Genij Ortopedii. 2022. Vol. 28, no. 2. P. 268-273.

Original article

https://doi.org/10.18019/1028-4427-2022-28-2-268-273

Osteoarticular pathology in Gaucher disease, complicated by tuberculosis (clinical observations)

Lyudmila A. Semenova[1]✉, Vladimir A. Khomenko[1], Kira A. Lukina[2]

[1] Central Research Institute of Tuberculosis, Moscow, Russian Federation
[2] National Hematology Medical Research Center, Moscow, Russian Federation

Corresponding author: Lyudmila A. Semenova, lu.kk@yandex.ru

Abstract

Introduction Gaucher disease belongs to the group of hereditary lysosomal orphan cumulative diseases caused by deficiency of the β-glucocerebrosidase enzyme. It features polysystemic affection, including bone tissue. The osteoarticular system in Gaucher disease is affected in 75–83 % of cases. Moreover, infectious processes may frequently develop, including tuberculosis. **Purpose** The aim of this work was to demonstrate the features and difficulties in diagnosing osteoarticular pathology in Gaucher disease complicated by tuberculosis infection in patients of different ages. **Material and methods** The following methods were used in the study: clinical material (including a retrospective case history), additional research methods, imaging diagnosis (radiography, computed tomography, magnetic resonance imaging), data from the protocols of surgical interventions, morphological study of biopsy / surgical material with microbiological confirmation. **Results** Two case reports are presented that demonstrate destructive changes in bones and joints developed due to Gaucher disease, and its further association with tuberculosis infection. One patient was diagnosed with Gaucher disease in childhood and gradually developed osteoarticular pathology that was later complicated by tuberculous. In the second case, the patient sought medical help due to pain in the lumbar spine as he already had osteoarticular manifestations. Upon further examination at the age of 32, Gaucher disease was diagnosed. Tuberculosis infection of the bones was suspected but was questioned several times by various medical institutions. **Conclusion** The clinical cases discussed confirm the difficulty of diagnosing osteoarticular pathology in Gaucher disease, especially in associated tuberculosis. This issue dictates the need for a specific examination algorithm.

Keywords: bone, joint, tuberculosis, Gaucher's disease

For citation: Semenova L.A., Khomenko V.A., Lukina K.A. Osteoarticular pathology in Gaucher disease, complicated by tuberculosis (clinical observations). *Genij Ortopedii*, 2022, vol. 28, no 2, pp. 268-273. https://doi.org/10.18019/1028-4427-2022-28-2-268-273

INTRODUCTION

The osteoarticular system in the patients with Gaucher disease is affected in 75–83 % of cases. Moreover, infectious processes of a certain etiology, for example, tuberculosis, may develop alongside. Gaucher disease is included in the group of hereditary lysosomal orphan storage diseases caused by a deficiency of the enzyme ß-glucocerebrosidase and multisystem lesions, including bone tissue [1–6]. Gaucher disease occurs when the gene for the lysosomal enzyme ß-glucocerebrosidase (GBAI gene) located on the long arm 1q21q is mutated [1, 6]. Insufficiency of ß-glucocerebrosidase leads to the accumulation of glucosylceramide, which consists of 497 amino acids and is part of the lysosomes of all organs and tissues [7, 8]. Thus, glucosylceramide, being insufficiently cleaved, accumulates in the lysosomes of macrophages, gradually turning into large cells with a foamy bluish cytoplasm (when stained with hematoxylin and eosin) and a large eccentric nucleus, the so-called Gaucher cells (macrophages of processed products overloaded with lipids).

One of the most favorite locations of these cells is the bone marrow [9–13]. The intertrabecular spaces are filled with infiltrates from Gaucher cells, that limit blood flow, disrupt nutrition, contributing to the formation of osteonecrosis. The mineral metabolism of calcium and phosphorus is disturbed resulting in a change in the strength and shape of bones [1, 14]. Abnormal bone tissue thickening occurs in the form of sclerotic areas along the medullary canal with a structural change, flattening of the upper third of the femoral head, and deformity, which is radiologically defined as an Erlenmeyer flask [15–17]. Disorder in the bone shape characterizes the process of remodeling in response to the accumulation of Gaucher cells in the medullary spaces. The presence of a small number of Gaucher cells in the medullary spaces may be asymptomatic.

