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Multicentric osteosarcoma as a rare type of osteosarcoma (case report)

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Multicentric osteosarcoma (M-OGS) is classified as a special type of osteosarcoma, which is characterized by multicentric bone lesions without visceral organs involvement in the tumor process. Synchronous type of the lesion is noted when several foci of osteosarcoma are diagnosed at the same time, whereas metachronous type may develop additional foci 6 months after the primary tumor diagnosis. This type of osteosarcoma is very rare with only a few articles describing this pathology. Objective. Present a clinical case of rare pathology — multicentric osteosarcoma. Materials and methods. Clinical, radiological, pathomorphological data of a patient with multicentric osteosarcoma. Data on the results of treatment of the patient. Results. Multicentric osteosarcoma It accounts for about 1.5 % of all cases reported worldwide. Fuchs et al described a multifactorial etiology of this pathology, considering it a part of hereditary diseases, such as Rothmund-Thomson, Li-Fraumani, Bloom syndromes. Patients with Paget's disease or McCune-Albright syndrome have also been diagnosed with multicentric M-OGS. Tumor genetic predisposition has been described as one of the etiology factors, where a genetic mutation is detected. While studying the nature of multicentric M-OGS, various scientists have created classifications of this lesion. Taking to account all clinical and radiological data, a differential diagnosis comes to multiple metastatic lesions of carcinoma, chronic recurrent osteomyelitis and hyperphosphatasia. Conclusions. Multicentric osteosarcoma is a highly malignant and aggressive tumor that has a characteristic clinical presentation in the form of multiple bone lesions without visceral organs involvement. Mandatory patient monitoring after a comprehensive treatment allows to detect a spread of tumor process, as well as verify this rare pathology and choose the best treatment course.

Мультицентрична остеосаркома (M-OGS) — це окремий особливий вид остеосаркоми, який характеризується багатоцентричним ураженням кісток без залучення до пухлинного процесу вісцеральних органів. Відмічають синхронний вид ураження, коли зафіксовано водночас декілька вогнищ остеосаркоми, а також метахронний — інші вогнища з'являються у період після 6 міс. від діагностики первинного пухлинного вогнища. Такий вид остеосаркоми зустрічається дуже рідко, у світовій літературі спостерігається декілька статей з описом цієї патології. Мета. Навести клінічний випадок виняткової патології — мультицентричної остеосаркоми. Методи. Клінічні, рентгенологічні, патоморфологічні дані пацієнтки з M-OGS. Проаналізовано лікування хворої. Результати. M-OGS складає майже 1,5 % усіх остеосарком. Fuchs та співавт. описали багатофакторну етіологію цього захворювання. Таким чином, це захворювання розглядається як частина генетичних і спадкових захворювань — синдроми Rothmund-Thomson, Li-Fraumani, Bloom. У пацієнтів із хворобою Педжета або синдромом McCune-Albright також діагностовано M-OGS. Наявність таких захворювань в анамнезі може бути схильністю до розвитку остеосаркоми. Під час вивчення природи M-OGS деякі вчені створили класифікації цього ураження. Диференційну діагностику цього захворювання проводять із множинними метастатичними ураженнями карцином, хронічним рецидивуючим остеомієлітом і гіперфосфатемією. Висновки. Мультицентрична остесаркома — високозлоякісна, агресивна пухлина, яка має характерні властивості у вигляді множинного ураження кісток скелета без ураження вісцеральних органів. Це дуже нечастий вид пухлинного ураження. Обов'язковий моніторинг пацієнтів після проведеного комплексного лікування дозволяє виявити розповсюдження пухлинного процесу, а також діагностувати цю патологію та призначити курс подальшого лікування. Ключові слова. Мультицентрична остеосаркома, метахронний тип, кісткові ураження.

