MOYAMOYA SYNDROME IN A PATIENT WITH GROWTH HORMONE DEFICIENCY AND HYPERGONADOTROPIC HYPOGONADISM: TO TREAT OR NOT TO TREAT WITH GROWTH HORMONE THERAPY?

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Background

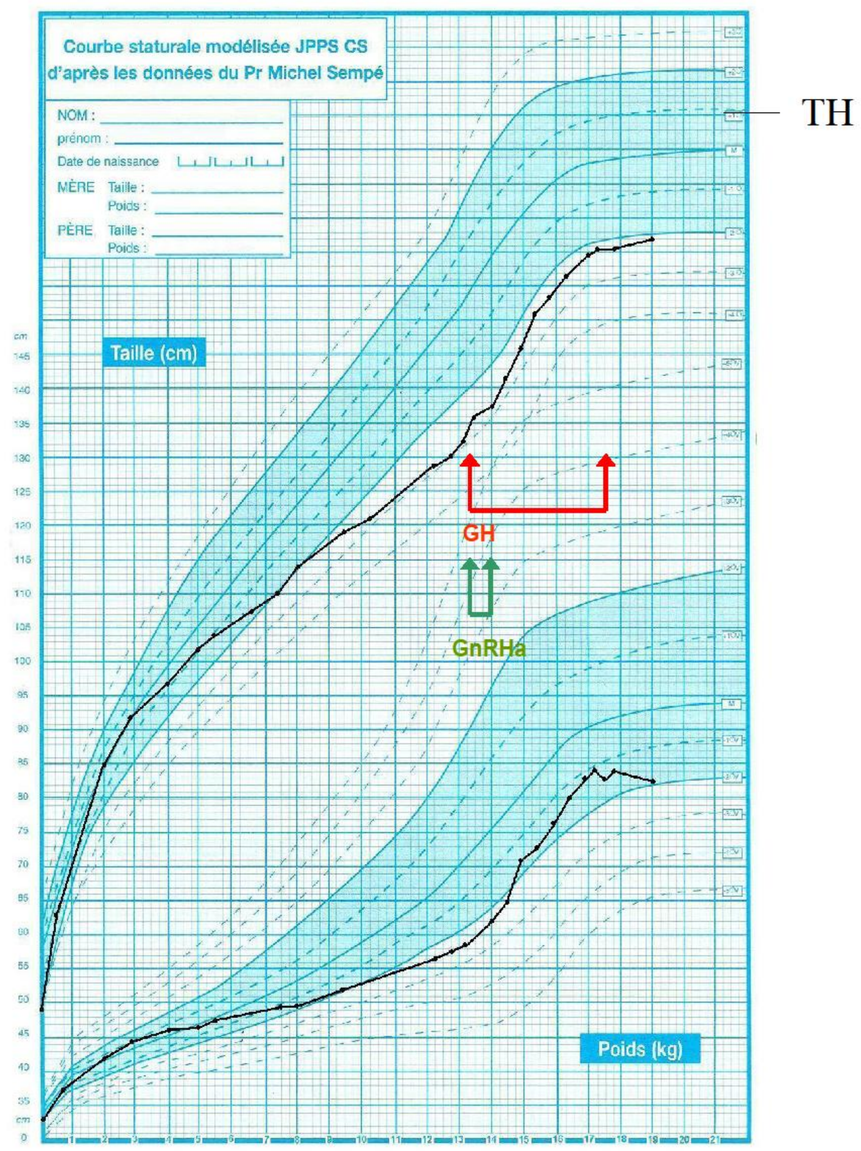
Moyamoya disease is a chronic cerebrovascular angiopathy consisting in a progressive stenosis of terminal part of internal carotid vessels and the compensatory development of thin and fragile collateral vessels.

This angiopathy may be isolated (Moyamoya disease), or appear in association with different conditions, such as neurofibromatosis, Down syndrome, and cranial radiotherapy.

Clinical case

A 12.9 year-old boy of Serbian origin was referred to our Hospital because of growth failure (height: -3SDS).
- Tanner puberty stage was 2.
- Initial work-up revealed **isolated GHD** (low GH peak after 2 stimulation tests, low IGF1 levels), normal for pubertal stage testosterone level (1.2 ng/mL) and normal pituitary assessed by MRI.

