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Clinical and Morphological Characteristics and Treatment of Gaucher Disease

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ABSTRACT

Background. Gaucher disease is a rare genetic pathology with an incidence of 1/50,000. Types II and III of the disease require special attention, manifesting in children and adolescents, with a severe course, disability, and high mortality. Purpose. The purpose is to evaluate clinical and morphological data from a patient with Gaucher disease type 1, a rare disease, in a single centre.

Methods. Data from a patient with type 1 Gaucher disease treated in a surgical department of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology Fergana Branch Republic of Uzbekistan in 2020 were assessed.

Results. We examined a male patient who was admitted to our center. Did this patient have a tumor of the spleen - lymphoma? liver cirrhosis, ascites, hepatosplenomegaly, moderate anemia, chronic calculous cholecystitis, chronic catarrhal gastroduodenitis. 2–3-degree varicose veins of the esophagus. esophagitis. were performed splenectomy.

Conclusion. Gaucher disease is a rare lysosomal storage disease that affects many systems. It causes irreversible morbidity in patients in whom diagnosis is delayed. The main treatment modality was enzyme replacement therapy. Because it is a rare and multisystem disease, with many complications, it is especially important for types 2 and 3 of the disease in children and adolescents, which have an acute course and high mortality. therefore, for early detection and diagnosis in patients with Gaucher disease, molecular genetic research methods should be introduced.

Keywords: Gaucher disease, β-glucocerebrosidase, pathomorphology, cytology, splenectomy.

INTRODUCTION

Gaucher disease (GD) - (ICD-10 code - E75.2 - impaired metabolism of β-glucocerebrosidase) - a rare orphan genetic lysosomal disease with an autosomal recessive type of inheritance, leading to lipid accumulation and dysfunction in various organs.

The pathogenesis of the disease is based on a hereditary deficiency in the activity of β-glucocerebrosidase, a lysosomal enzyme involved in the breakdown of cellular

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metabolic products. Mutations of the glucocerebrosidase gene located in the q21 region on chromosome 1 form the genetic basis. About 200 different mutations have been studied that lead to a defect in the enzyme (a decrease in its stability or activity), and which are associated with a wide polymorphism of the clinical symptoms of HD. The most common mutations are N370S, L444P, IVS2+1, and 84GG [6,9,15].

The lysosomal enzyme β-D-glucosidase is responsible for the breakdown of the complex lipid glucocerebroside into glucose and ceramide. Due to the low activity of this enzyme, complete cleavage of glucocerebrosides does not occur, resulting in their accumulation in macrophages and monocytes. As a result, we observe cells "filled" with lipids - Gaucher cells [1,8,12].

Gaucher disease is a systemic disease with similar clinical manifestations (hepato- and splenomegaly, cytopenia, bone lesions), but an extremely heterogeneous clinical course. Gaucher's disease was first described in 1882 by the French physician PCE Gaucher, who identified lipid-accumulating macrophage cells pathognomonic for this disease, later called Gaucher cells [4,5].

Due to the low activity of this enzyme, complete cleavage of glucocerebrosides does not occur, resulting in their accumulation in macrophages and monocytes. As a result, we observe cells "filled" with lipids - Gaucher cells [1,8,12].

EPIDEMIOLOGY

Gaucher disease affects people of any ethnic group or race. The disease is equally common among both women and men. The incidence is from 1/40,000 to 1/60,000 births, which is less than 10,000 patients in the world. And among Ashkenazi Jews, it rises to 1 case per 450-500 people. GD variants with primary CNS involvement occur in 5-10% of patients in most countries. To date, more than 200 mutations have been identified, of which 4 are the most common and account for about 90% of all mutations in the population of patients with Gaucher disease (Fig. 1).

The presence of two mutant alleles of the gene (homozygous inheritance) is associated with a decrease (or absence) of the catalytic activity of glucocerebrosidase, which leads to the accumulation of unutilized lipids in the cytoplasm of cells [4,16].

Glucocerebrosidase is found in all cells of the body, however, the deficiency of this enzyme is of the greatest importance for antigen-processing macrophages, since an important function of these "scavenger" cells is the degradation of blood cells that have completed their life cycle [2,11].

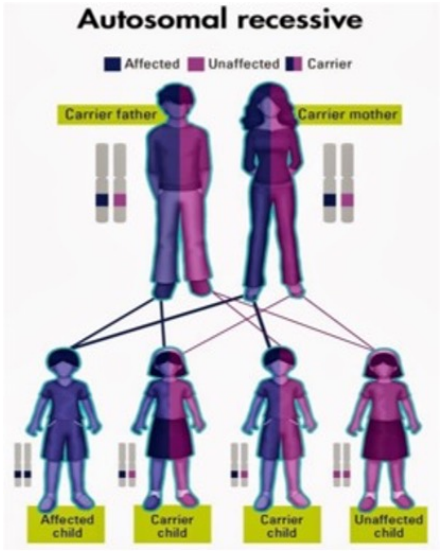

Fig.1. Inheritance of Gaucher disease by Autosomal Recessive type in which 25% are healthy, 75% are carriers and 25% are sick.

The absence or low activity of acid β-glucocerebrosidase leads to the accumulation of unutilized lipids in macrophage lysosomes and the formation of characteristic accumulation cells, or Gaucher cells, large elements ranging in size from 20 to 100 microns with a small, eccentrically located nucleus and abundant cytoplasm, which has a typical "wrinkled "or striped look (Fig. 2,3).

