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CLINICAL CASE REPORT

Metastatic lesions of the uterus, fallopian tubes and ovaries in undifferentiated pleomorphic sarcoma of the left tibia (clinical case)

O. I. Kit, E. V. Verenikina, A. P. Menshenina, L. Yu. Vladimirova, E. A. Kalabanova✉, T. O. Lapteva, A. A. Barashev, K. S. Eremin, A. Yu. Ardzha

National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
✉ alenakalabanova@mail.ru

ABSTRACT

Undifferentiated pleomorphic osteosarcoma belongs to the group of rarely occurring tumors. Despite the treatment, the disease progresses in 30–40 % of patients with osteosarcomas. The main route of metastasis of bone tissue sarcomas is hematogenous, while lymphogenic spread is observed less frequently. As a rule, secondary metastatic changes occur in the lungs. Less often there is a secondary lesion of the bones of the skeleton and brain. Metastatic lesion of uterus, fallopian tubes and ovaries in malignant undifferentiated pleomorphic sarcoma is extremely rare. Therefore, we found it interesting to describe a clinical case of such a rare metastatic lesion. Patient K. underwent amputation of the left limb at the level of the lower third of the femur for undifferentiated pleomorphic sarcoma of the left tibia in 2019, and 4 courses of adjuvant polychemotherapy were performed. In 20 months after completion of complex treatment of the primary tumor, complaints of lower abdominal pain, increased body temperature up to 37.8 °C in the evenings appeared. According to the results of follow-up examination, a voluminous, multinodular, solid mass of merging character was detected in the pelvis, with total dimensions of up to 11 cm, and a cavitary mass of up to 5 cm was detected in the posterior vault. A trepan-biopsy of the mass in the projection of the right ovary was performed. The morphological picture in the volume of trepan biopsy specimens is characteristic of spindle cell sarcoma. Metastasis of undifferentiated pleomorphic bone sarcoma (malignant fibrous histiocytoma) is most likely. Due to metastatic lesions of the uterus, fallopian tubes, ovaries, omentum, mesentery and serous membrane of the colon loops, peritoneum of the bladder, surgical intervention in the volume of removal of the distal part of the sigmoid colon, rectosigmoid, upper ampullary parts of the rectum, uterus with fallopian tubes and ovaries, appendix was performed. Immunohistochemical study of the postoperative material revealed that the immunophenotype of tumor cells confirmed the morphological picture typical for undifferentiated pleomorphic bone sarcoma. The patient was further prescribed antitumor drug therapy. This clinical case demonstrates a rare, atypical metastasis of undifferentiated pleomorphic osteosarcoma, which allows to expand the knowledge about the flow of malignant diseases of this localization.

Keywords: undifferentiated pleomorphic sarcoma of bone, metastasis to the uterus, fallopian tubes and ovaries, surgical treatment of metastatic lesions, immunohistochemical analysis

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For correspondence: Elena A. Kalabanova – Cand. Sci. (Med.), senior researcher at the Medical Therapy Department, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
Address: 63 14 line str., Rostov-on-Don 344037, Russian Federation
E-mail: alenakalabanova@mail.ru
ORCID: https://orcid.org/0000-0003-0158-3757
SPIN: 9090–3007, AuthorID: 734992
ResearcherID: V-2943–2019
Scopus Author ID: 57046062200

Compliance with ethical standards: the ethical principles presented by the World Medical Association Declaration of Helsinki, 1964, ed. 2013 were observed in the study. The study was approved by the ethics committee of the National Medical Research Centre for Oncology (extract from the protocol of the meeting No. 26 dated 09/11/2023. Informed consent was received from all participants of the study

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КЛИНИЧЕСКОЕ НАБЛЮДЕНИЕ

Метастатическое поражение матки, маточных труб и яичников при недифференцированной плеоморфной саркоме левой большеберцовой кости (клинический случай)

О. И. Кит, Е. В. Вереникина, А. П. Меньшенина, Л. Ю. Владимирова, Е. А. Калабанова✉, Т. О. Лаптева, А. А. Барашев, К. С. Еремин, А. Ю. Арджа