GH treatment was started (30-35 µg/Kg/day).
GnRH analogs were also prescribed, only during 10 months because of the patient's reluctance to perform this treatment.



Response to GH was moderate with a final height of 1.62m (target height: 1.80 m) with rather slow pubertal evolution.

At 17 yrs, endocrine evaluation showed low testosterone (3.8 ng/mL), high LH (13 U/L) and FSH (38 U/L) levels, low inhibin B (7 pg/mL, normal: 95-323).
Spermogram revealed azoospermia.
Blood karyotype was normal (46XY).

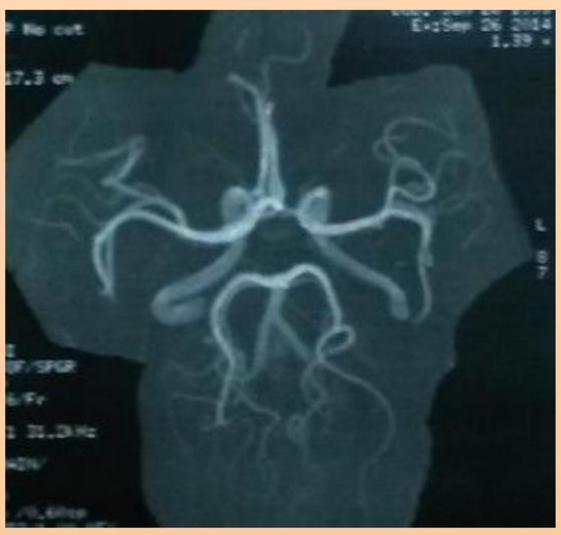
GHD was confirmed at re-evaluation by ITT:
GH peak: 4.7 mUI/l; IGF1: 154 µg/l (normal >167).

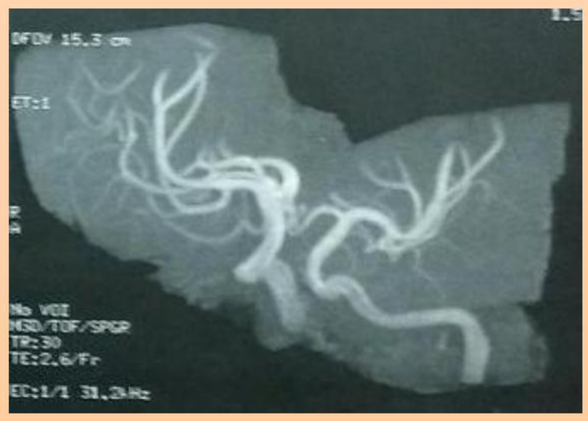
The association of GHD and primary gonadal insufficiency suggested the possibility of Moyamoya syndrome, which was confirmed by molecular analysis: **deletion of BRCC3 and MTCP1 genes**

BRCC3 encodes for a deubiquitinating enzyme and seems to play an important role in angiogenesis, MTCP1's function is unknown to data.

A brain angio-MRI was performed which initially suggested Moyamoya vessels anomalies. Reevaluation showed **absence of angiopathy**.

Close MRI follow-up is needed since anomalies may develop over time.





Discussion

Syndromic Moyamoya must be suspected when GHD and testicular insufficiency are associated.

This X-linked syndrome associates
-**facial dysmorphism** (hypertelorism, long philtrum, premature white hair locks),
-**postnatal onset short stature**,
-**partial GHD** (with normal pituitary gland),
-**hypergonadotropic hypogonadism**.

There may be heart involvement, with enlarged left ventricle to severe dilated cardiomiopathy. Our patient has a normal cardiac evaluation.

Moyamoya angiopathy may be present at diagnosis or appear in the years that follow.

Concerns are raised about the use of GH treatment in patients with GHD and cerebral vascular anomalies in whom the risk of ischemic and hemorrhagic brain damage may be increased by the background disease.

GH therapy was stopped in our patient as soon as the diagnosis of Moyamoya had been established. But soon after, he complained about asthenia, and GH therapy was again prescribed with regular control of IGF1 levels.

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