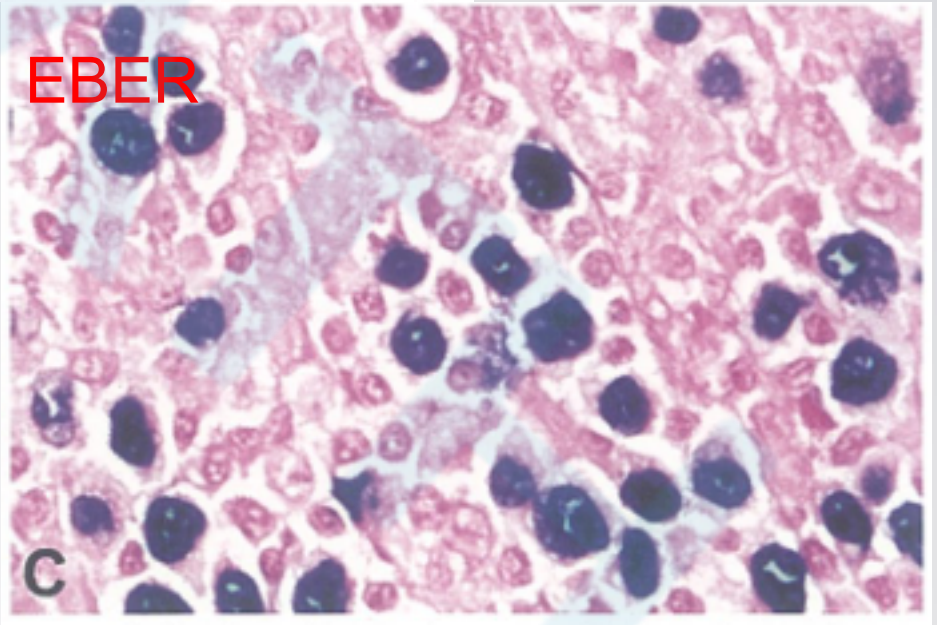

A


CD20
B


EBER
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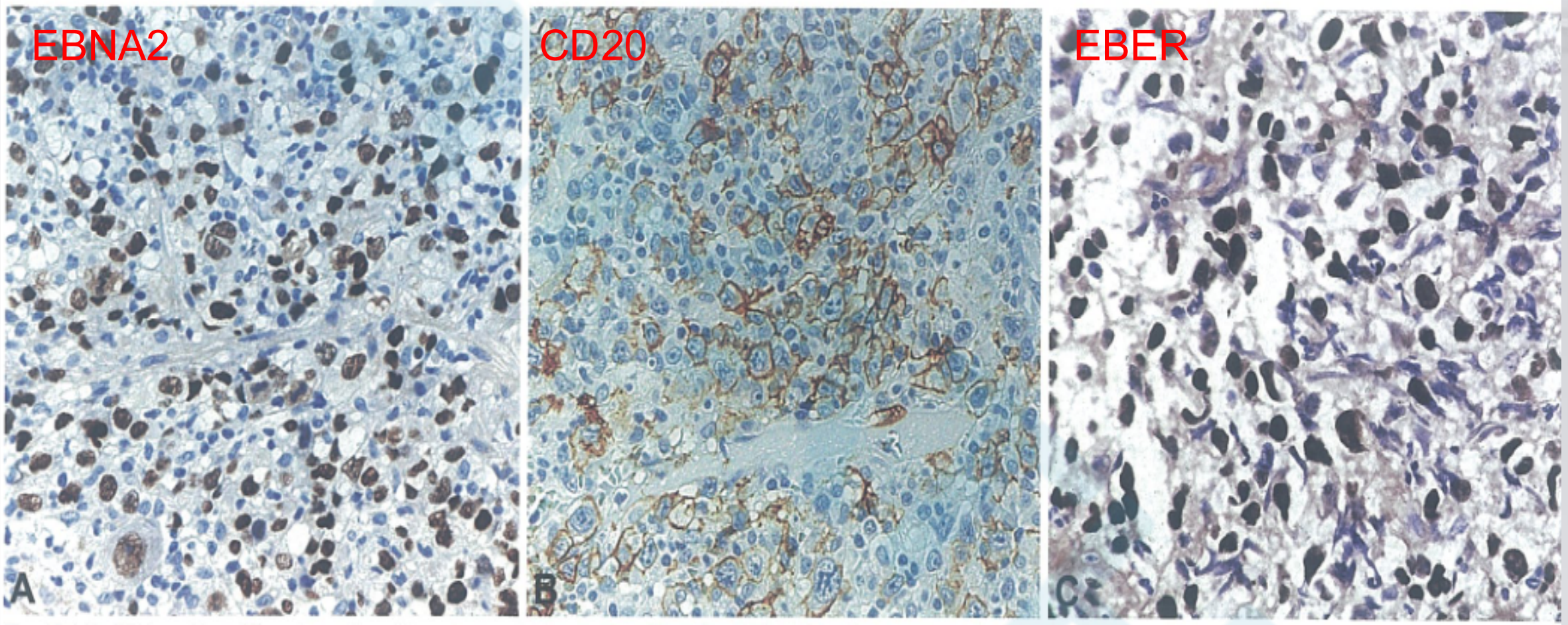

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EBV阳性粘膜皮肤溃疡（EBV-positive mucocutaneous ulcer，EBVMCU）

是一种新发现的临床病理学实体，与患者年龄或医源性免疫抑制相关，通常具有霍奇金样特征和典型的惰性进展病程，在某些情况下会自发消退。常出现在皮肤或粘膜。最常见的受累部位是口腔，包括牙龈。EBV阳性细胞的生长可能与局部创伤或炎症有关。

EBVMCU

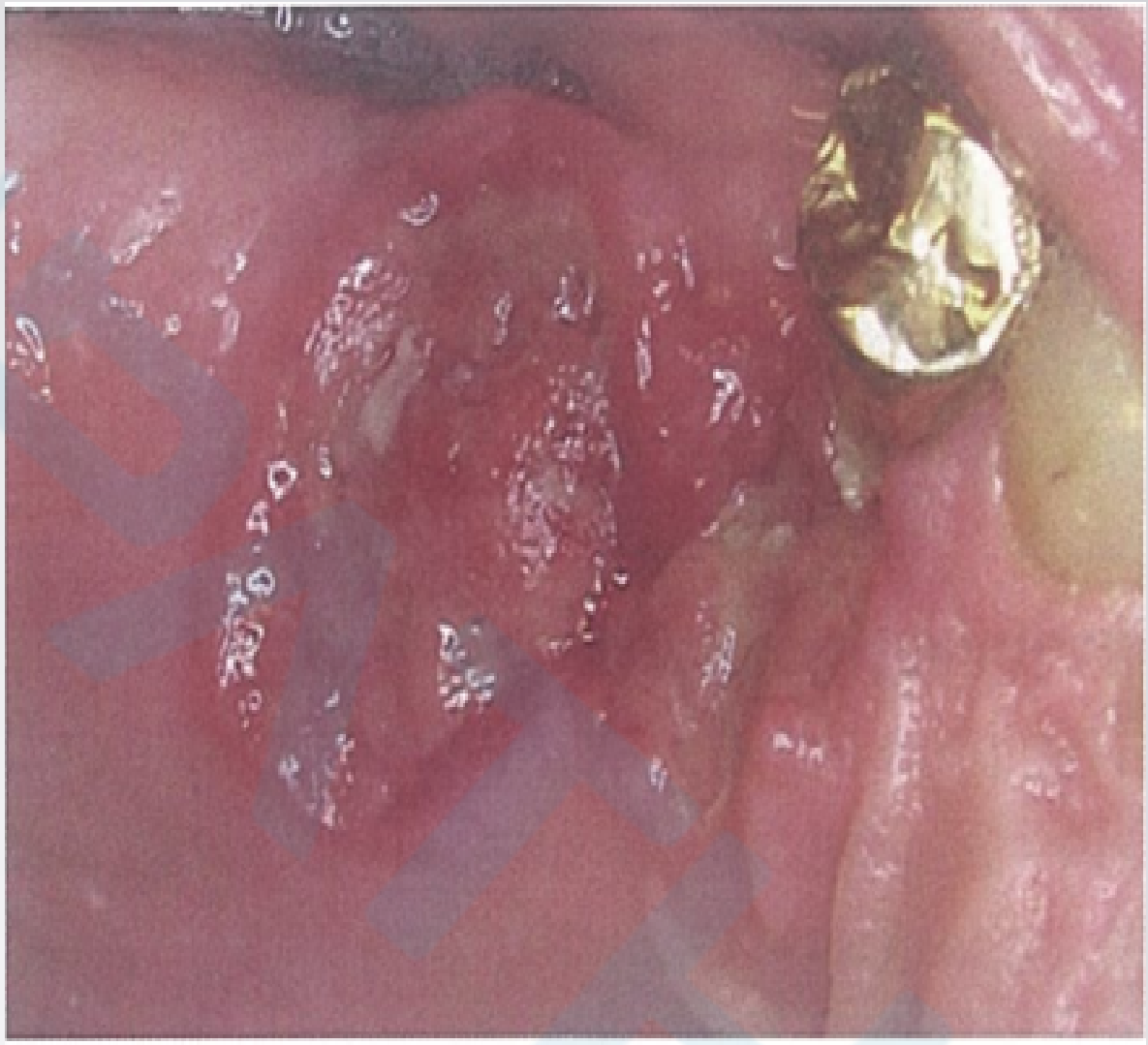
大B细胞表达：CD20 CD79 PAX5 OCT2 CD30 EBER MUM-1，BOB-1不同程度表达；部分表达CD15 ； CD10、BCL6(-)
背景为丰富的CD8+T CD3+T细胞