Keywords. Multicentric osteosarcoma, metachronous type, bone lesion

Introduction

Multicentric osteosarcoma (M-OGS) is classified as a special type of osteosarcoma, which is characterized by multicentric bone lesions without visceral organs involvement in the tumor process. Synchronous type of the lesion is noted when several foci of osteosarcoma are diagnosed at the same time, whereas metachronous type may develop additional foci 6 months after the primary tumor diagnosis. This type of osteosarcoma is very rare with only a few articles describing this pathology. For many decades it has been debated that this type of lesion characterizes metastatic lesions. The first case report describing this pathology was published only in 1936 by Silverman[1]. The largest analysis on M-OGS was conducted in a joint study by Mayo clinic in Rochester, MN (1900-2005) and Rizzoli institute in Bologna, Italy (1975-2004) [2]. During this period, 56 patients with confirmed diagnosis were identified, including 22 subjects with synchronous lesion and 34 with metachronous lesion. As for the cause and pathogenesis of this type of tumor the literature reports are still inconclusive. The most common M — OGS localization, along with the classic variant ofosteosarcoma, is the knee joint. Histologically there is no difference between synchronous and metachronous types, mostly represented by osteoblastic and fibroblastic subtypes, always high-grade stage 4 or 3. On radiologic examinations mixed bone structure destruction is commonly seen (sclerotic and lytic) with a wide area of the lesion, including a central part of the bone, a cortical layer and a soft tissue component. Prognostically synchronous osteosarcoma has a more aggressive course and a worse long-term patient survival compared to the metachronous variant. However, the use of aggressive individual treatment regimens, as polychemotherapy and/or surgery, allows to obtain better survival results of these patients.

Objective: present a clinical case of rare pathology — multicentric osteosarcoma.

Materials and metods

Case report

A 30 years old female presented with pain and slight edema in the distal part of her left leg. The above complaints have been noticed for about 1 month. The patient was not treated elsewhere on early stages and a primary comprehensive examination was conducted in clinic. Distal tibia lesion (osteoblastic type) was observed on plain radiographs and CT scan of the lower leg. The location of the foci was central without damage to the cortical layer but with evidence of a tumor soft tissue component (Fig. 1). No metastatic lesions were detected on CT oncological screening.

A pathological lesion biopsy of the left distal femur was performed (Fig. 2). For histological examination, biopsy material was delivered in a form of bone density gray-white columns. Microscopy revealed the formation of atypical bone tissue and sarcoma-like intermediate with pronounced polymorphism of cells and nuclei. Based on clinical, radiological and histological data the further diagnosis was established: osteogenic sarcoma of the distal part of the left tibia $T_2N_0M_0$ GIII, stage II, clinical group II.

Surgical intervention included removal of the tumor en block (left tibia segmental resection at the mid shaft) and replacement of the tibia lower third defect with a segmental articulating allograft. Step-cut osteotomy at the graft and recipient's bone sites was used for a stable fixation. To provide additional mechanical support and scaffold for vascular ingrowth along with osteoblastic cells infiltration, a cortical and cancellous autograft was added. Osteosynthesis was achieved with a blocking intramedullary rod (Fig. 3).

Histological specimen included a fragment of the distal tibia 13 cm long with a tumor measuring 8×3×6 cm. The tumor expanded on entire metaphyseal part of the fragment as well as extra-osseous (Fig. 4). Macroscopical examination characterized tissue of fibrous and bone density, mostly gray-white color with red and yellow foci (Fig. 5). Microscopy revealed the formation of osteoblastic atypical bone substance, having osteoid trabeculae in the form of deeply homogeneous eosinophilic substance cluster (Fig. 6). Intermediate cells with pronounced polymorphism contained nuclei of various shapes, mostly oval and spindle-shaped. The specimen included moderate number of wide lumen vessels filled with erythrocytes.

