Growth Hormone excess and pseudoprecocious puberty in a 8 year old boy with McCune-Albright Syndrome

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Introduction

McCune-Albright Syndrome is a pathological entity defined by skin, bone and endocrine disorders, due to activating mutations in the GNAS-1 gene. Reported cases exhibit heterogeneous clinical symptoms. The genetic analysis is an adjuvant investigation, reserved for the mild, subclinical cases. Some of the patients with clear clinical McCune- Albright features have negative results regarding GNAS mutations, as the positive detection rate has been reported to range between 23%-100% in different studies.

Case report

The 8 year old boy, previously diagnosed with mono-ostotic fibrous dysplasia of the skull involving the frontal and temporal region and left optic canal, was referred due to signs of pubertal development since the age of 6 years. There was facial asymmetry due to abnormal skull bone formation (**Fig. 1 and 2**),with only one café-au-lait spot in the right subscapular area (**Fig.1**). **Genetic analysis** of ***GNAS*** in peripheral lymphocytes was normal, suggesting somatic mosaicism.

After clinical and biochemical assessment we had evidence that at least three hormonal axis were affected:

GH/IGF-I:

-growth above 97th percentile and accelerated bone age.
-GH basal 11,4 ng/ml, IGF-I levels +4 SDS, GH excess after oral glucose load (minimal suppression of 7,7ng/dl)

Androgen:

-pubic hair stage Tanner IV with asymmetric testicular development; testicular volume (6 and 10ml) (**Fig.3**)
-elevated testosterone levels for age, but low for testicular size
-basal gonadotropins measurable, with minimal stimulation after LHRH (maximal LH 2,1 mU/ml and FSH 0,8mU/ml)

Prolactin:

Hyperprolactinemia (224,8 ng/ml, n.r. 4-15,2ng/ml)

Therapy

-Pegvisomant (Somavert ®): 10 mg daily s.c.
-Cabergoline (Dostinex ®): 2x 0,5 mg per week

During therapy growth decelerated and GH and prolactin levels normalised (**Fig. 4**)

An anti-androgenic therapy has so far not been started due to low testosterone levels, good height prognosis and the peripubertal age of the patient (**Fig. 5**)

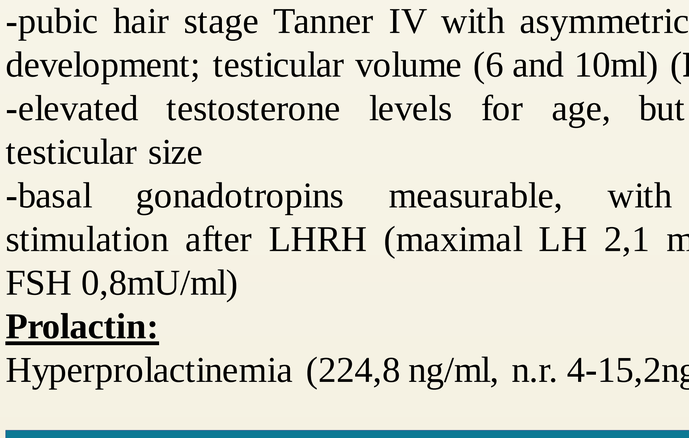

Fig. 5: Serum testosterone follow-up

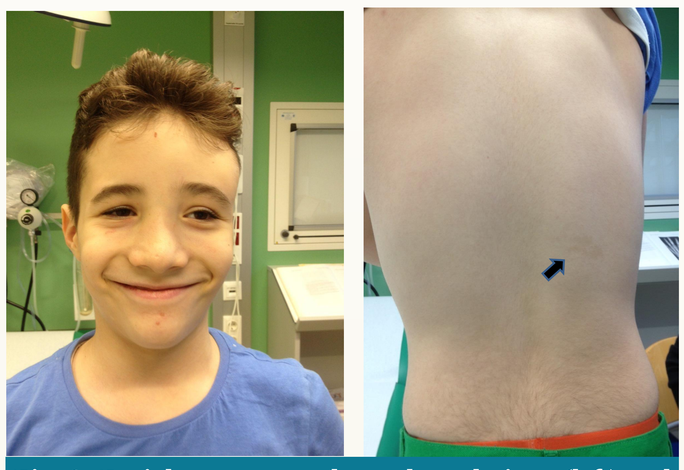

Fig. 1: Facial asymmetry due to bone lesions *(left)* and fainted cafe-au-lait spot *(right)*

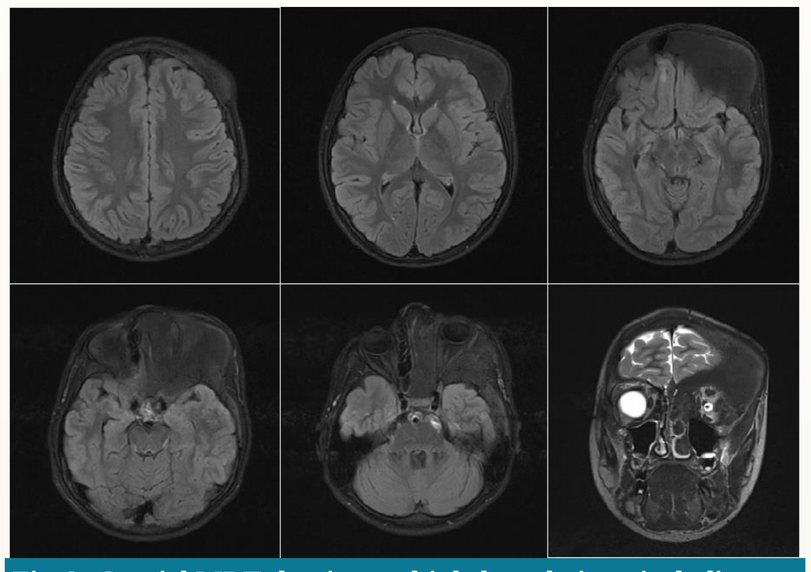

Fig. 2: Cranial MRT showing multiple bone lesions, including orbital, maxilar and mandibular involvement

