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Clinicopathological and genetic analyses of thyroid large B-cell lymphoma in a Japanese population Ayumi Numata,1) Rika Sakai,1) Kae Kawachi,2,3) Yasufumi Ishiyama,1) Yukako Hattori,1) Hirotaka Takasaki,1) Tomoyuki Yokose,2) Naoya Nakamura,4) Hideaki Nakajima5)

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原発性甲状腺リンパ腫のうち大細胞型 B 細胞リンパ腫 (LBCL) は、予後良好であるがその理由は未だ不明である。甲状腺 LBCL の良好な臨床転帰に影響を及ぼす因子を同定するために甲状腺 LBCL 21 例の臨床病理学および免疫組織化学、FISH、MYD88 変異の解析を含む遺伝学的解析を行った、

患者の年齢中央値は 70 歳 (範囲、54-80 歳) であった。5 年全生存率は 83% (95%信頼区間: 56%-94%)。中枢神経系 (CNS) の再発は認められなかった。21 例中 15 例は DLBCL, NOS、残りの 6 例は indolent B-cell lymphoma からの transformation であった。

FISH による解析では、MYC のスプリットシグナルが 2/17 例、BCL6 のスプリットシグナルが 3/15 例に認められた。MALT1 のスプリットシグナルは前例で認められず MYD88 変異は検出されなかった。甲状腺 LBCL における良好な臨床経過の要因は、GCB 表現型の割合が高いこと、DLBCLnos および T-IBCL に MYD88 変異がないことであった。なお MYC-R 症例でさえも予後は良好であった。

甲状腺を含め節外臓器における LBCL の大規模シリーズを含むさらなる研究が、本研究の所見を検証するために必要である。

Table 1. Clinical presentation and outcome of the patients

Case No.	Age	Sex	Clinical Stage	IPI	History of Hashimoto's thyroiditis	pathological diagnosis	Treatment	PFS (y)	OS (y)	Outcome (cause of death)
1	79	M	II	LI	Yes	T-IBCL ^m	ChT with R	1.28	1.28	Alive
2	70	F	II	L	Yes	DLBCLnos	ChT with R	2.06	2.06	Alive
3	59	M	II	L	Yes	DLBCLnos	ChT with R	1.48	1.48	Alive
4	76	F	II	LI	Yes	DLBCLnos	ChT with R	0.29	0.29	Alive
5	59	F	II	L	Yes	DLBCLnos	ChT with R	1.38	1.38	Alive
6	71	M	II	LI	Yes	DLBCLnos	ChT with R	0.05	0.05	Alive
7	54	M	II	HI	Yes	DLBCLnos	ChT with R	1.12	1.12	Alive
8	69	M	II	HI	Yes	DLBCLnos	ChT with R	6.61	6.61	Alive
9	70	F	II	HI	Yes	T-IBCL ^l	ChT with R	3.08	3.08	Died (lung cancer)
10	63	F	II	L	Yes	T-IBCL ^m	refusal of treatment	0.16	0.16	Alive
11	64	F	II	L	No	T-IBCL ^m	ChT without R + RT	10.42	10.42	Alive
12	80	F	II	LI	Yes	DLBCLnos	ChT without R + RT	6.43	6.43	Alive
13	54	F	II	H	No	DLBCLnos	ChT without R	0.38	0.71	Died (PD)
14	80	F	II	HI	Yes	DLBCLnos	ChT without R	0.34	0.40	Alive
15	68	F	II	H	Yes	DLBCLnos	ChT without R + RT	8.81	8.81	Alive
16	72	M	II	HI	No	DLBCLnos	ChT with R	1.32	3.66	Alive
17	71	M	II	L	No	T-IBCL ^m	ChT without R + RT	0.47	0.50	Died (PD)
18	61	F	II	L	No	DLBCLnos	ChT with R	8.15	8.15	Alive
19	71	F	II	HI	Yes	DLBCLnos	ChT with R	4.72	4.72	Alive
20	70	F	II	L	No	T-IBCL ^l	ChT with R	0.51	0.51	Alive
21	67	M	II	L	No	DLBCLnos	ChT with R	0.36	0.36	Alive

