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THE DETECTION OF CD56 AND EPSTEIN-BARR VIRUS IN T-CELL LYMPHOMAS*

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Objective: To study the relationship between EBV infection and the expression of CD56 in T-cell lymphomas (TCLs). Methods: 46 cases of TCLs and 15 cases of reactive hyperplasia of lymphonodes (RHs) were detected CD56 by immunohistochemistry and EBERs by *in situ* hybridization. Results: 8 cases of 46 TCLs (17.4%) showed CD56-positive. On sites, CD56 positive rate of nasopharyngeal TCLs was highest (5/17, 29.4%), and on subtypes, that of DLs was highest (6/16, 37.5%). Additionally, 4 RHs were also CD56-positive. Of 46 TCLs, 24 showed expression of EBERs. There were only 4 TCLs expressing both CD56 and EBERs. Conclusion: The expression of CD56 was not especially for TCLs that EBV infected. EBV infection was not related with CD56-positive TCLs. The findings also suggested the expression of CD56 in TCLs be possibly related to original sites and subtypes of TCLs.

Key words: T-cell lymphoma, Epstein-Barr virus, CD56.

Recently, the importance of EBV in TCL pathogenesis was noticed more and more.[1] Further, it has been discovered that TCLs with EBV infection often express an especial immunotype, CD2+CD3-CD56+,[2] and EBV infection in TCLs was thought being closed to CD56 expression.

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MATERIALS AND METHODS

Case Selection

All cases were collected from Department of Pathology, Sun Yat-Sen University of Medical Sciences from 1990 to 1997. 46 cases of TCLs selected, including 13 lymphonodal cases, and 33 extranodal samples (17 cases of nasopharyngeal, 8 cases of gastrointestimal tract and 8 cases of other sites). Additionally, 15 cases of RHs were chosen as the control group.

Immunohistochemical Study

The process of immunohistochemistry detecting CD56 (MONOSAN MON9006) on paraffin sections was based on labeled Streptacidin-Biotin Peroxidase (LSAB). Especially, the sections were disposed with microwave 13 minutes and placed in 4 refrigerator one night after adding the first antibody. The CD56-positive lymphoma was used as a positive control (Provided by MONOSAN).

In Situ Hybridization

Detection of EBV small RNAs by *in situ* hybridization using EBER oligonucleotides was performed on formalin-fixed parffin-embedded sections. Briefly, the Dako hybridization kit was used with a cocktail of fluorescein isothiocyanate (FITC)-labeled EBER oligonucleotides (DAKO, Y0017) hybridization products were detected using a monoclonal anti-FITC

(DAKO, KOO46). B95-8 cells were used as a positive control.

RESULTS

Histopathological Type

Fouty-six cases of TCLs were divided based on Working Formulation: 6 cases of the lymphoblastic (LB), 1 cases of the immunoblastic (IBL), 15 cases of the diffuse large lymphocytic (DL), 22 cases of diffuse middle lymphocytic (DM), 2 cases of small lymphocytic (SL). 46 cases were testified by immunohistochemistry as TCLs (Figure 1).

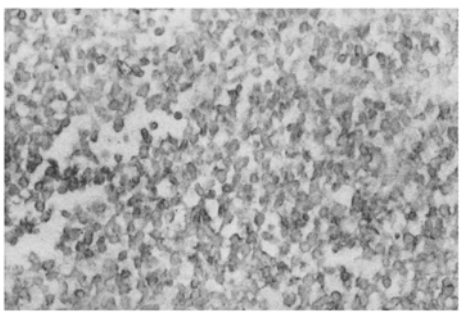

Fig. 1. The lymphoma immunoreacting with T-lineage associated UCHL1 (yellow-brown ×100)

Expression of CD56

Positive immunostaining for CD56 was observed on embrance (Figure 2). CD56 was detected in 8 cases of 46 TCLs, 4 cases of RHs, there was no significant difference statistically ($P>0.05$). On sites, 8 cases of 33 extranodal TCLs were CD56-positive (24.2%), while all cases of 13 nodal TCLs were CD56-negative. Among extranodal TCLs, 5 cases were nasopharyngeal TCLs (5/17, 29.5%), 2 gastrointestinal TCLs (2/8, 25%), 1 other site (1/8, 12.5%). On types, 6 CD56-positive cases were DLs (6/15, 40%), and the other 2 cases were DM and SL respectively. There was no CD56 expression in any cases of 6 LBs and 1 IBL.

