Identification of novel recurrent ETV6-IgH fusions in primary central nervous system lymphoma

Titre	Identification of novel recurrent ETV6-IgH fusions in primary central nervous system lymphoma
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Résumé en anglais	Background: Primary central nervous system lymphoma (PCNSL) represents a particular entity within non-Hodgkin lymphomas and is associated with poor outcome. The present study addresses the potential clinical relevance of chimeric transcripts in PCNSL discovered by using RNA sequencing (RNA-seq). Methods: Seventy-two immunocompetent and newly diagnosed PCNSL cases were included in the present study. Among them, 6 were analyzed by RNA-seq to detect new potential fusion transcripts. We confirmed the results in the remaining 66 PCNSL. The gene fusion was validated by fluorescence in situ hybridization (FISH) using formalin-fixed paraffin-embedded (FFPE) samples. We assessed the biological and clinical impact of one new gene fusion. Results: We identified a novel recurrent gene fusion, E26 transformation-specific translocation variant 6-immunoglobulin heavy chain (ETV6-IgH). Overall, ETV6-IgH was found in 13 out of 72 PCNSL (18%). No fusion conserved an intact functional domain of ETV6, and ETV6 was significantly underexpressed at gene level, suggesting an ETV6 haploinsufficiency mechanism. The presence of the gene fusion was also validated by FISH in FFPE samples. Finally, PCNSL samples harboring ETV6-IgH showed a better prognosis in multivariate analysis, P = 0.03, hazard ratio = 0.33, 95% CI = 0.12-0.88. The overall survival at 5 years was 69% for PCNSL harboring ETV6-IgH versus 29% for samples without this gene fusion. Conclusions: ETV6-IgH is a new potential surrogate marker of PCNSL with favorable prognosis with ETV6 haploinsufficiency as a possible mechanism. The potential clinical impact of ETV6-IgH should be validated in larger prospective studies.
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