BACKGROUND: PCNS-DLBCL is a rare subgroup of DLBCL occurring in the brain, eyes, meninges or spinal cord without system involvement. Recently, c-myc gene translocation and MYC protein expression have been found in PCNS-DLBCL while their effect on outcomes was unknown. It is well known that PCNS-DLBCL mostly occurs in Immunodeficient patients and associates closely with EBV infection. However, it seems that EBV associates less closely with PCNS-DLBCL in immunocompetent patients and the influence on survival is not clear.

HYPOTHESIS: We detected MYC protein expression and EBV infection in 24 Chinese PCNS-DLBCL patients and tried to find the relationship between these two elements and survival.

METHODS: IHC for BCL-2, BCL-6, CD10, MUM-1 and MYC, ISH for the EBV-RNA (1/2 EBER) were performed for 24 PCNS-DLBCL cases, detection for aberration of c-myc, Bcl-6 and Bcl-2 genes by FISH was applied for 6 cases with enough tissues. Information for clinical test, treatment and survival was collected. Relationship between these variables and outcome was analyzed by univariate survival analysis and multiple COX hazard regression analysis.

RESULTS: Twenty four patients were all immunocompetent. The male to female ratio was 1:1. The median age was 61 years old. Six cases had multiple lesions and 5 cases were affected in deep brain regions. BCL-2, BCL-6, CD10 and MUM-1 expressed in 79.2%, 66.7%, 8.3% and 91.7% cases respectively, MYC highly expressed (≥40%) in 16.70% cases. Three cases (12.50%) with multiple lesions were positive for EBER. Gene aberrations were found in 4 cases: 2 cases showed increased copy number (ICN) of c-myc gene, one showed coexistence of ICN of c-myc gene and Bcl-2 gene break apart, one harbored amplification of Bcl-6 gene. Protein in CSF and LDH in serum were found elevated in 11 and 8 cases respectively. Two patients showed high ECOG scores (> 1). All patients underwent totally or partially tumor resection. Five patients received merely whole brain radiotherapy (WBRT) after surgery as supplement treatment, 7 patients received combination of WBRT and high–dose methotrexate (HD-MTX) based chemotherapy as consolidation, 5 received HD-MTX based chemotherapy without WBRT. Six cases received no therapy after surgery. Detailed treatment information was unreached for 1 cases because of losing follow-up. Two case received rituxmab. The follow-up intervals ranged from 1 to 90 months, with a median interval of 8 months. The two-year survival was 28.61% and average survival time was 13.97±2.07 months. Univarite survival analysis indicated that deep brain region affection (p=0.019), multiple lesion (p=0.022) and high MYC expression (p=0.005) were associated with poor survival, while BCL-6 expression (p=0.019) and High-Dose MTX based chemotherapy (p=0.001) were favorable for survival. Multiple COX hazards regression analysis found that CSF protein elevation (95% Hazard Ratio CI: 3.11~162.88), high MYC expression (95% Hazard Ratio CI: 13.43~ 8488.16), EBV infection (95% Hazard Ratio CI: 2.04 ~1473.28) were adverse for survival, however High-Dose MTX based chemotherapy was (95% Hazard Ratio CI:0.031 ~0.504) advantageous for outcome. EBV infection associated with multiple lesion (p=0.005), while MYC expression had no relationship with ICN of c-myc gene (p=0.600).