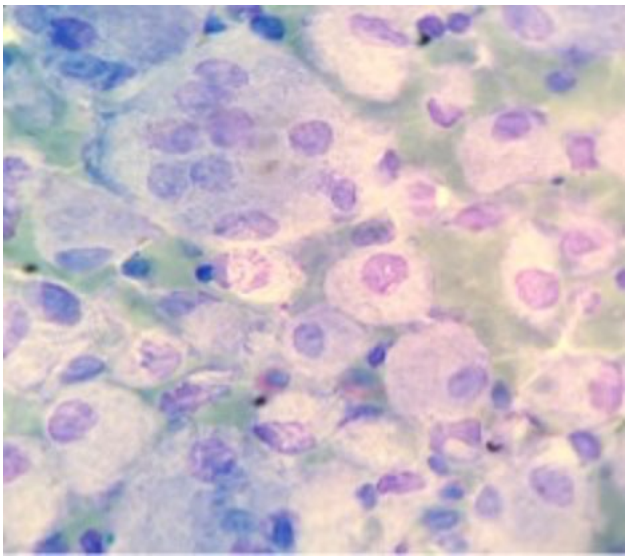

Fig.2. Cytological examination spleen imprint Increase x400. Romanowsky-Giemsa staining

The consequences of functional overload of macrophages are:

1) autocrine stimulation of monocytopoiesis and an increase in the absolute number of macrophages, which is manifested by hepato- and splenomegaly, infiltration of bone marrow, lungs, and other organs by macrophages;

2) violation of many physiological functions of macrophages, incl. regulation of hematopoiesis and bone metabolism, which presumably underlies the cytopenic syndrome and lesions of the osteoarticular system. Pathological effects of pro-inflammatory cytokines (IL-1, TNF-α, IL-6) and cytotoxic mediators (reactive oxygen species, nitroxide, proteolytic enzymes, complement components), which are secreted by activated macrophages overloaded with lipids [10,16].

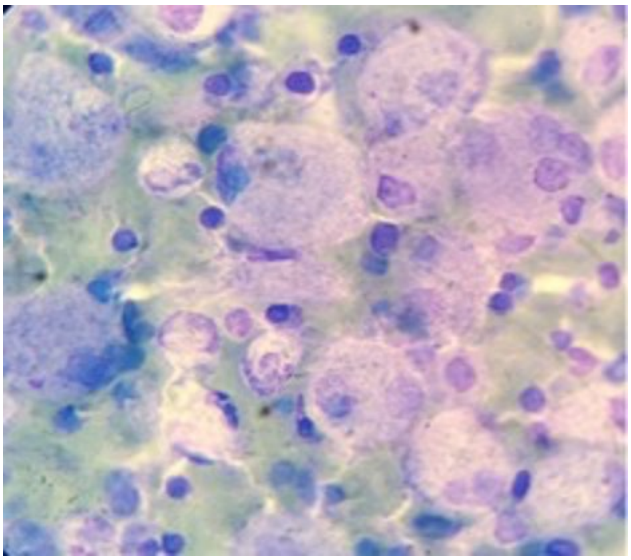

Fig.3. cytological examination of spleen imprint. Increase x400. Romanowsky-Giemsa staining.

CLINICAL PICTURE

There are three types of Gaucher disease:

I type - (adult or chronic) - non-neuronopathic form. The clinical manifestations of type 1 HD are varied. The age of manifestation of the disease varies from 0 to 60 years. Type 1 HD is chronic. The most common signs and symptoms are splenomegaly (95%), hepatomegaly (87%), bone radiographic changes (81%), thrombocytopenia (50%), anemia (40%), growth retardation (34%), bone pain (27%), as well as bone crises (9%) [2,10,13]. Severe bone loss occurs in childhood and adolescence. The causes of bone disorders are associated with extensive growths of pathological cells in the bones.

The involvement of bones in the process can be local or diffuse. At the same time, severe skeletal deformities are determined due to the development of osteoporosis, osteosclerosis, osteonecrosis, thinning of the cortical layer of tubular bones, and pathological fractures.

Osteonecrosis is the most debilitating manifestation of the disease and occurs with severe bone pain, causing the greatest concern to patients. On radiographs, the expansion of the ends of long tubular bones and the thinning of their cortical layer are revealed. Splenomegaly is a constant and the earliest sign of HD; on palpation, the spleen has a dense texture. In exceptional cases, the mass of the spleen can be 20% of the child's body weight. It occupies the entire abdomen and puts pressure on the stomach, reducing appetite. Infiltration with Gaucher cells and the development of infarcts in the spleen leads to organ fibrosis, scarring, and abdominal pain.

Hepatomegaly in HD is less pronounced than splenomegaly and develops, as a rule, later. The volume of the organ increases by 1.5–2 times. Many patients develop liver fibrosis with symptoms of portal hypertension. Significant disturbances are also found in the hematopoietic system. Normocytic, normochromic anemia, and severe thrombocytopenia are detected, in connection with which bleeding is noted. Haematological manifestations of the disease are mainly associated with infiltration of the bone marrow by Gaucher cells, displacement of normal hematopoietic elements, and hypersplenism [6, 8,17].

Type II (infantile) - acute neuronopathic form. The main symptoms of the disease in this type of HD occur in the first 6 months of life.

The clinical symptom complex includes signs of damage to the nervous system and internal organs. In the early stages of the disease, there is muscle hypotension, delay, and regression of psychomotor development. As the disease progresses, spasticity appears with type 2 neck retraction, flexion of the limbs, and oculomotor disturbances with the development of convergent strabismus, laryngospasm, and dysphagia.

