



CONGENITAL HYPOGONADOTROPIC HYPOGONADISM ASSOCIATED WITH X-LINKED ICHTHYOSIS DUE TO X-CHROMOSOME MICRODELETION IDENTIFIED BY CHROMOSOMAL MICROARRAY

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INTRODUCTION

Congenital hypogonadotropic hypogonadism due to KAL1 pathological variants manifest with micropenis, cryptorchidism, delay of puberty, and not associated with disorder of sex development. This condition can be associated with ichthyosis due to deletion of X chromosome region with genes KAL1 and STS (steroid sulphatase gene).

AIM

to assess diagnostic usefulness and accuracy of different diagnostic tools in patients with Kallmann syndrome and ichthyosis due to X-chromosome microdeletion.

MATERIALS

We report the clinical cases of 2, XY siblings with Kallmann syndrome without anosmia associated with ichthyosis and different clinical features of the disease.

The arm of one of the reported patients with ichthyosis and Kallmann syndrome



RESULTS

PATIENT 1

Younger brother
 At birth: ichthyosis, micropenis, bilateral cryptorchidism
 7 months: height SDS 0.28, LH 0.001 IU/ml, FSH 0.4 IU/ml, AMH 0.58 ng/ml, testosterone 1.6 nmol/l.
 No uterus on US.
 hCG stimulation test - testosterone up to 1.82 nmol/l.
 12 months of topic androgens penis length increased to 2.5 cm.

Micropenis
 bilateral cryptorchidism → DSD → MAMLD1
 uncertain significance defect

Ichthyosis
 Micropenis, bilateral cryptorchidism in younger brother → Chromosomal Microarray Analysis → Microdeletions in Xp22.3 KAL1 and STS → CONTIGUOUS GENE SYNDROME
 Testes hypoplasia in elder one

PATIENT 2

Elder brother
 At birth: ichthyosis.
 12 years: testes hypoplasia. Height SDS 0.87. Tanner 1. Penis length ~ 5.1 cm, both testes were in scrotum. D=S= 0.45 ml by US.
 Bone age was 11-12 years.
 LH 0.06 IU/ml. FSH 0.84 IU/ml, AMH 23.7 ng/ml, inhibin B 11 pg/ml.

CONCLUSIONS

1. Micropenis Bilateral cryptorchidism → Sex disorders? Hypogonadism? → NGS → Uncertain significance defect → NGS RESULTS + CLINICAL FEATURES INTERPRETATION
2. Clinical features analysis → Best diagnostic tool → TIMELY INITIATION OF THERAPY

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