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Research Article

MULTIPLE MYELOMA AND SHERSHEVSKY TERNER'S SYNDROME (CLINICAL CASE)

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Maxamadalieva G.Z.
Republican Specialized Scientific And Practical Center Of Hematology, Uzbekistan

Gulmirzaev J.A.
Republican Specialized Scientific And Practical Center Of Hematology, Uzbekistan

Xamidova F.I.
Republican Specialized Scientific And Practical Center Of Hematology, Uzbekistan

Isxakov E.D.
Republican Specialized Scientific And Practical Center Of Hematology, Uzbekistan

ABSTRACT

A clinical case of a patient with multiple myeloma with Shereshevsky-Turner syndrome was analyzed. The effectiveness of treatment according to the VRD protocol in the first line in the treatment of multiple myeloma with concomitant congenital mutations was assessed. An early relapse of the disease was revealed, requiring polychemotherapy with monoclonal antibodies.

KEYWORDS

Multiple myeloma, chemotherapy, Turner syndrome, chromosome.

INTRODUCTION

Shereshevsky-Turner syndrome is a genetically determined pathology that develops exclusively in girls. In this chromosomal disease, the second of the sex X chromosomes is lost. In some cases, only part of it is missing. Changes in the chromosome set also manifest themselves phenotypically (1,5,9,10). The

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prevalence of the anomaly is quite high - 1 case per 2–2.5 thousand newborn girls. The pathology is one of the three most common genetic diseases along with Klinefelter syndrome and Down disease (2,7,12).

Shereshevsky-Turner syndrome was described in 1925 by the Soviet endocrinologist N.A. Shereshevsky, who believed that it was caused by underdevelopment of the gonads and the anterior pituitary gland and was combined with congenital malformations of internal development. In 1938, Turner identified a triad of symptoms characteristic of this symptom complex: sexual infantilism, skin pterygoid folds on the lateral surfaces of the neck and deformation of the elbow joints (3,4,13). The following chromosomal aberrations are possible, leading to the STS phenotype:

- X monosomy (45, XO);
- Partial or complete deletion of the short arm of the X chromosome (delXp);
- Complete deletion of the long arm of the X chromosome (delXq);
- Isochromosome of the long arm of the X chromosome (i (Xq));
- ring X chromosome (r (X));
- marker chromosome (46, X + m);
- mosaicism, that is, the presence of more than two cell lines in one person, most often 45,X/46,XX and 45,X/46,XY.

Depending on the size of the lesions, clinical symptoms differ. In cases of mosaicism, the full range of symptoms may also be absent (1,2,3). Mapping the X chromosome and studying some of its genes made it possible to associate some features of TTS with dysfunction of certain genes. It also turned out that the variability of the cytogenetic image is expressed in the variability of the phenotype of patients with STS, which is important in predicting the course of the disease (2,7,12,8).

According to the literature, a clear connection between the occurrence of Shereshevsky-Turner syndrome and age and any diseases of the parents has not been identified. In the embryo, primary germ cells are formed in almost normal numbers, but in the second half of pregnancy they undergo rapid involution (reverse development), and by the time the child is born, the number of follicles in the ovary is sharply reduced compared to the norm or they are completely absent. This leads to severe deficiency of female sex hormones, sexual underdevelopment, and in most patients to primary amenorrhea (absence of menstruation) and infertility (6,9,10,13). The resulting chromosomal abnormalities are the cause of developmental defects. It is also possible that concomitant autosomal mutations play a certain role in

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the appearance of developmental defects, since there are conditions similar to Shereshevsky-Turner syndrome, but without visible chromosomal pathology and sexual underdevelopment. Other pathological findings are consistent with the clinical presentation. The most important changes in the osteoarticular system are shortening of the metacarpal and metatarsal bones, aplasia (absence) of the phalanges of the fingers, deformation of the wrist joint, and osteoporosis of the vertebrae. Radiologically, in Shereshevsky-Turner syndrome, the sella turcica and the bones of the cranial vault are usually not changed (3,6,8). All regions of the world and culture are affected by this pathology approximately equally. It is estimated to occur in 3% of all human fetuses. However, only 1% of these fetuses survive birth. Normal skeletal development is inhibited due to a wide variety of factors, mainly hormonal. The average height of a woman with STS without growth hormone treatment is 140 cm. Patients with mosaic STS can reach a normal average height. Due to insufficient estrogen production, many people with TTS develop osteoporosis. This can further reduce height and also worsen the curvature of the spine, which can lead to scoliosis. It also leads to an increased risk of bone fractures (4,6,7,9).

