Aggressive B-cell Lymphoma in Extreme Age Groups; Review of a Series of 760 Cases

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Abstract

Background
Diffuse large B-cell lymphoma (DLBCL) and related entities are the commonest type of non-Hodgkin lymphomas. Lymphomas of the extreme ages are relatively rare and with only few studies. In this study, we focus on aggressive B-cell lymphomas (ABL) in patient's younger than 30 and older than 90 years old.
Design
We analyzed a cohort of 760 consult cases that were diagnosed as ABL. They 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). 28 cases (3%) of patients were less than 30 years old (<30) and 20 cases (2%) were patients older than 90 years (>90) were evaluated further.
Results
Majority of cases were DLBCL [57% (16/28) of <30, and 90% (18/20) of >90 group], followed by Burkitt lymphoma [21% (6/28) of <30, and 10% (2/20) of >90 group]. Almost all cases were CD20 positive (93% of <30, 100% of >90). Most cases were extranodal (71% in <30, 60% in >90). EBER stain was performed on most cases and was only positive in 20% of <30 group. C-MYC expression was higher in <30 group (~92%) compared to 55% in >90 group. Available FISH study results show 21% MYC rearrangement in both groups, however BCL2 and BCL6 rearrangements (e.g. double hit lymphomas) were seen more frequently in >90 group (38% and 21% respectively). 54% (<30) and 27% (>90) of the cases showed CD30 positivity. Based on Hans and tally classification, majority of cases were germinal center in <30 group, comparing to non-germinal center in >90.
Conclusion
Our series shows that aggressive lymphomas are rare in patients younger than 30 and older than 90 years old. They show immunophenotype and genetics differences from the population >30 and <90 years.

Background

Diffuse large B cell lymphoma and related entities are the commonest type of non-Hodgkin lymphomas. Lymphomas of the extreme ages are relatively rare and with only few studies. In this study, we focus on aggressive B-cell lymphomas (ABL) in patient's younger than 30 and older than 90 years old.

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 and compared the immunophenotypic and genetic findings of different age groups, and found distinctive features in patents in <30 and >90 years old group.

Materials & Methods

Cases were consultation cases 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 [57% (16/28) of <30, and 90% (18/20) of >90 group]. Burkitt lymphoma was the second most common subtype of lymphoma in these age groups [21% (6/28) of <30, and 10% (2/20) of >90 group].

Almost all cases were CD20 positive (93% of <30, 100% of >90). Most cases were extranodal (71% in <30, 60% in >90).

EBER staining was performed on most cases and was only positive in 20% of <30 group. C-MYC expression was higher in <30 group (~92%) compared to 55% in >90 group. Available FISH study results show 21% MYC rearrangement in both groups.

Lymphomas with combined BCL2 and BCL6 rearrangements were seen more frequently in >90 group (38%) compared to the <30 group (21%). 54% of cases <30 and 27% of cases >90 showed CD30 positivity.

Based on Hans and tally classification, the majority of cases were germinal center type in <30 group, compared to non-germinal center in >90.

	Age <30	Age >90	Overall age groups
Number of cases	28	20	760
CD10	13/22 (59%)	10/19 (52%)	300/760 (39%)
BCL2	17/25 (68%)	15/19 (78%)	556/708(78%)
BCL6	22/25 (88%)	18/18 (100%)	625/725 (86%)
MUM1	17/25 (68%)	10/19 (52%)	373/652 (57%)
CD30	7/13 (53%)	3/11 (27%)	95/402 (23%)
Hans classifier	GC 9 NGC 7	GC 12 NGC 7	- -
Tally classifier	GC 2 NGC 4	GC 4 NGC 8	- -
MYC translocation	5/19 (26%)	4/15 (26%)	94/491 (19%)
IgH/BCL2 translocation	1/19 (5%)	5/13 (38%)	103/492 (20%)
BCL6 translocation	3/16 (18%)	3/14 (21%)	118/483 (24%)

Discussion

- Majority of cases were DLBCL (57% of <30, and 90% of >90 group)
- Most cases were extranodal (71% in <30, 60% in >90).
- EBV positivity was seen in 20% of <30 group compare to the large group of lymphoma in all ages (8%).
- MYC expression was higher in <30 group (~92%) compared to 55% in >90 group and 19% in large group of lymphoma in all ages.
- 54% of cases <30 and 27% of cases >90 showed CD30 positivity, as oppose to 23% in large lymphoma group.
- Combined BCL2 and BCL6 rearrangements were seen more frequently in >90 group compared to the <30 and all age groups (38%, 21% and 24% respectively).
- Based on Hans and tally classification, majority of cases were germinal center in <30 group, comparing to non-germinal center in >90.
- Both <30 (59%) and >90 (52%) groups showed more CD10 positivity than the large group of lymphomas (39%).
- The immunophenotype in all groups showed similar expression for BCL2 and MUM1.

References

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