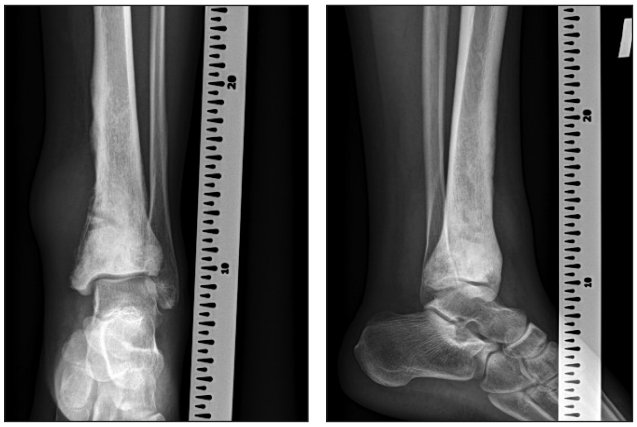

Fig. 1. Radiographs of the lower leg and supracalcaneal-tibial joint of patient Sh., 30 years old, with a diagnosis of osteogenic sarcoma of the distal part of the tibia

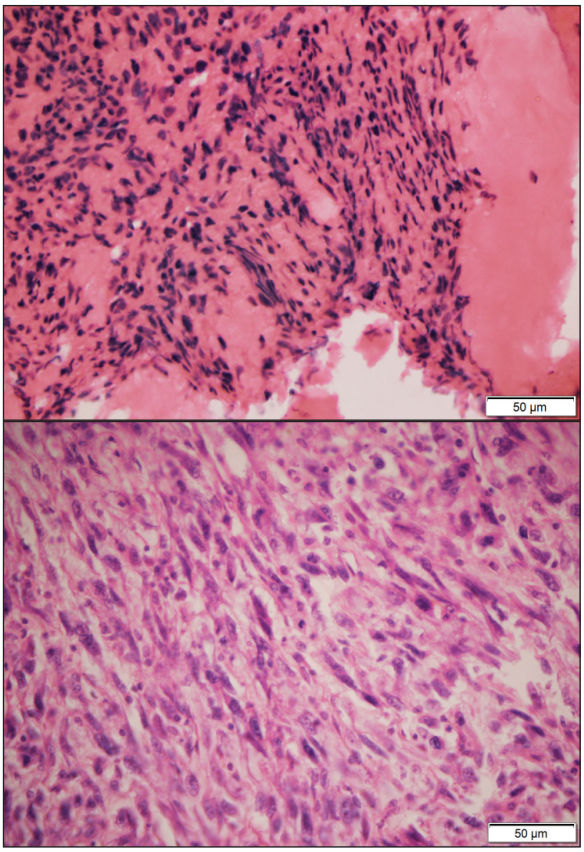

Fig. 2. Formation of atypical bone substance with a sarcoma-like intermediate zone. Hematoxylin and eosin

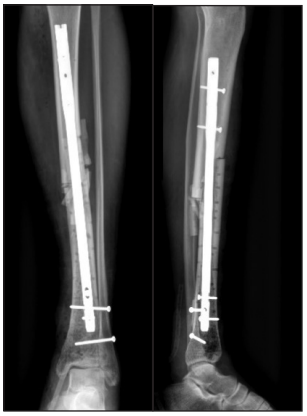

Fig. 3. X-rays of patient Sh. after surgery: removal of the tumor en block, replacement of the post-resection defect

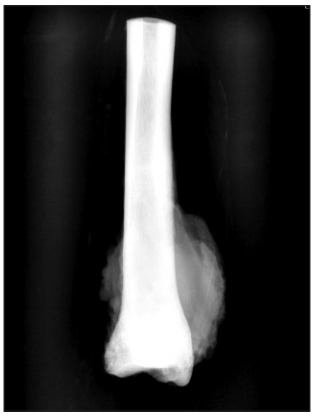

Fig. 4. X-ray of the removed tumor preparation

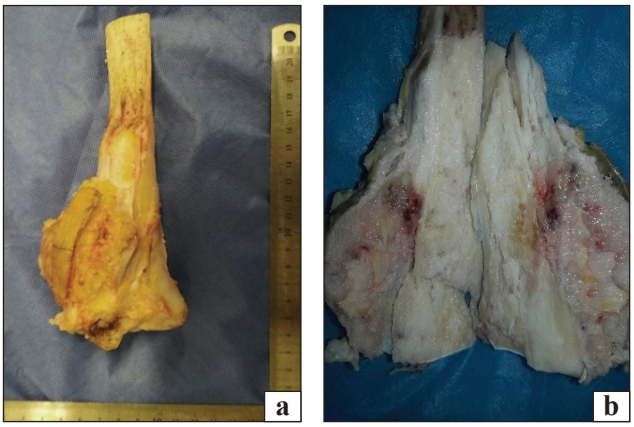

Fig. 5. Distal section of the tibia a) extraosseous location of the tumor, b) a gray-white tumor on cross-section, replacing the metaphyseal part of the bone

