The clinical and genetic characteristics of patients with gigantism


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**Objective:**
To analyse a large series of patients with gigantism.

**Design:**
A multicentre retrospective study.

**Patients:**
The gigantism was considered in patients with current/previous abnormal, progressive, excessively rapid growth velocity for age and/or a height greater than 2 SD above normal for their population and/or absolute height more than 200 cm or greatly (−75 cm) in excess of the calculated midparental height in the absence of constitutional tall stature. 184 patients were included. Data of patients systematically collected in centres was recorded in case report forms.

**Results:**
In most of cases gigantism was due to GH-overproduction by pituitary adenomas (PA) (92%), in 1.8% by pituitary hyperplasia, in 1 case because of ectopic GHRH secretion. In 3% radiographic findings showed no evidence of PA or hyperplasia. 2.7% had Klinefelter's syndrome. Males/Females ratio was 49/35. 26% of patients were taller than 200cm (max 250cm). Median age of rapid growth velocity was 12yr. 151 patients stopped growing at age of 20yr. [18;22] with the height 194.5cm [184;200]. Median height of 27 still growing patients was 191cm [171;199]. The first symptoms developed at age of 15 yr [11;19]. 93% had facial changes and/or acral overgrowth at time of diagnosis. Age at diagnosis PA in females were younger than in males (16.5yr vs 23yr) with delay in diagnosis of PA of 5 yr. Most of PA were macroadenomas (84%, even giant PA in 13%) and in 12% microadenomas with maximal tumor size of 25 mm [14.5;37]. In more than half of cases there was extrasellar extension (77%) and invasion (54%) of the tumor. Pituitary hyperplasia observed in 4%. 145 patients were operated with the remission after 1st operation in 14% and 0% in those who were reoperated (26pts). Multimodal treatment approach was in 40%. Median follow on treatment was 7yrs. [2;16]. Overall control of the disease was achieved in 43%. Hypopituitarism increased in frequency from 24% at baseline to 69% at last follow-up. Genetic features presented in 34% (17 FIPA, 2 AIPmut familial cases, 10 AIPmut sporadic/simplex cases, 6 McCune-Albright, 3 Carney complex, 1 case of familial pituitary diffuse hyperplasia). Germline mutations in AIP gene were found in 43.6% (24/55).

**Conclusion:**
In most of cases gigantism was due to PA, which are mostly large (with extrasellar extension and invasion in more than half of cases) and difficult to control. Syndromic features are presented in 1/3 of cases and AIP mutations are common in gigantism.