不同程度检出IgH和T细胞受体基因的克隆性重排。

目前认为该组病变部分为自限性病程。

EBVMCU

85岁男患
上颚



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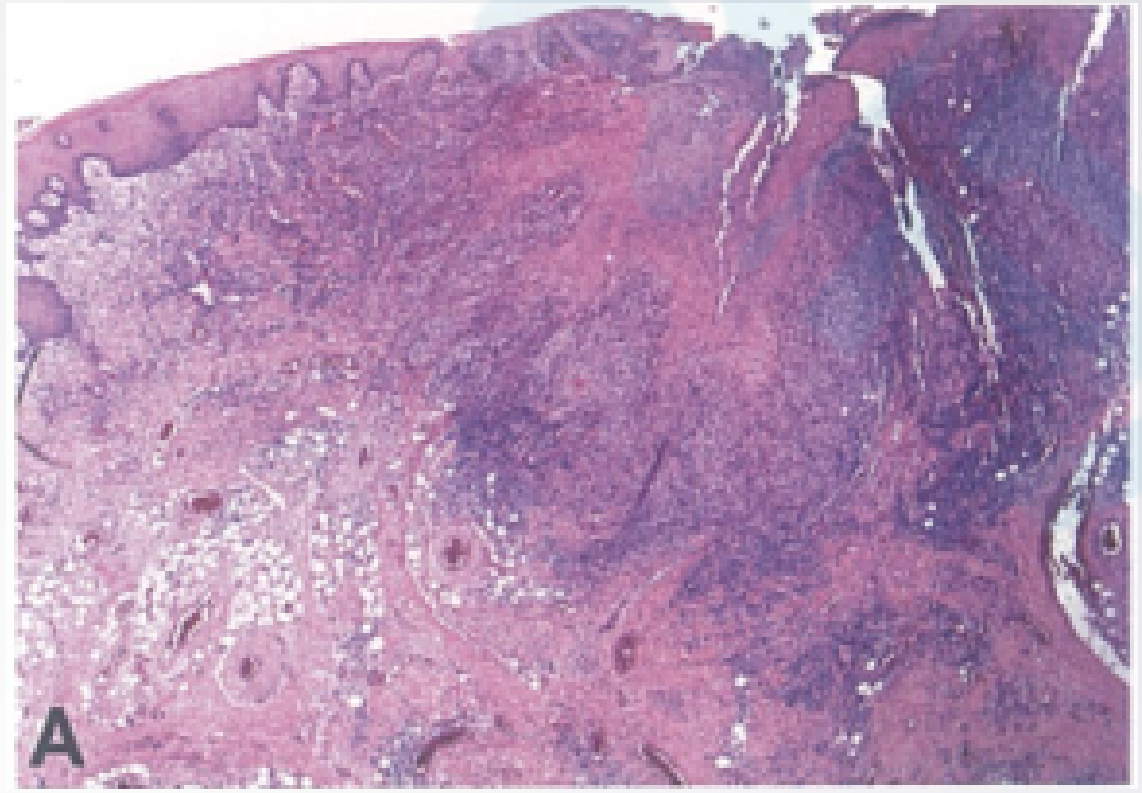

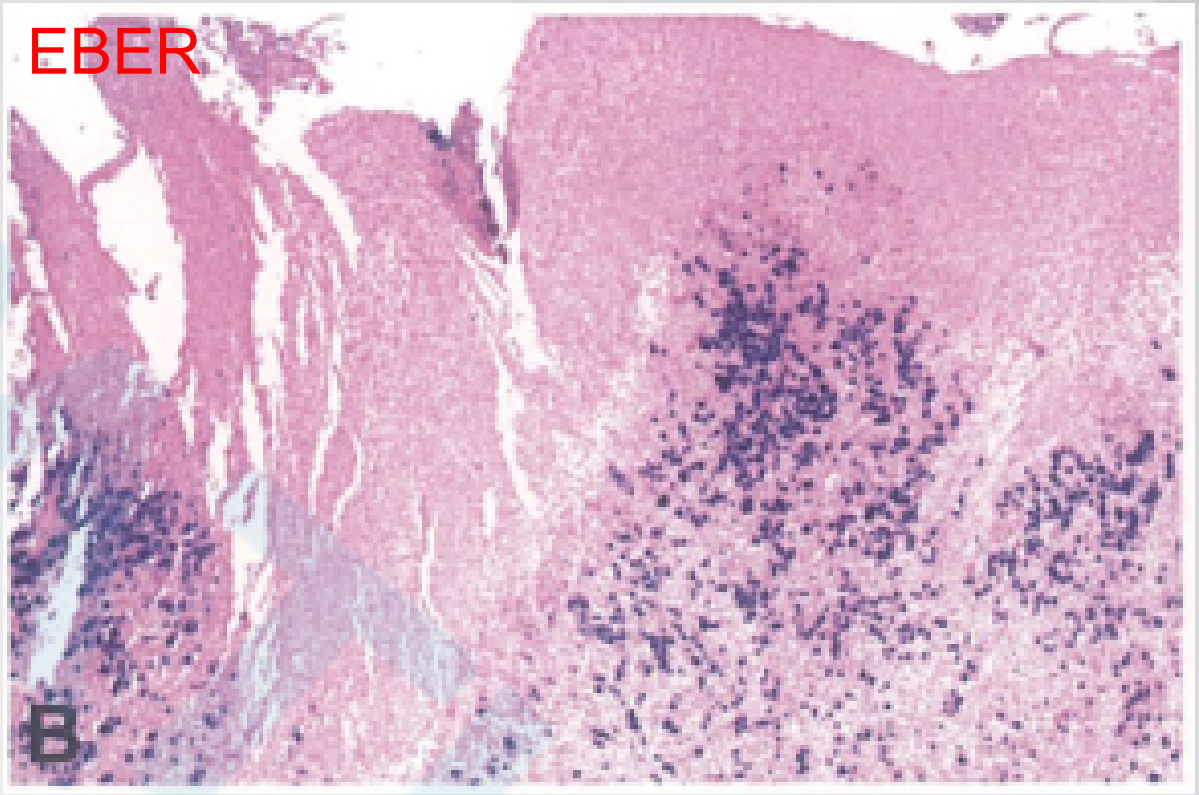

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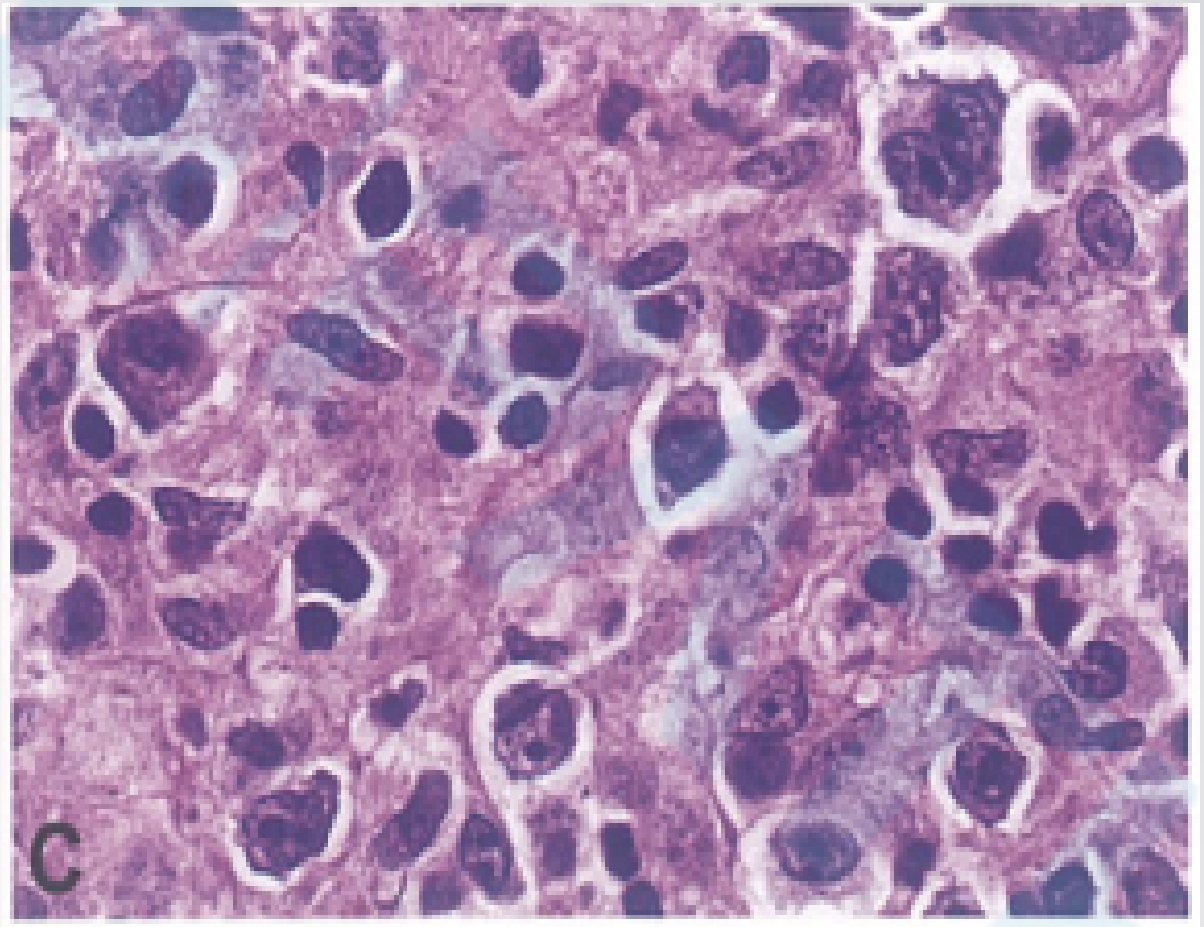

