

McCune-Albright syndrome: clinical and genetic study in a large cohort of pediatric patients

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Objectives:

McCune-Albright-Syndrome (MAS) is an extremely rare multisystem disorder that affects bones (fibrous dysplasia), skin (cafe-au-lait spots) and endocrine organs (hyperfunctioning endocrinopathies) and is caused by somatic mutations in *GNAS* gene. We describe a large cohort of pediatric patients with MAS.

Methods:

Patients: 44 girls (F) and 11 boys (M).

Screening for components of MAS: physical examination; blood tests to reveal endocrine disorders; head CT, bone scintigraphy, ultrasound of the thyroid and gonads, MRI of the pituitary.

Mutation analysis: CAST-PCR and NGS for *GNAS* mutations in peripheral leukocytes of 39 MAS patients.

Results:

Figure 1. First clinical manifestations

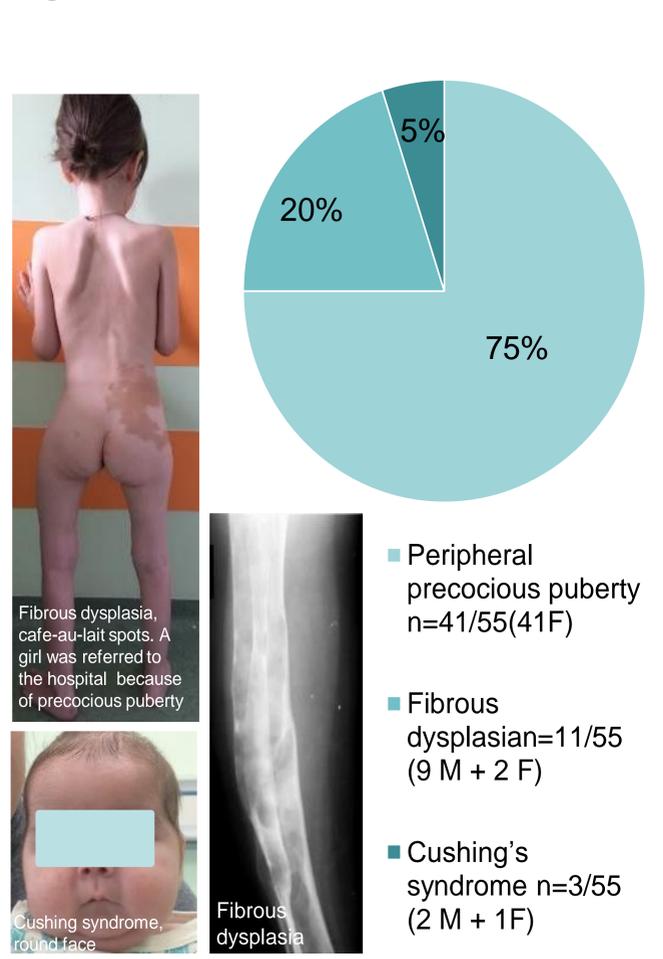


Figure 2. Spectrum and frequency of MAS components (n=55, 44 F + 11M)