Bulbar disorders with frequent aspirations are characteristic, leading to the death of the patient from apnea, aspiration pneumonia, or dysfunction of the respiratory centre of the brain [7,19]. Tonic-clonic seizures usually occur in the late stages of the disease and are resistant to prescribed anticonvulsant therapy. The course of the disease is rapidly progressive with a lethal outcome at 1–2 years of age [2, 5, 16].

III type (juvenile)- Chronic neuropathic form. The main feature of the clinical manifestations of HD of this type is that, along with damage to parenchymal organs (splenomegaly, hepatomegaly), neurological manifesta-

tions are also observed. Neurological symptoms usually occur between the ages of 6 and 15 and later [2,13].

A characteristic symptom is paresis of the muscles innervated by the oculomotor nerve, which for a long time may be the only neurological manifestation. There may be myoclonus, generalized tonic-clonic convulsions. Gradually progressing extrapyramidal rigidity, decreased intelligence, trismus, facial grimaces, dysphagia, and laryngospasm. Intellectual disabilities range from minor changes to severe dementia. Perhaps the development of cerebellar disorders, as well as disorders of speech and writing, behavioural changes, and episodes of psychosis. In most cases, the course of the disease is slowly progressive. Death occurs with severe damage to the lungs and liver. The life expectancy of patients with HD type 3 is 12–17 years, but cases of survival up to 30–40 years have been described [2,3].

Here is our clinical case.

Patient A.A., ethnic uzbek, was born in 1975 and lives in Kushtepa district, Ferghana region. He has considered himself a patient since 2004, when he first felt a feeling of heaviness in the left hypochondrium, an increase in the size of the spleen was clinically determined. April 2020 examined at FOMPMC. Ultrasound: gallbladder 65x29 mm, stones in the cavity 4x4, 25x19 mm; the spleen is enlarged 221x93 mm, contours are uneven, echogenicity is increased, with multiple spherical formations from 4 to 56 mm. In the abdominal cavity up to 2 liters of ascitic fluid.

Fibroesophagogastroduodenoscopy: chronic catarrhal gastroduodenitis. Varicose veins of the esophagus 2-3 degrees. Esophagitis.

MRI of the abdominal cavity: deformation of the gallbladder, dimensions 59x25 mm. Spleen: 243x12x151 mm, enlarged, in the parenchyma there are multiple spherical formations 18x24mm.

Tumor markers: AFP-6.7 ng/ml, CEA-8.2ng/ml. Patient 04.08.2020 was sent to the Fergana Branch of RSNPMTSOiR and examined.

X-ray of the lungs: no pathology.

Ultrasound of the abdominal cavity: in the gallbladder stones up to 24 mm. The structure is homogeneous, the density is 52-59 units. X. Spleen: 190x76 mm with multiple spherical formations 20x48 mm, hyperechoic. Retroperitoneal, cervical and inguinal lymph nodes are not enlarged.

Conclusion: hepatosplenomegaly. Calculous cholecystitis.

04.10.2020 hospitalized in the Department of Surgery of the Fergana Branch of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology. On general examination of the patient: In consciousness. The general condition is of moderate severity. Peripheral lymph nodes are not enlarged. The musculoskeletal system is deformed. Auscultation of the lungs revealed vesicular breathing. There are no complaints from the cardiovascular system. Heart sounds are rhythmic, pulse is 84 beats/min. Rhythmic, medium fullness. BP -120/80 mm Hg. Gastrointestinal tract: the tongue is moist with a whitish coating. The abdomen is soft on palpation, slightly swollen, pain in the navel. The liver is not enlarged, the spleen is enlarged and protrudes +10 cm beyond the edge of the costal arch.

Ultrasound of the abdominal cavity: in the gallbladder stones up to 24 mm. The structure is homogeneous, the density is 52-59 units. X. Spleen: 190x76 mm with multiple spherical formations 20x48 mm, hyperechoic. Ascitic fluid up to 2 litres. Retroperitoneal.

Laboratory blood tests.

Laboratory examination dated 04.11.2020: gemoglobin - 120 g/l, er - $3.9x10^{12}$/l, L - $4.0x10^{9}$/l, tr - $270x10^{3}$/l, p - 2%, segmented - 61%, lymphocyte - 28%, monocyte - 5%, eosinophils - 4%, ESR – 6 mm/h.

General urine analysis: 04.11.2020: urine density-1015, protein- abs, glucose - neg., leykocyte - 0-1 in field of view, Er-0-1 in field of view.

Biochemical blood analysis: on April 11, 2020: total protein - 60.7 g/l, ALT - 38 U/l, AST - 32 U/l, total bilirubin - 42.3 mmol/l, urea - 6.4 mmol/l, creatinine - 89.2 mmol/l, glucose - 4.5 mmol/l, LDH - 355.6 U/l.

Coagulogram on April 11, 2020: prothrombin time - 17.6 seconds, prothrombin index - 70%., fibrinogen - 4.7 g/l, prothrombin ratio - 1.42, MHO - 1.43. Blood type - AB (IV) Rh +.

Cytological examination of ascitic fluid on April 13, 2020: no atypical cells were found.

The main clinical diagnosis: neoplasm of the spleen? Lymphoma?

As of 04/14/2020 operation was scheduled: laparotomy, splenectomy.

