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ARTICLE

Study of Molecular Cytogenetic Abnormalities in Lymphoma and Their Clinical Relevance

Yudi Miao[1] and Qiaojiajie Zhao[2*]

[1]Department of Hematology, Shaanxi Provincial People's Hospital, 256 Youyi West Road, Xi'an City, Shaanxi Province, China

[2]Blood Research Department, Shaanxi Provincial People's Hospital, 256 Youyi West Road, Xi'an City, Shaanxi Province, China

*Corresponding author (E-mail: miaoyudi26@163.com)

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Abstract: Objective: To investigate the issue of molecular cytogenetic abnormalities in lymphoma and to study their clinical relevance. Methods:First, medium-term chromosomes of healthy men and women were prepared. Normal human peripheral blood lymphocytes were stimulated with PHA, treated with MTX synchronization, blocked with colchicine, cultured for 3 days, routinely treated with hypotonicity, cells were obtained, and steam-dried method was used to drop slices for backup. Next, comparative genomic hybridization. Preparation of probes; processing of normal human mid-term split images; hybridization; washing of slices after hybridization; staining; fluorescence microscopy observation, uptake and analysis of fluorescence signals. Results:Lymphoma CGH test results; Relationship between CGH abnormalities and lymphoma histological subtypes: Hodgkin's lymphoma CGH abnormalities, diffuse large B-cell lymphoma (DLBCL) CGH abnormalities, follicular lymphoma (FL) CGH abnormalities, and follicular lymphoma (FL) CGH abnormalities; Correlation between CGH test results and lymphoma clinical features: CGH test results and lymphoma patients, the type of CGH abnormality correlated with the clinical features of lymphoma, simple CGH abnormalities and complex CGH abnormalities correlated with the clinical features of lymphoma patients, and CGH abnormalities at specific chromosomal sites correlated with the clinical features of lymphoma. Conclusion: Conventional model analysis examines both chromosomal translocations and gene deletions or spreads, fails to observe the full picture of the lymphoma genome, and fails to detect new chromosomal abnormalities.

Keywords: lymphoma; molecular cytogenetics; abnormalities; clinical relevance study

Lymphoma is a malignant tumor derived from lymphocytes with complex biological behavior, and clinical classification and treatment are relatively difficult. The complex biological behavior of lymphoma is manifested by molecular cytogenetic abnormalities in lymphoma. According to the study, there are multiple abnormal forms of lymphoma in molecular cytogenetics; according to cytogenetics, it is manifested as both chromosome number abnormalities and chromosome structural mutations; whether it is activated oncogenes or inactivated oncogenes, they are all important manifestations of molecular genetic alterations in lymphoma, and these molecular cytogenetic abnormalities cause lymphocytes to develop differentiation and developmental disorders and eventually These molecular cytogenetic abnormalities cause lymphocytes to develop differentiation disorders and eventually form lymphoma. Therefore, in-depth study of molecular cytogenetic abnormalities in lymphoma can inform the pathogenesis of lymphoma, which provides both diagnosis and classification for clinical purposes, as well as prognosis determination for clinical purposes, and also makes it possible to implement targeted therapy for lymphoma accordingly. In lymphoid tissue, lymphoma is a solid tumor originating from this tissue and occupies an important position among tumors. Because of the biological characteristics of lymphoma cells, the mitotic rate of cells is low when multiple cells are cultured, and the quality of the obtained mid-phase divisions cannot be ensured. Conventional karyotype analysis limits the study of molecular cytogenetic

abnormalities in lymphoma, and it is more difficult to study genetic alterations using this method, both in the process of lymphoma occurrence and in the process of lymphoma development. The method is limited in that only specific genetic alterations can be studied in a single experiment, or alterations in chromosomal regions, and it is not possible to scan the genome over a large area. The method examines both chromosomal translocations and gene deletions or spreads, does not allow the observation of the full picture of the lymphoma genome, and does not allow the detection of new chromosomal abnormalities.