About a third of all women with STS have one of three kidney pathologies:

- One horseshoe-shaped kidney on one side of the body (instead of the usual two)
- Incorrect urine collection system
- Poor blood flow to the kidneys

Some of these conditions can be corrected with surgery. Even with these abnormalities, the kidneys of most women with STS function normally. However, as noted above, kidney problems can be associated with hypertension.

Approximately one third of all women with TTS have thyroid disease (10,11, 23). This is usually hypothyroidism, specifically Hashimoto's thyroiditis. Once detected, it can be easily treated with thyroid hormones. Women with TTS have a moderately increased risk of developing diabetes in childhood and a significantly increased risk of developing diabetes in adulthood (1,5,7) . A rare type of TTS, known as Ring-X Turner syndrome, is associated with mental retardation in 60% of cases. This type accounts for about 2–4% of all cases of STS (6).

People with TTS are almost always infertile. Although some women with TTS have successfully conceived and survived pregnancy, it is very rare and usually occurs in those women whose karyotype is not 45, Xo. The literature does not describe a case of multiple myeloma in patients with STS.

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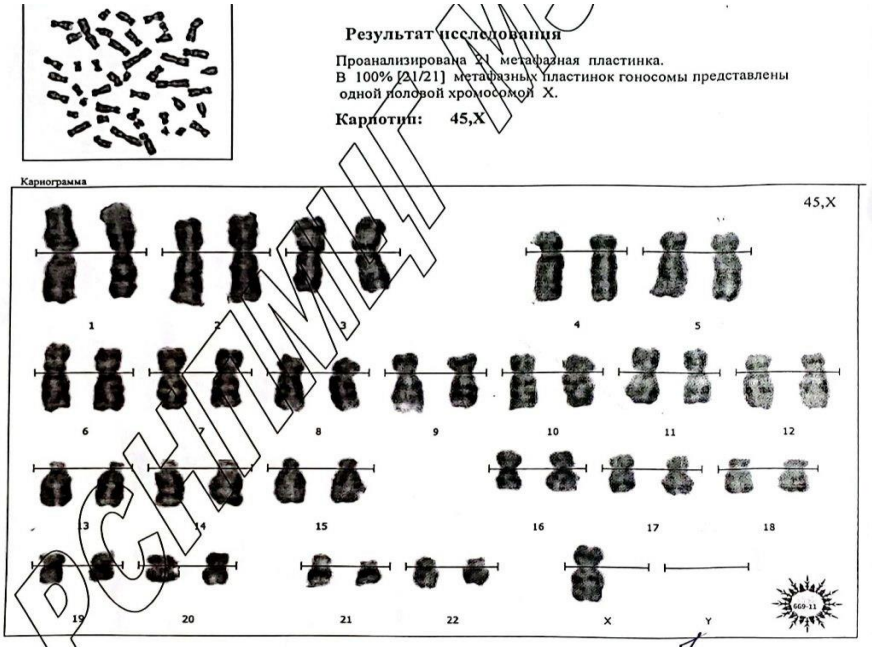
Purpose of the study: To analyze a clinical case of a patient with multiple myeloma with Shereshevsky-Turner syndrome

Patient V., 45 years old (Russian language teacher) with Shereshevsky-Turner Syndrome (TST) complete X-monosomy, was admitted to the Republican Specialized Scientific and Practical Medical Center of Hematology with complaints of general weakness, dizziness, bone pain, decreased appetite, and palpitations.