ФГБУ «Национальный медицинский исследовательский центр онкологии» Министерства здравоохранения Российской Федерации, г. Ростов-на-Дону, Российская Федерация
✉ alenakalabanova@mail.ru

РЕЗЮМЕ

Недифференцированная плеоморфная саркома костей относится к группе редко встречающихся опухолей. Несмотря на проводимое лечение, у 30–40 % пациентов с остеосаркомами заболевание прогрессирует. Основным путем метастазирования сарком костной ткани является гематогенный, реже наблюдается лимфогенное метастазирование. Как правило, вторичные метастатические изменения возникают в легких. Реже наблюдается вторичное поражение костей скелета, головного мозга. Метастатическое поражение матки, маточных труб и яичников при злокачественной недифференцированной плеоморфной саркоме является крайне редким. В связи с чем нам представилось интересным описать клинический случай такого редкого метастатического поражения. У пациентки К. по поводу недифференцированной плеоморфной саркомы левой большеберцовой кости в 2019 г. выполнена ампутация левой конечности на уровне нижней трети бедра, проведено 4 курса адъювантной полихимиотерапии. Через 20 месяцев после завершения комплексного лечения первичной опухоли появились жалобы на боли внизу живота, повышение температуры тела до 37,8 °С в вечернее время. По результатам дообследования в малом тазу выявлено объемное, многоузловое, солидное образование сливного характера, общими размерами до 11 см, в заднем своде выявлено полостное образование до 5 см. Выполнена трепан-биопсия образования в проекции правого яичника. Морфологическая картина в объеме трепан-биоптатов характерна для саркомы веретеноклеточного строения. Наиболее вероятен метастаз недифференцированной плеоморфной саркомы кости (злокачественной фиброзной гистиоцитомы). В связи с метастатическим поражением матки, маточных труб, яичников, большого сальника, брыжейки и серозной оболочки петель толстой кишки, брюшины мочевого пузыря выполнено хирургическое вмешательство в объеме удаления дистального отдела сигмовидной кишки, ректосигмоидного, верхне-ампулярного отделов прямой кишки, матки с маточными трубами и яичниками, аппендиксом. При проведении иммуногистохимического исследования послеоперационного материала выявлено, что иммунофенотип опухолевых клеток подтверждает морфологическую картину, характерную для недифференцированной плеоморфной саркомы кости. Далее пациентке назначена противоопухолевая лекарственная терапия. Данный клинический случай демонстрирует редкое, нетипичное метастазирование недифференцированной плеоморфной саркомы кости, что позволяет расширить знания о течении злокачественных заболеваний этой локализации.

Ключевые слова: недифференцированная плеоморфная саркома костей, метастазирование в матку, маточные трубы и яичники, хирургическое лечение метастатического поражения, иммуногистохимический анализ

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Для корреспонденции: Калабанова Елена Александровна – к.м.н., старший научный сотрудник отдела лекарственного лечения опухолей, ФГБУ «Национальный медицинский исследовательский центр онкологии» Министерства здравоохранения Российской Федерации, г. Ростов-на-Дону, Российская Федерация
Адрес: 344037, Российская Федерация, г. Ростов-на-Дону, ул. 14-я линия, д. 63
E-mail: alenakalabanova@mail.ru
ORCID: https://orcid.org/0000-0003-0158-3757
SPIN: 9090-3007, AuthorID: 734992
ResearcherID: V-2943-2019
Scopus Author ID: 57046062200

Соблюдение этических стандартов: в работе соблюдались этические принципы, предъявляемые Хельсинкской декларацией Всемирной медицинской ассоциации (World Medical Association Declaration of Helsinki, 1964, ред. 2013). Исследование одобрено этическим комитетом
ФГБУ «НМИЦ онкологии» Минздрава России (протокол № 26 от 11.09.2023 г.). Информированное согласие получено от участника исследования

Финансирование: финансирование данной работы не проводилось

Конфликт интересов: Кит О. И. является членом редакционной коллегии журнала «Южно-Российский онкологический журнал» с 2019 г., но не имеет никакого отношения к решению опубликовать эту статью. Статья прошла принятую в журнале процедуру рецензирования. Об иных конфликтах интересов авторы не заявляли

