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.

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.

**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=5= 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.

| Micropenis | bilateral cryptorchidism | DSD | MAML1 | uncertain significance defect |
| Ichthyosis | Micropenis, bilateral cryptorchidism in younger brother | Testes hypoplasia in elder one | Chromosomal Microarray Analysis | Microdeletions in Xp22.3 KAL1 and STS | CONTIGUOUS GENE SYNDROME |

CONCLUSIONS

1. Micropenis
   Bilateral cryptorchidism

2. Clinical features analysis
   Best diagnostic tool

| Sex disorders? Hypogonadism? | NGS | Uncertain significance defect | NGS RESULTS + CLINICAL FEATURES INTERPRETATION |
| TIMELY INITIATION OF THERAPY |

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