1 Information and methods

1.1 Basic information

From 2018.04 to 2022.04, 40 patients with lymphoma were admitted to our hospital. Among them, the number of male patients was 28 and the number of female patients was 12, with ages ranging from approximately 9 to 70 years old, with an average age of approximately (53.21+2.12) years. According to WHO related criteria, it was possible to clarify both the diagnosis and Ann arbor staging of patients, as well as the presence or absence of systemic symptom grouping and the determination of treatment effects. First treatment:MOPP was used to treat Hodgkin's lymphoma. On the first and eighth days, NH2 6mg/m2 was administered intravenously; on the first and eighth days, VCR 1.4mg/m2 was administered intravenously; on the first to fourteenth days, PCB 100mg/m2 was administered orally; on the first to fourteenth days, PRD 40mg/m2 was administered orally. Hodgkin's lymphoma was treated with CHOP protocol. On day one, intravenous CTX 700mg/m2; on day one, intravenous ADM 40mg/m2; on day one, intravenous VCR 1.4mg/m2; and on days one through five, a dose of PRD 100mg/m2 in a 21-day cycle. For a small number of DLBCL patients, the CHOP regimen was used for treatment, along with treatment with melphalan (450 mg/m2 once a week for a cycle of 4-6 times). Also, peripheral blood was selected from one normal healthy male and one healthy female.

1.2 Methods

First, medium-term chromosomes of healthy men and women were prepared. Normal human peripheral blood lymphocytes were stimulated by PHA, synchronized with MTX, blocked by colchicine, cultured for 3 days, routinely treated with hypotonicity, cells were obtained, and steam-dried method was used to drop slices for spare. Next, comparative genomic hybridization. Prepare the probe; process the normal human mid-term division image; hybridization; wash the film after hybridization; staining; fluorescence microscope observation, uptake and analysis of fluorescence signal.

1.3 Observation indexes

Observe CGH test results of lymphoma; observe the relationship between abnormal CGH and lymphoma histological subtypes: abnormal CGH in Hodgkin's lymphoma, abnormal CGH in diffuse large B-cell lymphoma (DLBCL), abnormal CGH in follicular lymphoma (FL), and abnormal CGH in mantle cell lymphoma (MCL); correlate CGH test results with clinical features of lymphoma: correlate CGH test results with clinical characteristics of lymphoma patients, clinical correlation of CGH abnormal types with lymphoma, clinical correlation of simple CGH abnormalities and complex CGH abnormalities with lymphoma patients, and clinical correlation of CGH abnormalities at specific chromosomal sites with lymphoma.

1.4 Statistical methods

SPSS software was used for statistics, and relevant data processing was done.

2 Results

2.1 Results of CGH testing in lymphoma

Among all lymphoma patients, abnormal CGH was detected in 24 cases, and the positive rate was 60%. From the test results, because of CGH abnormalities, chromosomes 1, 8 and 9 were involved (all 33.33%, 8/24), followed by 6 (25%, 6/24). Among all CGH abnormalities, not only 40 amplified regions but also 24 deletion regions were detected, and the frequency of abnormal amplification was higher than that of deletion. Chromosomal amplified regions were involved in 8q and 18q (10%, 4/40); followed by 9q (5%, 2/40) and 17q (5%, 2/40). The chromosomal deletion regions were 6q (25%, 6/24), 1p (16.67%, 4/24), 8p (16.67%, 4/24), 9q (12.5%, 3/24), and 9p (12.5%, 3/24), respectively.

2.2 Relationship between CGH abnormalities and histological subtypes of lymphoma

2.2.1 CGH abnormalities in Hodgkin's lymphoma. In one patient, the CGH assay was abnormal and occurred on chromosome 15, which was an amplified abnormality. (As shown in Table 1).

Table 1: Hodgkin's lymphoma CGH assay results.

Cases	Gender/Age	Clinical stage	Treatment response	Survival status/follow-up time (months)	Test result(normal)	Test result(deletion)	Test result(gain)
1	F/26	IVA	NR	52			15q12-14
2	F/52	IIB	CR	28	+		
3	F/44	IB	CR	19	+		

2.2.2 Diffuse large B-cell lymphoma (DLBCL) with abnormal CGH.

Among all patients, a total of 20 patients with DLBCL, CGH abnormalities were detected in 12 cases, and the detection rate was 60%. From the CGH test results, CGH abnormalities involved most chromosomes, chromosome 1 (33.33%, 4/12). The amplification site was 18q (10%, 3/30) and the deletion site was 6q (20%, 4/20). (As shown in Table 2)

Table 2: Results of CGH detection in diffuse large B-cell lymphoma.

