



REACHING A DEFINITIVE DIAGNOSIS OF HYPOGONADOTROPHIC HYPOGONADISM – EXPERIENCE OF A MULTIDISCIPLINARY DIAGNOSTIC SERVICE

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INTRODUCTION

Hypogonadotrophic hypogonadism (HH) is a rare condition caused by gonadotrophin deficiency, where a definitive diagnosis is often hard to reach

AIM

To describe the clinical, biochemical and genetic findings in cases with suspected HH in the West of Scotland who were referred for genetic analysis between 2016 and 2020

METHOD

Information was collected on clinical assessment including presenting symptoms, family history, gonadal and extra-gonadal features, biochemical and molecular genetic analysis using a panel of 21 HH genes (*ANOS1, CHD7, CUL4B, FEZF1, FGF8, FGFR1, FSHB, GNRH1, GNRHR, KISS1R, LHB, NR0B1, PROK2, PROK2R, SEMA3E, SOX10, SOX2, SPRY4, TAC3, TACR3, WDR11*)

RESULTS

Between 2016 to 2020, thirty cases with suspected HH (19 male, 11 female) and a median age of 18.3 yrs (range, 1.8, 48.3) had genetic analysis as part of routine clinical investigations

These patients included:-

- 11 (37%) with anosmic HH (aHH)
- 14 (47%) with normosmic HH (nHH),
- 1 (3%) with uncertain sense of smell (uHH)
- 3 (10%) with multiple pituitary hormone deficiency (MPHD)
- 1 (3%) with CHARGE syndrome

Major Findings:-

- A positive family history related to HH was present in 9/30 patients (30%)
- Delayed puberty was the commonest presenting symptom, found in 12/30 patients (40%)
- Apart from anosmia in the 11 patients with aHH, 6/30 (20%) had other extra-gonadal features
- Olfactory neuroimaging was abnormal in 5/22 patients (23%) who had MRI studies
- 19 gene variants of ACMG class 3-5 were identified in 8 genes in 14/30 (47%) (Figure 1)
- Although likelihood of a gene variant was greater in those with anosmic HH, there were several cases of nHH who also had a gene variant identified (Figure 2)

CONCLUSIONS

- Almost 50% of patients with HH who had undergone targeted genetic analysis had a variant identified
- A low threshold is required to suspect a diagnosis of HH even if classic features of HH do not exist

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