

TRIPLE-X SYNDROME ASSOCIATED WITH FAMILIAL HYPERLIPOPROTEINEMIA (case report)

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ABSTRACT: Triple-X syndrome was first described by Jacobs in 1959 under the name "superfemale". The authors present a case with triple-X syndrome associated with a hereditary anomaly of lipid's metabolism. The authors don't know the impact of the presence of chromosomal disease on familial hyperlipoproteinemia and they consider it an accidental association.

INTRODUCTION

The triple-X syndrome is a rare sex chromosome anomaly. The incidence rate of the syndrome has been reported to vary between 0,73 and 1 per 1,000 female births (1). The first published report of a woman with 47,XXX karyotype was by Jacobs and col. In 1959 (2).

The karyotype is usually not associated with a characteristic physical phenotype. The syndrome is associated with an increased risk of learning disabilities and delayed development of speech and language skills.

Hyperlipoproteinemias are hereditary troubles of the metabolism of the lipids. They represent an important risk factor for atherosclerosis.

The authors present a case with triple-X syndrome associated with familial hyperlipoproteinemia.

CASE REPORT

T.S (F.O.10243/1997), girl, 9 months old, was hospitalized in 3-rd Clinic of Pediatrics Iași, by transfer from Pediatric Surgery Clinic, for investigations because she was discovered with anomalies of metabolism of lipids.

▪Familial antecedents: mother – 22 years old, father – 26 years old, both healthy; a sister – 2 years and 6 months old, weight = 18 kg (+4SD), height = 96 cm (+2SD).

▪Personal antecedents: the girl is the second child of the family; birth weight – 3400g and height – 50 cm; APGAR score -7. Breast feeding till 7 months of age, than she received diverse nutrition.

▪History of the disease: mother related that she observed an abnormal increased of weight: the girl had 8 kg weight at 4 months of age. Because the baby had bilateral convex leg, she was hospitalized in Pediatric Surgery Clinic. The surgeon observed the excess weight and he investigated the metabolism of lipids. The investigations showed: hyperlipemia, hypercholesterolemia, hypertriglyceridemia, increased HDL, decreased LDL and VLDL. The girl was transferred in 3-rd Clinic of Pediatrics for continuation of the investigations and for establishing the therapy.

▪Physical examination showed:

-a girl, 9 months old, weight = 11 kg (+3SD), height = 73 cm, ponderal index = 1,27, cranial perimeter = 45 cm;

-almond eyes, epichantal folds;

-sharpen ears;

-unique palmar fold, clinodactyly bilateral on finger V;

-small labial anterior fused;

-bilateral convex leg.

▪Laboratory findings:

The modifications observed on clinical exam imposed the genetic exam: chromatinic sex positive, but with 2 Barr corpuscles; karyotype 46,XX/47,XXX.

The results of the investigation of the metabolism of lipids are presented in table 1.

Tabel 1. The modifications of the metabolism of lipids - patient T.S. and her family

| Parameter | T.S. | | T.I. father | T.F. mother | T.A. sister |
|---------------------|--------------------|---------------------|----------------|----------------|----------------|
| | Determination I | Determination II | | | |
| Lipids (g‰) | 10 (↑) | 6,1 (under diet) | 10,3 (↑) | 6,75 | 7,2 |
| Cholesterol (g‰) | 2,25 (↑) | 2,35 (↑) | 2,65(↑) | 2 | 1,65 |
| Triglycerides (mg‰) | 400 (↑) | 82 (↑) | 265 (↑) | 105 | 1,98 |
| TG/Chol | 1,77 | 0,35 | 1 | 0,52 | 0,01 |
| Lipidogramme (%) | HDL | 44 (↑) | 24,4 (↓) | 17 (↓) | 24,5 |
| | LDL | 46,7 (↓) | 53,6 (↓) | 63 (↑) | 60 |
| | VLDL | 9,3 (↓) | 22 (↑) | 20 (↓) | 10,5 |
| Serum aspect (4°C) | lactescent | lactescent | lactescent | normal | normal |

Other investigations (leucogramme, hemoglobin, hepatic and renal investigations, glycemia, ultrasonography) were normal. Ophtalmological exam: retinae edema, but without iridal and choroidal coloboma.