Cases	Test result(normal)	Test result(deletion)	Test result(gain)
4		+	+
5	+		
6	+		
7	+		
8	+		
9	+		
10		+	+
11		+	+
12		+	+
13		+	+
14		+	+
15		+	+
16		+	+
17		+	+
18		+	+
19			+
20			+
21			+
22			+
23			+
24	+		
25	+		
26	+		
27	+		

2.2.3 Follicular lymphoma (FL) CGH abnormalities. Among the five cases of FL, abnormalities were detected in two cases, located on chromosomes 6 and 8, and these abnormalities did not have common features. (As shown in Table 3)

Table 3: CGH abnormalities in follicular lymphoma (FL).

Cases	Gender/Age	Clinical stage	Treatment response	Survival status/follow-up time (months)	Test result(normal)	Test result(deletion)	Test result(gain)
28	F/40	IA	CR	26	+		
29	F/64	IA	CR	11	+		
30	F/52	IA	CR	13		8q13-22	
31	F/66	IIB	PR	15		6q14-21	6p12-ter
32	M/68	IVA	PR	20	+		

2.2.4 CGH abnormalities in set cell lymphoma (MCL). 2 cases were detected with deleterious CGH abnormalities, located on chromosome 1p, 9q, and 19. (As shown in Table 4)

Table 4: CGH abnormalities in mantle cell lymphoma (MCL).

Cases	Gender/Age	Clinical stage	Treatment response	Survival status/follow-up time (months)	Test result(normal)	Test result(deletion)	Test result(gain)
33	F/60	IA	CR	22		19	
34	F/67	IVB	PR	12		1P12-31, 9q34	

Clinical symptoms		CGH normal	CGH abnormal	P value
Ann arbor staging	I~II/III~IV	10/5	4/18	0.001
Systemic symptoms	Yes/No	2/13	13/9	0.019
Treatment outcome	CR/NR	11/4	3/19	0.003
Extra-nodal involvement	Yes/No	8/7	15/7	0.498
regression	Median survival time (months)	39.6	25.1	0.001

Figure 1: Correlation between CGH test results and clinical characteristics of lymphoma.

CGHabnormaln	Ann arbor staging		Systemic symptoms		Treatment outcome		Extra-nodal involvement		Median survival (months)
	I~II	III~IV	Yes	No	CR	NR	Involved	Not involved	
Chromosome deletion 8	3	5	5	3	4	4	3	5	33.7
Chromosome amplification 9	2	7	6	3	1	8	8	1	35.2
Deletion+Amplification 9	2	7	5	4	2	7	8	1	8.9
P	>0.05		>0.05		>0.05		>0.05		

Figure 2: Clinical correlation between abnormal types of CGH and lymphoma.

CGH abnormal n	Ann arbor staging		Systemic symptoms		Treatment outcome		Extra-nodal involvement		Median survival (months)
	I~II	III~IV	Yes	No	CR	NR	Involved	Not involved	
Simple anomaly 14	4	10	6	8	3	11	7	7	37.5
Complex anomaly 12	1	11	8	4	2	10	11	1	9.1
P	0.58		0.082		0.58		0.067		0.006

Figure 3: Clinical correlation between simple abnormalities of CGH and complex abnormalities of CGH and lymphoma patients.

2.3 Correlation between CGH test results and clinical characteristics of lymphoma

2.3.1 Correlation between CGH test results and clinical characteristics of lymphoma patients. (As shown in Figure 1).

2.3.2 CGH abnormality type and lymphoma clinical correlation. (As shown in Figure 2)

2.3.3 Clinical correlation between simple abnormalities of CGH and complex abnormalities of CGH and patients with lymphoma. (As shown in Figure 3)

2.3.4 Clinical correlation of CGH abnormalities at specific chromosomal sites with lymphoma. (As shown in Figure 4)

3 Discussion

With the gradual improvement of people's living standards, various dietary irregularities or wrong dietary methods, or environmental pollution and food contamination have led to an increase in lymphoma. In order to treat lymphoma, prior knowledge of their CGH test results, the relationship between abnormal CGH and lymphoma histological subtypes, and the correlation between CGH test results and clinical features of lymphoma should be obtained. This information will enable the health care provider to exercise a practical treatment plan for the patient and facilitate proper treatment as well as early recovery. If the patient has certain problems, the health care provider can also identify the cause of the problem and adjust the status for the patient according to the clinical characteristics; if the patient has an adverse reaction, the health care provider will also identify the cause and provide a treatment plan for the patient according to the patient's reaction. It can be seen that no matter what state the patient is in or what problems occur, the medical and nursing staff can provide or adjust practical treatment plans for the patient according to the specific situation, which makes the patient's treatment smoother and the effect is naturally more remarkable. From the results of CGH testing for lymphoma, among all lymphoma patients, abnormal CGH was detected in 24 cases, with a positive rate of 60%. From the test results, because of CGH abnormalities, chromosomes 1, 8 and 9 were involved (all 33.33%, 8/24), followed by 6

