Expression and Clinical Relevance of Programmed Cell Death-1 and Programmed Cell Death Ligands in Extranodal Natural Killer/T Cell Lymphoma

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Background: Programmed cell death-1 (PD-1)/Programmed cell death-ligands (PD-Ls) signal plays a vital role in regulating T-cell response. Several cancers aberrantly express PD-1/PD-Ls, leading to immunologic escape of tumor. Data on PD-1/PD-Ls in lymphoma are limitedly described in Hodgkin lymphoma. Extranodal Natural Killer/T cell lymphoma (ENKTL) is a relatively more common subtype in Asia. There is a lack of PD-1/PD-Ls data in ENKTL. Assessment of PD-1/PD-Ls expression in ENKTL is clinically relevant as a predictor for prognosis and treatment response.

Objective: To characterize PD-1/PD-Ls expression and its association with clinical characteristics and prognosis of ENKTL.

Methods: We included 39 ENKTLs diagnosed at King Chulalongkorn Memorial Hospital between 2008 and 2017. Immunohistochemical staining was performed to identify PD-1/PD-Ls expression within lymphoma and stromal cells. The 5% cutoff was adopted for positivity. Clinical, pathological data and outcome were reported.

Results: Of 39 cases, there was a high prevalence of PD-L1 and PD-L2 expression within lymphoma cells (27 cases; 69.2% and 29 cases; 74.4%) with median expression of 15% and 10%, respectively. Expression of PD-L1 and PD-L2 were noted on stroma of 32 (82.0%) and 0 (0%) patients. Median stromal PD-L1 expression was 5%. PD-1 positivity within stroma was seen in 8 cases (20.5%) with median positive cells of 5%. Whereas, there was no PD-1 expression within lymphoma cells. There was no difference in clinical features between positive and negative PD-1/PD-Ls expression, except higher proportion of impaired performance status among cases with negative PD-L1 within lymphoma cells (P=0.03). Positive PD-Ls expression within tumor cells was not associated with different EFS (2-year EFS 45.1 vs 54.7%; P=0.50 for PD-L1 and 42.8 vs 60%; P=0.31 for PD-L2) or OS (2-year OS 48.4 vs 74.1%; P=0.29 for PD-L1 and 51.7 vs 70%; P=0.36 for PD-L2). Neither PD-Ls nor PD-1 expression within tumor cells was associated with outcome, yet patients with positive stromal PD-1 had a trend towards inferior EFS (P=0.08). (Figure 1)

Conclusion: In ENKTL, PD-Ls are frequently expressed within lymphoma cells. Whilst, PD-1 and PD-Ls are variably expressed within stroma. Our study shows no association between PD-1/PD-Ls expression and outcome. However, there is a trend towards worse EFS in patients with positive stromal PD-1. Further studies are warranted to explore significance of PD-1/PD-Ls expression in ENKTL.

Keywords: Extranodal Natural Killer/T cell Lymphoma, Programmed cell Death-1, Programmed cell Death Ligands
Figure 1: Kaplan-Meier survival curves of ENKTL as stratified by PD-1/PDL1 expression within lymphoma and non-tumor stromal cells.