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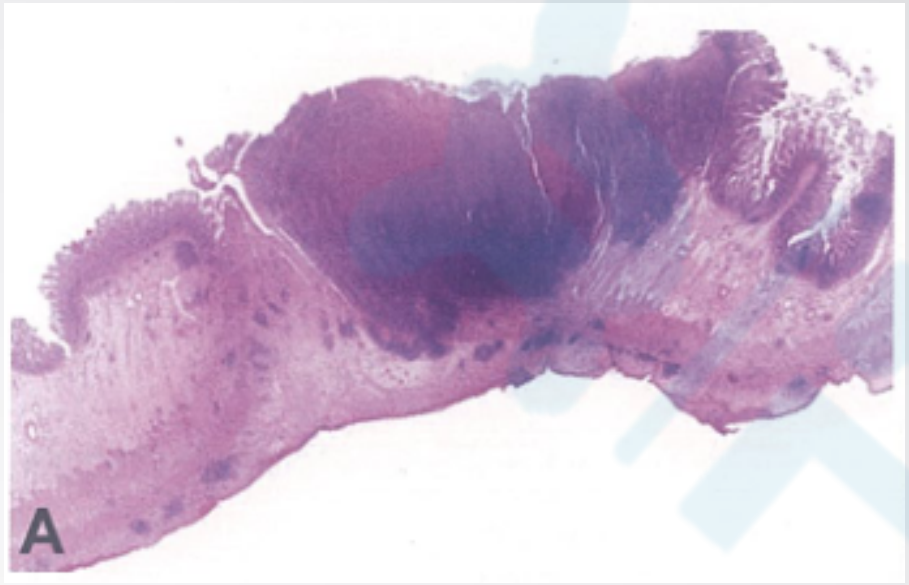
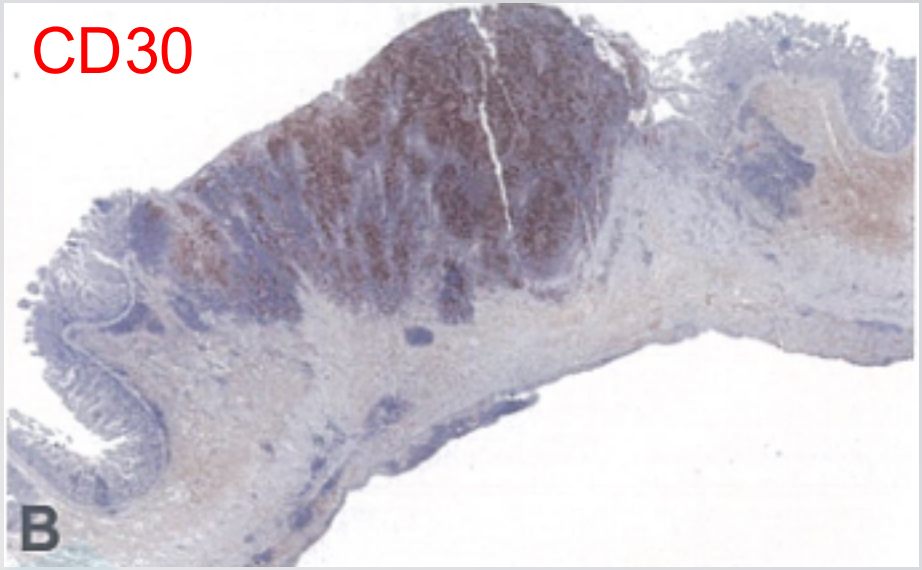
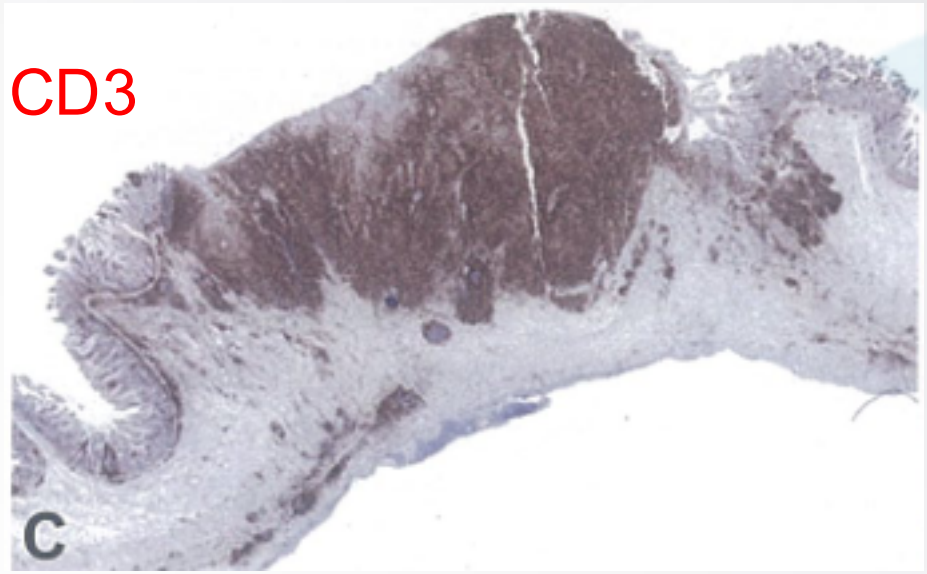
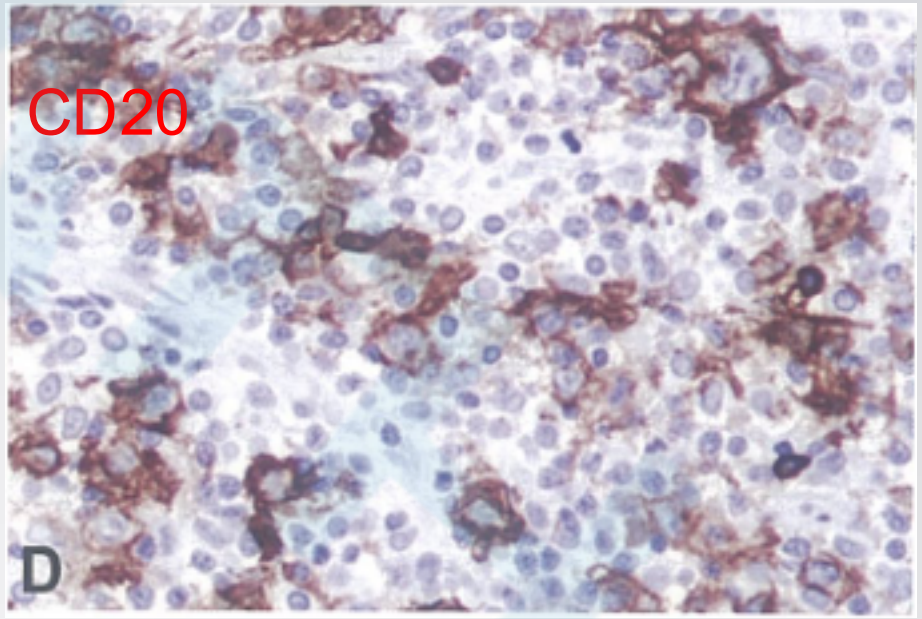








REevised 4th Edition WHO Classification of Tumour of Heamatopietic and Lymphoid Tissues

	EBV(+)DLBCL	EBVMCU
ICD-O code	9680/3	9680/1
流行病学	亚洲/拉丁美洲<5-15% 西方<5% 无易感性免疫缺陷记录；大多数患者年龄超过50岁，患病率在80岁达高峰 男女患病率1.2-3.6:1	高年龄，中位年龄>70 应用医源性免疫抑制剂的患者 器官移植
病因学	免疫衰老、免疫微环境的改变	EBV
部位	结内、结外（肺和胃肠道）	口腔黏膜（扁桃体、舌头、颊粘膜和上颚）、皮肤和胃肠道（食管、大肠、直肠和肛周）
临床特征	高或较高的（IPI）评分 大多数患者的血清或全血中EBV DNA+	溃疡
IHC	CD19 CD20 CD22 CD79a PAX5 IRF4/MUM1 CD30 EBER（+） CD10 BCL-6（-）	CD20 PAX5 OCT2 BOB1 IRF4/MUM1 CD30 EBER CD15(50%) CD79 LMP1（+） CD10 BCL-6（-） CD3 CD8（+）
基因谱	IG基因克隆性重排	<50%（IG基因克隆性重排）

根据组织病理学作出淋巴瘤的诊断和分类分型诊断后，还需根据淋巴瘤的分布范围，按照Ann Arbor(1966年)提出的HL临床分期方案（NHL也参照使用）分期；

I期：病变仅限于1个淋巴结区（I）或单个结外器官局部受累（I E）。

II期：病变累及横膈同侧两个或更多的淋巴结区（II），或病变局限侵犯淋巴结以外器官及横膈同侧1个以上的淋巴结区（II E）。

III期：横膈上下均有淋巴结病变（III）。可伴有脾累及（III S）结外器官局限受累（III E）或脾与局限性结外器官受累（III SE）。

IV期：1个或多个结外器官受到广泛性或播散性侵犯，伴或不伴淋巴结肿大。肝或骨髓只要受到累及均属IV期。累及的部位可采用下列记录符号：E结外；X直径10cm以上的巨块；M骨髓；S脾；H 肝；O骨骼；D皮肤；P胸膜；L肺。

每一个临床分期按全身症状的有无分为A、B二组，无症状者为A组，有症状者为B组。全身症状包括三个方面：①.发热38.0℃以上时间≥3天且排除感染性发热；②.6个月内体重减轻10%以上；③.盗汗：即入睡后出汗。

淋巴瘤 2014版Lugano分期标准

局限期	
I 期	仅侵及单一淋巴结区域 (I) 或单个结外器官局部受累 (I E)。
II 期	累及≥2 个淋巴结区域，但均在膈肌同侧 (II) ,可伴有同侧淋巴结引流区域的局限性结外器官受累 (II E) (例如：甲状腺受累伴颈部淋巴结受累，或纵膈淋巴结受累直接延伸至肺脏受累)
II 期大包块*	II 期伴有大包块者。
进展期	
III 期	侵及膈肌上下淋巴结区域，或侵及膈上淋巴结+脾受累 (III S)
IV 期	侵及淋巴结引流区域之外的结外器官 (IV)

根据2014年Lugano改良分期标准，不再对淋巴瘤的大包块（Bulky）病灶进行具体的数据限定，只需在病例中明确记载最大病灶的最大直径即可，II期伴有大包块的患者，应根据病例类型及疾病不良预后因素而酌情选择治疗原则，如伴有大包块的惰性淋巴瘤患者可选择局限期治疗模式，但是伴有大包块的侵袭性淋巴瘤患者，则应选择进展期治疗模式。

BACKGROUND

1. Epstein-Barr virus (EBV)-positive diffuse large B-cell lymphoproliferation encompasses a broad range of clinicopathologic findings, including specific subtypes, for example, EBV + mucocutaneous ulcer.
2. EBV harboring tumor cells are an independent adverse factor in both primary gDLBCL and iDLBCL.
3. EBVMCU affects extranodal sites (oropharynx in 52% of cases, skin in 29%, and GI tract in 19%), and is associated with the setting of iatrogenic IS in 56% to 66% of cases, primary immunodeficiency in 2% to 4%, and advanced age in 27% to 40%.