For pathomorphological examination, prints and tissue samples of the spleen were taken. In the cytological examination of the imprints, we observe large, voluminous cells, 30-100 u in diameter, with an indefinite shape, round, slightly polygonal, oval or elongated. The nucleus is small and eccentric. Many binuclear or multinuclear cells. The cytoplasm is abundant, pale, and full of crystalline substance arranged in plates, perinuclearly,

in the form of "crumpled paper" of "onion leaves", or vortices.

Pathological examination of the removed spleen. Macroscopy: dimensions 25.0x18.0 cm (normal 10.0x14.0 cm) (Fig. 2), In the parenchyma, there are multiple spherical formations of dark red colour 1-3 cm in size (Fig. 4,5).

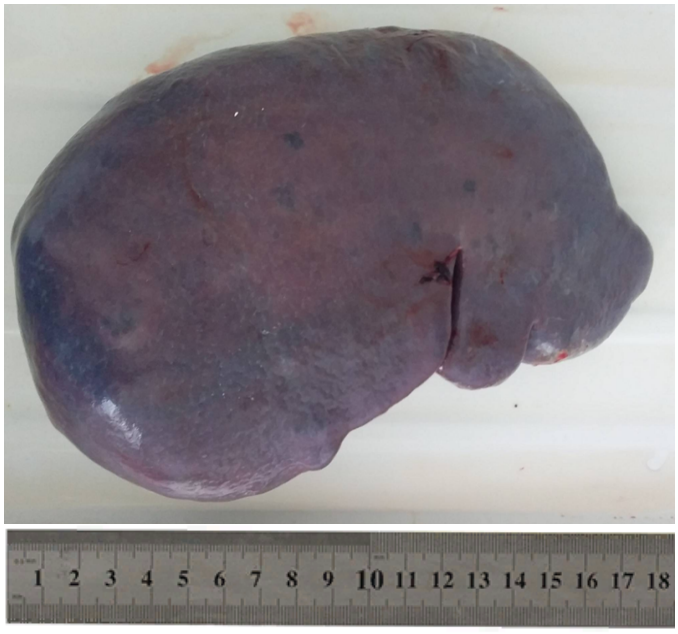

Fig. 4. Pathological examination of the removed spleen: spleen dimensions.

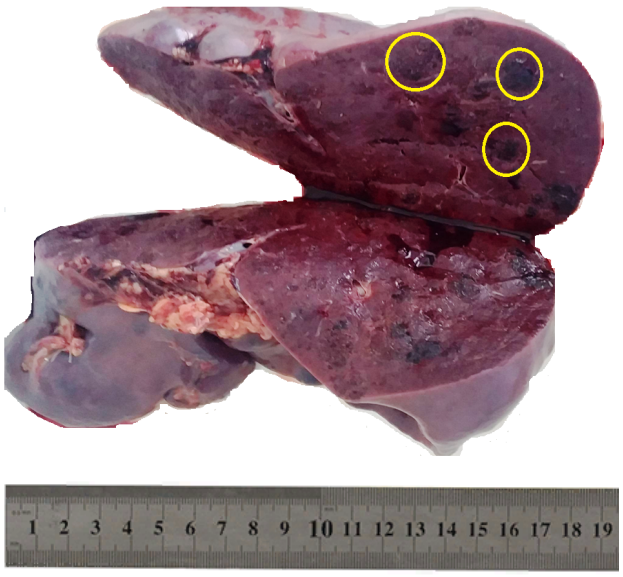

Fig. 5. Pathological examination of the removed spleen: Multiple spherical formations of dark red color (yellow circle).

Microscopy: Gaucher cells are dotted throughout the spleen parenchyma. Huge Gaucher cells with an eccentric nucleus, in places multinucleated large cells, are visible, the cytoplasm is foamy-lumpy, in the form of "onion leaves" or whirlwinds. There is Romanowsky-Giemsa stain was used for cytological studies. (Fig.6,7).

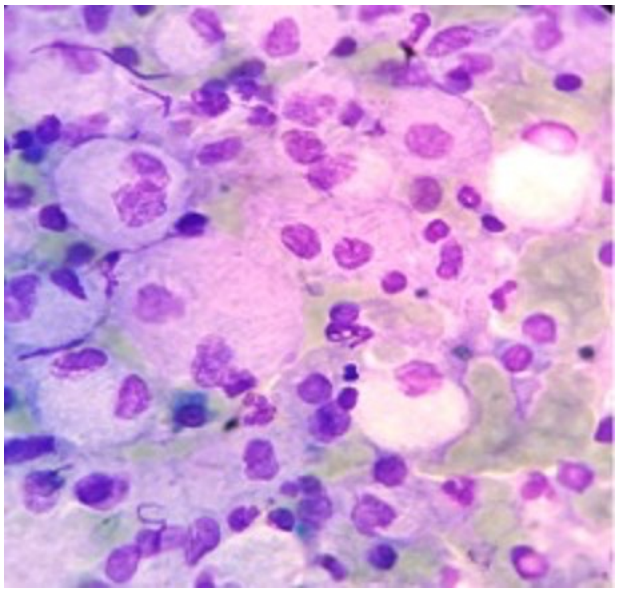

Fig.6. Cytological examination spleen imprint Increase x400. Romanowsky-Giemsa staining.