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INTRODUCTION

In 1964, malignant fibrous histiocytoma was first described as an independent nosological form by J. O'Brien and A. Stout [1]. According to the World Health Organization's classification of soft tissue and bone tumors from 2020, the term "malignant fibrous bone histiocytoma" has been changed to "undifferentiated pleomorphic bone sarcoma" [2]. Undifferentiated pleomorphic bone sarcoma belongs to a group of rare tumors. The frequency ranges from 0.2–1 % of the number of all malignant neoplasms. As a rule, bone sarcomas are diagnosed before the age of 35 [3]. According to E. K. Laryukova et al. (2018), in more than 70 % of cases, the long tubular bones of the lower extremities are affected, mainly those parts of them that form the knee joint [4].

Even despite the treatment, 30–40 % of patients with osteosarcomas experience disease progression, while more than 80 % of them show metastases in the lungs [5]. Usually, bone sarcomas metastasize hematogenically (up to 90 % of cases), lymphogenic metastasis is less common. Hematogenous metastasis usually affects the lungs, less often the bones of the skeleton, the brain [6]. In patients with bone sarcomas, isolated metastatic lung damage occurs in approximately 40 % of cases [7].

Osteosarcoma metastasis to the lymph nodes is quite rare, the frequency of metastases to the lymph nodes ranges from 4 to 11 % [8]. In clinical practice, both single and multiple lymph nodes are affected by metastases [9]. In addition to the lesion of regional lymph nodes, distant lymph nodes may also be involved. The literature describes metastases of osteosarcoma of the femur in the lymph nodes of the lung root [10]. We did not find data on metastatic lesions of the uterus, fallopian tubes and ovaries in undifferentiated pleomorphic bone sarcoma among the analyzed literature sources.

We found it interesting to describe a rare case of metastasis of an undifferentiated pleomorphic sarcoma of the left tibia into the uterus, fallopian tubes and ovaries, with damage to the large omentum, mesentery and serous membrane of the loops of the colon, peritoneum of the bladder.

The purpose of the study: reports of such rare cases of metastatic lesions allow us to expand knowledge about the course of malignant neoplasms, to form an optimal treatment strategy for the patient in atypical clinical situations.

In 2005, at the age of 17, patient K. noticed an increase in the volume of the left shin, after an examination, a clinical diagnosis of fibrous dysplasia of the bones of the left shin was established. Segmental resection of the fibula on the left was performed in the pediatric orthopedic department in Krasnodar, and a histological conclusion was obtained – fibrous dysplasia. In 2006, she was operated at the H. I. Turner National Medical Research Center for Children's Orthopedics and Trauma Surgery of the Ministry of Health of the Russian Federation (Moscow St. Petersburg), resection of the focus of fibrous dysplasia of the left tibia was performed within healthy tissues, morphological conclusion – fibrous dysplasia.

Upon obtaining the anamnesis data, it was established that the patient's mother during pregnancy in 1987 lived in an area located within a radius of less than 400 kilometers from the Chernobyl nuclear power station.

In 2018, when the patient was 30 years old, there were complaints of an increase in the volume of the

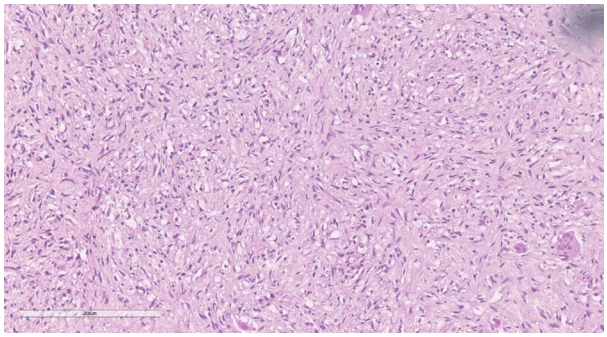

Fig. 1. Trepan biopsy – the picture is typical for spindle cell sarcoma (magnification × 200)