BACKGROUND

6. Although EBVMCU is generally featured by a solitary lesion, it is multifocal in 17% of reported cases. To date, the English literature includes only 14 reported cases of EBVMCU affecting the GI tract, other than oral mucosa.

7. Therefore, further studies are needed to elucidate the clinicopathologic characteristics of this disease in the GI tract.

Research purposes

- Observation and analysis of 36 primary EBV + giDLBCL cases,Investigate their clinicopathological characteristics to further clarify their biological behavior.

MATERIALS AND METHODS

Patient Selection

- This retrospective study included data from 36 patients with primary EBV + giDLBCL, diagnosed between1995 and 2018 at Nagoya University Hospital and 11 affiliated institutions. These cases were identified among 312 cases consecutively diagnosed as primary giDLBCL during the same time period.

- In all cases, the diagnosis was established according to histopathologic and immunohistochemical criteria, based on the 2017 World Health Organization (WHO) classification system.

MATERIALS AND METHODS

Patient Selection

- Because an optimal method has not yet been established for discriminating primary giDLBCL from systemic DLBCL involving the GI tract, in this study, lymphoma of the GI tract was considered primary if the main bulk of disease was located in the GI tract.

- Clinical stage was evaluated according to the Lugano classification for GI non-Hodgkin lymphoma.

Immunohistochemistry and In Situ Hybridization

- Tumor cells were considered positive for neoplastic programmed cell death ligand 1 when ≥5% of the neoplastic lymphoid cells exhibited moderate or strong membrane staining with a PD-L1-specific antibody(clone SP142).

- A case was considered positive for PD-L1 in the microenvironment when ≥20% of the total tissue cellularity in comprised nonmalignant cells exhibiting moderate or strong membrane or cytoplasmic PD-L1-specific staining.

Immunohistochemistry and In Situ Hybridization

- All cases were tested for Epstein-Barr virus–encoded small RNA (EBER) using in situ hybridization as described previously. Cases were considered positive for EBER when nuclear expression of EBER was observed in ≥80% of tumor cells.

RESULTS

- On the basis of the available clinical information, the 36 patients were divided into 3 groups as follows: 8 immunosuppressed patients, 7 nonimmunosuppressed patients with Lugano stage I disease, and 21 nonimmunosuppressed patients with Lugano stage II1/II2/IIE/IV disease.

- Four patients (1 in stage I [14%] and 3 in II-IV [17%]) with gDLBCL were caught by the medical checkup, while all of iDLBCL cases were diagnosed in a symptomatic setting (P=0.56).

TABLE 1. Characteristics of Patients With Primary EBV$^+$ giDLBCL (N = 36)

Characteristics	Immunosuppressed (N = 8), n/N (%)	Nonimmunosuppressed, n/N (%)		*P**	*P*†
		Stage I (N = 7)	Stage II-IV (N = 21)		
Male sex	2/8 (25)	3/7 (43)	11/21 (52)	0.24	1.00
Age, median (range) (y)	74 (35-82)	69 (42-76)	69 (37-84)	0.83	0.79
Age > 60 y	7/8 (88)	5/7 (71)	14/21 (67)	0.38	1.00
Stomach localization	1/8 (13)	7/7 (100)	18/21 (86)	0.001	0.55
B symptoms present	2/7 (29)	1/7 (14)	11/21 (52)	0.40	0.18
Perforation	2/8 (25)	0/7 (0)	0/21 (0)	0.069	—
PS 2-4	3/7 (43)	0/7 (0)	4/21 (19)	0.32	0.55
Serum LDH > normal	4/8 (50)	0/7 (0)	12/21 (57)	1.00	0.010
sIL-2R (≥ 1000 U/mL)	5/7 (71)	1/6 (17)	12/16 (75)	1.00	0.023
Extranodal involvement > 1 site	3/8 (78)	0/7 (0)	3/21 (14)	0.31	0.55
IPI high-int, high	5/7 (71)	0/7 (0)	8/21 (38)	0.20	0.075
Macroscopic type					
Ulcerative	8/8 (100)	3/7 (43)	13/19 (68)	0.14	0.37
Polypoid	0/8 (0)	2/7 (29)	3/19 (16)	0.53	0.59
Diffuse-infiltrating or other	0/8 (0)	2/7 (29)	3/19 (16)	0.53	0.59
Multiple lesions	5/8 (63)	0/5 (0)	8/19 (42)	0.42	0.13
Bulky mass present	1/7 (14)	2/7 (29)	3/21 (14)	1.00	0.57
Immunophenotype					
CD5	2/7 (29)	0/6 (0)	1/20 (5)	0.15	1.00
CD10	0/8 (0)	1/6 (17)	6/20 (30)	0.14	1.00
BCL-2	5/8 (63)	3/5 (60)	11/20 (55)	1.00	1.00
nPD-L1 ≥ 5%	1/8 (13)	1/3 (33)	1/14 (7)	1.00	0.33
miPD-L1 ≥ 20%	7/7 (100)	2/2 (100)	11/13 (85)	0.51	1.00
Non-GCB immunophenotype	8/8 (100)	5/7 (71)	14/20 (70)	0.14	1.00

TABLE 1. Characteristics of Patients With Primary EBV$^+$ giDLBCL (N = 36)

Characteristics	Immunosuppressed (N = 8), n/N (%)	Nonimmunosuppressed, n/N (%)		*P**	*P*†
		Stage I (N = 7)	Stage II-IV (N = 21)		
Treatment					
R-containing therapy	7/8 (88)	3/7 (43)	12/21 (57)	0.20	0.67
R-CTx	4/8 (50)	2/7 (29)	7/21 (33)	1.00	1.00
R-CTx+S	3/8 (38)	0/7 (0)	2/21 (9.5)	0.082	1.00
R-CTx+Rad	0/8 (0)	0/7 (0)	3/21 (14)	0.55	0.55
R-CTx+S+Rad	0/8 (0)	1/7 (14)	0/21 (0)	—	0.25
No. cycles, median (range)	6 (2-6)	8 (1-8)	5 (2-8)	0.61	0.82
CTx	0/8 (0)	4/7 (57)	4/21 (19)	0.55	0.14
CTx+Rad	0/8 (0)	0/7 (0)	1/21 (4.8)	1.00	1.00
Surgery	0/8 (0)	0/7 (0)	1/21 (4.8)	1.00	1.00
No treatment	1/8 (13)	0/7 (0)	3/21 (14)	1.00	0.55
Treatment response					
CR	5/7 (71)	5/7 (71)	11/20 (55)	0.66	0.66
PR	1/7 (14)	0/7 (0)	2/20 (10)	1.00	1.00
SD	0/7 (0)	0/7 (0)	3/20 (15)	0.55	0.55
PD	1/7 (14)	2/7 (29)	4/20 (20)	1.00	0.63
Treatment response (R-containing)					
CR	5/7 (71)	2/3 (67)	8/12 (67)	1.00	1.00
PR	1/7 (14)	0/3 (0)	2/12 (17)	1.00	1.00
SD	0/7 (0)	0/3 (0)	1/12 (8.3)	1.00	1.00
PD	1/7 (14)	1/3 (33)	1/12 (8.3)	1.00	0.37

*Immunosuppressed group versus nonimmunosuppressed group with stage II-IV.

†Nonimmunosuppressed group with stage I versus stage II-IV.

CTx indicates chemotherapy; GCB, germinal center B cell; high-int, high-intermediate; IPI, International Prognostic Index; LDH, lactate dehydrogenase; miPD-L1, microenvironmental programmed cell death ligand 1; PD, progressive disease; PR, partial remission; PS, performance status; R, rituximab; Rad, radiation; SD, stable disease; sIL-2R, soluble interleukin-2 receptors.

TABLE 2. Clinicopathologic Features of Immunosuppressed EBV+ giDLBCL Patients (N=8)