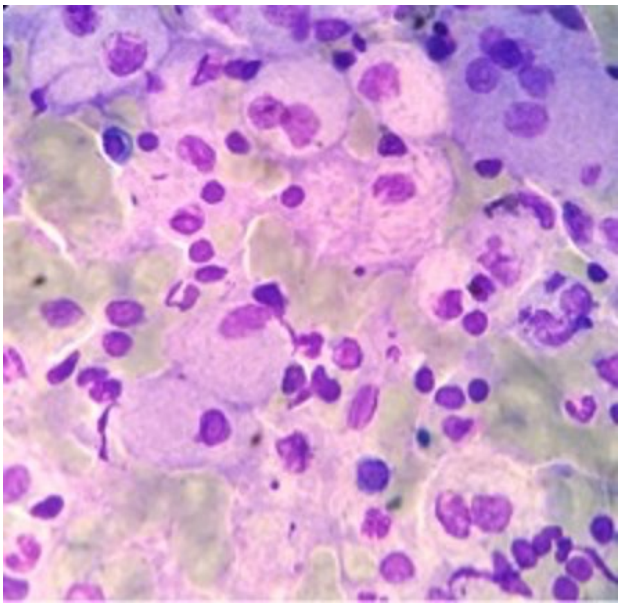

Fig.7. Cytological examination spleen imprint Increase x400. Romanowsky-Giemsa staining.

There is Hemotoxylin-eosin stain was used for histological studies. (Fig. 8,9,10,11).

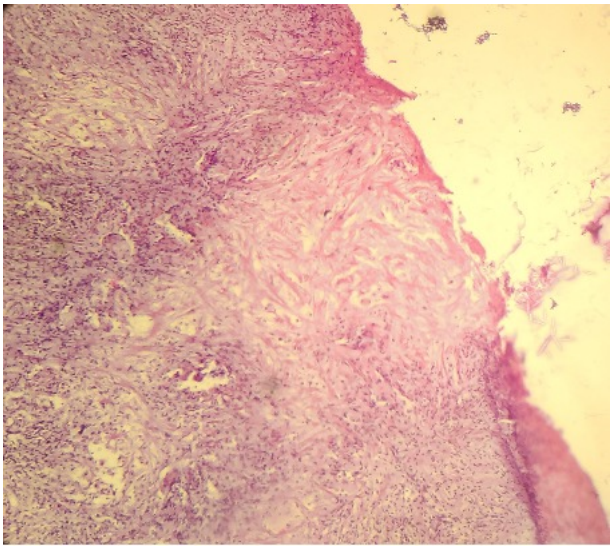

Fig.8. Histological specimen of the spleen. H&E. Increase x100

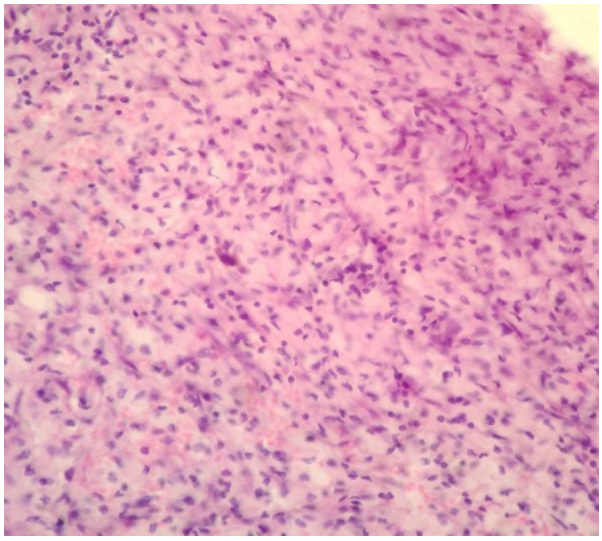

Fig.10. histological preparation, removed spleen. H&E. Increase x400

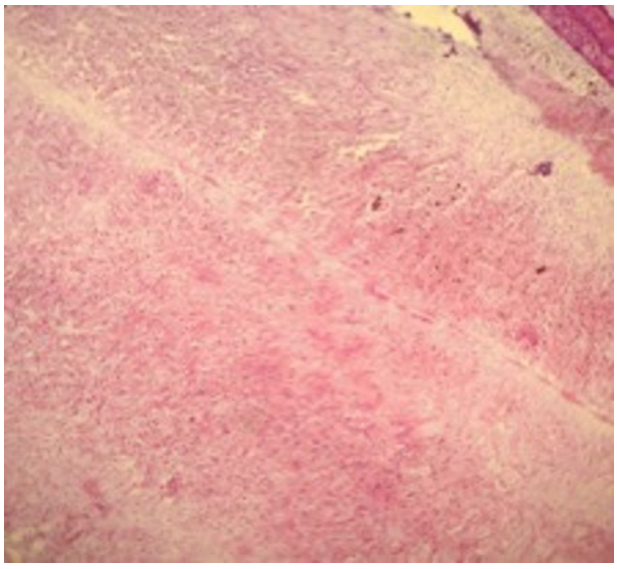

Fig. 9. Histological preparation of the spleen. H&E. Increase x100

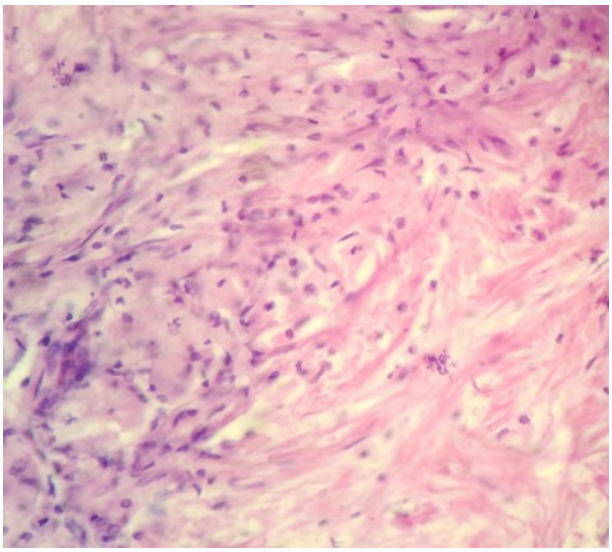

Fig.11. histological preparation, removed spleen. H&E. Increase x400

Diagnostics.