Abbreviations: M, male; F, female; IPI, international prognostic index; L, low; LI, low intermediate; HI, high intermediate; H, high; T-IBCL^m, transformations of indolent B-cell lymphomas from MALT lymphomas; T-IBCL^l, transformations of indolent B-cell lymphomas from follicular lymphomas; ChT, chemotherapy; R, rituximab; RT, radiotherapy; PFS, progression free survival; y, years; OS, overall survival; PD, progression disease

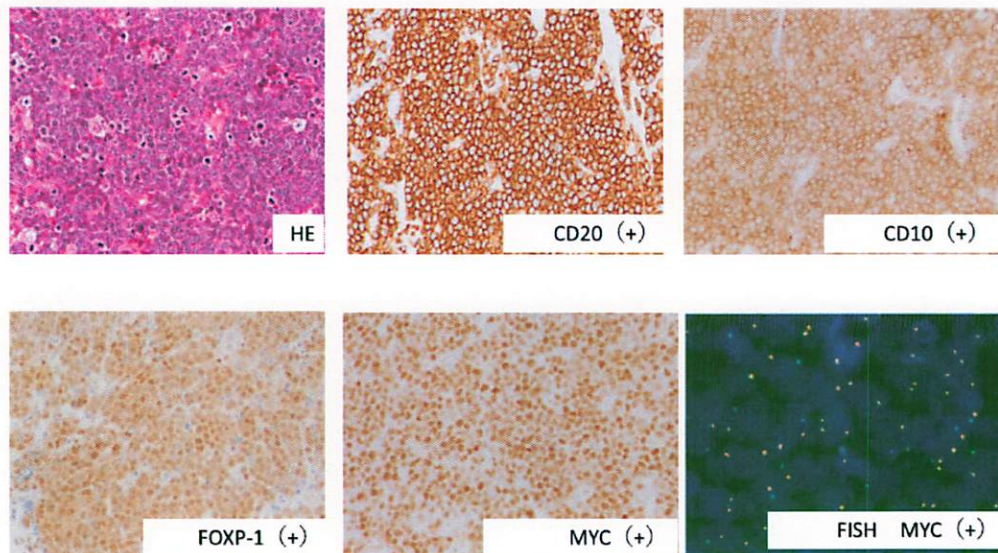


Fig. 1. Immunohistochemical study and FISH study. Immunohistochemical staining using antibodies against CD20, CD10, MYC and FOXP1. Plus and minus signs indicate positive and negative staining, respectively (Case 8). Original magnification, 200 $\times$.

Table 2. Results of immunohistochemical and genomic features

Case No.	pathological diagnosis ⁱ	Immunohistology							Hans classification ^h	FISH				MYD88 gene
		Ki-67 (%) ^a	CD10 ^b	BCL6 ^c	MUM1 ^d	BCL2 ^e	MYC ^f	FOXP1 ^g		MYC rearrangement	MALT1 rearrangement	BCL6 rearrangement	BCL2 rearrangement	
1	T-IBCL ^m	80	+	+	-	+	-	+	GCB	nd	nd	nd	nd	wild type
2	DLBCLnos	80	+	+	-	+	-	-	GCB	-	-	-	-	wild type
3	DLBCLnos	80	+	+	-	+	-	-	GCB	-	-	-	-	wild type
4	DLBCLnos	90	+	-	+	-	-	-	GCB	nd	nd	nd	nd	wild type
5	DLBCLnos	100	+	+	+	+	+	+	GCB	+	-	-	-	wild type
6	DLBCLnos	80	-	-	-	+	+	+	nonGCB	-	-	-	-	wild type
7	DLBCLnos	50	-	+	-	-	-	-	GCB	-	-	-	-	wild type
8	DLBCLnos	80	-	+	+	+	-	+	nonGCB	+	nd	nd	-	wild type
9	T-IBCL ^f	60	+	+	+	+	-	+	GCB	-	-	-	-	wild type
10	T-IBCL ^m	50	-	-	-	-	-	-	nonGCB	nd	nd	nd	nd	wild type
11	T-IBCL ^m	70	-	-	-	+	-	-	nonGCB	nd	nd	nd	nd	wild type
12	DLBCLnos	70	+	+	-	-	-	+	GCB	nd	nd	nd	nd	wild type
13	DLBCLnos	60	+	+	-	-	+	+	GCB	nd	nd	nd	nd	wild type
14	DLBCLnos	40	-	+	+	+	-	-	nonGCB	-	nd	nd	-	wild type
15	DLBCLnos	50	-	-	+	+	-	-	nonGCB	nd	nd	nd	nd	wild type
16	DLBCLnos	70	-	+	-	-	-	-	GCB	nd	nd	nd	nd	wild type
17	T-IBCL ^m	90	-	-	+	-	-	-	nonGCB	nd	nd	nd	nd	wild type
18	DLBCLnos	80	-	+	+	+	+	-	nonGCB	-	-	-	-	wild type
19	DLBCLnos	60	-	+	+	+	-	+	nonGCB	-	-	+	-	wild type
20	T-IBCL ^f	90	+	+	+	+	-	+	GCB	-	-	-	-	wild type
21	DLBCLnos	90	+	+	-	+	-	-	GCB	-	-	+	-	wild type