Karyotype 45.XO



Symptoms	Frequency by occurrence %	In our case
Intelligence preserved	50-60	+
Stunting	98	+
General dysplasticity (abnormal physique)	92	+
Lymphostasis (swelling) of the arms and legs	24	+

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Barrel chest and widely spaced nipples	75	+
Neck shortening	63	+
Low hairline at the back of the head	57	-
Low-set ears, ear deformation	46	-
Infertility	100	+
Vestigial ovaries	80-100	+
Amenorrhea	80-100	+
Small nails	60-79	-
Specific facial features	60-79	-
Wing-shaped folds of skin in the neck area	46	+
• Bicuspid aortic valve	50	-
High waist-to-hip ratio (hips not much larger than waist)	80-100	-
Height below 140 cm.	80-100	160 CM
The fourth metacarpal may be unusually short, as may the fifth.	40-59	+
Osteoporosis and scoliosis.	40-50	+
bone fractures.	-	+

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According to the literature on cardiovascular malformations, complications of aortic dilatation are usually associated with a 45.X karyotype, but in our case, no pathology with cardiovascular pathology was identified.[27].

Survey results:

In the hemogram dated 08/03/23: hemoglobin 52.0 g/l, erythrocytes 1.70 million, c.p.-0.9, leukocytes 5.83 thousand/µl, platelets 30.0 thousand/µl, p.o.-6.0, s.o. -45.0, lymphocytes 45.0 thousand/µl, mon.-4.0%, ESR-20mm/hour.

Serum β2-microglobulin - 14,240.0 ng/mL, LDH - 180 U/l.

Considering the anemic syndrome and bone pain, immunofixation of pathological serum proteins was done: M protein was detected, free kappa was detected 294.33 mg/l.

Test Name	Result	Unit(s)	Biological reference interval
Total Protein (Biueret)	7.5	gdL	6.4-8.2
Albumin (Gel Hecfophoresis)	2.72	S/dL	3.57-5.42
Alpha 1 Globutin {Gel Ebcnrophoresis)	0.14	S/dL	0.19-0.40
Alpha 2 Globutin	0.37	g/dL	0.45-0.96
Beta Globutin	0.45	S/dL	0.30-0.59
Gamma Globulin	3.83	g/dL	0.71-1.54
AlbuminlGlobulin Ratio	0.57	Ratio	1.0-2.2
'M" Band	Present	-	Absent

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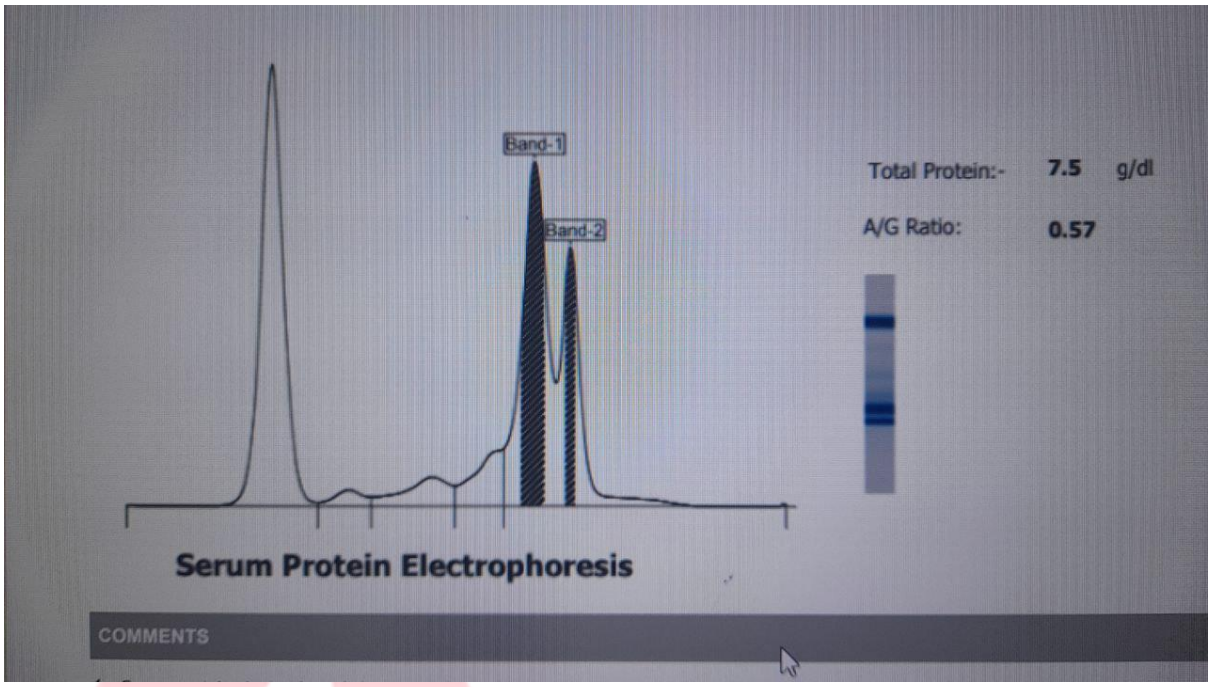

