VIA MEDICA

CASE REPORT

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A case of primary breast osteosarcoma

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ABSTRACT

Primary breast osteosarcoma (PBOS) makes up less than 0.125% of all breast neoplasms and 12.5% of breast sarcomas.

Here, the case of a 53-year-old patient is presented who was treated at The Maria Skłodowska-Curie Institute of Oncology in Warsaw. Histopathological examination of core needle biopsy specimen revealed a neoplasm composed of atypic oval and spindle cells with chondroid differentiation as well as osteoid-like bands and myxoid stroma. The patient underwent a simple mastectomy with lymph node dissection. Histopathological evaluation of the surgical specimen confirmed the diagnosis of osteosarcoma G3, any features of metaplastic carcinoma as well as phyllodes tumor were excluded. Patient was given adjuvant radiotherapy after the operation. Seven months subsequent, multiple metastases in the lungs were found in a CT scan. The patient received chemotherapy, which, after three courses, resulted in a significant decrease of the metastases.

Addressed in discussion was the origin of this tumor, which is ambiguous, and a review the prognostic factors, of which, the most reliable is the size of the lesion and treatment methods, where wide excision definitely plays a major role.

Keywords: primary breast osteosarcoma, osteosarcoma, breast malignancy

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Introduction

Around 150 cases of primary breast osteosarcoma (PBOS) have been reported to date, however it is possible that many of those cases were in fact metaplastic breast carcinoma with the loss of epithelial components [1]. Hence every case of this neoplasm is a diagnostic and therapeutic challenge.

Case description

In January 2022, a 53-year-old woman came for her first visit because of a lump in her left breast that she identified during a breast self-examination.

In ultrasonography (USG) scan, breast tissue was heterogeneously dense. The right breast did not present any suspicious focal lesions. A solid-cystic nodule measuring 55 × 50 × 37 mm was detected in the left breast. Left axillary fossa did not contain any nodal lesions. According to BI-RADS, the nodule fitted category 4B; moderate suspicion for malignancy.

An ultrasound-guided core needle biopsy was performed. The histopathological examination of the biopsy specimen indicated a neoplasm composed of oval and spindle cells with strongly expressed cellular atypia. Multinucleated cells without atypia were also present. Chondroid differentiation, osteoid-like bands and myxoid stroma occurred in the neoplasm area. Necrosis made up around 50% of the specimen. 8 mitoses per 10 high power fields (HPF) were present. Immunohistochemistry results of the biopsy were negative for cytokeratin (CKAE1/3 "–", CKHMW "– ") and hormone receptors [estrogen eeceptor (ER) 0%, progesterone receptor (PGR) 0%, human epidermal growth factor receptor 2 (HER2) (0)]. Ki67 was elevated

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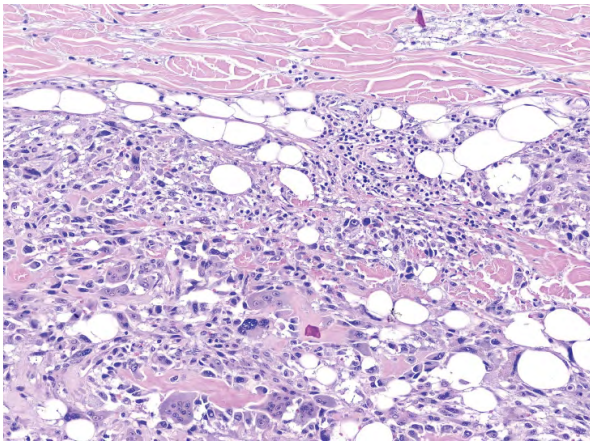

