Genetic analysis does not confirm NCCAH in almost half of the women who had received this diagnosis. Preliminary results of an audit.

Valeria Alcántara Aragón[1], Diana Tundidor Rengel[1], Susan M. Webb[1,5] ,Gemma Carreras González[2], Juan José Espinos[4], Ana Isabel Chico Ballesteros[1], Silvia Martínez Couselo[3], Francisco Blanco Vaca[3], Rosa Corcoy Pla[1]

Endocrinology[1], Pediatrics[2], Biochemistry[3], Gynecology[4] Hospital de la Santa Creu I Sant Pau, CIBERER 747 [5]

Introduction

Non-classical congenital adrenal hyperplasia (NCCAH) due to 21-hydroxylase deficiency is one of the most frequent autosomal recessive diseases.[1]

Genetic analysis performed for genetic counseling revealed a miscorrelation with the clinical diagnosis in several patients at our centre.

Objectives

To confirm the genetic diagnosis of NCCAH in women attended for this condition.

Methods

Consecutive patients attended at our centre are to be included. So far 26 patients have undergone medical record study collecting clinical, hormonal, and therapeutic information at diagnosis and follow-up into a standardized database.

Analysis of the 21-hydroxilase gene has been performed through polymerase chain reaction, sequencing, and family genetic testing when possible.

Statistics: descriptive analysis; data are expressed as percentages and medians(P25, P75).

Results

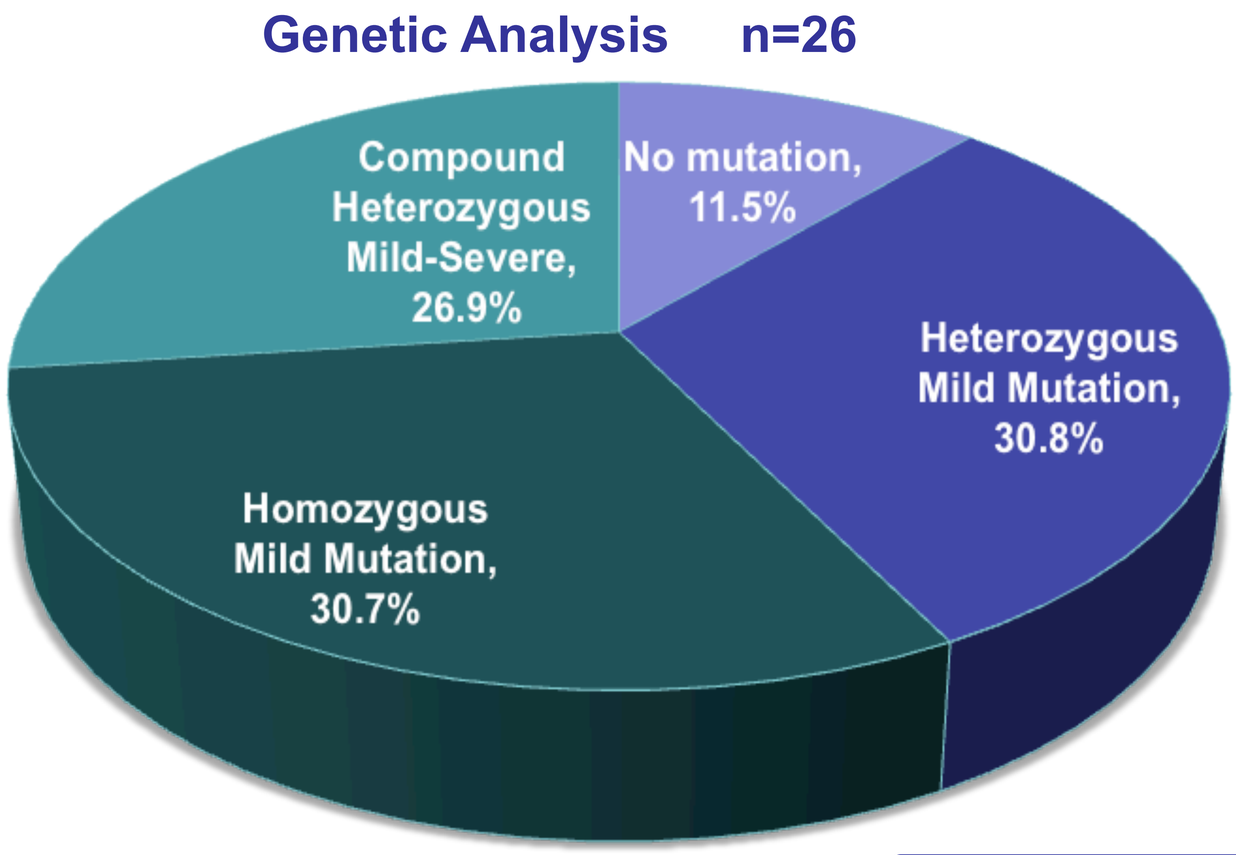
Patient characteristics n=26	
Sex	100% female
Index case	84.6%
Age at first symptom (P25, P75)	16 (9, 23)
Number of symptoms (P25, P75)	2 (1-3)
Most common manifestations:	
Hirsutism	66.7%
Oligomenorrhea	50%
Infertility	15.4%
Acne	11.5%
Alopecia	11.5%

Hormonal workup at diagnosis		
	Studied patients	**Median (P25,P75)**
Basal 17OH-P	73%	21.6nmol/l (6.97, 41)
ACTH stimulation 17OH-P	23%	30 min: 141.9nmol/l (52, 175.2)

Pharmacological treatment *	
Corticosteroid treatment (%)	80.7%
Other treatments for NCCAH (%)	88.46%

*at any time during follow-up

Seventy-five percent of the patients whose genetic diagnosis was not confirmed had received a corticosteroid treatment at some point during follow-up.



The genetic diagnosis was confirmed in **81.3%** of those with a sufficient hormonal diagnosis and in **20%** of those with an insufficient one.

Most frequent mutations	
Mild Exon 7 Val281Leu	58.53%
Mild Exon 10 Pro453Ser	9.7%
Severe Exon 7 His282Tyr	4.87%
Severe IVS2 290-13 C>G	4.87%

Conclusions

In a substantial subset of patients in follow-up for NCCAH, hormonal work-up at diagnosis was inadequate. In almost half of the patients the genotype did not confirm the diagnosis. These results compel us to reconsider the diagnostic and therapeutic requirements of these patients.

References

1.Bidet M, et al, J Clin Endocrinol Metab **94: 1570–1578, 2009**