A familial form of DSD due to NR5A1 mutation in a father and his son

Claire-Lise Gay[a], Daniela Gorduza[d], Aude Brac de la Perriere[b], Ingrid Plotton[c], Pierre Mouriquand[d], Marc Nicolino[a] & Yves Morel[c]

[a] Pediatric Endocrinology, Hopital Femme Mère Enfant; [b]Endocrinology Federation, [c]Laboratory of Molecular and Endocrine Biology, Centre de Biologie Est, [d]Pediatric Urology, Hôpital Femme Mère Enfant, [a,b,c,d] Hospices Civils de Lyon, Bron, France

Introduction

NR5A1 mutations in 46,XY patients lead to various degrees of disorders of sex development (DSD) and are generally de novo mutation. Familial cases have been described where the mother transmitted the mutation (mimicking a X-linked transmission mode) and presented primary ovarian failure. Little is known about testicular function at puberty but most patients have biological markers of gonadal dysgenesis, raising fears of infertility.

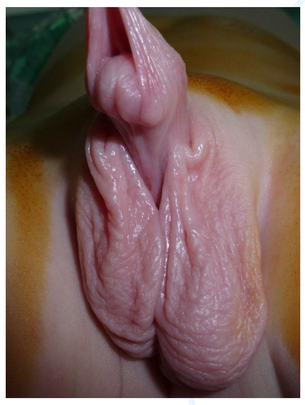
Objectives

To describe a familial form of DSD due to NR5A1 mutation transmitted by the affected father

Results

Clinical presentation

The index case presented at birth a 25 mm penis with perineal hypospadias and bifid scrotum containing 2 testis.
He needed testosterone therapy for increasing penile length and hypospadias surgery. The right testis was brought down at 4 years for secondary ascension



The father has a perineal hypospadias operated during the childhood but no micropenis. Puberty occurred spontaneously and he had no testosterone treatment. His wife became twice pregnant without medical assistance.

Hormonal profil

Index case

	7 weeks	3 months	After hCG test * 6 months	21 months	4 years
Testosterone (nmol/l)	3,42	2,66	4,9		
AMH (pmol/l)	475	616	442	203	209
Inhibin B (ng/l)				21	23
LH (UI/l)	7,3	2,2			
FSH (UI/l)	3,3	2,6			

Father

	35 years
Testosterone (nmol/l)	17
AMH (pmol/l)	7,2
Inhibin B (ng/l)	85
LH (UI/l)	4
FSH (UI/l)	10

* Test hCG: 6 injections of 1500U every 2 days.

The son has a partial testicular dysgenesis. His father has a normal leydig function but FSH and inhibin B suggested a partial balanced Sertoli dysfonction . Father and son were heterozygous for c.269delG mutation of NR5A1. They had no adrenal insufficiency.

Conclusions

NR5A1 mutations may be transmitted by the affected father. Gonadal dysgenesis is variable and spontaneous puberty and fertility is possible in some cases. Puberty should be carefully monitored and as progressive gonadal dysgenesis is likely, early sperm cryopreservation should be considered.

References

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Claire-Lise GAY
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