In a significant accumulation of Gaucher cells, the patients experience so-called bone crises with severe pain that may persist from several hours to several days. Bone involvement in Gaucher disease occurs in 75–83 % of patients. In most cases, the process of bone involvement begins in childhood or adolescence. Long bones are mostly affected: the femur, tibia, and humerus [18]. Gaucher cells can stimulate the release of pro-inflammatory cytokines, interleukins IL-1, IL-6, IL-10, tumor necrosis factor α, macrophage colony stimulating factor. It is suggested that IL-6 simulates bone resorption, contributing to the onset of osteopenia and osteoporosis [1]. Infection may penetrate into the bone tissue.

Purpose of the study To demonstrate the features and complexity of diagnosing osteoarticular pathology in patients of different ages with Gaucher disease complicated by tuberculosis

MATERIAL AND METHODS

We report two clinical cases with Gaucher disease. The methods used for their study are clinical examination including previous history of the disease, additional methods of study, radiological imaging (radiography, computed tomography, magnetic resonance), findings of surgical interventions, morphological investigation of the biopsy/surgical material and microbiological confirmation.

RESULTS

Case 1 A male, born in 1981, was diagnosed with Gaucher disease when he was four years of age. At the age of 13, a splenectomy was performed for hepatosplenomegaly. At the age of 17, arthrodesis of the left hip joint was performed due to osteonecrosis of the head of the left femur (Fig. 1).

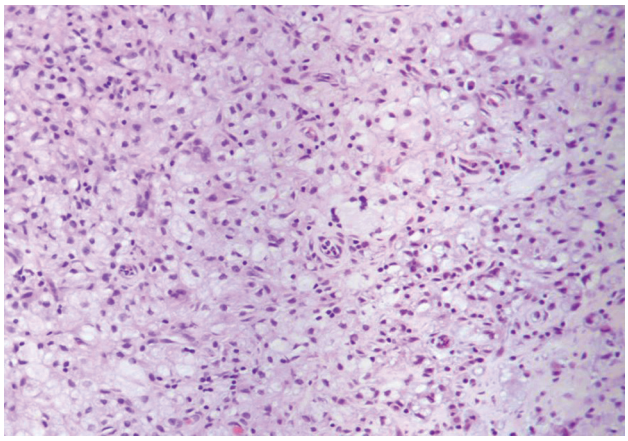

Fig. 1 Histological preparation. Gaucher disease. Deposits of the Gaucher cells in the femur bone marrow. Staining with hematoxylin and eosin, × 100

At the age of 27 years, he started complaining of pain and non-weight bearing on the right hip. Left limb shortening of 5 cm was revealed and sharp limitation in the range of motion in the hip joints: due to arthrodesis on the left side and due to pain on the right side. At admission to the treatment, his condition was severe. He could walk only with crutches. The patient was exhausted and weighed only 55 kg, being 185 cm tall. There were no sinuses or wounds in the area of the right hip. There was expressed adduction of the right hip and severe pain. Radiological study (radiography, CT and MRI) revealed signs of osteonecrosis of the left head and medial fracture of the right femoral head, and formed subluxation (Fig. 2). Due to the above symptoms and his orthopedic condition, total arthroplasty of the right hip joint was performed. The postoperative period ran smoothly. The patient had a simultaneous pathogenetic therapy with enzymes for Gaucher disease.

Three months after the surgery, a divergence of the sutures appeared in the area of the postoperative scar. A decision was made on surgical intervention and revision of the surgical area. A purulent cavity was found in the region of the right hip joint, fistulous tracts communicating with the components of the endoprosthesis. A lavage system was installed, and secondary sutures were applied to the area of the surgical wound. Despite the lavage system, wound dressing, antibiotic therapy, an inflammatory infiltrate appeared in the left gluteal region, communicating with the left hip joint, and another fistulous tract in the same area. Tuberculous sacroiliitis was suspected and diagnosed, which was confirmed by microbiological cultures from the fistulous discharge. Anti-tuberculosis therapy was prescribed according to an individual regimen. Due to positive clinical dynamics, after 2 months, a necrosequestrectomy of the left sacroiliac joint was performed with excision of the sinus and a histological examination of the surgical material, which confirmed the tuberculous etiology. Despite subsequent treatment with anti-tuberculosis drugs, a new fistulous tract appeared in the left gluteal region. In November (4 months after the date of the last operation), a second revision and necrosequestrectomy of the left sacroiliac joint and sacrum were performed. Anti-tuberculosis therapy continued. As a result, the temperature returned to normal, the patient gained weight.

