Introduction

In sporadic acromegaly, downregulation of AIP protein of the adenomas associates with invasive tumour features and reduced response to somatostatin analogue treatment. AIP is a regulator of Gαi signaling, but it is not known how the biological function of the Gαi pathway is controlled.

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To study somatic GNAS and AIP mutation status, AIP and Gαi₂ protein expressions, Ki67 proliferation indices, and clinical parameters in patients having primary surgery because of acromegaly at a single centre between years 2000-2010. We demonstrate, for the first time, that AIP protein expression associates with Gαi₂-2 proteins in sporadic somatotropinomas. The upper panel shows a diffuse cytoplasmic AIP immunoreaction intensity. The deleted region is colored red in the WT sequence.

Results

Sixty patients (F/M 31/29, mean age 49 (median 50), mean follow-up 7.7 (range 0.6-14.0) yrs) underwent primary surgery. Of the 60 adenoma specimens, four (6.8%) harboured an AIP and 21 (35%) an activating GNAS (Gsp⁺) mutation. All adenomas stained positive for Gαi₂, and 55/56 AIP mutation negative adenomas stained positive for AIP protein. Altogether 13/56 (23%) adenomas had negative adenomas stained positive for AIP. The majority (43%) was associated with lower KNOSP grade (p=0.006 **). The deleted region is colored red in the WT sequence. Table 3 shows a diffuse cytoplasmic AIP immunoreaction intensity and the lower Gαi₂ immunoreaction intensity.

Conclusions

We demonstrate, for the first time, that AIP protein expression associates with Gαi₂ protein intensities in sporadic somatotropinomas. This may indicate a synergetic effect on somatostatin signaling. Low AIP protein levels associate with higher proliferative activity and higher postoperative serum GH, indicating more aggressive adenomas. The AIP mutation rate of 6.8% is fairly high and probably reflects the genetic composition of the Finnish population.