Background:

Treatment with growth hormone (GH) receptor antagonist, pegvisomant, results in improvement in clinical and biochemical symptoms of acromegaly but experience with this drug in pituitary gigantism is limited. We present results of pegvisomant therapy in two girls with invasive GH pituitary macroadenomas.

Case 1:

A somatotroph pituitary macroadenoma was diagnosed in a 8-year-old girl with progressive tall stature (height: 148 cm, >3 SD; growth velocity (GV): 11 cm/year), GH hypersecretion without suppression during oral glucose loading (serum GH nadir: 34 mU/l), high serum IGF-I (691 ng/ml) and high serum prolactin (270 mU/l) levels. Bone age was 10 years without onset of puberty (Tanner stage P2S1). Pituitary MRI showed an invasive pituitary macroadenoma [1]. Transphenoidal surgical tumour removal was incomplete. Histological examination showed a mixed GH and prolactin-secreting adenoma. Serum IGF1 and GH levels remained high after surgery (GH serum nadir during oral glucose loading: 5 mU/l, IGF1: 908 ng/ml) and after cabergoline treatment (10.6 mU/l, 590 ng/ml).

Pegvisomant 10mg/d in combination with cabergoline quickly led to IGF1 normalization (180, 115, 208 and 80 ng/ml after respectively 1, 4, 7 and 10-months treatment) and growth arrest (GV: 0 cm/7 months, 2 cm/12 months) [2].

Case 2:

A 15-year-old girl presented with clinical and biochemical evidences of acromegaly: tall stature (182 cm, >3 SD, no GV available), pubertal stage IV, bone age 13 years, high IGF1 and GH serum levels (776 ng/ml, 109 mU/l). Pituitary MRI revealed a large and invasive mass [3]. An AIP mutation was found. She was treated with a combination of oestrogen -to accelerate epiphyseal fusion-, somatostatin analogs and pegvisomant titrated up to 40 mg/day. Medical treatment failed to normalize IGF1 and stop growth (GV: 2 cm/6 months) but major weight gain was noticed (+14 kg/6 months). Therefore tumour was partially resected by a trans-sphenoidal surgical approach. Histological characterization confirmed the diagnosis of GH-secreting adenoma. Pegvisomant adjuvant therapy 40mg/d was resumed to improve IGF-I serum level control (IGF1 571 ng/ml after surgery, 447 after 3-months post-surgery treatment, 221 and 204 ng/ml respectively by month 5 and 8) and stop physical growth (0 cm/7 months) [4].

Conclusion:

In childhood acromegaly, pegvisomant appears to be effective in stunting growth and normalizing IGF-I but only after pituitary tumor debulking.