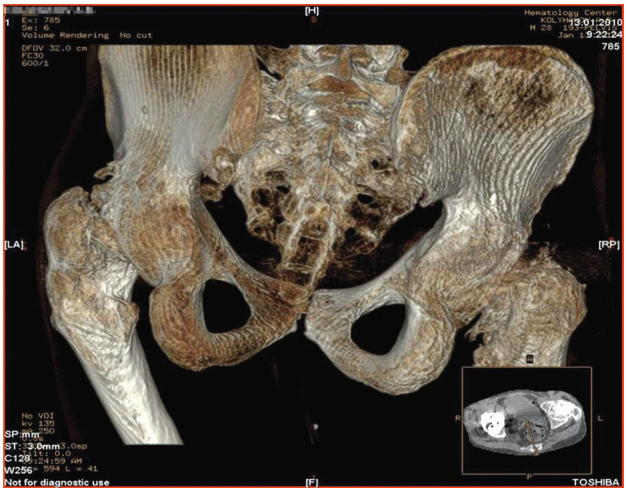

Fig. 2 3D computed tomography of the pelvis and hip joints in Gaucher disease. Ankylosis of the left hip joint. Neoarthrosis of the right hip joint

However, new sinuses in the left gluteal region led to the decision to remove the endoprosthesis from the right hip joint with excision of the fistulous tracts, sequestrectomy of the sacroiliac joint and sacrum that was performed two years after the THA. To ensure the fusion of fragments of the right femur, a coxite bandage was applied. Over the next two years, the patient followed the recommendations for the treatment of Gaucher disease and tuberculosis. During a routine examination, flexion adduction contracture, neoarthrosis of the right hip joint with a shortening of the lower limb by 8 cm, pelvic and lumbosacral spine inclination and altered gait were

revealed. Computed tomography detected destruction of the bones of the sacrum, extensive areas of destruction, massive osteosclerosis of the ilium. Prophylactic anti-tuberculosis chemotherapy according to an individual regimen continued and at the urgent request of the patient, three years after the first total arthroplasty, revision THA of the right hip joint was performed. The postoperative period proceeded without complications. However, after two years, the fistulous tract in the area of the right hip joint reopened, which did not close, despite ongoing antibacterial and anti-tuberculosis therapy. Due to recurrent suppuration in the area of the operation, three years after the repeated arthroplasty, a decision was made to remove the implant. In the postoperative period in the following 12 months, the patient was prescribed an individual regimen of anti-tuberculosis chemotherapy and anti-tuberculosis drugs of the 1st and 2nd line according to sensitivity. The patient is currently receiving enzyme replacement therapy for Gaucher disease on a regular basis. There are no signs of tuberculous inflammation of the osteoarticular system, so the therapy for osteoarticular tuberculosis was completed.