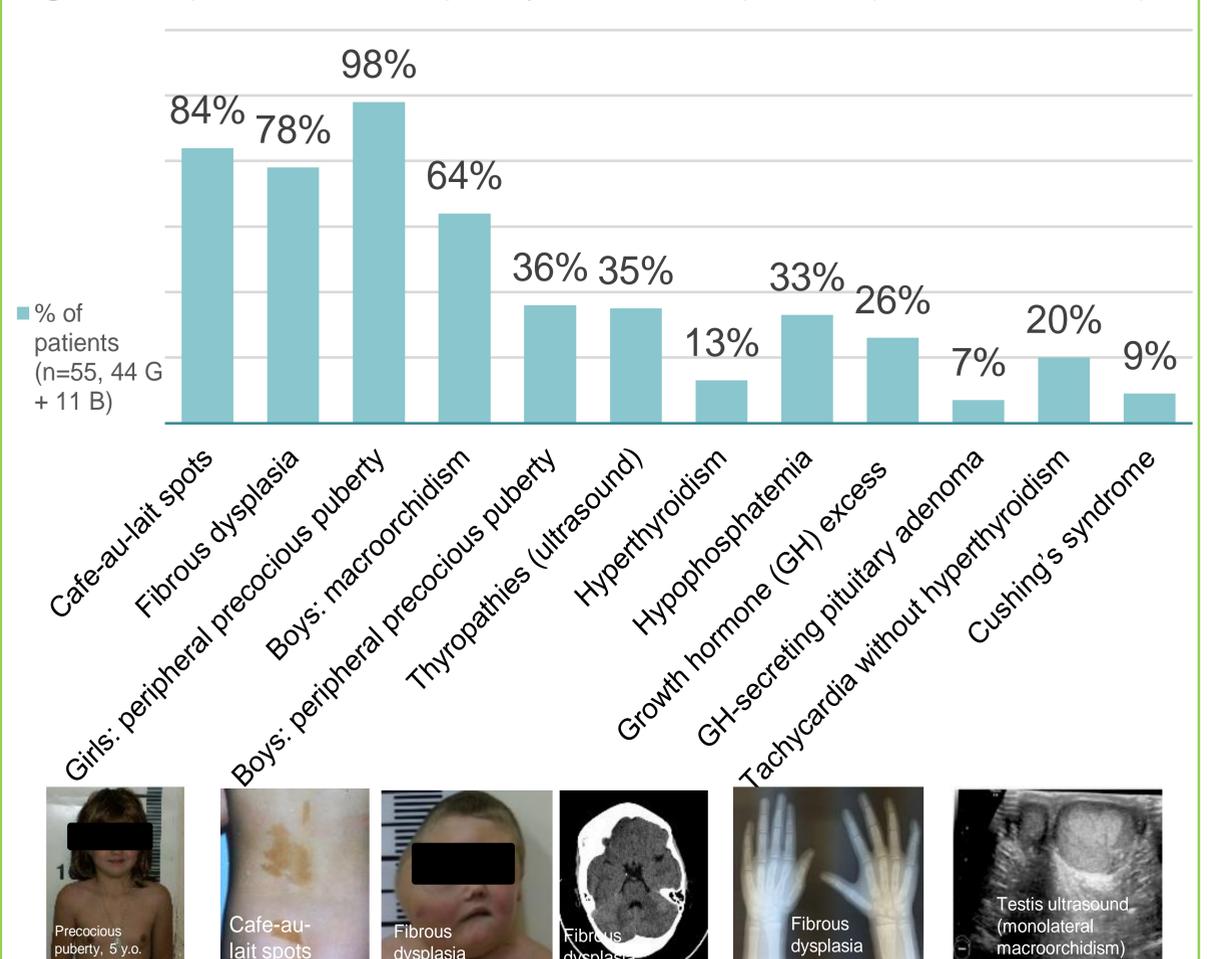


Figure 3. Age of component's manifestation (n=55)

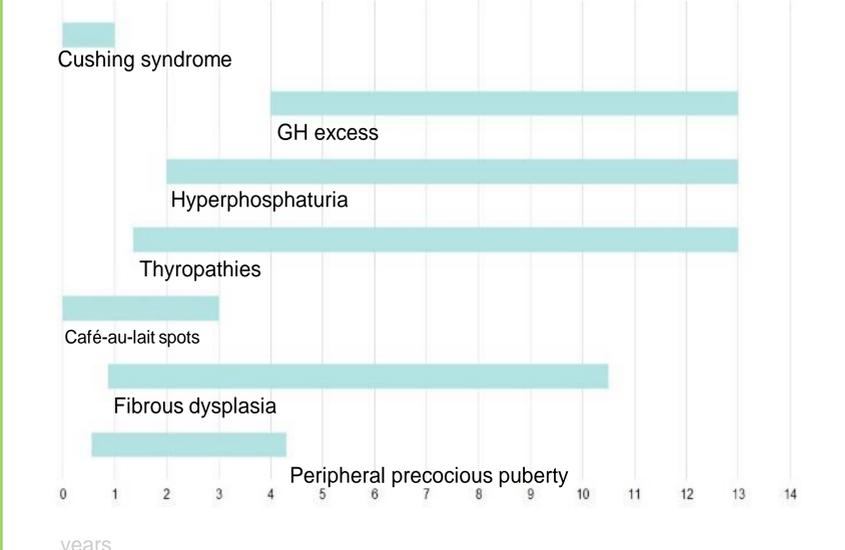
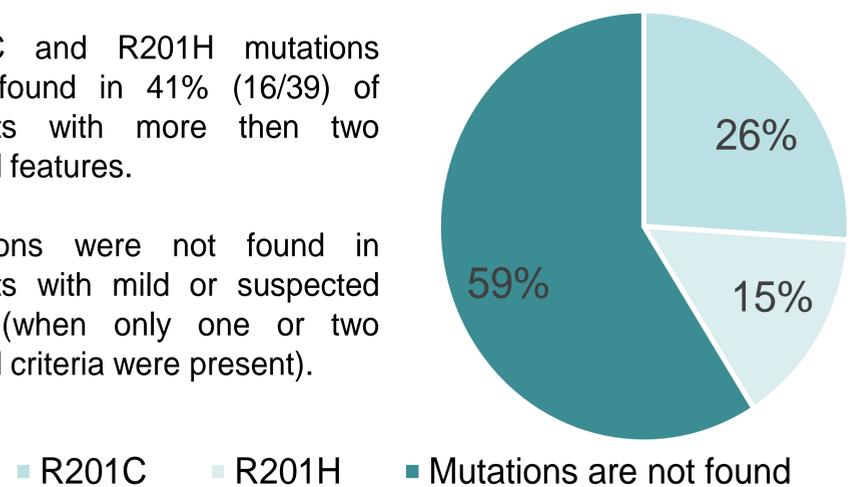


Figure 4. Mutational analysis

R201C and R201H mutations were found in 41% (16/39) of patients with more than two clinical features.

Mutations were not found in patients with mild or suspected MAS (when only one or two clinical criteria were present).



Conclusion:

- MAS can manifest during the first year of life with precocious puberty, fibrous dysplasia and/or Cushing's syndrome.
- The most common components of MAS develop in 78-98% of cases however other manifestations (Cushing's syndrome, GH-secreting adenoma) are very rare and are seen in 7-9% of patients.
- Mutation analysis of *GNAS* gene in peripheral lymphocytes with CAST-PCR and NGS methods is not useful for diagnosis of MAS in mild cases.