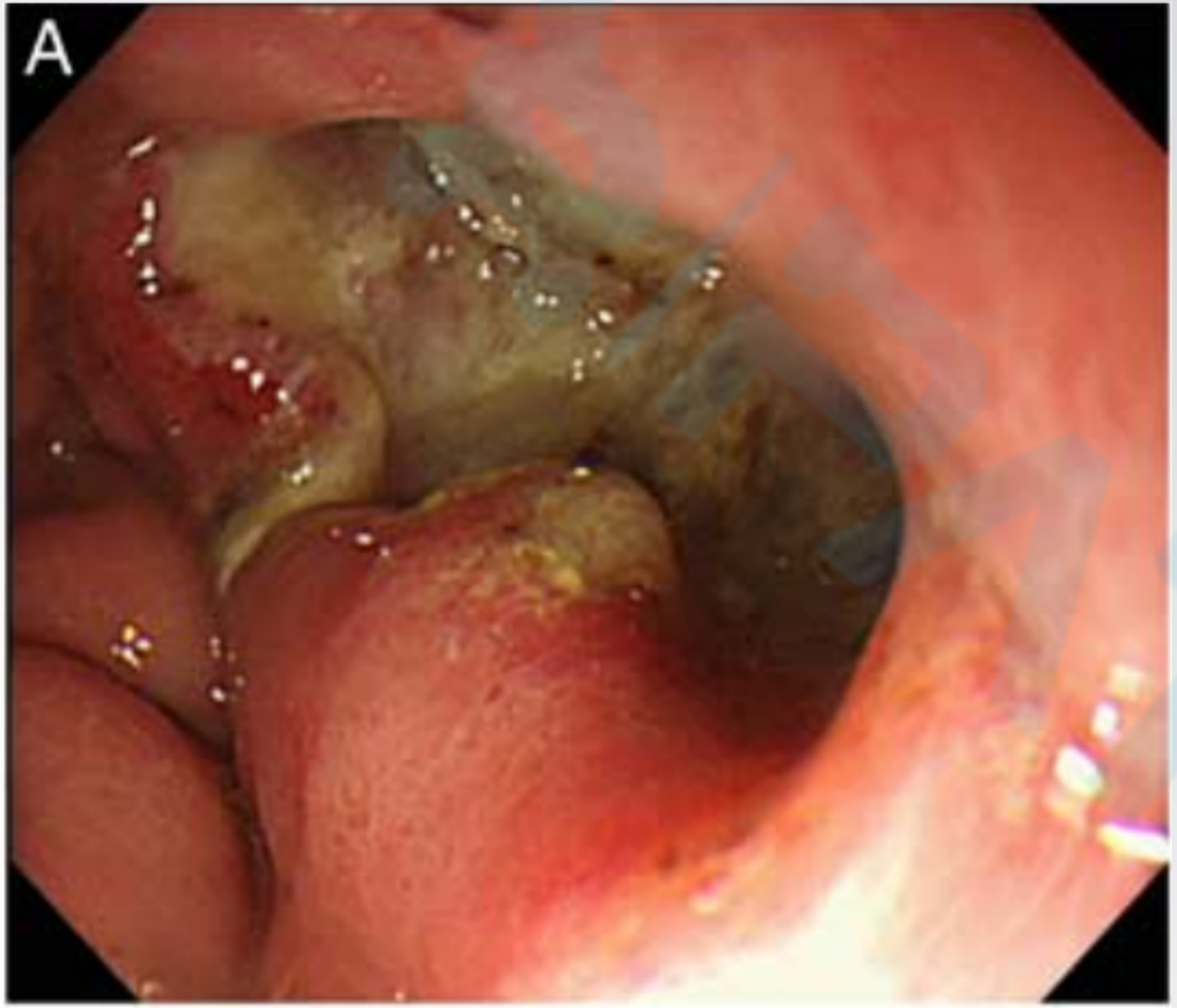
No.	Age (y)	Sex	Site	Source of IS	Endoscopic Finding	No. Lesions	nPD-L1 (%)	Stage	Treatment	Response	Time to Relapse (mo)	Status	Length of FU (mo)
1	35	Female	Stomach	MTX (RA)	Ulcerated	Multiple	0	IV	R-CTx	CR	—	NED	11
2	82	Female	Ileum end	MTX (RA)	Ulcerated	Multiple	0	IIE	R-CTx+S	CR	—	DOC	81
3	74	Male	Rectum	Infliximab (CD)	Ulcerated	Single	0	II2	R-CTx	CR	52	DD	62
4	47	Female	Duodenum	Tacrolimus	Ulcerated	Multiple	0	IV	R-CTx	PD	—	DD	11.5
5	82	Female	Duodenum	CHL	Ulcerated	Single	0	IV	NT	—	—	DOC	0.4
6	80	Male	Jejunum	CHL	Ulcerated	Multiple	0	IIE	R-CTx+S	PD	—	DD	12
7	74	Female	Ileum end	PTCL-NOS	Ulcerated	Single	20	IV	R-CTx+S	CR	22	DD	26
8	70	Female	Ileocecum	PTCL-NOS	Ulcerated	Multiple	0	IV	R-CTx	CR	11	DD	46

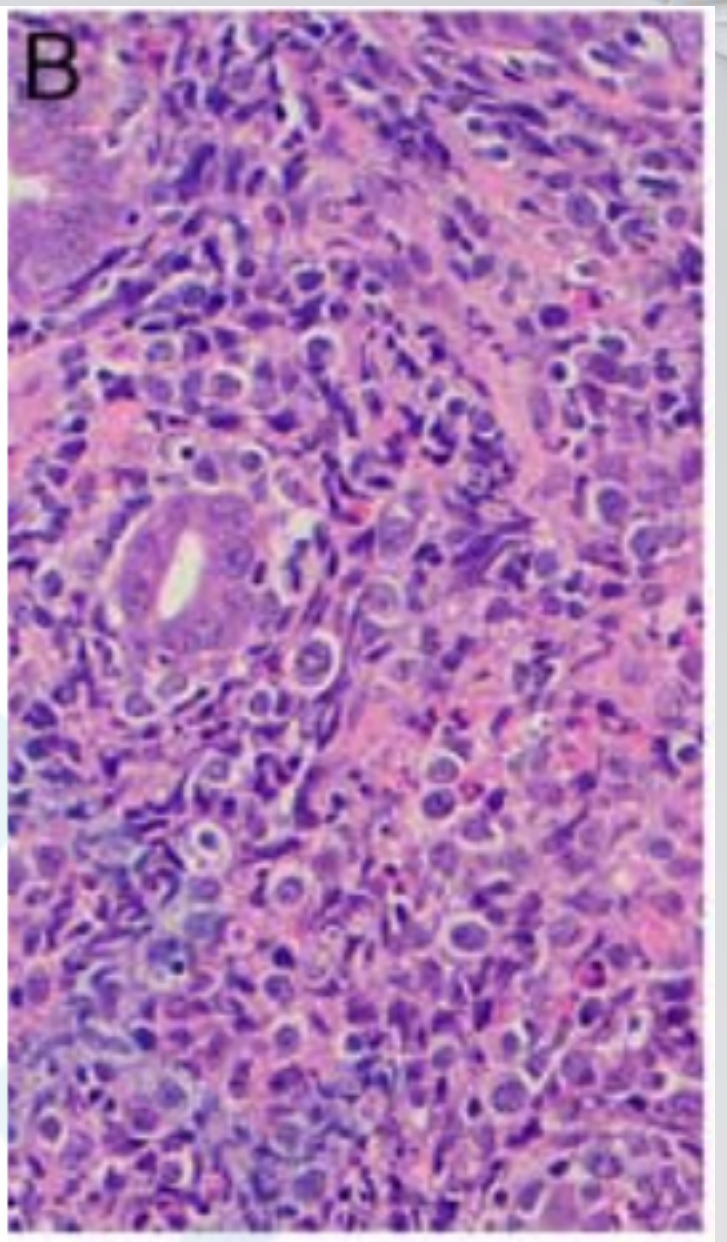
AWD indicates alive with disease; CD, Crohn disease; CTx, chemotherapy; DD, died of disease; DOC, died of other causes; FU, follow-up; MTX, methotrexate; NED, no evidence of disease; NOS, not otherwise specified; NT, no treatment; PD, progressive disease; PR, partial remission; PTCL, peripheral T-cell lymphoma; R, rituximab; RA, rheumatoid arthritis; S, surgery.

TABLE 3. Clinicopathologic Features of Nonimmunosuppressed EBV$^+$ giDLBCL Patients With Lugano Stage I (N = 7)

No.	Age (y)	Sex	Site	Endoscopic Finding	No. Lesions	nPD-L1 (%)	Treatment	Response	Status	Length of FU (mo)
9	69	Female	Stomach	Ulcerated	Single	0	CTx	CR	NED	148
10	72	Female	Stomach	Ulcerated	Single	NA	CTx	CR	NED	112
11	60	Male	Stomach	Ulcerated	Single	90	R-CTx	PD	NED	11
12	76	Female	Stomach	Polypoid	Single	NA	CTx	CR	NED	130
13	73	Male	Stomach	Polypoid	Single	0	R-CTx	CR	NED	71
14	42	Male	Stomach	Bulky mass	Unknown	NA	R-CTx+S+Rad	CR	NED	132
15	64	Female	Stomach	Bulky mass	Unknown	NA	CTx	PD	DD	6.1

CTx indicates chemotherapy; DD, died of disease; FU, follow-up; NA, not available; NED, no evidence of disease; PD, progressive disease; R, rituximab; Rad, radiation; S, surgery.