Case 2 A female, born in 1984, had a history of splenectomy at the age of 13 but the diagnosis was not established. She delivered twins at the age of 27 by cesarean section. At the age of 30, MRI revealed protrusion of intervertebral discs at L4–SI level, extrusion of L5–SI with signs of root compression. Two paravertebral injections of diprospan were done without effect. At the age of 31, the patient sought medical help for subfebrile temperature and pain in the lumbar region, shoulder, knee, ankle joints, and painful formations in the right arm, left forearm, and hands. The patient was hospitalized in the rheumatology department with a diagnosis of septicopyemia and arthritis of the left hip joint and had antibiotic therapy without positive dynamics. Further examination revealed osteomyelitis of the body of the right iliac bone; lateral masses of the sacrum; abscesses in the right iliac, lumbar muscles; left femur; abscesses in the medial muscle group of the left thigh; phlegmon of adjacent retroperitoneal fatty tissue. A biopsy of the left femur was performed. According to its results, she was transferred to the department of extrapulmonary tuberculosis with a diagnosis of tuberculosis of the osteoarticular system (tuberculous coxitis on the left and sacroiliac joint on the right), where the "cold" leak was opened and drained. The diagnosis of tuberculosis was confirmed bacteriologically by studying the wound of the left hip joint and discharge from the active drainage, (Mycobacterium tuberculosis was detected). Anti-tuberculous therapy was prescribed according to regimen I, followed by a positive effect (significantly decreased pain). However, the patient went to another medical institution, where the diagnosis of tuberculosis was questioned and the patient was operated on. An attempt was made to replace the left hip joint, which was complicated by dislocation of the femoral head due to damage to the posterior wall of the acetabulum. The operation was completed with partial resection of the femoral head, necrectomy of the tissues of the left hip joint (2016). Histological and microbiological studies of the surgical material were performed. Osteomyelitis was determined microscopically without signs of specificity. Bacteriological examination did not reveal mycobacterium tuberculosis. Based on it, the tuberculous etiology of the inflammatory process was rejected and another diagnosis was made: the consequences of reactive arthritis. In the next hospital, at the age of 32, for the first time (taking into account the history of splenectomy), Gaucher disease was suspected and verified. An enzymatic diagnosis was performed, which confirmed the presence of hereditary fermentopathy (beta-glucocerebrosidase enzyme activity 0.78 μmol/liter/hour; GDF gene mutation: T 370S/M162T). A mutation was detected in one allele of the prothrombin gene (heterozygous inheritance). The patient was transferred to a specialized medical institution for correction and treatment of Gaucher disease. Upon admission, the severity of the condition was due to a disabling orthopedic status: she moved with the help of crutches due to the inability to support the left lower limb with a shortening of 4–5 cm. She felt sharp pain during active and passive movements of the left hip joint. Radiologically, dislocation, coxarthrosis and osteonecrosis in stage 2 of the head of the left femur was detected (Fig. 3).

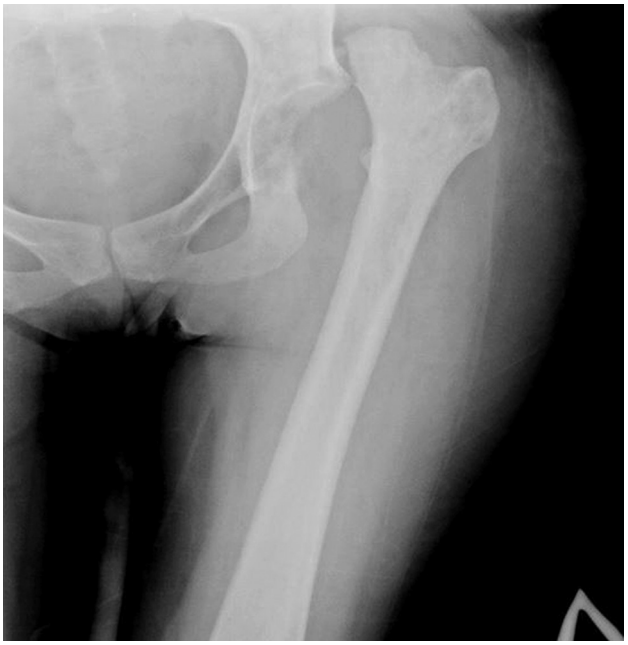

Fig. 3 Radiograph of the left hip joint. Tuberculosis coxitis, left femoral head dislocation

A bulb-shaped expansion of the distal parts of both femurs, bone marrow infiltration caused by the underlying disease was revealed. Small-focal disseminations were found in the lungs, which were interpreted as manifestations of pneumonia, and axillary lymphadenopathy. Changes in the bones of the pelvis

