NEUROGENETIC ASPECTS IN INFERTILE MEN WITH KLINEFELTER SYNDROME

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Introduction

- Klinefelter's syndrome (SK) is characterized by the additional presence of one or more X chromosome in a male person.

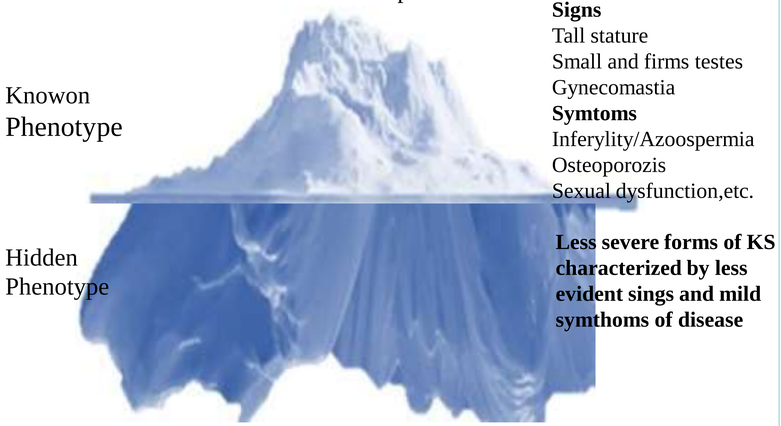

Figure 1: Signs and symptoms of KS according to the severity of clinical phenotype

- Most genes from the extra X undergo inactivation, but some escape (10% of PAR1 and PAR2) and play a role in klinefelter pathogenesis, and could be responsible for cognitive disorders of KS patients.

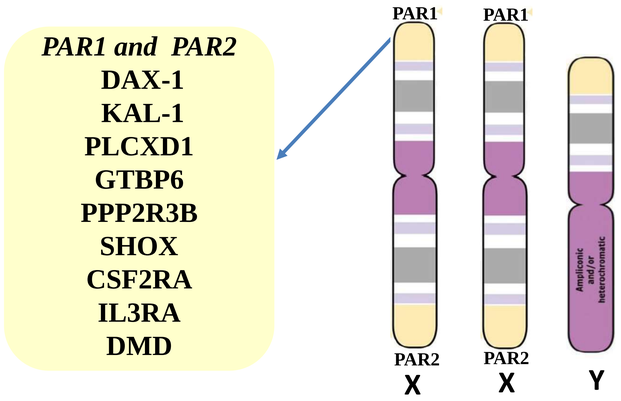

Figure 2: The gene from PAR 1 and PAR 2 in the X chromosome

- The severity of the clinical features being directly proportional to the number of additional X chromosomes. **(47,XXY, 48,XXXY, 49,XXXXY) !!!**

Key whords

- Cytogenetic variants, 47,XXY, gene, neurologic, infertile, karyotype, Klinefelter Syndrome

Purpose

- To study the neurological and cytogenetic peculiarities of KS in infertile men in order to initiate measures to improve their quality of life.

Material and methods

- The study was performed on 110 men with infertility, selected during medical genetic counseling, having as selection criteria, lack of sperm in the ejaculate, elevated values of FSH and LH, the following phenotypic aspects: developmental anomalies of the external genitalia - peno-scrotal hypospadias, small testes, cryptorchidism, cranio-facial dysmorphism, waist high and disproportionate, hypogonadism, gynecomastia, mental retardation, psychosocial problems.
- Karyotyping was performed on peripheral blood lymphocytes according to standard methods G-banding of metaphase chromosomes. For reporting the results, the 2016 International System of Cytogenetic Nomenclature was used.

Results

- The most common chromosomal abnormality diagnosed in the 33 patients with SK was homogeneous free trisomy 47,XXY (30 cases - 90.9%), followed by the forms: mosaic (47,XXY/46,XY: 1 case), polysomy X-Y (variant 48,XXYY: 1 case - and 49,XXXXY: 1 case).