A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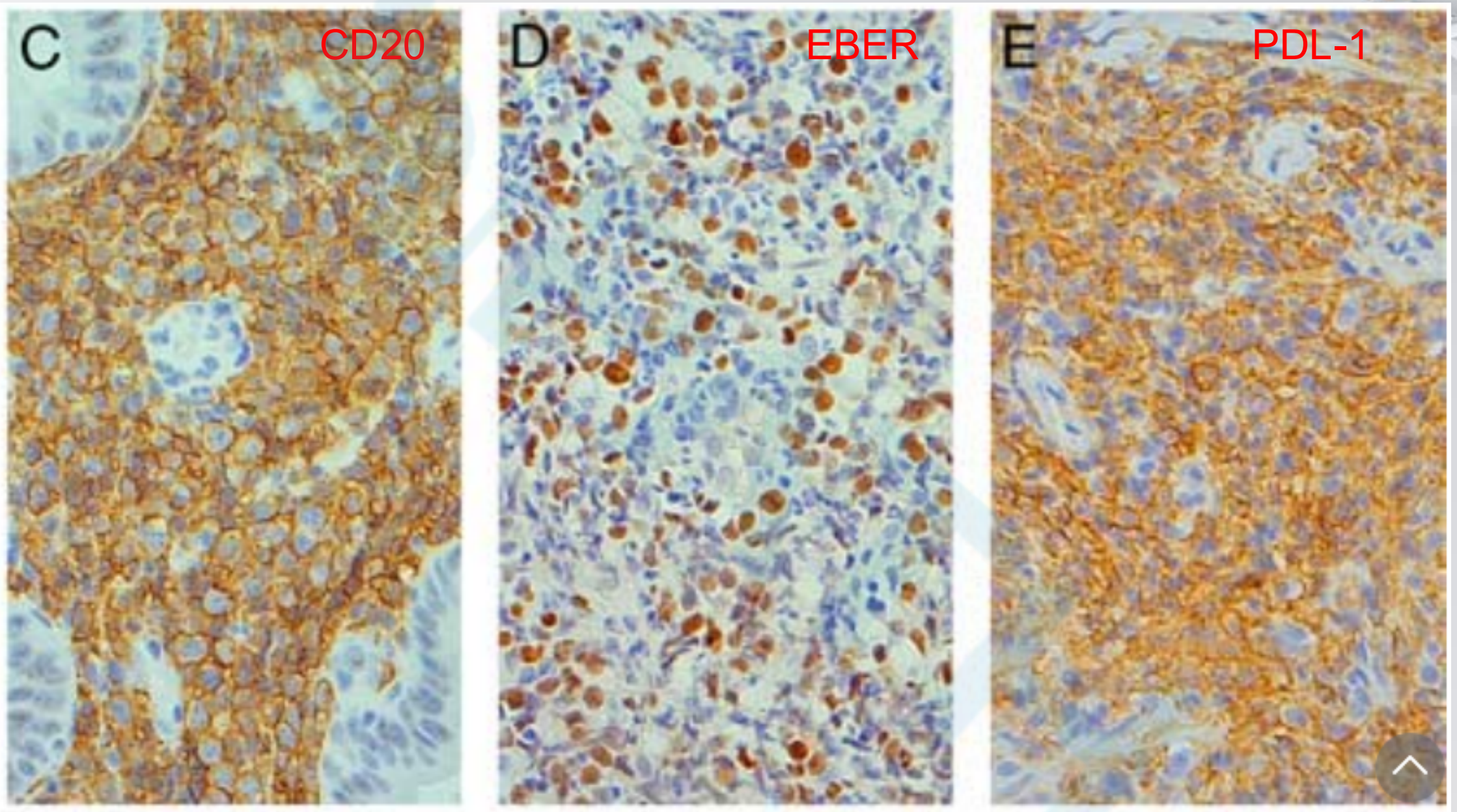
C
CD20
D
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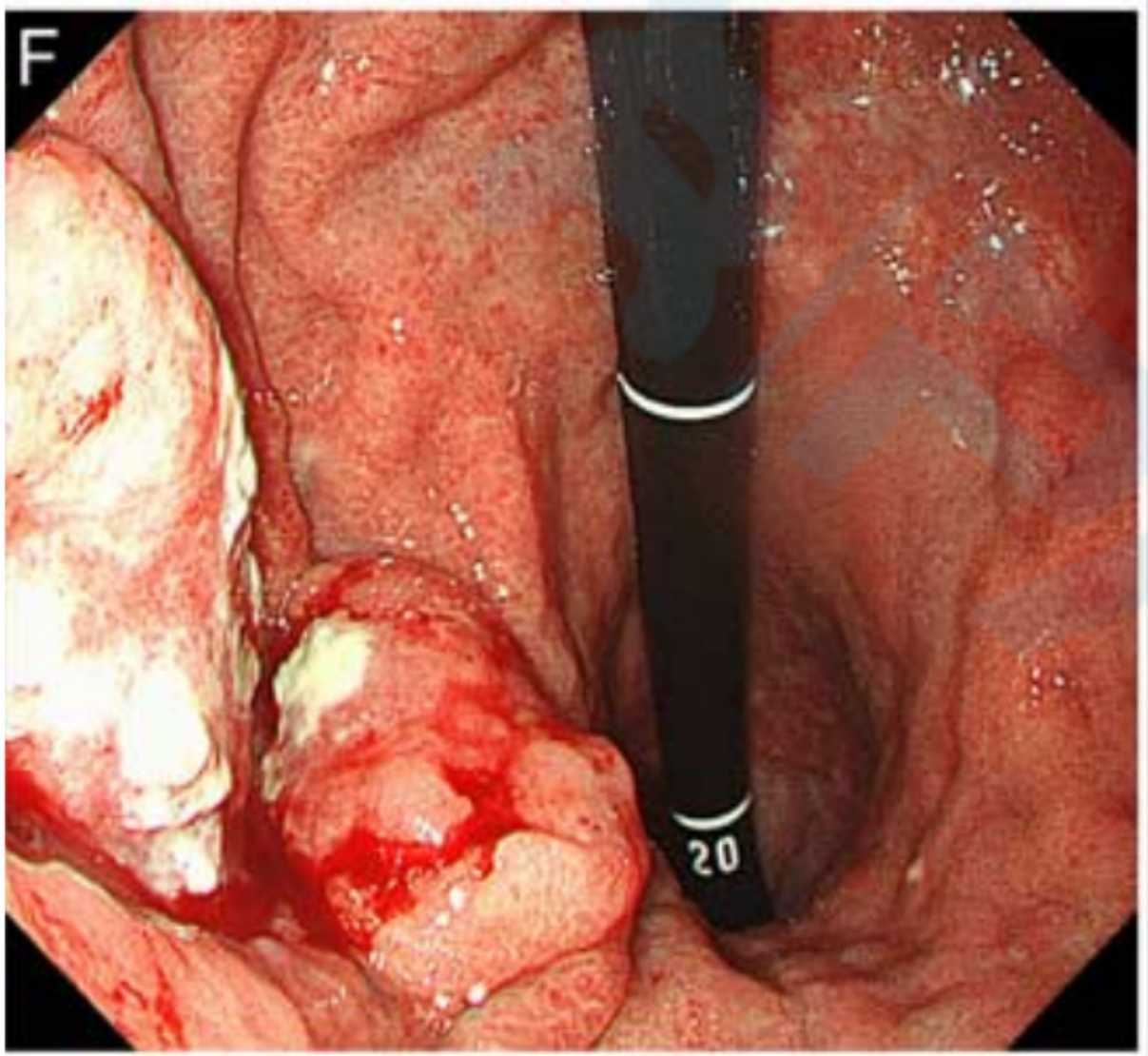
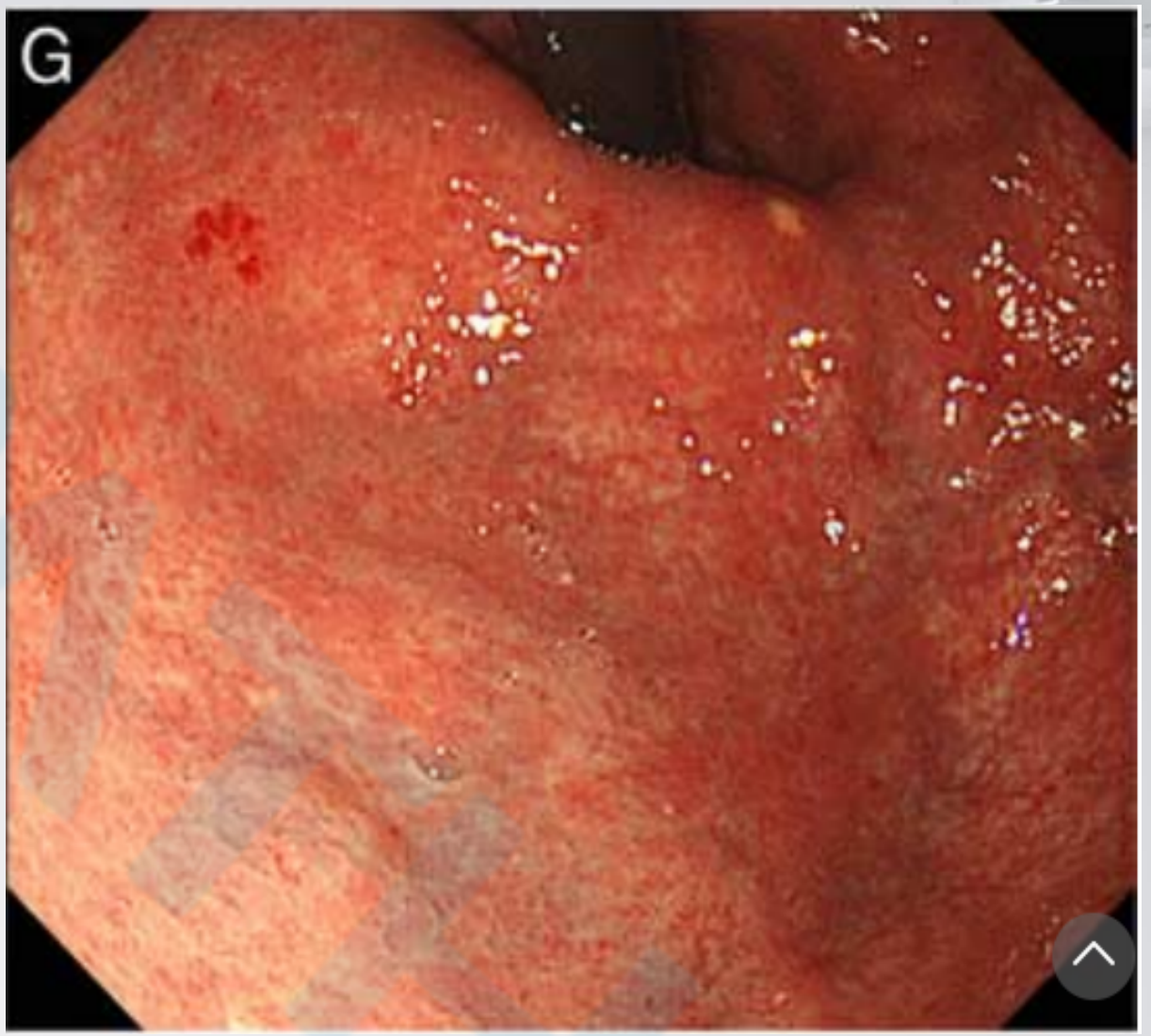
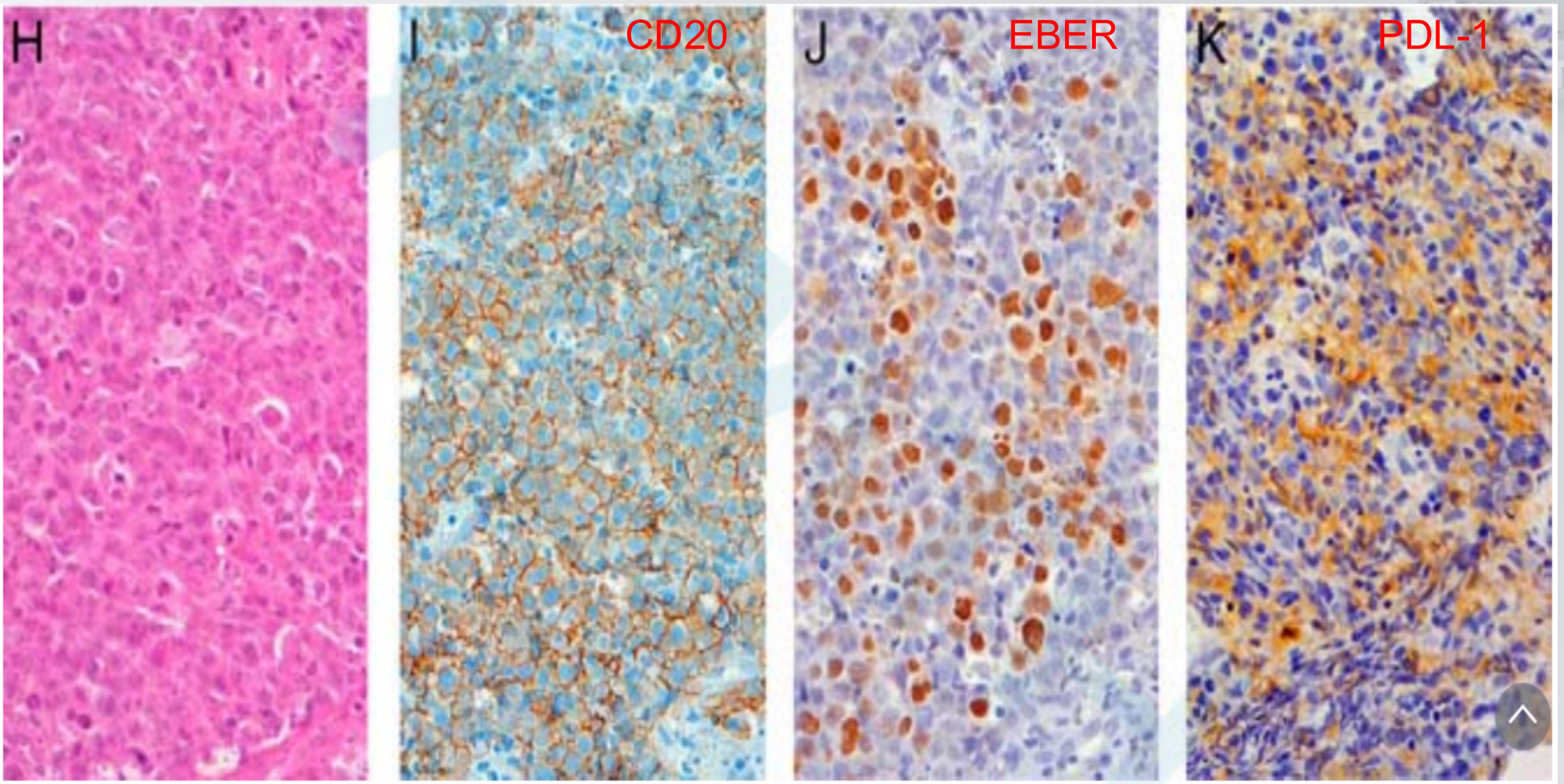
E
PDL-1