and hip joints were regarded as the consequences of a long-term purulent inflammatory process with spread to the region of the sacroiliac joint on the right and sacral vertebrae. A decision was made to perform surgical intervention with sequestrectomy of the left hip joint, revision with possible unipolar arthroplasty or placement of an articulating spacer. As preoperative preparation, anti-tuberculosis chemotherapy for 4 weeks was carried out according to regimen 1, substitution (Gaucher disease) and metabolic therapy. In 2017, it was possible to perform total arthroplasty of the left hip joint. The operation was technically difficult due to previous surgical interventions on the joint. The joint cavity was opened through an anterolateral approach, and about 50 ml of a light, transparent, odorless liquid and flakes were released. The revision revealed a posterior dislocation of the head of the left femur, damage to the posterior sections of the joint capsule, a defect in the posterior edge and posterior sections of the roof of the acetabulum. The neck of the femur was treated for the installation of the femoral component of the endoprosthesis. The head and neck of the femur were completely resected. The proximal femur was treated to size 7 of the femoral component of the Ilsa endoprosthesis. After removal of adhesions, the acetabulum was released. In attempt to install a monopolar modular head with a diameter of 44 mm, a tendency to posterior dislocation was noted. It meant unipolar prosthesis could be unstable, the same referred to the installation of an articulating spacer. Based on the above, a decision was made to perform total arthroplasty. The acetabulum was treated with cutters up to 48 size. Due to the possibility of a specific infectious process, the pelvic and acetabular components of the endoprosthesis were placed on bone cement with gentamicin in the maximum possible horizontal position (to prevent dislocation of the femoral head). After the installation of the Ilza-7 femoral component, the implant was reduced. The Ilsa-standard size 7 stem was implanted; cementless acetabular component of size 46 mm according to the "Press-fit" type with additional cement fixation; insert size 44–46 mm; "S" size of the head. Reduction of the components of the implant was performed. The tissues removed during surgery, including a part of the resected femoral head, were sent for morphological examination (Fig. 4).

In the postoperative period, blood transfusions were administered; combined antibiotic-enzyme therapy; anticoagulant prophylaxis. The course of the postoperative period proceeded without complications, the wound healed by primary intention. The sutures were removed on the 14th day. The patient was discharged with a diagnosis of tuberculosis of multiple locations: left-sided coxitis, right-sided sacroiliitis, S1 spondylitis, active phase. Condition after sequesternecrectomy of the left hip joint. Complete dislocation of the head of the left femur. Condition after total arthroplasty of the left hip joint. Over the next 24 months, anti-tuberculosis therapy was prescribed, the regimen of which was adjusted depending on clinical and laboratory data. Prescribed anti-tuberculosis drugs were well tolerated. X-ray control of the osteoarticular system and chest organs followed after 3, 6, 12 months and then annually (Fig. 5).

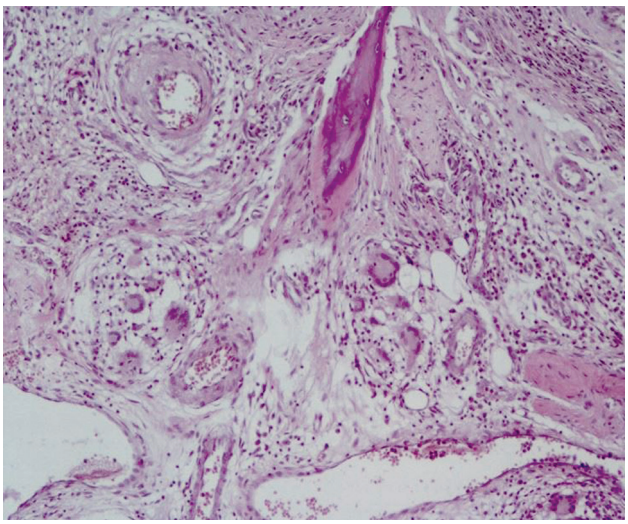

Fig. 4 Histological preparation. Tuberculosis of the femur. Epithelioid cell granulomas, giant multinucleated Pirogov-Langgans cells. Staining with hematoxylin and eosin, × 100

