Growth Hormone Excess in McCune-Albright Syndrome

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BACKGROUND AND OBJECTIVES

McCune-Albright Syndrome is a combination of polyostotic fibrous dysplasia (BFD), café'-au-lait skin pigmentation and hyperfunctioning endocrinopathies. It results from postzygotic mutations in a-subunit of the Gsalfa protein and the consequent phenotype is a mosaic with high degree of clinical variability.
The aim of the study is determine prevalence and characteristics of GH hypersecretion (GHH) in MAS.

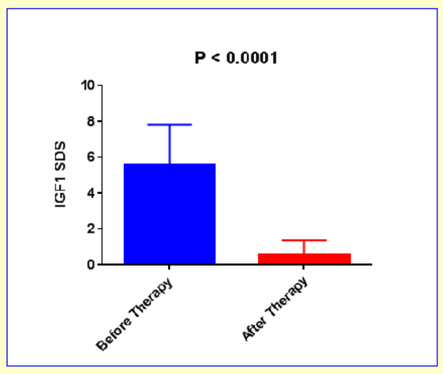
METHODS

We screen GH excess in two cohort of MAS patients. 3/34 cases identified in Italian cohort = 8.8 %; 28/129 cases identified in NIH cohort = 21.7 %. Average age at diagnosis is 13.9 y.o. (from 3 to 36). Male are 18/31 (58%), female are 13/31 (42%), age range at last evaluation 5-49 y.o. (mean age 21.1 y.o.). In all we study auxological data, biochemical GHH (IGF1 Z score, random GH, GH after OGTT), association with prolactin hypersecretion (PH), possible abnormal pituitary MRI, BFD, response to medical and other treatment. 30 MAS cases with GH excess were matched with 30 MAS controls without GH excess for sex, age (± 7 y.o.) and total bone scan score at Technetium Tc 99m bone scintigraphy (± 3 units) to evaluate association between comorbidities and GH hypersecretion. At the end we divided patients with GH excess in two groups: Group A (17 MAS, therapy before 20 y.o.) and Group B (13 MAS, no therapy or therapy after 20 y.o.).

RESULTS

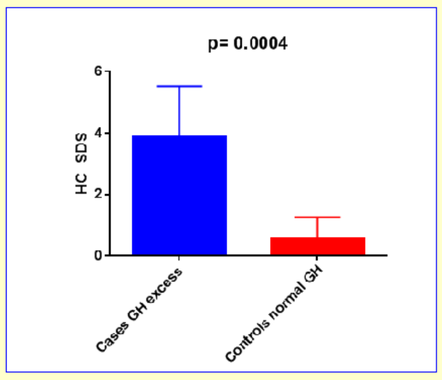
PH occurs in 27/31 (87%). Pituitary adenoma is evidenced in 16/31 (52%), while craniofacial and long bone FD are evidenced in 100%. 23/31 have also Hyperprolactinemia (74.1%), Medical treatment was performed in 25/31: in 17 ocreotide 10-30 mg im/month, in 5 ocreotide 30 mg im/month and pegvisomant 20 mg s.c./day, in 1 ocreotide 30 mg i.m./month, pegvisomant 20 mg s.c./day and pipuitary irradiation, in 2 ocreotide 30 mg i.m./month and transphenoidal pituitary surgery (1 died for post-operative complications). 19/24 (79%) have complete control of GHH (-2 <IGF-1 Z-score< +2), 3 patients are non-compliant to therapy.

What is the response to therapy? (MT+RT+Surgical) SDS IGF1



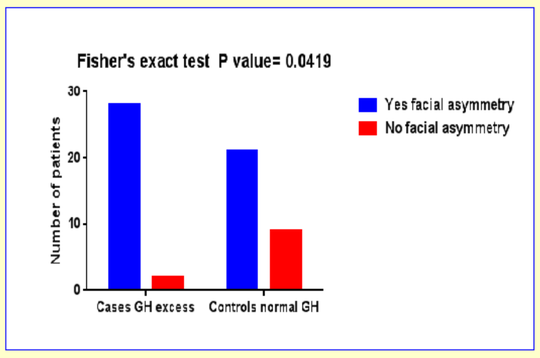
Mean SEM of column IGF1 SDS BT 5.618 1.086, n=26
Mean SEM of column IGF1 SDS AT 0.5737 0.3907, n=26