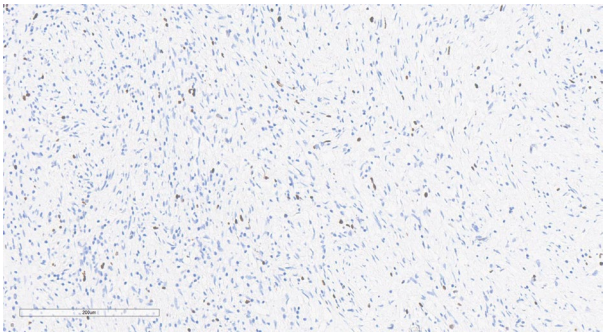

Fig. 2. IHC study, 2019 (the marker of proliferative activity Ki67 is positive in 30 % of tumor cell nuclei)

left shin and pain in this area. As is known, the main symptoms of primary undifferentiated pleomorphic bone sarcoma are pain and clinically detectable tumor formation. Almost half of the patients have these symptoms at the same time [11]. In December 2018, a follow-up examination was conducted at the medical center of the city of Krasnodar, which revealed a pathological focus in the left tibia, a biopsy was performed, a morphological conclusion was obtained fibrous bone dysplasia, no special treatment was carried out. In August 2019, the patient independently applied to the National Medical Research Centre for Oncology of the Russian Federation in Rostov-on-Don. A trepan biopsy of the pathological focus of the left tibia was performed, a histological conclusion was obtained – a morphological picture of spindle cell sarcoma, differentiated with fibrosarcoma, undifferentiated pleomorphic bone sarcoma (malignant fibrous histiocytoma). To determine the immunophenotype of tumor cells, an immunohistochemical study is recommended (Fig. 1).

The conclusion was obtained according to immunohistochemical analysis, the morphological picture and immunophenotype of tumor cells are most characteristic of undifferentiated pleomorphic bone sarcoma (Vimentin +, CD68+, Ki-67 30 %) (Fig. 2).

In September 2019, at the age of 31, the patient underwent amputation of the left lower limb at the level of the lower third of the thigh, the histological conclusion was an undifferentiated pleomorphic sarcoma (malignant fibrous bone histiocytoma). In the adjuvant mode, 2 courses of antitumor drug therapy were performed according to the HD AI scheme (doxorubicin 25 mg/m^2/day intravenously on days 1–3 (72-hour continuous infusion) + ifosfamide 2500 mg/m^2 (+ mesna 100 % of the dose of ifosfamide) intravenously on days 1–4 + granulocyte colony stimulating factor 5 mcg/kg subcutaneously on days 5–15) and 2 courses of antitumor drug therapy according to the HD I scheme (ifosfamide 2000 mg/m^2 intravenously on days 1–7 (+ mesna) + granulocyte colony stimulating factor 5 mcg/kg subcutaneously on days 8–16, every 3 weeks).

Further, the patient was observed by an oncologist at the place of residence, no signs of progression were detected. Thus, according to computed tomography of the chest, abdominal cavity and pelvic organs from 02/03/2021, no pathological changes were detected. In August 2021, the patient had a new coronavirus infection, after which there were complaints of pain in the lower abdomen, an increase in body temperature to 37.8 °C in the evening. In September 2021, the patient applied to the National Medical Research Centre for Oncology, examined by an oncogynecologist. During gynecological examination: the external genitalia are formed correctly, in the mirrors the cervix is without pathological changes, pushed back to the womb. During vaginal examination, the uterus is of normal size, pushed forward, in the posterior vault and above the body of the uterus, a solid volumetric formation is palpated, doubtfully mobile, the arches are free. Computed tomography of the chest organs, magnetic resonance imaging of the abdominal cavity and pelvic organs, ultrasound examination of the pelvic organs were performed. According to the results of the examination, a voluminous, multi-nodular, solid formation, of a draining nature, with total dimensions up to 11 cm, with uneven contours, in the posterior vault and close to the main substrate, a cavity, liquid formation up to 5 cm, with wall-mounted, hyperechogenic, intracavitary structures, in the form of "papillae", in the iliac region on the left mesenterically and close to the omentum, there are hypoechoic nodes up to 11–18 mm. No data were found for secondary changes in other organs.