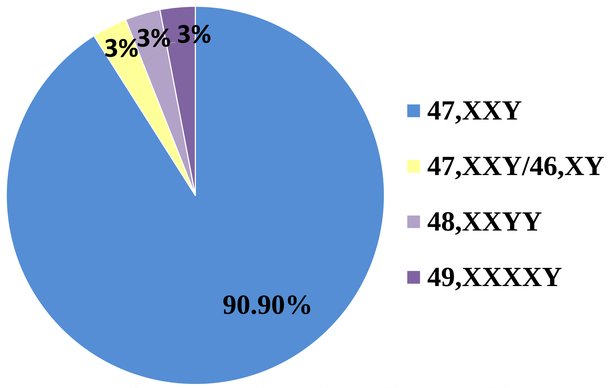

Figure 3: Frequency of cytogenetic variants diagnosed in SK

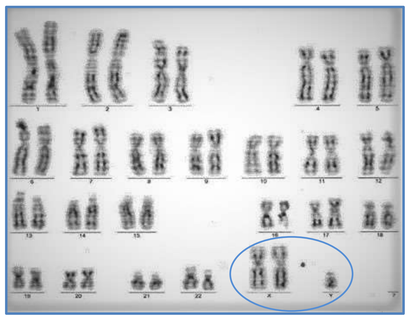

Figure 4: Cytogenetic variant 47,XXY diagnosed in SK

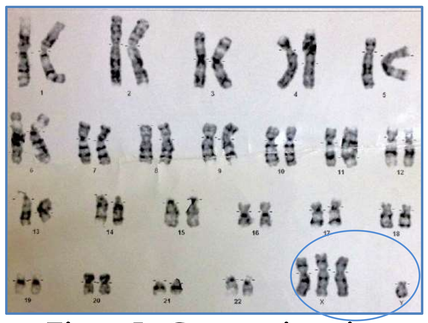

Figure 5: Cytogenetic variant 48,XXXY diagnosed in SK

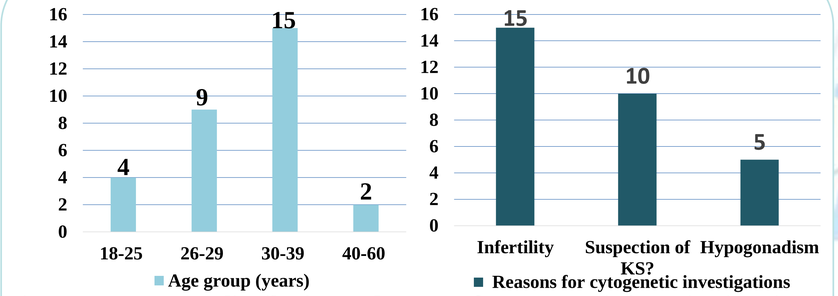

Figure 6: Age group distribution and reasons for cytogenetic investigations in KS

47,XXY–the classical and ***47,XXY/4,XY***- mosaic form - a mild to moderate mental retardation, language disorders with cognitive-verbal retardation, slow motor development, coordination disorders, immature behavior, waist high, gynecomastia, hypogonadism, azoospermia.

48,XXXY and 49,XXXXY–moderate to severe mental retardation, severe cognitive-verbal retardation, behavioral problems and life-threatening problems were found, waist high and disproportionate, gynecomastia, developmental anomalies of the external genitalia - hypospadias, small testes, azoospermia .

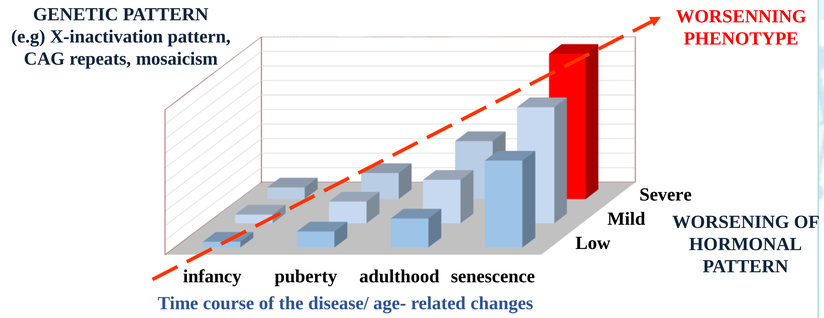

Figure 7: *The broad spectrum of phenotypes in KS depends on the severity of all its components (number of supernumerary X chromosome, genetic impact of supernumerary X, severity of hypogonadism) as well as on the time duration of the disease, the delay in the diagnosis of testosterone deficiency, and advancing age coupled with increasing other comorbidities*

Conclusions

- The diagnosis of the cytogenetic variant in patients with KS is of neurological importance, as the severity of the neurodevelopmental phenotype in subjects with KS is directly proportional to the number of the supernumerary X chromosome.

References

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