Introduction

- CDKN1B (p27) underexpression and Ribosomal proteins (RP) have been related to the pathogenesis of pituitary adenomas (1, 2).
- In gastric cancer, RPS13 down-regulates p27 and promotes cell cycle progression (3); these mechanisms have not yet been explored in pituitary adenomas.

Objective

- To evaluate the relationship between RPS13 and CDKN1B, CDK2, CCNE1, MYC gene expression in pituitary tumorigenesis and its association to clinical findings.

Methods

We studied four groups: corticotrophinomas (n=12), somatotrophinomas (n=18), non-functioning pituitary adenomas (NFPA, n=21), and normal pituitaries (NP, n=07). Clinical and pathological data of tumors are shown in table 1, 2 and 3. RNA was isolated by TRIzol method. Gene expression was assessed by qRT-PCR. Kruskal-Wallis test was used for continuous variables between groups and Fisher Exact test for categorical data.

Results

We observed CDKN1B underexpression (fold=2.0) in somatotrophinomas compared to NP (p=0.03), CCNE1 overexpression (fold=2.0) in NFPA versus NP (p=0.02) and MYC underexpression (fold=10.0) in NFPA compared to corticotrophinomas (p=0.002). No differential gene expression among the groups were observed in RPS13 (p=0.1) and CDK2 (p=0.07) (table 4; figure 1).

In corticotrophinomas: no association between gene expression and tumor size, remission or immunohistochemistry (IHC).

In somatotrophinomas: no relationship between gene expression and tumor size, visual field, IGF-1 levels, basal and post-oGTT GH levels, IHC, post-surgery remission and disease control. Tumors with higher CDKN1B expression tended to achieve control with somatostatin agonist (p=0.08).

In NFPA: higher CDK2 expression was associated to null cell subtype (p=0.03) with a tendency to correlate with tumor size (p=0.08). Higher CCNE1 expression was associated with remission (p=0.02).

Conclusion

The p27-CDK2-CCNE1 pathway seems dysregulated in pituitary adenomas and may interact with other aberrant pathways, leading to an environment that may have putative role in pituitary tumorigenesis. Overexpression of RPS13, however, does not seem to be the underlying mechanism.

References