CGH abnormal	Case	Gender/Age	Pathological diagnosis	Clinical staging	Treatment response	Survival status/follow-up time (months)
6q-	17	F/18	DLBCL	IVBSE	NR	10(Death)
	4	M/56	DLBCL	IVBE	NR	59
	10	M/29	DLBCL	IVA	NR	9(Death)
	11	M/49	DLBCL	IVBE	CR	9(Death)
	12	F/76	DLBCL	IVBSE	NR	8(Death)
	31	F/67	FL	IA	CR	22
8P-	14	F/27	DLBCL	IVAS	NR	4(Death)
	15	M/68	DLBCL	IAE	CR	18
	16	F/66	DLBCL	IVBSE	NR	6(Death)
	1	F/31	PTL	IVBE	NR	3(Death)
18q+	18	F/30	DLBCL	IVBS	NR	10(Death)
	19	F/26	DLBCL	IVAS	NR	4(Death)
	20	M/49	DLBCL	IVBE	CR	9(Death)
	21	F/74	DLBCL	IVBSE	NR	6(Death)

Figure 4: Clinical correlation between CGH abnormalities at specific chromosomal sites and lymphoma.

(25%, 6/24). Among all CGH abnormalities, not only 40 amplified regions but also 24 deletion regions were detected, and the frequency of abnormal amplification was higher than that of deletion. Chromosomal amplified regions were involved in 8q and 18q (10%, 4/40); followed by 9q (5%, 2/40) and 17q (5%, 2/40). The chromosomal deletion regions were 6q (25%, 6/24), 1p (16.67%, 4/24), 8p (16.67%, 4/24), 9q (12.5%, 3/24), and 9p (12.5%, 3/24), respectively. Implementing different treatment plans for patients according to their different clinical characteristics can lead to not only proper treatment, but also rapid treatment and rapid turnaround of patients, which in turn can lead to the eradication or remission of malignant tumors. Through the clinical characteristics of patients with different malignant tumors, treatment is carried out according to the grade to promote proper treatment on the one hand, and to promote remission on the other hand, which is conducive to the further work of medical and nursing staff. Generally speaking, patients in the low-risk group are relatively easy to treat and the treatment methods adopted are relatively simple, and they can recover quickly; patients in the high-risk group are relatively complicated to treat and the treatment methods adopted are relatively complex, and the treatment process takes more time and the patients recover relatively slowly. Therefore, in order to promote early recovery or alleviate the condition of patients, we should understand the clinical characteristics of patients, and provide patients with practical treatment plans according to all clinical characteristics of patients, so as to promote patients to better accept surgical treatment and avoid postoperative infection, which may affect postoperative recovery or even lead to death. At the same time, the clinical experience will be summarized, the clinical treatment effect of patients will be analyzed, and the clinical experience will be summarized and effective clinical experience will be promoted to make positive contribution to the treatment and research in this field. In terms of the relationship between CGH abnormalities and histological subtypes of lymphoma, firstly, Hodgkin's lymphoma CGH abnormalities. Among them, one patient had an abnormal CGH test, which occurred on chromosome 15 and was an amplified abnormality; secondly, diffuse large B-cell lymphoma (DLBCL) had abnormal CGH. Among all patients, there were 20 patients with DLBCL and 12 cases were detected with abnormal CGH, with a detection rate of 60%. From the CGH test results, CGH abnormalities involved most chromosomes, chromosome 1 (33.33%, 4/12). The amplification site was 18q (10%, 3/30) and the deletion site was 6q (20%, 4/20); furthermore, follicular lymphoma (FL) had CGH abnormalities. Among the 5 cases of FL, abnormalities were detected in 2 cases, located on chromosomes 6 and 8,