Computed tomography of the chest organs was performed, which did not reveal any pathological

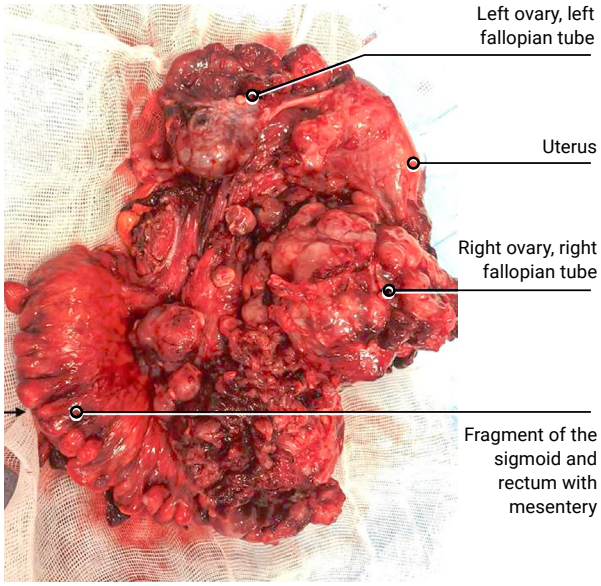

Fig. 3. Macro specimen view

changes in the lungs, lymph nodes and bone structures of the examined area.

Computed tomography of the left femur revealed a stable picture of the condition after amputation of the lower third of the left thigh, no signs of continued growth were revealed.

The level of cancer markers was determined, Ca-125 increased to 175.8 units/ml, Ne-4 increased to 74.08 pmol/l, ROMA index = 19.3 %.

A trepan biopsy of the formation in the projection of the right ovary was performed. The morphological picture in the volume of trepan biopsies is characteristic of spindle cell sarcoma. The most likely metastasis is undifferentiated pleomorphic bone sarcoma (malignant fibrous histiocytoma).

Taking into account the metastatic lesion of the pelvic organs, the absence of other distant metastases, a consultation of doctors of the National Medical Research Centre for Oncology decided on surgical treatment in the amount of removal of a pelvic tumor.

09/30/2021: in the supine position of the patient, a lower-median laparotomy was performed, minor ascites was observed during the revision of the abdominal cavity and pelvis, about 500 ml of straw-yellow effusion was evacuated. A tumor conglomerate lies in the wound, including a metastatically altered large omentum, a uterus with a tumor-like transformed right ovary, loops of the colon with multiple metastatic nodes along the serous membrane and mesentery, and the peritoneum of the bladder. The capsule of the liver is smooth, the peritoneum of the subdiaphragmatic space, the parietal and visceral peritoneum of the abdominal cavity are smooth, without metastatic lesion. Retroperitoneal lymph nodes are not enlarged. It was decided to remove the tumor conglomerate in a single block, for which it was necessary to perform anterior rectal resection with preventive ileostomy, pangisterectomy, appendectomy, extirpation of the large omentum. The distal sigmoid colon, rectosigmoid, upper ampullary rectum, uterus with fallopian tubes and ovaries, appendix was mobilized and removed as a single unit. Peritonectomy of the anterior arch was performed. A loop ileostomy has been formed in the right iliac region, at 30 cm from the dome of the cecum. Description of the macro specimen: as a single block, the body of the uterus is 5 × 5 × 4 cm, the cervix is 4 × 4 × 3 cm, a fragment of the sigmoid and rectum with mesentery, a large omentum, peritoneum of the bladder, appendix, metastatic nodes. Uterus with metastatic nodes along the serous membrane along the anterior and posterior surfaces, along the mesentery and serous lining of the intestine, multiple dense metastatic nodes from 1 to 3 cm in diameter, the left ovary is 4 × 3 cm with small cysts, the peritoneum of the bladder is totally affected by a metastatic process from 0.5 to 1 cm in diameter, the right ovary is totally replaced a tumorous tuberous tissue about 15 cm in diameter with cluster-like tumor growths along the outer capsule. A large omentum with multiple dense metastatic nodules, on an incision of a macroscopically sarcomatous nature (a type of "fish meat") (Fig. 3).

