Immunohistochemical (IHC) expression of epigenetic regulators (EZH-2 and H3K27) as well as cell cycle regulators (P16, P53 and RB) in patients diagnosed with primary Diffuse Large B-Cell Lymphoma (DLBCL) and association with therapy response rates and survival

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Background

- Diffuse large B cell lymphoma (DLBCL) is the most common lymphoma worldwide, accounting for about 30% of all non-Hodgkin lymphomas.
- Despite many advances the overall survival rate of DLBCL is only 50% with current chemotherapies.
- Apart from genetics, epigenetics also has major role in pathogenesis of many malignancies, including DLBCL.
- In recent years, the role of polycomb receptor complex (PRC) in DLBCL is in major focus.
- Genomic studies have revealed that Enhancer of zeste homolog 2 (EZH2) is the catalytic subunit of PRC involved in malignant transformation.
- In this study, we compare the cell cycle regulators with expression of epigenetic regulators EZH2 and H3K27 expression in DLBCL.

Objectives

- To evaluate IHC expression of epigenetic regulators and cell cycle regulators in DLBCL, NOS and correlate with cell of origin (GCB type and non-GCB type), therapy response and patient survival.
- To compare the cell cycle regulators with expression of epigenetic regulators EZH2 and H3K27 expression in DLBCL.

Materials and Methods

STUDY DESIGN:

- A retrospective study of patients diagnosed with primary DLBCL, NOS in 2014-2015 who were followed-up till April 2022.
- DLBCL was classified by Han's Algorithm and IHC for EZH-2, H3K27, P16, P53, RB was done & scored semi-quantitatively.
- Various clinical parameters at baseline as well as treatment modalities given were also noted.

STUDY SETTING:

- Study conducted at a Tertiary Referral Cancer Care Centre on patients visiting the out-patient department (OPD).

PATIENTS:

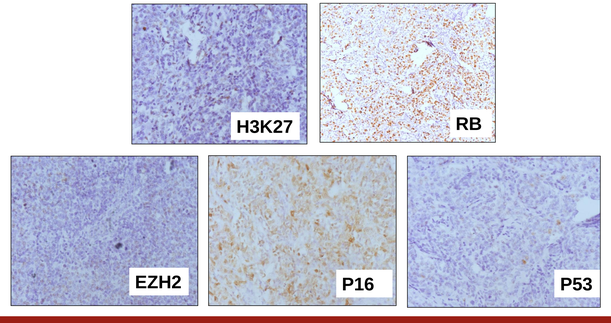
- Patients were selected continuously from the out-patient records of the Department of Medical Oncology during 2014-2015.
- 37 patients were included, out of which follow-up data was available for 21 patients.

MAIN OUTCOME MEASURES:

- Association between IHC expression and various clinical parameters as well as correlation with cell of origin, therapy response and patient survival.

Results

- Out of 37 patients, 62.16% were males with male to female ratio of 1.64.
- Age (48.6±14.1) ranged from 22-78 years. 15/37(40.5%) patients were diagnosed as DLBCL-GCB type.
- 18/37(48.6%) patients presented with at least one of the B-symptoms.
- 20/37(54%) patients presented at higher stage of disease (3 or 4), while, 17/37(46%) had extra-nodal involvement.
- Derived neutrophil-lymphocyte ratio (dNLR) was ≥ 2.2 in 13/37(35%) patients.
- Association of H3K27 with RB(p=0.024) and EZH-2 with P53(p=0.001) was found to be statistically significant.



Results (contd.)

- No other significant association was found between the various markers as well as with the cell of origin.
- However, association of H3K27 with response rate (RR)(p=0.012) and EZH-2 with RR(p=0.028) was found to be statistically significant.

Conclusions

- EZH-2 pathway has been described in GCB type of DLBCL.
- Though IHC expression contributed to a statistically significant difference in RR, the expression was not limited to GCB subtype as defined by Han's Algorithm.
- Therefore, further larger studies are required for validation of IHC based expression.

References

1. Strong expression of EZH2 and accumulation of trimethylated H3K27 in diffuse large B-cell lymphoma independent of cell of origin and EZH2 codon 641 mutation, Leukemia & Lymphoma
2. EZH2 Is Required for Germinal Center Formation and Somatic EZH2 Mutations Promote Lymphoid Transformation, Cancer Cell
3. EZH2 mutations are frequent and represent an early event in follicular lymphoma, Blood

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