Expression of EBERs

Positive signal for EBERs was observed in nuclear (Figure 3). It was found in 24 cases of TCLs, while all RHs were EBERs-negative ($P<0.05$). Among EBERs-positive TCLs, 3 cases were the lymphonodal (3/13, 23%), 21 cases were the extranodal (21/33, 63.6%).

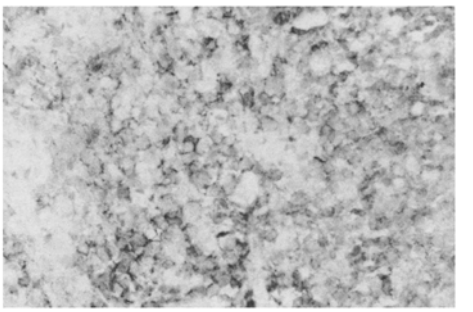

Fig. 2. The T-cell lymphoma immunocreating with CD56 (yellow-brown ×100)

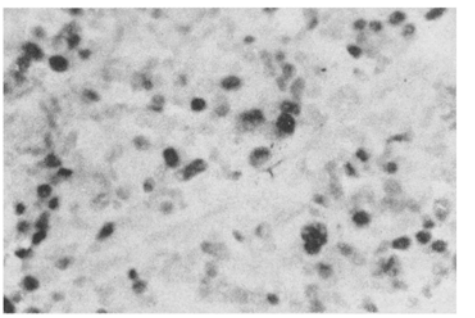

Fig. 3. In situ hybridization for Epstain-Barr virus RNA in a T-cell lymphoma showing diffuse nuclear staining (blue-purple ×200)

The Relationship between CD56 and EBERs

There was much difference between expression of CD56 and EBERs in TCLs (Table 1). Only four cases expressed CD56 and EBERs commonly, suggesting that CD56-positive TCLs were not associated with the EBV infection ($P>0.05$).

Table 1. The expression of EBERs and CD56

EBERs	CD56		Total
	–	+	
+	20	4	24
–	18	4	22
Total	38	8	46

DISCUSSION

It was reported that the pathologenesis of TCLs, especially the extranodal TCLs was testified having some relationship with EBV infection.[3] In our study, EBERs-positive rate was 52.2% (24/46) totally, 63.6% (21/33) extranodally. It confirmed that EBV infection may playing an important role in pathogenesis of TCLs.

CD56 is an isoform of neural cell adhesion molecule (NCAM), which is expressed on essentially all human NK cells and on a subset of T lymphocytes and IL-2-actived thymocytes that mediate MHC-unrestricted cytotoxicity.[4] Like NCAM in neural and muscle tissues, CD56 on NK cells does contribute to NK cell binding when the target cells express CD56, and the binding is homotypic, i.e., CD56 on NK cells binds to CD56 on target cells.[5]

Recently, some author reported that EBV infection in extranodal TCLs is related to CD56 expression. Tsang WY considered that lymphomas with CD56-positive expression, irrespective of the site of involvement (but always extranodal), show 100% association with EBV, the strongest association among the various lymphoma types.[6] But in our study, CD56 expression was highly inconsistent with EBV infection. 8 cases of CD56-positive TCLs, only 4 cases expressed EBERs, and 20 cases of EBERs-positive TCLs were CD56-negative. Additionally, there were also 4 RHs CD56-positive while EBERs-negative. Conclusively, we considered expression of CD56 is not special, and they may be no relationship between CD56 and EBV infection. The reason why our conclusion is different with those authors abroad need to be researched continually.

In the other hand, it was found that expression of CD56 is related with site and type of TCLs. On sites, CD56-positive rate of nasopharngeal TCLs was highest. On types, that of DLs was the highest.

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