



Primary Chondroblastic Osteosarcoma of the Uterus: Immunohistochemical Examination and Differential Diagnosis with Malignant Mixed Mullerian Tumor

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Abstract

Extraskelletal osteosarcomas are rarely observed tumors. Besides this, primary osteosarcomas of uterus are rarer, and only 21 cases have been reported in the literature. It is generally seen at the postmenopausal period, and it progresses quite aggressively. Particularly, malignant mixed mullerian tumors (MMMTs) are important for differential diagnosis. Histopathological and immunohistochemical examination of a mass that was detected in the uterus of a 61-year-old postmenopausal patient revealed the diagnosis of primary chondroblastic osteosarcoma, and this very rare case is presented here.

Keywords: Chondroblastic, Osteosarcoma, Uterus

Introduction

Primary sarcomas of the uterus constitute approximately 3%–5% of malignant uterine corpus tumors (1, 2). According to the classification systems proposed by the World Health Organization and College of American Pathologists, uterine sarcomas can be divided into the following seven histological groups based on the differentiation/growth pattern of neoplastic cells: (i) leiomyosarcoma, (ii) low-grade endometrial stromal sarcoma, (iii) high-grade endometrial stromal sarcoma, (iv) undifferentiated uterine/endometrial sarcoma, (v) adenosarcoma, (vi) adenosarcoma with sarcomatous overgrowth, and (vii) others (3, 4). Pure heterologous uterine sarcomas, which are quite rare, may arise from mesenchymal tissues that are unfamiliar to the uterus (5). Primary osteosarcomas belong to this group, and characteristically, they do not contain epithelial and other mesenchymal components. These tumors generally resemble the mesenchymal component of malignant mixed mullerian tumors (MMMTs) and behave quite aggressively with early relapses and metastasis (6-8).

Case Report

A 61-year-old patient was admitted to a gynecology clinic due to postmenopausal bleeding, pelvic pain, and vaginal discharge. On pelvic examination, there was a mass causing cervical dilatation and protruding towards the vagina. Pelvic ultrasound examination revealed an approximately 15 cm solid mass in the uterus. The preliminary diagnoses were leiomyoma, leiomyosarcoma, or a malignant mesenchymal tumor. After informing the patient about the clinical condition, a decision for surgery was made. Because she was postmenopausal, total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed. During the operation, uterine dimensions were 15x10x9 cm, and bilateral ovaries were macroscopically normal. Sections of the uterus revealed an intramural 15x8x8 cm solid mass at meat consistency which was compressing the endometrium and was resembling either a degenerated leiomyoma or leiomyosarcoma. In an area where the myometrium was as thin as 2 cm, it was seen that the mass infiltrated the myometrium by up to 1.8 cm. The cross-sections included wide areas of bleeding and focal areas of grayish-yellow colored, degenerated areas with a soft consistency. Microscopically, the tumor was widely cellular, containing irregular oval-fusiform, apparently pleomorphic, atypical cells. In some areas, tumor cells were in the form of bizarre and giant cells containing apparent eosinophilic cytoplasm. In focal areas, chondroid tissue consisted of atypical chondrocytes; prominent osteoid production and lace-like architectural formation of atypical osteoblasts and osteoclast-type giant cells were remarkable (Figures 1, 2). There were a few atypical mitosis, and mitotic index was high in cellular areas (10–15/10 high-power field) (Figure 3). The tumor showed minimal atypia and mild pleomorphism in focal areas. All of the material was analyzed by taking more than 100 samples; any epithelial or different components of sarcomas (endometrial stroma, skeletal muscle, adipose tissue, and smooth muscle) were not present. Immunohistochemically, stromal cells were positive with vimentin and negative with panitokeratin, CK 5/6, CK 7, CK 20, CD 10, EMA, and SMA. Atypic-