F
20


G


H
I
CD20
J
EBER
K
PDL-1

One nonimmunosuppressed stage I case (case 13) exhibited spontaneous regression, and had an immunophenotype of CD3 − , CD5 − , CD10 − , CD20 + , BCL-2 + , BCL6 + , MUM1 − , and EBNA2 + (latency type III), and a Ki67 index of 90%. Fluorescence in situ hybridization in this case revealed unusual aberrant CCND1 expression without any detectable t(11;14)(q13;q32).

RESULTS

Histopathology

- The cases shared similar histologic features, regardless of whether they were in the setting of IS. Hodgkin and R-S cells were scattered in variable numbers among the cases. In the background, the cases showed varying degrees of polymorphic inflammatory infiltrate of lymphocytes, plasma cells, histiocytes, and eosinophils.

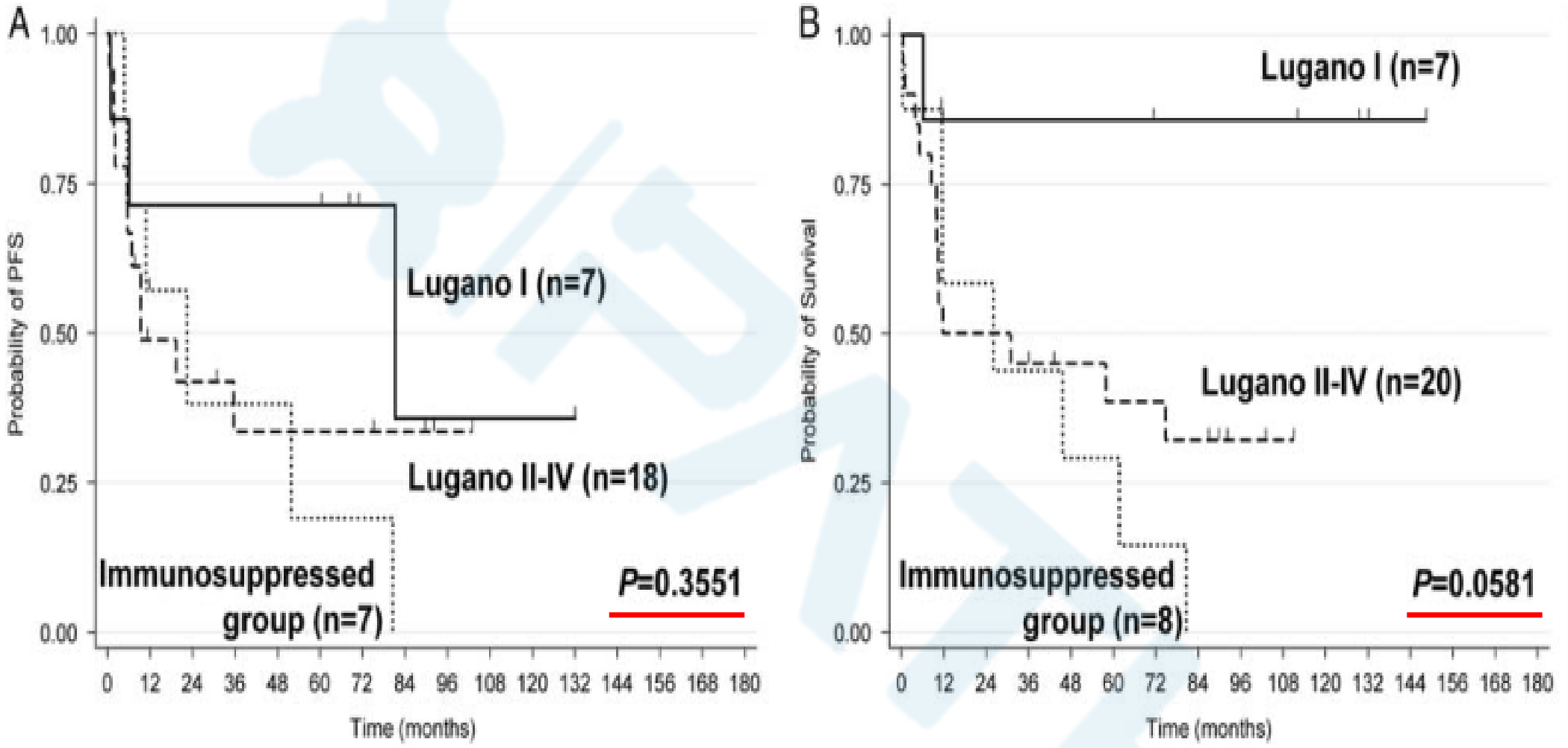


FIGURE 2. PFS (A) and OS (B) according to the immunosuppressed state and Lugano stage classification in patients with EBV$^+$ giDLBCL.

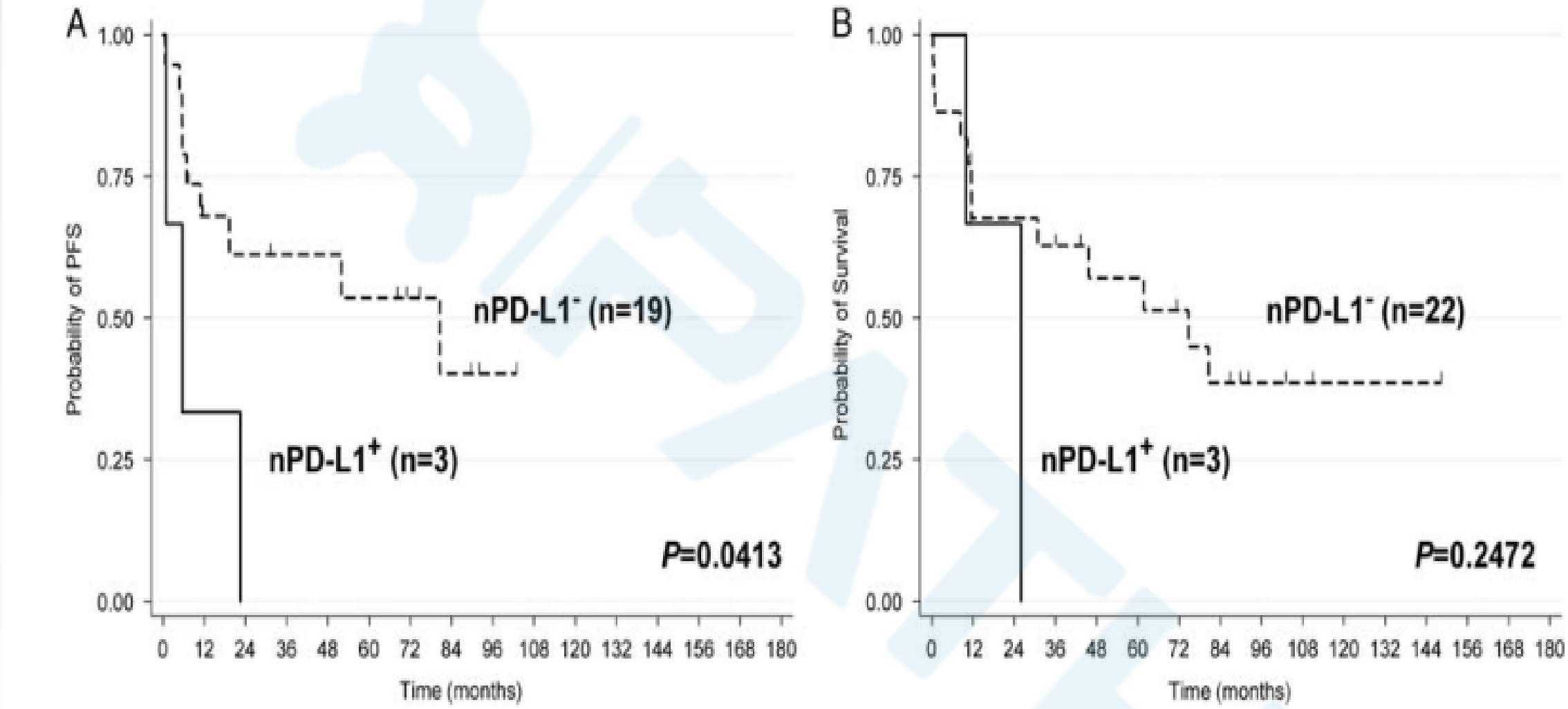


FIGURE 3. PFS (A) and OS (B) according to the PD-L1 expression in patients with EBV$^+$ giDLBCL.