▪The positive diagnosis based on anamnestic, clinical and paraclinical data was:

- Triple-X syndrome;
- Familial hyperlipoproteinemia type IIb – homozygote form;
- Convex bilateral leg.

The treatment recommended consisted of:

- diet: restriction of total fat and reducing the intake of saturated fat (egs, milk, cheese, butter).

We also recommended a decreased powder-milk (Beba, Enfamil).

- medical treatment (Clofibrat 1g/m²/day).

Under the treatment, the values of parameters of lipid's metabolism decreased.

The control effectuated at the age of 5 revealed:

- mental deficiency (QD= 47%);
- comportamental troubles (narcissism, masturbation) that were observed at the next controls too (at 8, 10 and 12 years of age).
- learning difficulties and problems in relation to speech development.

The girl presented a growth acceleration than other girls up till the age of 8 years, being taller than average (table 2).



Foto T.S. 12 ani



Foto T.S.-aspectul mâinilor

Tabel 2. T.S. – the evolution of weight and height between 8 and 12 years.

| | | | | | |
|---------------------|-------|-------|-------|-------|------|
| Age (years) | 8 | 9 | 10 | 11 | 12 |
| Height (cm) | 128 | 135 | 137 | 143 | 149 |
| Height average (cm) | 121,9 | 127,1 | 132,3 | 137,7 | 144 |
| Weight (kg) | 21 | 28 | 30 | 32 | 36 |
| Height average (kg) | 22,4 | 24,6 | 27,3 | 30,9 | 35,2 |

DISCUSSION

By definition, triple-X syndrome is a sex chromosome abnormality occurring in females that is characterized by the presence of an extra X chromosome 1. Triple-X syndrome is not inherited, but usually occurs as an event during the formation of reproductive cells.

5 to 10 girls with triple-X syndrome are born in USA each day and in Denmark with a population of 5 mill. are approximately 3,000 women with triple-X (3).

During the first years after the triple-X constitution had been described, these women were occasionally described as “superfemales”. But they are neither more, neither less females than other women with normal sex chromosomes 46,XX.

Girls with triple-X have no increased risk of any diseases in childhood.

The majority of females with triple-X syndrome appear normal at birth, and without specific congenital malformations (4). They are usually no distinguishable differences to the naked eye between girls with triple-X and the rest of the female population.

If symptoms appear, they may include: microcephaly, epichantal folds, tall stature, clinodactyly, delayed development of certain motor skills, speech and language, learning disabilities (dyslexia) and infertility (rare) (2).

The girl presented had some of these features: epichantal folds, clinodactyly, tall stature, but she didn't appear thin. She presented certain learning difficulties during the first years of school that can't be remedied by an increased pedagogical effort. These problems were in relation to speech development and she required speech therapy. It is possible that learning disabilities and delayed development to lead to a variety of other issues like behavioral and emotional difficulties, poor socialization skills that can cause social isolation. The girl and her family received psychological counseling.

Familial hyperlipoproteinemia is an autosomal dominant disorder. The prevalence of homozygous familial hyperlipoproteinemia is 1 case per 1 million persons. The homozygous children have a risk for a very early cardiovascular event and sudden death or acute myocardial infarction may occur in patients as young as 1- 12 years (5,6)

Because each must have a parent with heterozygous familial hyperlipoproteinemia, a history of significant hypercholesterolemia and premature coronary heart disease can be traced to the patient's second degree relatives (5).

These children may have cutaneous xanthomas by early childhood and corneal arcus.

Children with homozygous familial hyperlipoproteinemia should be referred to a pediatric cardiologist for consideration of vascular imaging studies that can direct treatment for hypercholesterolemia.

CONCLUSIONS

1. We presented a sex-chromosome disease associated with familial hyperlipoproteinemia – disease with an important risk for atherosclerosis.

2. Triple-X is not a disease; girls with this syndrome should definitely not be considered patients.

3. Triple-X girls have no special disorders or increased risk of any disorders.

4. We don't know the impact of the presence of chromosomal disease on familial hyperlipoproteinemia and we considered it an accidental association.

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