The diagnosis of Gaucher disease should be considered in a patient with unexplained splenomegaly, hepatomegaly, cytopenia, and bone symptoms. The standard of modern diagnostics is the biochemical analysis of the activity of acid β-glucocerebrosidase in blood leukocytes. The diagnosis is confirmed by a decrease in enzyme activity to 30% or less of the normal value. An additional characteristic biochemical marker is a significant increase in the activity of chitotriosidase in the blood serum (an enzyme presumably secreted by activated macrophages overloaded with unutilized lipids is a surrogate marker of Gaucher disease activity).

The diagnosis can be verified by molecular analysis of the glucocerebrosidase gene: the presence of two mutant alleles confirms the diagnosis of Gaucher disease [11,16].

Morphological examination of the bone marrow allows to identification of characteristic diagnostic elements - Gaucher cells and at the same time excludes the diagnosis of hemoblastosis or lymphoma as the cause of cytopenia and hepatosplenomegaly. The presence of numerous Gaucher cells in punctate and trephine biopsy of the bone marrow or liver biopsy is an evident sign of Gaucher disease. However, single cells with similar morphology (Gaucher-like) can occur in other diseases

accompanied by increased cell destruction, such as chronic myeloid leukemia and lymphoproliferative diseases [2,16].

On an optical microscope, Gaucher cells are easily recognized due to their aspect and size. These are voluminous cells, 30-100 μ in diameter and with an indefinite shape, round, slightly polygonal, oval, or elongated. The nucleus is small, eccentric, round, or stellate with spongy or compacted chromatin. Binuclear or multinuclear cells often appear. The cytoplasm is abundant, pale, and full of crystalline substance arranged in plates, perinuclearly, in the form of "onion leaves" or vortices. Rarely, cells contain small vacuoles and have a frothy appearance. Often in the cytoplasm are erythrocytes, erythroblasts, or pigment granules. The morphological changes in the spleen are manifested by the replacement of lymphoid tissue with Gaucher cells, they are of macrophage origin, and the contents of the cells have a characteristic autofluorescence and a characteristic appearance when microscopy in polarized light.

X-ray of the bones of the skeleton is used to identify and assess the severity of damage to the musculoskeletal system. Densitometry and MRI are more sensitive methods and make it possible to detect bone lesions (osteopenia, bone marrow infiltration) at early stages that are not available for visualization by radiography.

Differential diagnosis.

Gaucher disease should be differentiated from all diseases that occur with hepatosplenomegaly, cytopenia and bone lesions [2,16]:

- hemoblastoses and lymphomas;
- chronic cholestatic liver diseases;
- cirrhosis of the liver as a result of chronic viral and non-viral hepatitis;
- other hereditary fermentopathy (Niemann-Pick disease);
- thalassemia and other forms of hereditary pathology of erythron;
- rheumatic diseases (Felty's syndrome).

Diagnosis of HD currently consists of several successive stages:

1) detection of characteristic clinical signs of the disease;

2) measuring the activity of β-D-glucosidase in leukocytes; detection of characteristic Gaucher cells;

3) pathomorphological examination of biopsy specimens;

4) molecular genetic analysis [1,3,5]

Treatment.

Treatment for Gaucher disease is lifelong enzyme replacement therapy (ERT) with recombinant glucocerebrosidase (imiglucerase, ceresyme, velaglucerase, or taliglucerase). Orally administered inhibitors of glucosylceramide biosynthesis (miglustat or eliglustat) can also be used. In severe Gaucher disease (type I) in adults, the initial dose of Cerezyme is 30 units/kg/infusion. The drug is administered intravenously drip with an interval of 2 weeks. (2 times a month). In some cases, for example, with severe damage to the bones of the skeleton with multiple pathological fractures, the dose of Cerezyme can be increased to 60 U/kg per administration (120 U/kg/month) [2,11,16,18].

Treatment goals include: 1) prevention of irreversible damage to the musculoskeletal system and other vital organs (liver, lungs, kidneys); 2) regression or weakening of the cytopenic syndrome, 3) reduction in the size of the spleen and liver. Monitoring the effectiveness of enzyme replacement therapy includes monitoring of hemogram parameters, blood biochemistry, including the determination of a surrogate marker of macrophage activity - serum chitotriosidase; determination of the size of the spleen and liver; assessment of the state of the osteoarticular system (densitometry, MRI, bone radiography once every 1–2 years). When the goals are achieved, maintenance treatment with Cerezyme is prescribed at a dose of 10-15 U/kg as an infusion 2 times a month (for life).

DISCUSSION

Gaucher disease is one of the most common storage diseases inherited in an autosomal recessive manner. The disease is definitively diagnosed by detecting the mutations and enzyme deficiency in patients who present with symptoms and signs [4,6].

At our clinic, enzyme level determination is performed first in patients with suspected GD, and genetic analysis is performed in patients with low enzyme levels. In the Gaucher Registry study published in 2000, the data of 522 clinicians and 1698 patients with GD from 38 different countries were compiled. The genetic analysis of 766 of these patients was obtained, and the N409S (N370S) mutation was detected in 53% of the 1532 alleles. The L483P (L444P) mutation was the second most common mutation observed (16%). In the Gaucher Registry study, osteopenia was seen in 42% of the patients, and skeletal system involvement was higher in the group without a spleen than in the group with a spleen. In our

study, except for two patients, the lumbar z-score was < – 1 in five patients and ≤ –2.5 in six patients. [19].