Postoperative histological analysis – in the tissues in the projection of the uterine appendages on the right and left, on the serous membrane of the uterus, in the mesentery of the colon, the growth of tumor tissue with foci of necrosis, represented by intertwining bundles of atypical fibroblast-like and epithelioid cells, with moderate nuclear polymorphism, mitosis

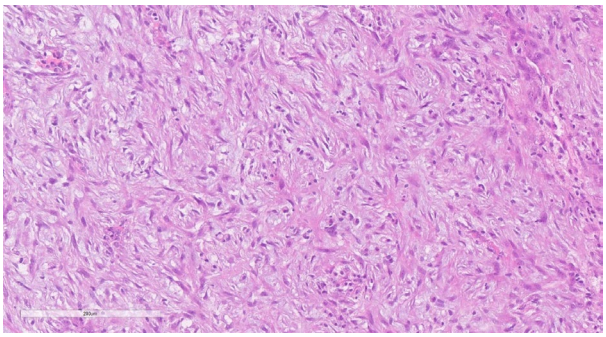

Fig. 4. Postoperative material – undifferentiated sarcoma (magnification × 200)

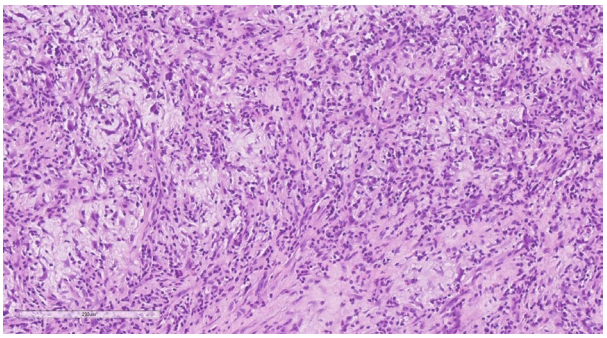

Fig. 5. Postoperative material presented with undifferentiated sarcoma with inflammatory infiltration (magnification × 200)

figures, with sections of myxoid stroma, with pronounced inflammatory (lymphocytic, granulocytic eosinophilic (and neutrophilic) infiltration, with lymphovascular invasion. Conclusion: the morphological picture is characteristic of undifferentiated sarcoma with growth into the uterine appendages and serous lining of the uterus, mesentery of the colon, appendix and omentum tissue, lymphovascular invasion. No tumor growth was detected in the resection lines of the vagina, colon and appendix (Fig. 4, 5).

During immunohistochemical examination, the immunophenotype of tumor cells confirms the morphological picture characteristic of undifferentiated pleomorphic bone sarcoma (Vimentin+, SMA+/-, CD68+/-) (Fig. 6).

The next stage of treatment was antitumor drug therapy.

DISCUSSION

The patient's first signs of bone pathology were revealed at the age of 17, when fibrotic dysplasia of the bones of the left shin was diagnosed. The causes of fibrotic dysplasia are currently not clear enough. The disease is based on a tumor-like process associated with the abnormal development of osteogenic mesenchyma. As a rule, fibrous dysplasia prevails in females aged 15–19 years [12].

Anamnestic data on the place of residence of the patient's mother during pregnancy in the territory located from the Chernobyl nuclear power plant within a radius of less than 400 kilometers were interesting. As is known, on April 26, 1986, as a result of the destruction of the reactor of the fourth power unit, a significant amount of radioactive substances was released into the environment. There is no doubt about the high radiosensitivity of the fetus at all stages of its development. We do not know for sure whether the radiation background had an effect on the patient's mother. However, it has been proven that intrauterine exposure to ionizing radiation can cause severe pathological consequences for the fetus. Among these consequences can be both gross violations of somatic development, as well as a decrease in intelligence, mental retardation [13].

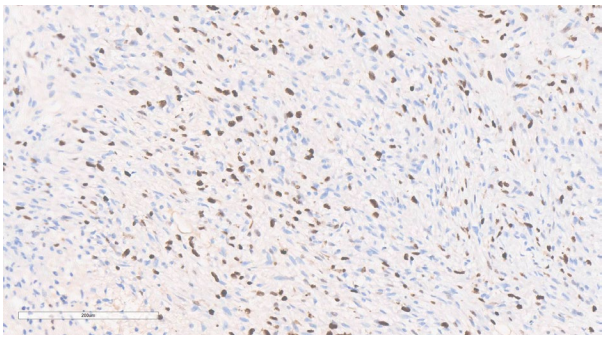

Fig. 6. IHC study, 2021 (marker of proliferative activity of Ki-67 in 60 % of tumor cell nuclei)