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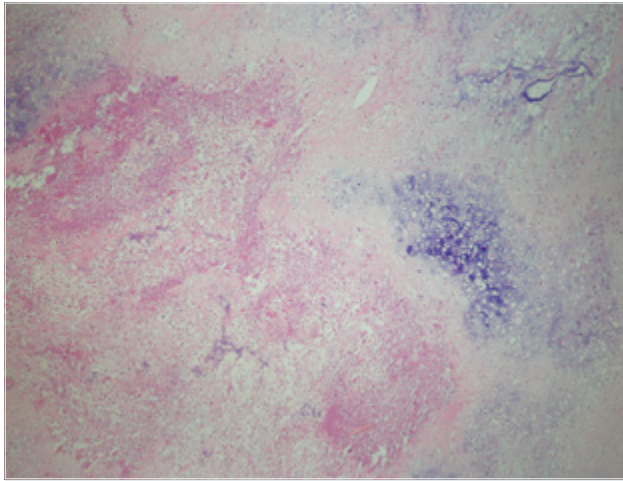


Figure 1. Atypical osteoblasts in osteosarcoma area and osteoclast type giant cells (H/E, x200)

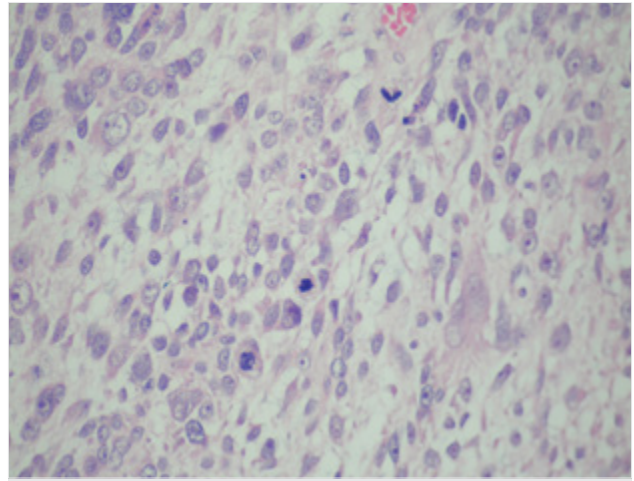


Figure 3. High mitotic index in cellular areas (H/E, x400)

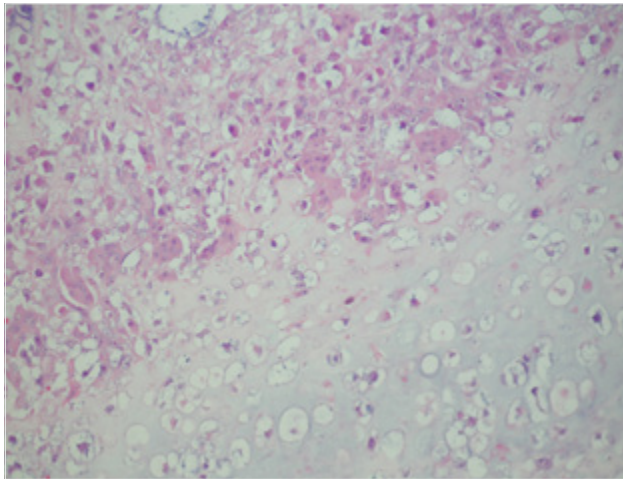


Figure 2. Osteosarcoma and chondrosarcoma areas forming the tumor (H/E, x100)