To fully diagnose this type of pathology, it is necessary to conduct a molecular genetic study, which, unfortunately, is not available in our clinic. With a more thorough history taking, bone densitometry, trephine biopsy of the liver and/or bone marrow, and pathomorphological and molecular genetic studies, it might be possible to avoid surgical intervention with removal of the spleen and refer it to a specialist for conservative enzyme replacement therapy [9,13,15].

In our case, the 35-year-old man had suffered from GD, onset before 15 years old, with hepatosplenomegaly, splenectomy, ascites, bone destruction, myelofibrosis and MPGN. The activity of β-glucosidase was decreased, 1.95nmol/1 h/mg and gene detection demonstrated variant Leu483Pro. The diagnosis of type 1 GD (GD1) was verified. Splenomegaly is observed in more than 90% of GD patients and hepatomegaly is noted in 60-80% of GD patients [20]. Persistent liver enlargement, with or without liver enzyme alteration, fibrosis, cirrhosis, and portal hypertension, is the consequence of the intra-hepatic accumulation of Gaucher cells and secondary inflammatory response. Portal hypertension in GD is not just secondary to the presence of liver cirrhosis, since the overflow in the portal system is secondary to splenomegaly or the massive infiltration of Gaucher cells in liver parenchyma especially in splenectomized patients [21, 22].

In this case, peritoneal tap for ascites and its routine test indicated that it was non-inflammatory, which was thought to be related to portal hypertension and hypoalbuminemia. This patient is diagnosed with Gaucher disease type I - (adult or chronic) - non-neuronopathic form, with damage to the spleen, liver, and bones. Paraclinical manifestations: portal hypertension with oesophagal varices of 2-3 degrees, esophagitis, chronic catarrhal gastroduodenitis, anemia of 1 degree.

CONCLUSIONS

Thus, Gaucher disease is a rare disease that belongs to the group of lysosomal storage diseases and is characterized by polymorphic clinical symptoms with damage to many organs and systems and a progressive course without adequate replacement therapy. Timely diagnosis of the disease in children has certain difficulties associated with the lack or insufficiency of information among paediatricians and general practitioners.

The polymorphism of clinical manifestations and the absence of pathognomonic symptoms impede the diagnosis in the early stages, and the polysystemic nature of the lesion disguises Gaucher's disease as a variety of diseases.

Hereditary diseases that lead to disability and a decrease in the quality of life of the population are of social importance with financial consequences for both the patient and the state. In this regard, it is advisable to make early diagnosis using molecular genetic research methods and conduct timely pathogenetic therapy to prevent disability.

GD is a rare lysosomal storage disease that affects many systems. It can cause irreversible morbidity in patients in whom the diagnosis is delayed. The main treatment modality is enzyme replacement therapy. Because it is a rare and multisystemic disease, patients should be followed up at centres that have experience in treating the Gaucher disease.

Consent for publication - The author agrees to open publication.

Availability of data and material - Available

Competing interests - No

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REFERENCES:

1. Adar T, Ilan Y, Elstein D, Zimran A. Liver involvement in Gaucher disease - Review and clinical approach.Blood Cells Mol Dis. 2018 Feb;68:66–73. https:// doi. org/ 10. 1016/j. bcmd. 2016. 10. 001.
2. Beutler E., Gelbart T., Scott C.R. Hematologically important mutations: Gaucher disease // Blood Cells Mol. Dis. 2005; 35(3):355-64.
3. Beyer E.M., Bukina T.M., Tsvetkova I.V. Biochemical and genetic diagnosis of Gaucher disease and phenotypic heterogeneity of the disease // Vopr. medical chemistry. 2000.;5:9-12.
4. Brady R.O., Kanfer J.N., Shapiro D. Metabolism of glucocerebrosides: evidence of an enzymatic deficiency in Gaucher disease. Biochem. Biophys. Res. commun. 1965; 18:221–5.
5. Carubbi F, Cappellini MD, Fargion S, Fracanzani AL, Nascimbeni F. Liver involvement in Gaucher disease: a practical review for the hepatologist and the gastroenterologist. Dig Liver Dis. 2020;52(4):368–73. https:// doi.org/ 10. 1016/j. dld. 2020. 01. 004.
6. Charrow J, Andersson HC, Kaplan P, et al. The Gaucher registry: demographics and disease characteristics of 1698 patients with Gaucher disease. Arch In-