Abbreviations: T-IBCL^m, transformations of indolent B-cell lymphomas from MALT lymphomas; T-IBCL^f, transformations of indolent B-cell lymphomas from follicular lymphomas; nd, not done;

a Percentage of MIB1 (Ki-67) positive staining cells.

b CD10 expression — cutoff: 30% positive staining cells.

c BCL6 expression — cutoff: 30% positive staining cells.

d MUM1 expression — cutoff: 30% positive staining cells.

e BCL2 expression — cutoff: 30% positive staining cells.

f MYC expression — cutoff: 40% positive staining cells.

g FOXP1 expression — cutoff: 60% positive staining cells.

h Classification according to the immunohistochemical algorithm proposed by Hans et al

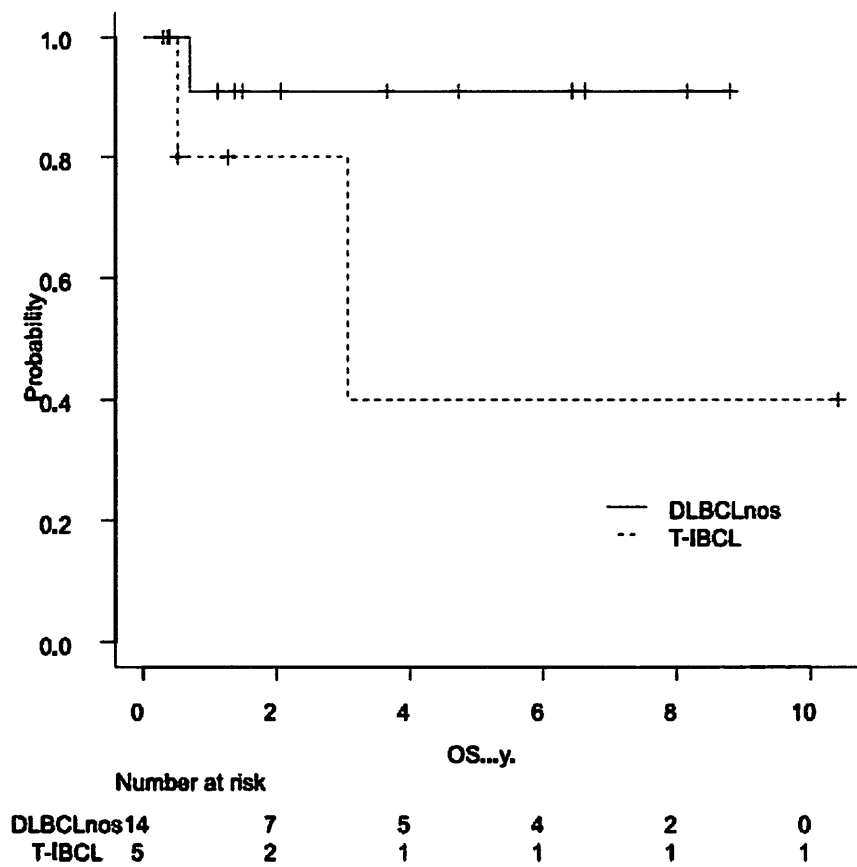


Fig. 2.
Kaplan–Meier analysis of survival fraction in 19 patients showed no statistical difference between DLBCLnos and T-IBCL.