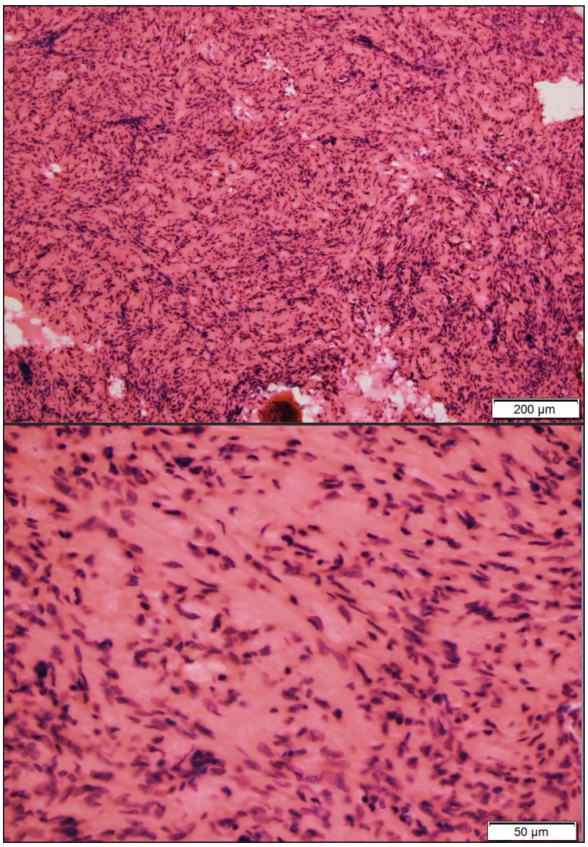

Fig. 6. Atypical bone substance, formation of osteoid trabeculae, pronounced cellular and nuclear polymorphism of intermediate substance. Hematoxylin and eosin

Patient underwent a course of poly-chemotherapy. At one year follow up, there was evidence of allograft and recipient bone fusion, however complete osseous restructuring was not achieved. Patient walked without any additional support or ankle external fixation. CT onco-screening, radiographic and clinical examination was performed every 6 months.

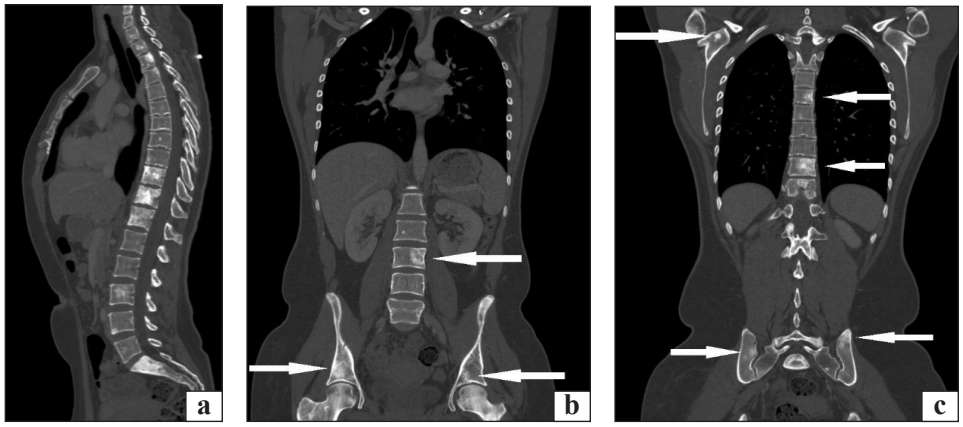

Fig. 7. CT scan of patient Sh. Multiple osteoblastic tumor lesion is determined: a) vertebrae, b) pelvic bones, c) scapula. Multicentric osteosarcoma