tern Med. 2000;160(18):2835–43. https:// doi. org/ 10. 1001/archi nte. 160. 18. 2835
7. Grabowski G.A. Phenotype, diagnosis, and treatment of Gaucher's disease // Lancet. 2008; 372(9645):1263-71.
8. Guggenbuhl P., Grosbois B., Chalus G. Gaucher disease: review // Joint Bone Spine. 2008;75(2):116-24.
9. Gundobina O.S., Komarova E.V., Namazova-Baranova L.S., Gevorkyan A.S., Movsisyan V.S. Gaucher disease in children. // Pediatric pharmacology. 2013; 10 (6):72-5.
10. Koprivica V., Stone D.L., Park J.K. Analysis and classification of 304 mutant alleles in patients with type 1 and type 3 Gaucher disease // Am. J. Hum. Genet. 2000; 66(6):1777-86.
11. Krasnopolskaya K.D. Hereditary metabolic diseases. M.2005; 20–2.
12. Lee R.E. The pathology of Gaucher disease. Prog. Clin. Biol. Res. 1982; 95:177–217.
13. Lukina E.A. Gaucher's disease: the current state of the issue // Russian Medical News. 2008; 12 (2):51-6.
14. Mistry P.K. Gaucher disease: a model for modern management of a genetic disease. J. Hepatol. 1999; 30:1–5.
15. Niederau C. Gaucher disease. Bremen: UNI-MED; 2006: 84.
16. Poll L.W., Terk M.R. Skeletal aspects of Gaucher disease. Brit. J. Radiol. 2002; 75(1): A1–A42.
17. Stirnemann J, Belmatoug N, Camou F, Serratrice C, Froissart R, Caillaud C, Levade T, Astudillo L, Serratrice J, Brassier A, Rose C, de Billette T, Berger MG. A Review of Gaucher Disease Pathophysiology, Clinical Presentation and Treatments. Int J Mol Sci. 2017;18(2):441. https:// doi. org/ 10. 3390/ijms1 80204 41
18. Stirnemann J., Belmatoug N., Camou F. A Review of Gaucher Disease Pathophysiology, Clinical Presentation and Treatments. Int J Mol Sci. 2017;18(2):441. doi:10.3390/ijms18020441
19. Vorobyov A. I. Rational pharmacotherapy of diseases blood systems. Moscow: Litterature. 2009; 563–6.
20. Weinreb N.J. Type I Gaucher disease in elderly patients. Gaucher Clin. Persp. 1999; 7(2): 1–8.
21. Yassin N.A., Muwakkit S.A., Ibrahim A.O. A novel genotype c.1228C>G/c.1448C-1498C (L371V/RecNciI) in a 3-year-old child with type 1 Gaucher disease // J. Appl. Genet. 2008;49(4):421-24.
22. Zimran A., Kay A., Beutler E. Gaucher disease: clinical, laboratory, radiological and genetic features of 53 patients. Medicine. 1992; 71:337–53.

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GOSHE KASSALIGINING KLINIK-MORFOLOGIK HARAKTERISTIKASI VA DAVOLANISHI

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ABSTRAKT

Dolzarbligi. Gaucher kasalligi kam uchraydigan genetik patologiya bo'lib, 1/50 000 ni tashkil qiladi. Kasallikning II va III turlari og'ir kechishi, nogironligi va o'lim darajasi yuqori bo'lgan bolalar va o'smirlarda namoyon bo'ladigan alohida e'tibor talab qiladi.

Usullar. O'zbekiston Respublikasi Farg'ona filiali Respublika ixtisoslashtirilgan onkologiya va radiologiya ilmiy-amaliy tibbiyot markazi jarrohlik bo'limida 2020-yilda davolanayotgan 1-toifa Gosher kasalligi bilan og'rigan bemorning ma'lumotlari o'rganildi.

Natijalar. Markazimizga murajjaat qilgan erkak bemorni tekshiruvlardan o'tkazildi. Bu bemorga dastlabki tashxis taloq neoplasmasi – limfoma qo'yildi. Hamroh patologiya: jigar sirrozi, astsit, gepatosplenomegaliya, o'rta og'ir daraja anemiya, surunkali kalkulyoz xoletsistit, surunkali kataral gastroduodenit. Qizilo'ngachning tomirlarining 2-3 darajadagi varikoz kengayishi. ezofagit. Bemorga splenektomiya jarrohlik tashrihi o'tkazilgan.

Xulosa. Gaucher kasalligi - bu bir nechta tizimlarga ta'sir qiladigan kam uchraydigan lizosomalarni saqlashini buzilishi. Bu tashxis kechiktirilgan bemorlarda qaytarilmas asoratlarni keltirib chiqaradi. Asosiy davolash usuli fermentlarni almashtirish terapiyasidir. Chunki bu juda kam uchraydigan va ko'p tizimli kasallik bo'lib, ko'plab asoratlarni keltirib chiqaradi.

Kalit so'zlar: Gosher kasalligi, b-glyukotserebrosidaza, O'zbekiston, patomorfologiya, sitologiya, splenektomiya

КЛИНИКО-МОРФОЛОГИЧЕСКАЯ ХАРАКТЕРИСТИКА И ЛЕЧЕНИЕ БОЛЕЗНИ ГОШЕ

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АБСТРАКТ

Актуальность. Болезнь Гоше является редкой генетической патологией с частотой встречаемости 1/50000.

Методы. Изучены данные пациента с болезнью Гоше 1 типа, находившегося на лечении в хирургическом отделении Республиканского специализированного научно-практического медицинского центра онкологии и радиологии Ферганского филиала Республики Узбекистан в 2020 году.

Полученные результаты. Мы обследовали пациента мужского пола, поступившего в наш центр. Предварительный диагноз этому больному выставлен опухоль селезенки – лимфома. Сопутствующая патология: цирроз печени, асцит, гепатоспленомегалия, умеренная анемия, хронический калькулезный холецистит, хронический катаральный гастродуоденит.

Заключение. Болезнь Гоше — редкое лизосомальное мультисистемное ззаболевание накопления, поражающее многие системы, имеющее множество необратимых осложнений, особенно у пациентов, которым диагноз ставится поздно. Основным методом лечения является заместительная ферментотерапия.

Ключевые слова: болезнь Гоше, β-глюкоцереброзидаза, Узбекистан, патоморфология, цитология, спленэктомия.