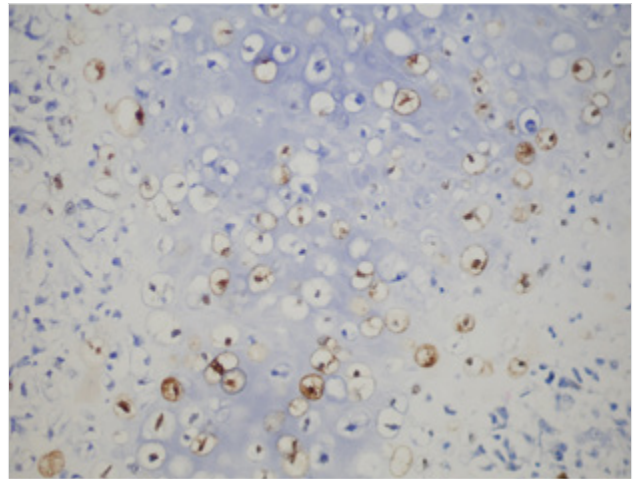


Figure 4. Atypical chondrocytes shows S100 positivity (x200)

cal chondrocytes in chondrosarcoma areas were S100 (+) (Figure 4). Ki-67 index of the tumor was approximately 25%.

The patient was given two doses of chemotherapy (iphosphamide +paclitaxel) postoperatively, and she had no relapse during the postoperative 6 months. Consent form was taken from the patient.

Discussion

There are a limited number of case reports and reviews about full heterologous sarcomas of the uterus. The review by Fadare O published in 2011, which was about primary homologous and heterologous sarcomas of the uterus, gives information about 19 primary uterus osteosarcomas (4). These tumors, which are rarely seen, generally show their peak incidence at the postmenopausal period and are quite aggressive clinically (2). The most important signs and symptoms are vaginal bleeding, pelvic pain, and uterus growth (2). Our patient also presented to the clinic with complaints of postmenopausal bleeding and pelvic pain.

A few theories were asserted about the formation of primary uterine sarcomas, including osteosarcoma in the literature. There are

studies supporting that osteosarcomas can occur by the development of MMMTs in the monomorphic direction, by the transformation of multipotent cells in the myometrium into different mesenchymal components, or by the malignant transformation of osseous metaplasia areas in smooth muscle tumors (8, 9).

Some criteria have to be fulfilled for the definitive diagnosis of primary osteosarcoma (10). These criteria are as follows: absence of osteosarcoma in any part of the skeleton of a patient, apparent osteoid production in the microscopic examination of the mass, and absence of epithelial component and any homologous or heterologous component in the tumor after adequate sampling. In our patient, a lesion was not seen on the bone scan. As a result of histopathological examination of adequate samples taken from the mass, osteosarcoma areas that showed lace-like set-up and produced prominent osteoid adjacent to chondrosarcoma areas were seen; any epithelial or different type of mesenchymal component was not encountered.

Histopathologically, distinction between primary uterine osteosarcomas and other malignant mesenchymal tumors of the uterus (such as leiomyosarcoma, MMMT, and endometrial stromal sarcoma) requires scrutiny. For our patient, we performed numerous samplings from the tumor to exclude the diagnosis of MMMT.

Moreover, immunohistochemical staining is helpful for diagnosis. The suspicious cellular areas showed negative staining with pancytokeratin. Rhabdomyosarcoma is the most frequent type among pure heterologous sarcomas of the uterus, but the tumor can include mixed heterologous components such as chondrosarcoma, osteosarcoma, and liposarcoma (2). In our patient, there were no areas in the sections showing differentiation in the direction of smooth muscle, striated muscle, or adipose tissue apart from chondrosarcoma and osteosarcoma components histopathologically and immunohistochemically.

Macroscopic growth is also important for differentiation between pure heterologous sarcomas and MMMTs. While MMMTs grow as polypoid masses towards the inside of the endometrial cavity, pure heterologous sarcomas generally grow as an intramural mass that compress the endometrium (9, 11-13). In our case, tumor infiltrated the myometrium and grew as an intramural mass. Endometrium was compressed at broad areas and gained the appearance of an atrophic endometrium.

Conclusion

Pure heterologous sarcomas of the uterus and primary osteosarcoma included in this category are malign mesenchymal tumors that are rarely seen. Their prognosis is quite bad. Therefore, many samplings from the mass should be performed and should be immunohistochemistry used for the differential diagnosis, particularly from MMMT and for the exclusion of the epithelial component.

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