Figure 1. Histopathological examination

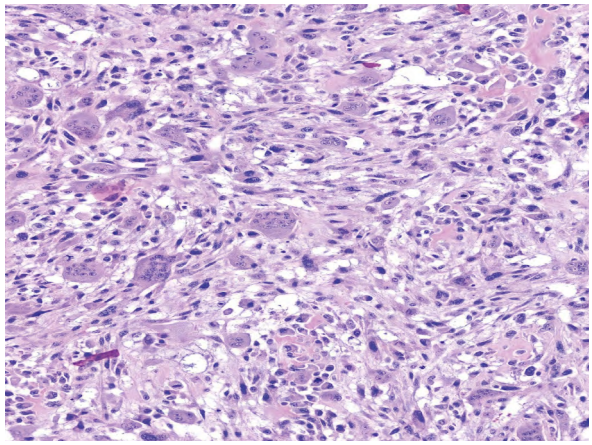

Figure 2. Histopathology high power magnification

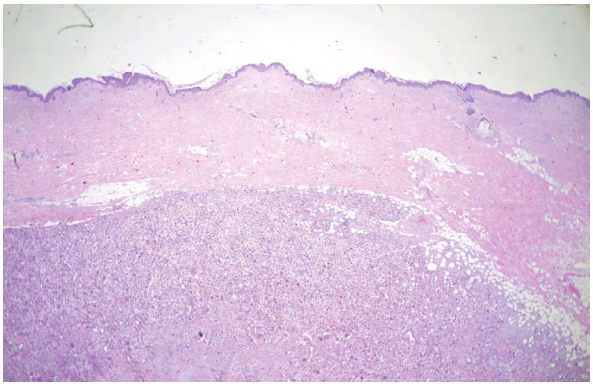

Figure 3. Histopathology low power magnification

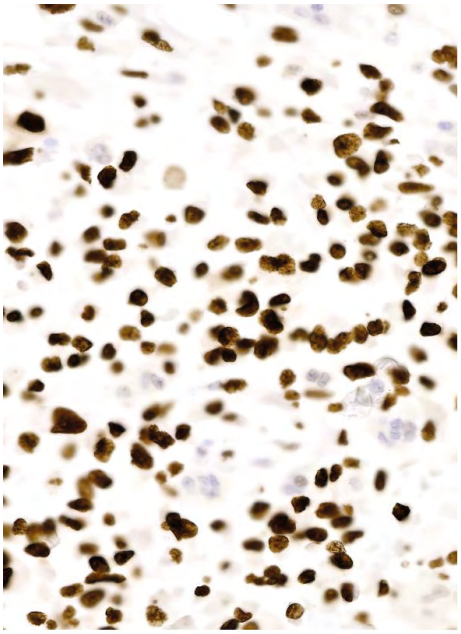

Figure 4. Immunochemistry special AT-rich sequence-binding protein 2 (SATB2)

to 50%. This description reinforced the diagnosis of mesenchymal malignancy with chondroid and osteosarcomatous differentiation — high grade sarcoma. Even so, based on these results, exclusion of phyllodes tumor and metaplastic carcinoma was not possible and required further exams.

Chest radiograph in February 2022 did not reveal any abnormalities.

In accordance with the decision made at a multidisciplinary consultation meeting the patient underwent a simple mastectomy with sentinel node and level I armpit lymph nodes dissection.

Histopathological examination of the surgical specimen confirmed tissue morphology of high-grade sarcoma (Fig. 1–3). The tumor reached up to 7 cm in dimension. Morphological features and immunohistochemistry were indicative of osteosarcoma G3. Based on this pathological evaluation with IHC staining the metaplastic carcinoma as well as phyllodes tumor were excluded. All margins of the specimen were free of tumor.

Panel of immunohistochemical markers: special AT-rich sequence-binding protein 2 (SATB2) (+) (Fig. 4), p53(+/–) (Fig. 5); cytokeratin AE1/AE3 (CKAE1/AE3) (–) (Fig. 6), CAM5,2(–), CK5/6(–), p63(–), CD10(–); SMA(–), Desmina(–), Caldesmon(–), S100(–), MDM2(–); ER(–), PGR(–), HER2(–); CD163(–), H3F3A/B(–).

In March of 2022 computed tomography (CT) scans did not show any metastases. The patient was given adjuvant radiotherapy of her left thoracic area in fraction dose of 1,8/2,0 Gy and total dose 54/60 Gy.

In October of 2022 CT scan showed multiple metastases in both lungs, the biggest measured 21 mm (segment 8, left lung), 21 mm (segment 9/10, right lung), 14 mm (segment 5, right lung) (Fig. 7). A nodule in the lung parenchyma or an enlarged lymph node measuring 26 × 19 mm was also identified on the level of hilum of the lung.