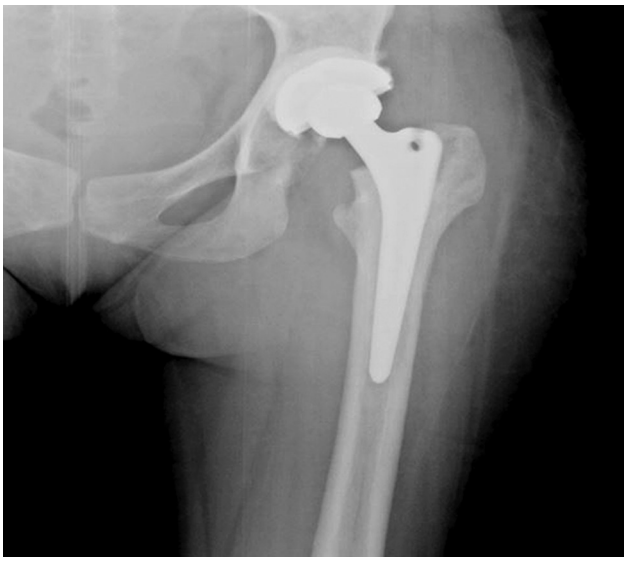

Fig. 5 X-ray of the left hip joint two years after total arthroplasty

At present, three years after the operation, the patient's condition is satisfactory. She walks without additional support. The assessment of the function of the left hip arthroplasty according to Harris score was: pain – 42 points, daily activity – 12 points, function – 44 points, amplitude / movement – 4 points, deformity – 4 points. Gaucher disease is being corrected by appropriate enzyme therapy. Treatment of osteoarticular tuberculosis was completed on the basis of the absence of signs of tuberculosis recurrence.

DISCUSSION

The current classification divides Gaucher disease into two types: non-neuropathic and neuropathic. The non-neuropathic type can manifest at any age and is characterized by a chronic course. Radiological diagnostics (radiography, magnetic resonance imaging, densitometry, scintigraphy) helps to identify early changes in the bones, the dynamics of the pathological process. Radiography allows diagnosing deformities, fractures, determine the thickness of the cortical layer of the bone and the presence of osteonecrosis. Magnetic resonance imaging evaluates the state of the bone marrow. Densitometry shows the density of bone tissue, the content of inorganic calcium phosphate compounds, and severity of osteopenia [19, 20].

In the presented two clinical cases, the patients had a non-neuropathic type of Gaucher disease. In the first patient, Gaucher disease was diagnosed early, in childhood. Despite the therapy, the problems of the osteoarticular system manifested themselves at the age of 17, when osteonecrosis of the head of the left femur was diagnosed, and therefore arthrodesis of the left hip joint was performed. Over the following 10 years, the state of health was satisfactory. Then, the patient developed a serious condition with a significant shortening of both limbs and severe pain. At the age of 27, the first total arthroplasty of the right hip joint was performed. However, the postoperative period was complicated by tuberculosis infection and sacroiliitis. Though the prophylactic anti-tuberculosis chemotherapy was administered, an attempt of repeated arthroplasty of the right hip joint was not successful, but then the endoprosthesis had to be removed.

In the second clinical observation, the Gaucher disease was first detected at the age of 32, when serious problems with the osteoarticular system and corresponding complaints appeared. For several years, the patient was examined at medical institutions of the country. However, Gaucher disease was not immediately identified. Similar to the first case, tuberculosis infection joined the osteoarticular pathology.

In modern conditions of active preoperative treatment, the morphological diagnosis of tuberculous features some peculiarities as there is no clear classical structure. This is evidenced by the second clinical case. Under the treatment provided, there were no signs of granulomatous inflammation characteristic of tuberculosis. The diagnosis of tuberculosis was rejected and the course of the pathological process aggravated. The histological picture consists of a combination of signs characteristic of tuberculous inflammation: scattered foci of caseous necrosis, a few epithelioid cell granulomas, giant multinucleated macrophages of different age, including Pirogov-Langhans, lymphoid infiltration, and the presence of leukocytes.

CONCLUSION

Our study demonstrates the features and difficulties in diagnosing osteoarticular pathology in patients of different ages with Gaucher disease complicated by tuberculosis. Diagnostics requires the use of a wide range of diagnostic methods: analysis of clinical material (including retrospective anamnesis), additional research methods, imaging techniques (radiography, computed tomography, magnetic resonance imaging), data from surgical interventions, morphological examination of biopsy/surgical material with microbiological confirmation.