and these abnormalities did not share common features; finally, CGH abnormalities in follicular lymphoma (MCL). deleterious CGH abnormalities were detected in 2 cases, located on chromosomes 1p, 9q, and 19. It can be seen from the relationship between the two that regardless of the above four lymphomas, the presence of CGH abnormalities is also an important reason for the formation of malignant tumors, and if they cannot be controlled, the patient's organism will gradually deteriorate. From the correlation between CGH test results and clinical characteristics of lymphoma, firstly, CGH test results are correlated with clinical characteristics of lymphoma patients; secondly, the type of CGH abnormality is clinically correlated with lymphoma; furthermore, simple CGH abnormalities and complex CGH abnormalities are clinically correlated with lymphoma patients; finally, CGH abnormalities in specific chromosomal sites are clinically correlated with lymphoma. It can be seen that there is a direct relationship between CGH abnormalities leading to clinical features in lymphoma patients and the reason why lymphoma patients develop the disease. In conclusion, regarding the molecular cytogenetic abnormalities in lymphoma and their clinical correlation, it is important to understand both the CGH test results in lymphoma, the relationship between CGH abnormalities and histological subtypes of lymphoma, and the correlation between CGH test results and clinical features of lymphoma. After understanding these aspects, patients can be treated properly, and relevant experiences as well as drawbacks can be summarized to adopt effective treatment plans accordingly and to provide patients with proven clinical experience to facilitate patients to reduce pain while receiving treatment, recover as soon as possible after receiving treatment, avoid risks as much as possible, and provide patients with better opportunities and conditions for recovery.

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The authors declare no conflict of interest.

References

[1] Shi Pei-Qin,Wang W-T,Zhu X-T,et al. Molecular cytogenetic abnormal correlation in multiple myeloma[J]. *Journal of Modern Laboratory Medicine*, 2014,(5):77-80.

[2] Guan W,Jing Y,Yu L. Prognostic value of molecular genetic and epigenetic abnormalities in T-lymphoblastic lymphoma/leukemia[J]. *Chinese Journal of Experimental Hematology*, 2017,25(2):587-591.

[3] Yang YN. Research progress of gene mutation detection in normal-nucleated acute myeloid leukemia in adults[J]. *Leukemia-Lymphoma*, 2012,21(2):122-125.

[4] Su Miao. Progress in the study of microRNAs in acute leukemia with genetic abnormalities[J]. *Leukemia-Lymphoma*, 2014,23(10):632-635.

[5] Wang Dongmei,Fan Lei,Fang Cheng,et al.Cytogenetic study of 18 cases of condylomatous lymphoma[J]. *Chinese Journal of Medical Genetics*. 2011,(3).283-286.

[6] Cao X, Fan L, Fang C, et al. Expression studies of SOX11, cyclin D1, cyclin D2 and cyclin D3 in B lymphoproliferative disorders[J]. *International Journal of Blood Transfusion and Hematology*. 2011,(1).4-9.

[7] Zhao F. Correlation of morphological and subpopulation characteristics of peripheral blood lymphocytes with the diagnosis of non-Hodgkin's lymphoma[D]. Hebei North College, 2020.

[8] Chen Zhaogun. Clinical characteristics and survival of patients with set cell lymphoma[J]. *Huaihai Medicine*. 2020,(2).

[9] Hong Y,Yuan L,Yuan HF. A case of maternal cell type condylomatous lymphoma involving the lacrimal gland[J]. *Journal of Aerospace Medicine*. 2018,(11).

[10] Lin Ling. A study on the clinicopathological characteristics associated with treatment strategies and prognosis of patients with paired cell lymphoma [D]. Tianjin Medical University, 2017.

[11] Yin Xue,Gu Kansheng.Retrospective analysis of clinical characteristics and prognosis of 50 cases of condyloma lymphoma[J]. *Anhui medicine*. 2017,(6).1010-1015.

[12] Dong Ru-Nan,Zhou Shu-Ya,Lu Ying-Juan. Clinical characteristics and prognostic survival analysis of patients with paired cell lymphoma[J]. *PLA Journal of Preventive Medicine*. 2017,(5).467-470.

[13] Zhang XL. Exploration on the clinicopathological characteristics of condylomatous lymphoma [J]. *Imaging research and medical applications*. 2017,(12).216-218.

[14] Liang Rong,Wang Zhe,Zhu Mina,et al.Analysis of clinical characteristics and prognosis-related factors in 23 patients with condylomatous lymphoma[J]. *Chinese Journal of Hematology*. 2016,(6).491-496.

[15] Chen JJ,Chen JJ. Comparison of the application of citric acid and EDTA on cyclinD1 and TdT antigen repair[J]. *Anhui Med*. 2015,(10).1901-1904.

[16] Xiao X.B.,Zhong K.L.,Zhao S.H.,et al. Clinical characteristics and efficacy observation of 15 cases of paired cell lymphoma[J]. *Military Medicine*. 2015,(11).859-862.