



Trabalhos Científicos

Título: Sonic Hedgehog Pathway Is Up-regulated In Adamantinomatous Craniopharyngiomas (acp)

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Resumo: Objectives: To evaluate the expression pattern of SHH pathway genes in ACP. Patients and Methods: Fourteen ACP patients (8 children; 57% male; median age 15.5 yrs) were analyzed. Pituitary hormone deficiency and beta-catenin mutations were found in 86% and 50% of these cases, respectively. The mRNA expression levels of SHH pathway genes (SHH, PTCH, SMO, GLI1, GLI2, GLI3, SUFU and ZIC2) evaluated by qPCR. SMO, GLI1, GLI3 and SUFU protein expression evaluated by immunohistochemistry (IHC). Seven normal pituitaries tissues used as controls. Results: Compared to normal pituitaries, ACP presented higher mRNA levels of SHH (fold: 4.6x10³; p<0.01) and GLI1 (fold: 1.2x10³; p<0.001) and GLI3 mRNA levels (fold: 17; p<0.001). Interestingly, ACP GLI2 mRNA expression level was not different from normal pituitaries (fold: 2.6; p=0.09). PTCH, SMO, ZIC2 and SUFU ACP mRNA levels were similar to normal pituitaries. Moreover, compared to beta-catenin WT, beta-catenin mutated ACPs presented higher expression of GLI1 (fold: 32; p=0.04) and SMO (fold: 5; p=0.03). There was no association between abnormal ACP SHH pathway genes expression and age at diagnosis or disease progression, suggesting that SHH pathway abnormalities may occur at an early stage of tumor formation. SMO, GLI1, GLI3 and SUFU immunostaining was found in 90%, 80%, 92% and 67% of the ACP evaluated. IHC showed that normal pituitaries (4 adults; 3 children) presented focal and weak expression of SMO, GLI1, GLI3 and SUFU. Conclusions: SHH pathway is up-regulated in human ACP and may play an important role in the pathogenesis of these tumors.