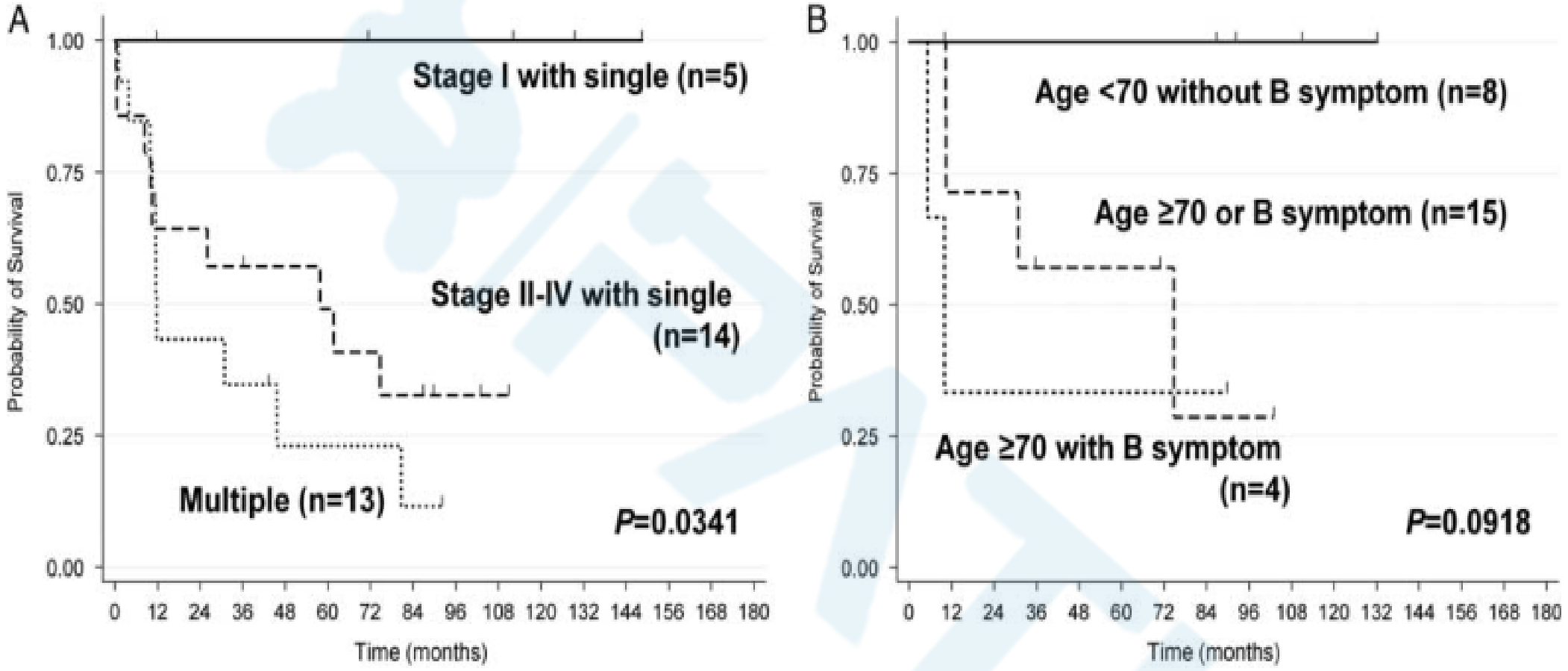


FIGURE 4. A, OS according to the combination of Lugano stage classification and the number of GI lesions in patients with EBV$^+$ giDLBCL. B, OS according to the combination of age and the presence of B symptoms in patients with EBV$^+$ giDLBCL treated with rituximab-containing chemotherapy in nonimmunosuppressed group.

Reassessment with Reference to EBVMCU

- Among the 36 cases in our present series, we identified 5 nonimmunosuppressed stage I cases (14%) that were unique in exhibiting both a localized disease in the stomach and a long-standing favorable prognosis after CR. None of these patients developed lesions at other sites.

- These findings prompted us to compare these 5 cases with previously reported cases of EBVMCU affecting the GI tract. In the English literature, we identified 23 cases of EBVMCU affecting the GI tract (Table 4), of which 20 exhibited pathogenesis associated with iatrogenic immunodeficiency.

Reassessment with Reference to EBVMCU

- Interestingly, these cases often showed local progression—that is, multiple, deeper, and/or larger ulcerations with perforation, as contrasted with the shallow and sharply circumscribed mucosal ulcers more commonly described affecting the oropharynx and skin. Selected cases were treated with chemotherapy including rituximab.

- The 5 nonimmunosuppressed stage I patients in our present study might be considered cases of EBVMCU of the GI tract, based on the observation of favorable outcome regardless of a polypoid appearance.

TABLE 4. Summary of Reported Cases of EBVMCU of the GI Tract

No.	Age (y)	Sex	Ulcer Location(s)	Preceding Disease	Source of IS	Treatment	Outcome	Length of FU (mo)	References
1	69	Female	Colon	RA	AZA	NA	NA	NA	8
2	78	Male	Rectum	UC	CYA	Reduction of IS	CR	23	8
3	75	Female	Esophagus	RA	AZA	Reduction of IS	CR	17	8
4	64	Female	Colon	HSCT (ET, SMD, RISSCT*)	CYA	Reduction of IS	CR	6	8
5	51	Female	Stomach	ATLL	mLSG15	No therapy	CR, but DOC	4	14
6	35	Female	Ileum, colon, rectum	ATLL	mLSG15, CHASE, M, HSCT, T	Reduction of IS	CR	19	14
7	61	Male	Esophagus	SOT (kidney)	MMF, P	Reduction of IS	CR	16	21
8	70	Female	Rectum	SOT (kidney)	MMF, P	Reduction of IS	CR	17	21
9	32	Male	Terminal ileum	SOT (bilateral lung)	MMF, P, T	Reduction of IS, R, V	CR, but DOC	60	21
10	61	Female	Esophagus	Hypogammaglobulinemia	PI	R, IVING, B	PD	<6	22
11	53	Female	Colon, rectum	CD	MTX, infliximab	Reduction of IS	PD (surgery), and HL†	18	23
12	26	Male	Rectum	CD	AZA, infliximab	Reduction of IS	PD (surgery)	12	24
13	64	Female	Ileocecum		Age	Surgery	CR, but DOC	6	25
14	54	Female	Rectum	SOT (kidney)	MMF	Reduction of IS	CR	4	26
15	57	Female	Rectum	IBD	NA	FU	PD	9	27
16	70	Male	Rectum	HIV	HIV	FU	CR	9	27
17	84	Female	Esophagus		Age	FU	CR	6	28
18	34	Male	Colon, rectum	UC	6-MP	Reduction of IS, R	CR	12	29
19	77	Male	Colon	Me, irColitis (ipilimumab [anti-CTLA-4])	P	Surgery	PD	<1	30
20	70	Male	Colon, rectum	Me, irColitis (ipilimumab [anti-CTLA-4])	P	Surgery	CR	>50	30
21	69	Male	Colon, rectum	Me, irColitis (ipilimumab [anti-CTLA-4])	P, infliximab	Surgery	CR	>60	30
22	66	Male	Colon	Me, irColitis (ipilimumab [anti-CTLA-4], nivolumab [anti-PD-1])	P	Surgery	CR	25	30
23	81	Male	Colon	Chronic kidney disease	Age	Surgery	CR	20	31

*ET, SMD, RISSCT, essential thrombocythemia (2000) and secondary myelodysplasia (2007) treated with reduced intensity sibling stem cell transplant (2007 and 2009).

†HL, Hodgkin lymphoma (EBV$^+$) developing in association with IS in IBD, which has been cured with adriamycin, bleomycin, vinblastine, and dacarbazine. Progression to HL (surgery).

ATLL indicates adult T-cell leukemia/lymphoma; AZA, azathioprine; B, brentuximab; CD, Crohn disease; CHASE, cyclophosphamide, etoposide, cytarabine, and dexamethasone; CTLA-4, cytotoxic T-lymphocyte-associated protein 4; CYA, cyclosporin-A; DOC, died of other cause; FU, follow-up; HIV, human immunodeficiency virus; HSCT, hematopoietic stem cell transplantation; IBD, inflammatory bowel disease; iCR, immune checkpoint regulator; irColitis, immune-related colitis; IVING, intravenous immunoglobulin; M, mogalizumab; Me, melanoma; mLSG15, modified LSG 15 chemotherapy; MMF, mycophenolate; 6-MP, 6-mercatopurine; NA, not available; P, prednisolone; methyl-prednisolone; or predomidnisolone; PD, persistent disease; PD-1, programmed cell death protein 1; PI, primary immunodeficiency; R, rituximab; RA, rheumatoid arthritis; SOT, solid organ transplant; T, tacrolimus; UC, ulcerative colitis; V, velcade.

DISCUSSION

- The reinvestigation led to our identification of 1case of EBV + gDLBCL with a single lesion in Lugano stage I, in which the patient exhibited spontaneous regression despite polypoid appearance. Our results from the present retrospective analysis also provided IS-associated cases are restricted to EBV + iDLBCLs.
- We classified our cases into 3 groups. This classification clearly revealed that stage I patients uniformly exhibited gastric lesions without IS, while immunosuppressed patients also exhibited intestinal lesions and advanced stage disease.

DISCUSSION

- We have theorized that cases of stage I EBV + giDLBCL may be classifiable as EBVMCU. Within our present series of 36 cases, 5 (14%) were identified as stage I without bulky mass (ie, small-volume disease), showing an incidence similar to that of EBVMCU (26/200 cases; 13%) originally described by Dojcinov et al.
- Our immunosuppressed cases were all diagnosed as EBV + iDLBCL with advanced clinical stage, which appeared to arise in patients who had a preceding episode of EBVMCU and a tendency to progress to a systemic disease.

CONCLUSION

- Our present results demonstrated that primary EBV + giDLBCL cases could be delineated into 3 groups based on their immune status and clinical stage, revealing distinguishing features that may be useful as a pragmatic guide for diagnostic and therapeutic approaches.

- The tiering system according to the combination of Lugano stage classification and the number of GI lesions was predictive of outcome in EBV+giDLBCL, regardless of affected anatomic sites and IS status.

感谢聆听