According to PET-CT data: metabolic active destructive foci in all bone structures - changes similar to myeloma? Pleurisy on both sides. Pericarditis.

In the myelogram dated July 25, 2023: The bone marrow punctate is medium cellular. Hematological cells - 100 cells are rare, mostly non-hematological cells - atypical cells are found.

According to MRI: signs of diffuse damage to the bone marrow of the skeleton. Hepatosplenomegaly. Bilateral hydrothorax. Anasarka.

According to trephine biopsy data during microscopic examination: conclusion: histological picture of plasma cell dyscrasia.

According to FISH data from 11/21/23:

1. 13q deletion (locus 13q14) not detected

2. Deletion of the TP53 gene (kjre 17p13.1) was not detected.

3. Translocation t(11;14), leading to the formation of a fusion signal of the IGH::CCTV1 gene. Not found.

4. Translocation t(4;14), leading to the formation of a fusion signal of the IGH: FGFR3 gene, was not detected.

Thus, the main diagnosis was established: Multiple myeloma with Kappa light chain secretion. Diffuse-focal form. Stage IIIA (according to B. Durie, S. Salmon). ISS III. R-ISS II.

Related: Q96.9 Turner syndrome, unspecified. I89.0 Lymphoedema, not elsewhere classified.

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Complication: Diffuse damage to the skeletal bones. Hepatosplenomegaly. Anasarka. Conducted No. 3 VRD:

From 09.12.23 to 11.23.23 3 courses of PCT "VRD" (Bortezomib 1.0 mg/m2, Lenalidomide 25 mg/day, Dexamethasone), Hemotransfusion 3p mark. er. wt. No. 5.

After the 3rd course of treatment, CR was achieved, maintenance therapy was prescribed with lenalidomide 25 mg orally, but after three months the disease relapsed, treatment with Daratumumab 16 mg/kg + Pomalide 4 mg + dexamethasone was started.

After two courses, partial remission was achieved.

Discussion: There are no cases of multiple myeloma with Shereshevsky-Turner syndrome described in the literature. In our case, the patient was not found to have pathogenetic mutations that play a role in the development of multiple myeloma. According to the authors Smith L, Barlogie B, Alexanian R.Smith L, et al. biclonal tumors often showed atypical myeloma protein changes with chemotherapy, suggesting that one clone was reduced while the other remained unchanged. These data suggest a genetic basis for the resistance of low-RNA tumors to chemotherapy, possibly accounting for early relapse. Based on the therapy performed, one can judge the effectiveness of PCT according to the VRD protocol in the first line in the treatment of multiple myeloma with combined congenital mutations, but early relapse of the disease requires polychemotherapy with monoclonal antibodies.

CONCLUSION

Thus, we can conclude that patients with multiple myeloma with combined congenital mutations should be classified as a high-risk group despite the absence of high-risk cytogenetic abnormalities by FISH. MM with biclonal proteins should be considered a high-risk group, although the R-ISS classification does not assess biclonality.

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