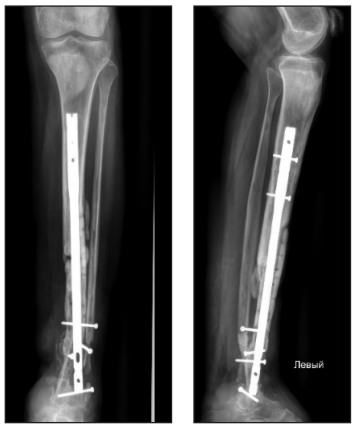

Fig. 8. Radiographs of the lower leg of patient Sh. 2 years after treatment, a focus of osteosarcoma was detected in the proximal part of the tibia

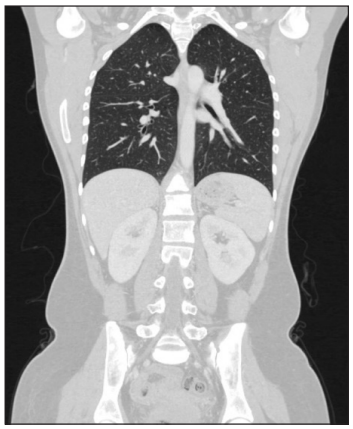

Fig. 9. CT oncoscreening of patient Sh., damage to visceral organs is not observed

On a follow-up examination at two years post-op CT onco-screening showed multiple tumor bone lesions: proximal left tibia, lumbar and thoracic vertebrae, pelvic bones and scapula (Fig. 7, 8). Visceral lesions were not detected (Fig. 9). Thus, metachronous type M-OGS diagnosis was confirmed. Given the presence of tibia tumor and lower leg pain it was decided to perform a lower limb amputation at the level of middle third of the thigh (Fig. 10).

On a specimen pathological preparation, multiple subdermal nodules up to 3 cm in size were found. Cross section tumor tissue was gray with fibrous density. Specimen dissection at proximal tibia reveled a tumor sized 3×5×7 cm, gray-white color, bone density. In the area of surgical intervention there was an evidence of a strong bone fusion between allograft and recipient site.

Microscopic examination of soft tissue nodes and proximal tibia tumor revealed a characteristic structure of osteogenic sarcoma (Fig. 11).

Currently patient receives polychemotherapy-a combination of cisplatinum, doxorubicin and metotrexate.

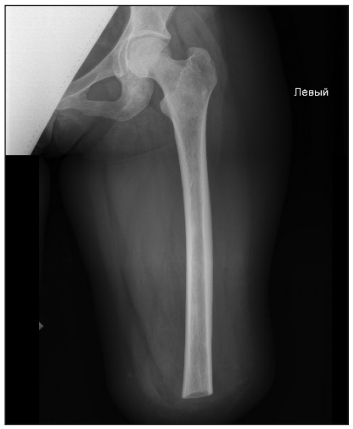

Fig. 10. X-ray of the left lower limb of patient Sh. after amputation

Discussion

Osteogenic sarcoma has been a known bone pathology for many decades. Tumor grade, extension and presence of distant metastases is crucial for patient survival. However, the histological response to chemotherapy depending on a subtype is a key component responsible for the remission.

For a long time, there has been a debate on cases with multiple tumor sites at various follow-up time frames. The main question remained an interpretation of these lesions - are those metastases or multiple primary tumors? It was then found that visceral