The case is interesting for the extremely rare localization of metastasis of undifferentiated pleomorphic bone sarcoma. It is known that more than 80 % of patients with bone sarcomas have lung metastases. According to the clinical recommendations of the Ministry of Health of the Russian Federation, in the treatment of metastatic forms of osteosarcoma, it is recommended to perform surgical treatment in combination with chemotherapy if possible [14]. According to the literature, in isolated metastatic lung damage, complete surgical removal of these metastases can ensure a 40 % 5-year survival rate [3]. The metastasis of malignant undifferentiated pleomorphic bone sarcoma into the uterus, fallopian tubes and ovaries has not been described in the available literature.

CONCLUSION

Following the completion of complex treatment of undifferentiated pleomorphic sarcoma of the left tibia, the progression of the disease with a rare localization of metastatic lesions of the uterus, fallopian tubes and ovaries was revealed in the patient in the given clinical case. Despite the spread of the tumor in the pelvis, secondary changes in the lungs were not detected. Due to the absence of other metastatic foci, it became possible to perform radical surgical intervention. Analyzing the above, it can be assumed that the complete surgical removal of metastatic focuses in combination with ongoing antitumor drug therapy will improve the prognosis of the disease. Currently, the period from the moment of initial diagnosis of undifferentiated pleomorphic sarcoma of the left tibia is 43 months.

Reports of such rare cases of metastatic lesions allow us to expand knowledge about the course of malignant neoplasms, to form an optimal treatment strategy for the patient in atypical clinical situations.

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Information about authors:
Oleg I. Kit – Academician at the Russian Academy of Sciences, Dr. Sci. (Med.), professor, general director, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0003-3061-6108, SPIN: 1728-0329, AuthorID: 343182, ResearcherID: U-2241-2017, Scopus Author ID: 55994103100

Ekaterina V. Verenikina – Dr. Sci. (Med.), head of the Department of Oncological Gynecology National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0002-1084-5176, SPIN: 6610-7824, AuthorID: 734269, Scopus Author ID: 57194271506

Anna P. Menshenina – Dr. Sci. (Med.), leading researcher, Section of Reproductive Tumors, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0002-7968-5078, SPIN: 6845-4794, AuthorID: 715810, Scopus Author ID: 57191983118

Liubov Yu. Vladimirova – Dr. Sci. (Med.), professor, head of Tumor Drug Therapy Department, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0002-4822-5044, SPIN: 4857-6202, AuthorID: 289090, ResearcherID: U-8132-2019, Scopus Author ID: 7004401163

Elena A. Kalabanova ✉ – Cand. Sci. (Med.), senior researcher at the Medical Therapy Department, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0003-0158-3757, SPIN: 9090-3007, AuthorID: 734992, ResearcherID: V-2943-2019, Scopus Author ID: 57046062200

Tatiana O. Lapteva – head of Pathoanatomical Department, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0002-6544-6113, SPIN: 2771-3213, AuthorID: 849370

Artem A. Barashev – Cand. Sci. (Med.), traumatologist-orthopedist, Department of Bone, Skin, Soft Tissue and Breast Tumors No. 1, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0002-7242-6938, SPIN: 4590-5745, AuthorID: 697517

Konstantin S. Eremin – MD, pathologist, Pathoanatomical Department, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0001-9331-3353, SPIN: 9865-0123, AuthorID: 1150930

Anna Yu. Ardzha – Cand. Sci. (Med.), MD, oncologist, Department of Oncological Gynecology, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0001-6787-3007, SPIN: 2519-7898, AuthorID: 951656

Contribution of the authors:
Kit O. I. – study concept and design, scientific editing, surgical treatment;
Verenikina E. V. – study concept and design, surgical treatment;
Menshenina A. P. – preparation of figures, surgical treatment;
Vladimirova L. Yu. – study concept and design, scientific editing;
Kalabanova E. A. – collection, analysis and interpretation of data, manuscript writing, material processing, preparation of references, preparation of the article;
Lapteva T. O. – morphological and immunological tests, preparation of figures according to morphological and immunological tests;
Barashev A. A. – surgical treatment;
Eremin K. S. – morphological and immunological tests;
Ardzha A. Yu. – technical editing, preparation of references.