Final height in a boy with McCune-Albright syndrome and precocious puberty treated with ketoconazole, cyproterone acetate and leuprolide acetate depot for more than 5 years

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Background
McCune-Albright syndrome (MAS) is a sporadic and rare disorder, clinically defined by the classic triad of café-au-lait skin lesions, polyostotic fibrous dysplasia and peripheral precocious puberty. Precocious puberty is common in girls, but has been reported in only 15% of affected boys. Clinical trials on therapeutic management of precocious puberty in MAS boys are limited to case reports or small patient cohorts and no data are reported about final height.

Objective
To describe the results in term of final height of a therapeutic combination ketoconazole-cyproterone acetate-leuprolide depot, a regimen that has never been experienced so far.

Case report
A 4.6-year-old boy presented to our clinic owing to a painless enlargement of right testis (10 ml). On physical examination no other signs of precocious puberty were noticed and left testis volume was 3 ml and penis size was infantile (4.5 x 1.2 cm). Patient’s height was 119.2 cm (+ 2.6 SDS) vs a target height of 181.2 cm (+ 1.2 SDS), weight was 19.2 kg (+ 0.8 SDS) and bone age 5.5 years. Endocrinological assessment excluded a central precocious puberty and an adrenal disorders. An atypical form of MAS was suspected and confirmed by molecular analysis (classic mutation R201C of GNAS1 gene). During the subsequent 2 years right testis volume, testosterone and free testosterone serum levels, growth velocity and bone maturation progressively increased. At the age of 6.6 years, a combined treatment with both ketoconazole (400 mg/daily in 2 divided doses) and cyproterone acetate (50 mg/daily), aiming at both suppressing testicular steroidogenesis and inhibiting the peripheral effects of testosterone was started and at 8.8 years an LHRH analogue was added to prevent central precocious puberty. The complex pharmacological scheme was definitely stopped at a chronological age of 13.6 and resulted in a final height of 188.5 cm (+ 1.6 SDS).

Conclusions
To the best of our knowledge, this is the first report in the literature in which a MAS boy with both peripheral and central PP has been treated with a complex pharmacological regimen up to final height. His excellent auxological outcome suggests that a combination of cyproterone acetate, ketoconazole and LHRH analogue may be effective in controlling both the peripheral and the central PP in MAS male patients, allowing the attainment of a final height in the normal range and very close to target height.