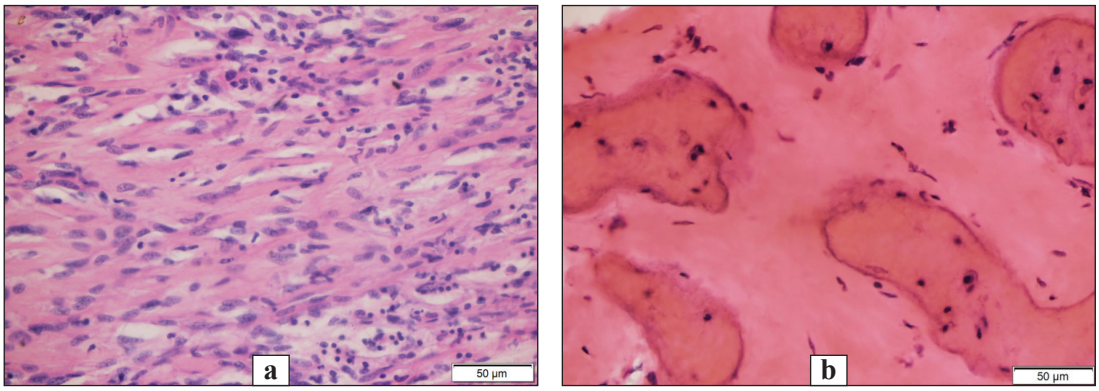

Fig. 11. Osteogenic sarcoma in the soft tissues around the distal femur. Sarcoma-like intermediate substance (a), osteogenic sarcoma in the tibia. Atypical bone formation (b). Hematoxylin and eosin

organs were not involved in the tumor process when multiple osseous foci were detected. Thus, a distinguished type of osteosarcoma was suggested- multicentric (metachronous or synchronous variant). It accounts for about 1.5% of all cases reported worldwide. Fuchs et al described a multifactorial etiology of this pathology, considering it a part of hereditary diseases, such as Rothmund-Thomson, Li-Fraumani, Bloom syndromes [3]. Patients with Paget's disease or McCune-Albright syndrome have also been diagnosed with multicentric M-OGS [2]. Tumor genetic predisposition has been described as one of the etiology factors, where a genetic mutation is detected. RB1, p53 tumor suppressor gene or de novo unidentified mutation are blamed for the cause of this pathology [3, 4, 5]. Hansen et al studied the genes of Paget's disease chromosomal abnormalities, correlating those with osteosarcoma and identifying certain prerequisites for further research in this are [6]. The obstacle is that inherited diseases are rarely screened in these patients.

Several conditions to identify multicentric M-OGS were suggested by Hameed et al [7]:

– absence of primary systemic bone pathology;

– no previous body radiation exposure;

– simultaneous appearance of multiple osseous pathological foci;

– absence of metastases in the lungs or other parenchymal organs.

While studying the nature of multicentric M-OGS, various scientists have created classifications of this lesion. Amstutz suggested 3 types and Mahoney included histological gradation, patient age and tumor location in his classification.

Studies with ample patient cohorts have shown a male gender and metachronous osteosarcoma type prevalance [2,7]. Among all clinical manifestations the most frequent are pain and local edema. Moreover, the first clinical signs in synchronous type mainly develop from a dominant lesion, whereas other foci are asymptomatic and detected during the follow up.

Tumor histological examination often identify high grade III and IV, rarely low grade lesions. 73 % of those are osteoblastic and 24 % are fibroblastic [2]. Radiologic examination also helps to define a multicentric M-OGS type. Metachronous lesions characterized by a lytic destruction with sclerotic component or a cortical destruction with soft tissue component. It is common to see an abnormal periosteal bone reaction. Synchronous lesions often present with sclerotic borders without cortical destruction or soft tissue component. Thus, radiological features of the metachronous type more resembles a primary osteosarcoma, whereas synchronous type — multiple metastatic lesions [2].

This also reflects on a patient survival, where synchronous lesions are found to be more clinically aggressive [8] Taking to account all clinical and radiological data, a differential diagnosis comes to multiple metastatic lesions of carcinoma, chronic recurrent osteomyelitis and hyperphosphatasia.

Conclusions

Multicentric osteosarcoma is a highly malignant and aggressive tumor that has a characteristic clinical presentation in the form of multiple bone lesions without visceral organs involvement. Mandatory patient monitoring after a comprehensive treatment allows to detect a spread of tumor process, as well as verify this rare pathology and choose the best treatment course.

Conflict of interest. The authors declare no conflict of interest.

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(CASE REPORT)

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