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Telomeres Length and Wnt/beta-catenin Pathway in Adamantinomatous Craniopharyngiomas

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Objectives: To evaluate how telomeres length behaves in adamantinomtous craniopharyngioma (aCP) and if it contributes to the pathogenesis of aCPs with and without CTNNB1 mutations. Design: Retrospective cross-sectional study enrolling 42 aCPpatients from two tertiary institutions. **Methods:** Clinicopathological features were retrieved from patient's charts. Fresh frozen tumors were used for RNA and DNA analyses. Telomere length was evaluated by qPCR (T/S ratio). Somatic mutations in TERT promoter (TERTp) and CTNNB1 were detected by Sanger and/or whole-exome sequencing. We performed RNA-Seq to identify differentially expressed genes in aCPs presenting with shorter or longer telomere lengths. **Results:** Mutations in CTNNB1 were detected in 29 (69%) tumors. There was higher frequency of CTNNB1mutations in aCPs from patients diagnosed under the age of 15 years (85% vs 15%; p=0. 04) and a trend to recurrent disease (76% vs 24%; p=0.1). No mutation was detected in the TERTp region. The telomeres were shorter in CTNNB1-mutated aCPs (0.441, IQR: 0.297-0.597 vs 0.607, IQR: 0.445-0.778; p=0. 04) but it was neither associated with clinicopathological features nor with recurrence. RNAseq identified a total of 387 differentially expressed genes, generating two clusters, being one enriched for short telomere and CTNNB1-mutated aCPs. **Conclusions:** CTNNB1 mutations are more frequent in children and adolescents and appear to associate with progressive disease. CTNNB1-mutated aCPs have shorter telomeres. This is the first evidence for a relationship between the Wnt/beta-catenin pathway and telomere biology in the pathogenesis of aCPs.

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