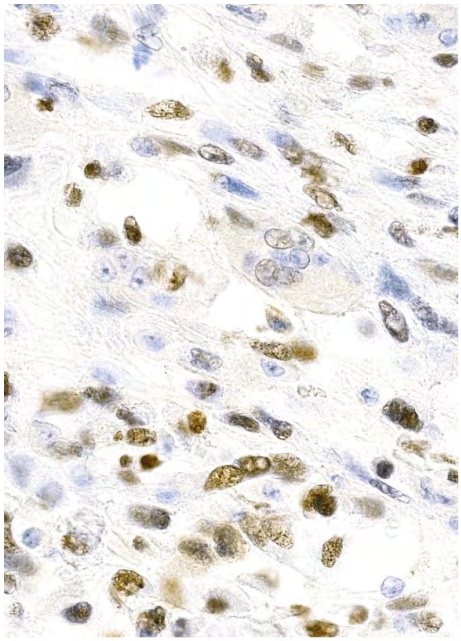

Figure 5. Immunochemistry p53

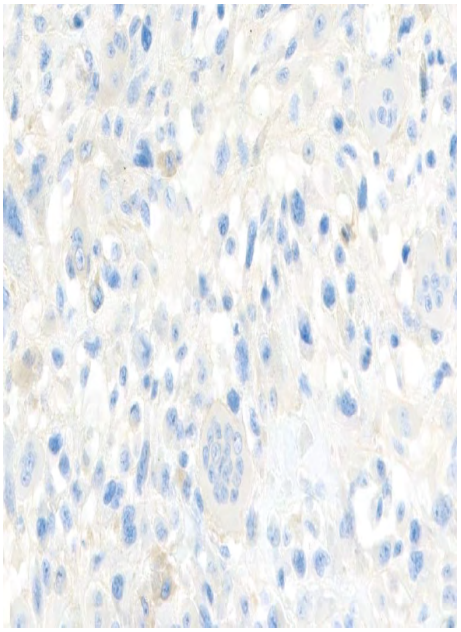

Figure 6. Immunochemistry cytokeratin AE1, AE3 (CKAE1, AE3)

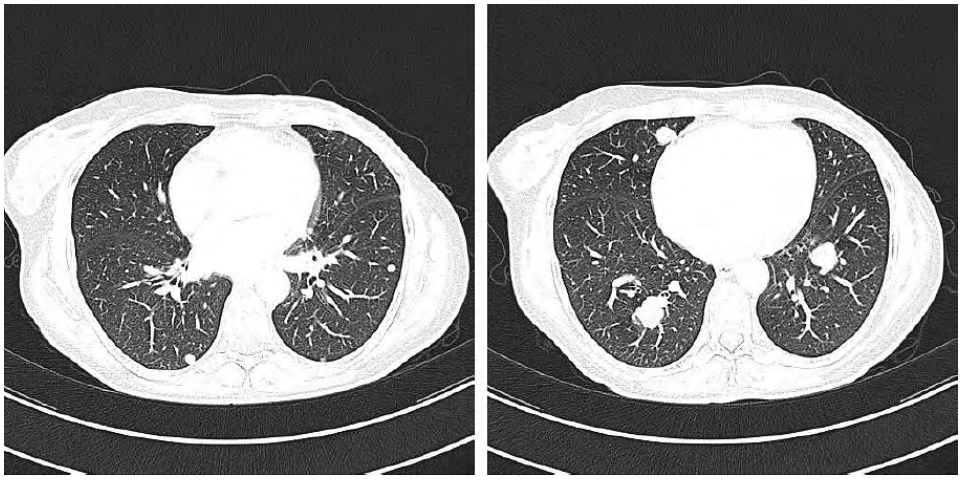

Figure 7. Computed tomography scan — October 2022

In October of 2022 patient got her first course of chemotherapy including doxorubicin *in venam* (*i.v.*) in a dose of 40 mg/day for two days and 30 mg on the third day. Ifosfamide *i.v.* in a dose of 4 g/day — on day 1, 2, 4 and 3 g on the third day. In addition, aprepitant, dexamethasone, ondansetron, mannitol and mesna were given.

After three courses of chemotherapy, the CT scan from December of 2022 showed a decrease in most metastases in the lungs. In segment 8 of the left lung: from 21 to 12 mm, in segment 9/10 of the right lung: from 21 to 8 mm.