What about comorbidities? Head Circumference (HC) SDS



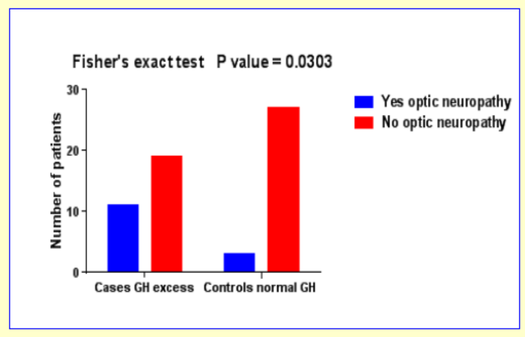
Mean ± SEM of column SDS Cases 3,874 ± 0,8053, n=29
Mean ± SEM of column SDS Controls 0,5752 ± 0,3350, n=29

What about comorbidities? Facial Asymmetry



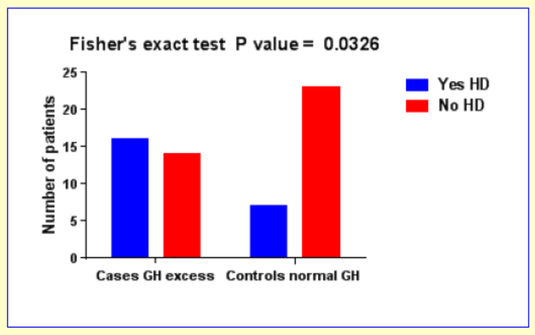
Odds ratio 6.000
95% confidence interval 1.171 to 30.74

What about comorbidities? Vision



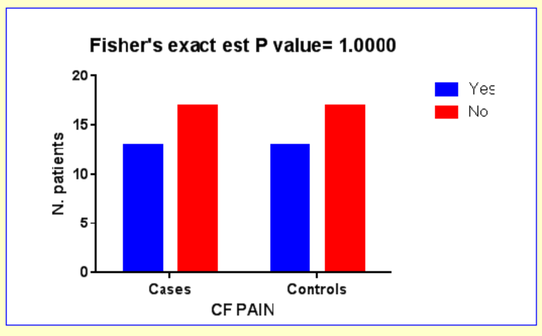
Odds ratio 5.211
95% confidence interval 1.278 to 21.24

What about comorbidities? Hearing deficit (HD)



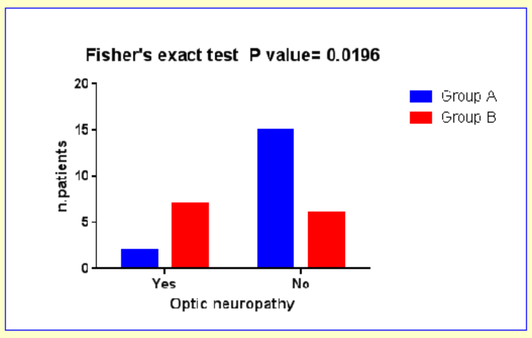
Odds ratio 3.755
95% confidence interval 1.238 to 11.39

What about comorbidities? Pain



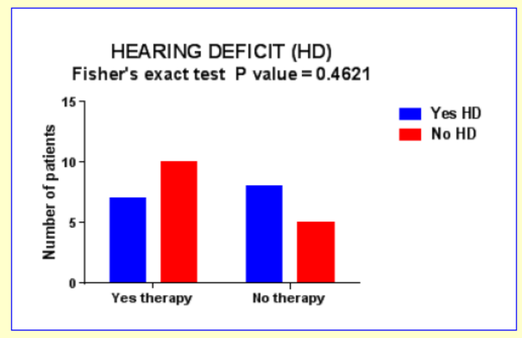
Odds ratio 1,000
95% confidence interval 0,3601 to 2,777

Comorbidities and therapy Vision



Odds ratio 0.1143
95% confidence interval 0.01824 to 0.7161

Comorbidities and therapy Hearing deficit



Odds ratio 0.4375
95% confidence interval 0.09986 to 1.917

CONCLUSIONS

GH excess is present in about 20 % of MAS patients. 76 % of them have also Hyperprolactinemia.
MAS phenotype with GHH is more severe because always associated with cranio-facial FD, head circumference expansion and more comorbidities (facial asymmetry, optic neuropathy and hearing deficit). Pain is not affected by GH Hypersecretion. Early therapy should be effective in preventing Optic Neuropathy.

References

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2. An instrument to measure skeletal burden and predict functional outcome in fibrous dysplasia of bone. Collins MT, Kushner H, Reynolds JC, Chebli C, Kelly MH, Gupta A, Brillante B, Leet AI, Riminucci M, Robey PG, Bianco P, Wientroub S, J Bone Miner Res. 2005 Feb;20(2):219-26.

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