The clinical cases above presented confirm the complexity of diagnosing osteoarticular pathology in Gaucher disease complicated by inflammation of tuberculous etiology. Therefore, it is necessary to identify signs of damage to the osteoarticular system as early as possible in order to timely resolve the issue of treatment tactics, primarily surgical intervention. There is always a risk of tuberculosis infection. Therefore, it is necessary to apply a certain algorithm to detect it at the first signs of inflammation, dysfunction of the joint, restriction of movements: Diaskin test, Mantoux reaction with 2 TU, T-SPOT TB. When fistulas appear, it is necessary to study microbiological cultures of the discharge not only for the presence of nonspecific flora, but also for the presence of Mycobacterium tuberculosis (luminescent microscopy, polymerase chain reaction). In the morphological study of biopsy or surgical material, staining of micropreparations by the Ziehl-Neelsen method is necessary to identify acid-resistant mycobacteria. For the final decision on the issue of tuberculous or non-specific inflammation of the osteoarticular system, the diagnosis is based on a combination of the results of clinical radiological, laboratory, microbiological and morphological studies.

REFERENCES

1. Volgina S.Ia., Iurov I.Iu., Belogurova M.B. *Redkie bolezni detei* [Rare diseases of children]. Kazan, Meditsina, 2018, pp. 20-27. (in Russian)
2. Lukina E.A. *Bolezn Goshe* [Gaucher disease]. M., Litterra, 2014, 56 p. (in Russian)
3. *Gaucher Disease*. 1st Ed. / Futerman A.H., Zimran A., eds. Boca Raton (USA), CRC Press, 2006, 544 p. DOI: 10.1201/9781420005509.
4. Kamath R.S., Lukina E., Watman N., Dragosky M., Pastores G.M., Arreguin E.A., Rosenbaum H., Zimran A., Aguzzi R., Puga A.C., Norfleet A.M., Peterschmitt M.J., Rosenthal D.I. Skeletal improvement in patients with Gaucher disease type 1: a phase 2 trial of oral eliglustat. *Skeletal Radiol*., 2014, vol. 43, no. 10, pp. 1353-1360. DOI: 10.1007/s00256-014-1891-9.