Discussion

Primary breast osteosarcoma usually manifests as a palpable lump. Typically it afflicts women after menopause. Nevertheless, it has been diagnosed in individuals aged 16 to 96 [1]. Lymphatic spread is uncommon and lymph node metastases strongly indicate a metaplastic origin of the neoplasm [2]. Osteosarcomas metastases are found typically in the lungs and bones [3, 4]. In microscopic evaluation a variable amount of osteoid tissue is present. Typically, cells of primary breast osteosarcoma in immunohistochemical (IHC) staining

are positive for vimentin and negative for hormone receptors [5]. Predisposing factors of this neoplasm are mostly unknown. However, the manifestation of PBOS many years after burning of the breast has been reported, which can indicate a possible role of physical trauma in the development of this tumor [6]. In addition, occurrence of extraskeletal osteosarcoma a few years after radiation therapy of the chest wall for breast cancer has been described in the literature as well [7, 8].

This neoplasm has ambiguous origins. Some authors claim, that breast osteosarcomas mostly originate from epithelial tissue that underwent neoplastic metaplasia (and are in fact metaplastic carcinomas with minimal or even hardly detectable residual epithelial components) and true pure extraosseous breast osteosarcomas arising out of totipotent mesenchymal cells is extremely rare [9]. The third possibility is a transformation from underlying primary benign lesion, for instance fibroadenoma or phyllodes tumor [4].

Histopathological evaluation plays a fundamental role in the diagnosis of primary breast osteosarcoma. Having in consideration the rarity of primary origin of osteosarcoma in the breast, PBOS should be differentiated from metaplastic carcinoma and others, especially phyllodes tumor [1, 2]. In order to exclude carcinoma it is necessary to confirm the lack of epithelial tissue in the biopsy and negative immunohistochemical staining for cytokeratins [2]. It is optimal to use more than one epithelial marker, including CKAE1/AE3, CK7, CAM5,2, epithelial membrane antigen (EMA). However, cartilaginous differentiation can be focally positive for EMA and positive cytokeratin staining can be exceptionally found in sarcomas samples [6]. It is also important to confirm the lack of any benign tumors in the surrounding areas during diagnostics [3, 5].

Diagnosis of the tumors primary origin in the breast should be supported by excluding the presence of lesions in skeleton to confirm the absence of bone origin. Especially a direct connection with underlying ribs or sternum raise suspicion of primary osseous osteosarcoma.

Some authors emphasize the role of bone scintigraphy with technetium 99-methylene diphosphonate (Tc-99m) in preoperative clinical diagnosis where intense uptake reinforces the thesis of a new bone formation in the lesion. It is also useful in excluding metastases [5].

Another helpful diagnostic tool is digital breast tomosynthesis mammography (DBT), which can support the differentiation between PBOS and benign calcified tumors like fibroadenoma. A densely calcified mass with a sunburst pattern of calcifications should prompt a suspicion of a malignant nature of the lesion [10].

Tumor size seems to be the most important prognostic factor [2]. Five-year survival rate was reported as 91% in case of tumor size not exceeding 5 cm in diameter and 50% with tumors larger than 5 cm. In opposition to the five-year survival rate, the risk of recurrence and metastases was not statistically significantly correlated with the size of the tumor [2]. Other prognostic factors include histopathological diagnosis, infiltrative features, presence of positive margins and age.

There are various therapeutic strategies. According to some authors, treatment should be the same as that provided for other extra-skeletal osteosarcoma, which consists of surgery or chemoradiation [1]. Other researchers suggest the same treatment as the one for triple negative breast cancer [9]. However, surgery seems to be the general principle of the treatment and achieving negative margins remains the most important matter [4, 5]. Patients treated with a simple excision tend to have a high risk of recurrence or metastases [2]. Simple mastectomy seems to be the optimal procedure.

Lymph node dissection is not considered to be necessary, due to the fact that osteosarcoma spreads mainly through the hematogenous route [3].

The role of chemotherapy has been emphasized especially when the tumor size exceeds 5cm in diameter. In most cases chemotherapy is employed [1]. Usually treatment is based on conventional medications for osteosarcoma, for example: doxorubicin, ifosfamide, cisplatin, methotrexate [3].

The prognosis in extraskeletal osteosarcoma is poor, especially because of a high risk of early recurrence and dissemination.

Conclusions

Currently there are no standardized guidelines for treatment of PBOS and gaining new insight from case reports can lead to improvement in clinical practice.

Article Information and Declarations

Ethics statement

This research did not require ethical approval from bioethics comittee, because the article is based only on review of scientific papers and clinical data.

Author contributions

K.M.B.: writing; A.Sz.-C.: supervision.

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Conflict of interest

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Supplementary material

None.

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