Aggressive B-cell Lymphomas of the Respiratory System: Histologic, Immunohistochemical and Genetic Evaluation of a Large Series

Yalda Naieni[1], Annie Wu[1], Dennis P. O'Malley[2,3]

1. UCLA Medical Center, Los Angeles, CA 2. NeoGenomics/Clarient, Aliso Viejo, CA 3. MD Anderson Cancer Center, Houston, TX

Abstract

Background
Diffuse large B-cell lymphoma and related entities are the commonest type of non-Hodgkin lymphomas. However primary involvement of respiratory system by aggressive B-cell lymphoma (ABL) is extremely uncommon, diagnostically challenging and poorly studied.
Design
760 consult cases that were diagnosed as ABL including Burkitt lymphoma (BL), B-cell lymphoma unclassifiable, including double hit lymphomas (DHL), and diffuse large B-cell lymphoma (DLBCL) were evaluated using an extensive panel of immunohistochemical stains (CD20, CD3, CD5, CD10, Cyclin D1, BCL6, BCL2, EBER, Ki-67, CD30) and a panel of FISH studies (including MYC, IgH/BCL2 and BCL6). Forty-four (5%) cases were identified in the respiratory tract; 43% were located in nasopharynx.
Results
The majority of cases were DLBCL (37/44; 84%), with two cases of BL (4%), three lymphomatoid granulomatosis (6%), one DHL (2%) and one plasmablastic lymphoma (2%) identified. *MYC* translocation was only identified in BL and DHL. Compared to a large group of lymphoma in other organs, respiratory tract lymphomas were more often positive for EBV (25% vs. 8%) and were of non-germinal center origin (~67%) by both Hans and tally classifiers (compared to 60% germinal center origin in other organs).
Conclusion
Our series shows that aggressive lymphomas in respiratory tract show heterogeneity of immunophenotype and genetics. Also the cell of origin in respiratory tract lymphoma differs from the large group of lymphoma in other organs (33% GC vs 60% GC).

Background

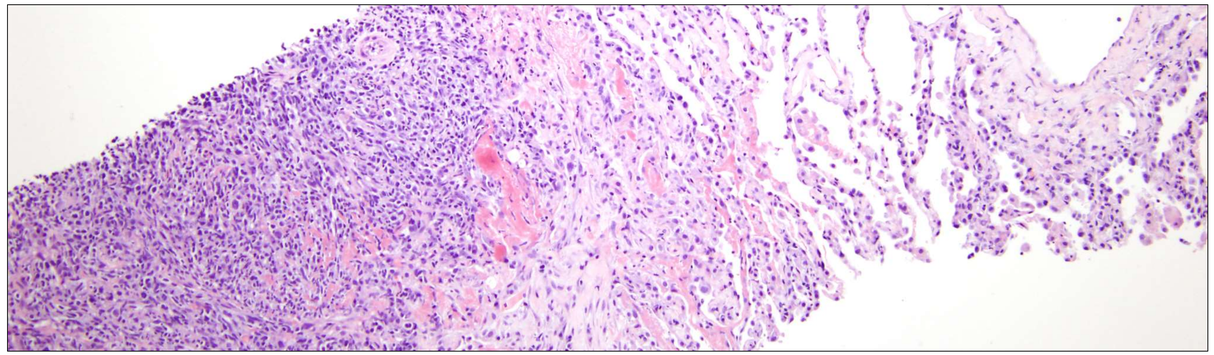
Diffuse large B-cell lymphoma and related entities are the commonest type of non-Hodgkin lymphomas. However primary involvement of respiratory system by aggressive B-cell lymphoma (ABL) is extremely uncommon, diagnostically challenging and poorly studied.

Many large studies have shown variation in immunohistochemical and genetic features of aggressive B cell lymphomas. The presence of a variety of immunohistochemical, genetic and clinical features have an impact on prognosis of these patients. Additional insight into prognosis and pathobiology of DLBCL will continue by using additional methods to subclassify cases. The goal of this study is to review a large number of cases of DLBCL and other aggressive B cell lymphomas using a relatively uniform immunohistochemical panel and genetic methods. We assessed the frequency of different locations, compared them to respiratory origin as well as documenting the distinctive immunophenotypic and genetic findings of subgroups of these cases.

Materials & Methods

Cases were consultations sent to Clarient Pathology Services/Neogenomics (Aliso Viejo, CA). All cases were reviewed and diagnosed by DPO. The diagnoses were made in accordance with the 2008 WHO classification for hematopoietic and lymphoid tumors using a combination of immunohistochemical, genetic and other studies, as appropriate, to establish the diagnosis. All research was performed in accordance with local standards for ethical research. The tissues were evaluated using both standard hematoxylin and eosin (H&E) staining and immunohistochemistry. Immunohistochemical stains were performed on a variety of platforms from Ventana (Tucson, AZ), Leica BioSystems (Buffalo Grove, IL), and Dako (Carpenteria, CA) using standard methodologies.

Most cases were evaluated using an extensive panel of immunohistochemical stains including CD20, CD3, CD5, CD10, Cyclin D1, BCL2, BCL6, Ki67, and CD30. In situ staining for Epstein-Barr virus (EBV) early RNA (EBER) was performed on a significant subset of cases using standard methods. A subset of cases was further evaluated with immunohistochemical stains MUM1, GCET1, LMO2, FOXP1, and MYC. Fluorescence in situ hybridization (FISH) studies were performed in a subset of cases using standard methods (Abbott Molecular; Des Plaines, IL).



Results

The majority of cases were DLBCL (37/44; 84%). The remainder included: two cases of Burkitt lymphoma (4%), three cases of lymphomatoid granulomatosis (6%), one DHL (2%) and one plasmablastic lymphoma (2%).
MYC translocation was only identified in BL and DHL.
Compared to a large group of lymphoma in other organs, respiratory tract lymphomas were more often positive for EBV (25% vs. 8%).
They were mainly of non-germinal center origin (~67%) by both Hans and tally classifiers (compared to 60% germinal center origin in other organs).

	DLBCL	BL	PBL	DHL	LYG
Number of cases	37	2	1	1	3
CD10	7/32	2/2	0/1	1/1	0/3
BCL2	31/36	0/2	0/1	1/1	0/2
BCL6	28/36	2/2	0/1	0/1	0/1
MUM1	21/32	0/2	1/1	-	2/2
CD30	4/21	0/1	-	-	2/3
Hans classifier	GC 11 NGC 21	GC 2 NGC 0	GC 0 NGC 1	GC 1 NGC 0	GC 0 NGC 3
Tally classifier	GC 5 NGC 14	- -	- -	- -	- -
MYC translocation	0/18	2/2	0/1	1/1	-
IgH/BCL2 translocation	3/18	0/2	0/1	1/1	-
BCL6 translocation	5/18	0/2	0/1	0/1	-

Discussion

- Aggressive lymphomas in respiratory tract show heterogeneity of immunophenotype and genetics.
- The majority of cases were DLBCL (37/44; 84%).
- The cell of origin in respiratory tract lymphoma differs from the large group of lymphoma in other organs (33% GC vs 60% GC). All cases of LYG were of non-GCB origin.
- Respiratory tract lymphomas were more often positive for EBV (25%) compared to a large group of lymphoma in other organs.(8%)
- Respiratory lymphomas showed MYC translocation in 14% of cases

References

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