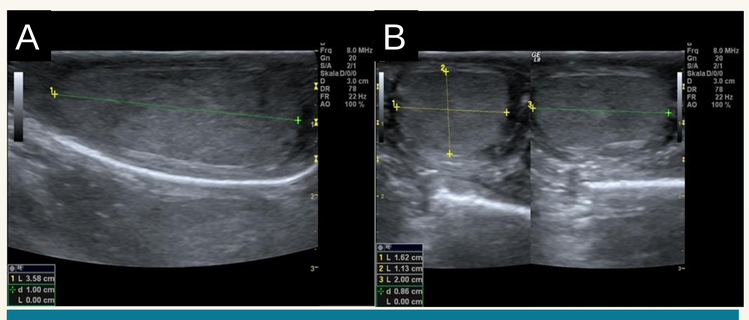

Fig. 3:Testicular ultrasound. A. longitudinal section of the left testicle: macroorhidism (10ml) and inhomogeneous structure. B. Transversal *(left)* and longitudinal *(right)* section of the right testicle: pubertal size (6ml) and normal structure

Discussion

There are few reports in the literature regarding therapy with Pegvisomant in the paediatric population with GH excess [1]. The main therapy target in this patient is lowering IGF-I, as high levels represent a risk for compression of the optic nerve by the fibrotic bone tissue [2]. Boys with MAS and signs of secondary sex characteristics are also rarely found in published reports, although testicular enlargement is common. The inconsistent result of LHRH testing with a rather low testosterone level in this case speaks for an intermittent testicular activation, like is has been described in girls with MAS and pseudo-precocious puberty. An alternative explanation is a direct stimulatory effect of IGF-I at the testicular level [3].

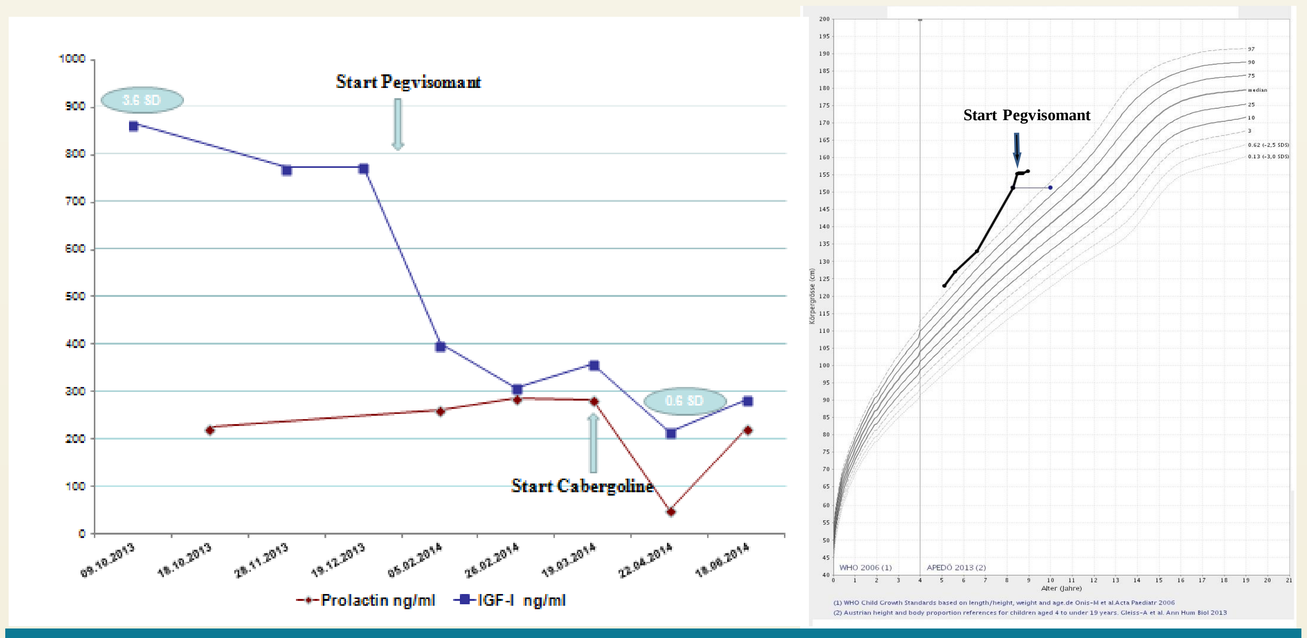

Fig. 4: Bioche mical and auxological follow-up under therapy

Acknowledgements

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References

1. Main KM, Sehested A, Feldt-Rasmussen U. Pegvisomant Treatment in a 4-Year-Old Girl with Neurofibromatosis Type 1. Horm Res 2006;65:1–5
2. Boyce AM, Glover M, Kelly MH, Brillante BA, Butman JA, Fitzgibbon EJ, Brewer CC, Zalewski CK, Cutler Peck CM, Kim J, Collins MT. Optic Neuropathy in McCune-Albright Syndrome: Effects of Early Diagnosis and Treatment of Growth Hormone Excess. J Clin Endocrinol Metab. Jan 2013; 98(1): E126–134.
3. Laron Z, Klinger B. Effect of insulin-like growth factor-I treatment on serum androgens and testicular and penile size in males with Laron syndrome (primary growth hormone resistance). Eur J Endocrinol. 1998 Feb;138(2):176-80

There is no actual or potential conflict of interest related to this poster

Photos presented with patient's consent