5. Zimran A. How I treat Gaucher disease. *Blood*, 2011, vol. 118, no. 6, pp. 1463-1471. DOI: 10.1182/blood-2011-04-308890.
6. Rosenthal D.I., Doppelt S.H., Mankin H.J., Dambrosia J.M., Xavier R.J., McKusick K.A., Rosen B.R., Baker J., Niklason L.T., Hill S.C. Enzyme replacement therapy for Gaucher disease: skeletal responses to macrophage-targeted glucocerebrosidase. *Pediatrics*, 1995, vol. 96, no. 4, Pt. 1, pp. 629-637.
7. Savostyanov K.V., Pushkov A.A., Murav'ova L.V., Movsisyan G.B., Rykunova A.I., Ponomarev R.V., Lukina K., Lukina E., Namazova-Baranova L. Glucosylfingosine (Lyso-GLi) maybe the primary biomarker for screening Gaucher disease in Russian patients. *Mol. Genet. Metab*., 2019, vol. 126, no. 2, pp. S130. DOI: 10.1016/j.ymgme.2018.12.334.
8. Weinreb N.J. The Bone in Gaucher Disease. *Clinical Therapeutics*, 2007, vol. 29, pp. S91-S92. DOI: 10.1016/S0149-2918(07)80462-0.
9. Semenova L.A., Khomenko V.A., Lukina K.A., Kalugina S.M. *Tuberkulez i bolezn Goshe* [Tuberculosis and Gaucher disease]. Aktualnye Voprosy Ftiziatrii: Sbornik nauchnykh trudov, 2017, no. VIII, pp. 208-211. (in Russian)
10. Khomenko V.A., Semenova L.A., Lukina K.A., Tokaev K.B. Tuberkuleznyi sakroileit s koksitom u patsienta s bolezniu Goshe [Tuberculous sacroiliitis with coxitis in a patient with Gaucher's disease]. *Tuberkulez i Bolezni Legkikh*, 2018, vol. 96, no. 8, pp. 55-58. (in Russian)
11. Vom Dahl S., Poll L., Di Rocco M., Ciana G., Denes C., Mariani G., Maas M. Evidence-based recommendations for monitoring bone disease and the response to enzyme replacement therapy in Gaucher patients. *Curr. Med. Res. Opin*., 2006, vol. 22, no. 6, pp. 1045-1064. DOI: 10.1185/030079906X104623.
12. Sims K.B., Pastores G.M., Weinreb N.J., Barranger J., Rosenbloom B.E., Packman S., Kaplan P., Mankin H., Xavier R., Angell J., Fitzpatrick M.A., Rosenthal D. Improvement of bone disease by imiglucerase (Cerezyme) therapy in patients with skeletal manifestations of type 1 Gaucher disease: results of a 48-month longitudinal cohort study. *Clin. Genet*., 2008, vol. 73, no. 5, pp. 430-440. DOI: 10.1111/j.1399-0004.2008.00978.x.
13. Weinreb N., Barranger J., Packman S., Prakash-Cheng A., Rosenbloom B., Sims K., Angell J., Skrinar A., Pastores G.M. Imiglucerase (Cerezyme) improves quality of life in patients with skeletal manifestations of Gaucher disease. *Clin. Genet*., 2007, vol. 71, no. 6, pp. 576-588. DOI: 10.1111/j.1399-0004.2007.00811.x.
14. Wenstrup R.J., Bailey L., Grabowski G.A., Moskovitz J., Oestreich A.E., Wu W., Sun S. Gaucher disease: alendronate disodium improves bone mineral density in adults receiving enzyme therapy. *Blood*, 2004, vol. 104, no. 5, pp. 1253-1257. DOI: 10.1182/blood-2003-11-3854.
15. Soloveva A.A., Ponomarev R.V., Lukina K.A., Mamonov V.E., Khomenko V.A., Kostina I.E., Iatsyk G.A., Lukina E.A. Differentsialnaia diagnostika luchevoi kartiny tuberkuleznogo sakroileita i spetsificheskogo porazheniia kostnoi sistemy pri bolezni Goshe na primere klinicheskogo sluchaia [Differential diagnosis of radiation picture of tuberculous sacroiliitis and specific lesions of the skeletal system in Gaucher disease on the example of a clinical case]. *Terapevticheskii Arkhiv*., 2019, vol. 91, no. 1, pp. 84-88. (in Russian)
16. Gotman L., Iatsyk G., Togonidze D. Vozmozhnosti rentgenologicheskoi diagnostiki bolezni Goshe. Materialy II Vserossiiskogo Natsionalnogo Kongressa po luchevoi diagnostike i terapii. Meditsinskaia Vizualizatsiia, 2008, special issue, pp. 73. (in Russian)
17. Maas M., Poll L.W., Terk M.R. Imaging and quantifying skeletal involvement in Gaucher disease. *Br. J. Radiol*., 2002, vol. 75, no. Suppl. 1, pp. A13-A24. DOI: 10.1259/bjr.75.suppl_1.750013.
18. Soloveva A.A., Iatsyk G.A., Ponomarev R.V., Mamonov V.E., Khomenko V.A., Lukina E.A. Opyt diagnostiki i lecheniia kostno-sustavnogo tuberkuleza u patsienta s bolezniu Goshe I tipa [Experience in the diagnosis and treatment of osteoarticular tuberculosis in a patient with type I Gaucher disease]. *Gematologiia i Transfuziologiia*, 2018, vol. 63, no. 1, pp. 182-183. (in Russian)
19. Robertson P.L., Maas M., Goldblatt J. Semiquantitative assessment of skeletal response to enzyme replacement therapy for Gaucher's disease using the bone marrow burden score. *AJR Am. J. Roentgenol*., 2007, vol. 188, no. 6, pp. 1521-1528. DOI: 10.2214/AJR.06.1410.
20. Vom Dahl S., Poll L., Di Rocco M., Ciana G., Denes C., Mariani G., Maas M. Evidence-based recommendations for monitoring bone disease and response to enzyme replacement therapy in Gaucher patients. *Curr. Med. Res. Opin*., 2006, vol. 22, no. 6, pp. 1045-1064. DOI: 10.1185/030079906X104623.

The article was submitted 09.12.2019; approved after reviewing 22.12.2021; accepted for publication 26.01.2022.

Information about the authors:

1. Lyudmila A. Semenova – Candidate of Medical Sciences, lu.kk@yandex.ru, https://orcid.org/0000-0002-1782-7763;
2. Vladimir A. Khomenko – Doctor of Medicine, khomenkov@mail.ru, https://orcid.org/0000-0001-8988-556X;
3. Kira A. Lukina – Candidate of Medical Sciences, https://orcid.org/0000-0002-6757-985X.

Informed consents were obtained from the patients

Conflict of interests *Not declared.*