Pathologic Quiz Case

A 60-Year-Old Woman With Diffuse Uterine Enlargement

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A 60-year-old woman presented with a 2-year history of abdominal pain. Previous medical history was unremarkable. Physical examination revealed an enlarged uterine corpus. Pelvic ultrasound showed the uterus to be displaced by multiple nodular ill-defined masses. Because of the uncertain nature of these masses, the patient underwent a hysterectomy. On gross examination, the uterus weighed 1145 g. The corpus was distorted and displaced by an intramural tumor with imprecise borders. The adnexa were normal. The cut surface of the tumor showed multiple nodular white areas of varying size diffusely infiltrating the myometrium. Two of these nodular areas are represented in the lower right-hand corner of Figure 1, which represents only part of the neoplasm (arrows). These areas were interspersed with foci of hemorrhage and calcification (not shown). The tumor had diffusely infiltrated through the myometrium, but there was no extrauterine extension. Lymph nodes were unremarkable.

The immediate postoperative course was uneventful. Microscopically, the major portion of the tumor consisted of anaplastic-appearing round to spindle-shaped neoplastic cells with marked pleomorphism, irregular nuclei, and prominent nucleoli (Figure 2, original magnification ×400). Intermingled with the tumor cells were irregular areas of neoplastic osteoid with scattered foci of calcification (Figure 3, original magnification ×100). The osteoid formed a fine meshwork separated from the sarcomatous areas. Many multinucleated osteoclast-like giant cells were observed (Figure 4, original magnification ×200). The average number of mitoses in 10 high-power fields was 7 (100 fields were counted). The neoplastic cells infiltrated diffusely through the normal-appearing muscular cells of myometrium. Despite extensive sampling of the tumor, neither epithelial nor any other mesenchymal component was observed throughout the tumor tissue. The tumor reached the uterine serosa but did not invade the cervix, the fallopian tubes, or the ovaries. Immunohistochemical stains, including vimentin, smooth muscle actin, desmin, S100, AE1/AE3, and epithelial membrane antigen (Novocastra, Newcastle upon Tyne, United Kingdom), were performed on a representative block of formalin-fixed, paraffin-embedded tissue using the avidin-biotin-peroxidase method. The neoplastic cells were strongly positive for vimentin. The atypical spindle cells showed focal positivity for smooth muscle actin and S100. The other markers were negative.

What is your diagnosis?

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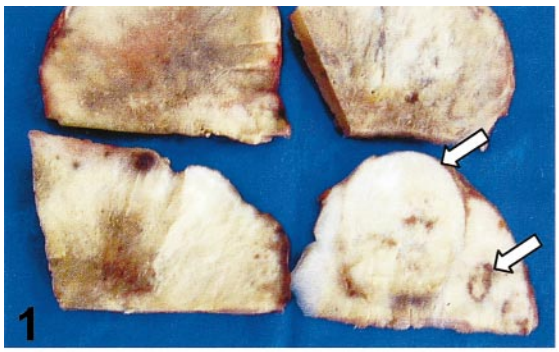

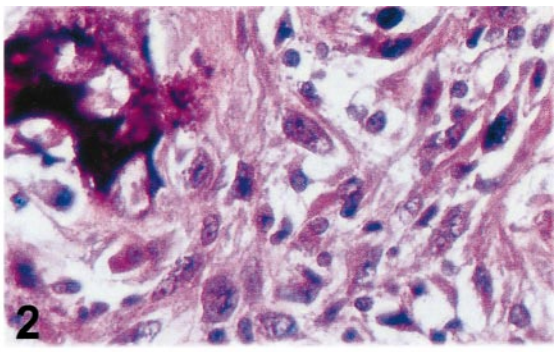

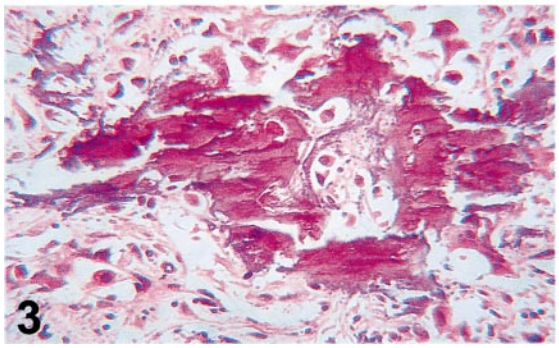

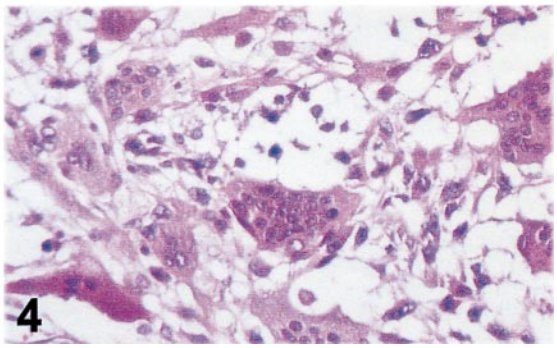

Pathologic Diagnosis: Primary Osteosarcoma of the Uterus

Uterine sarcomas are uncommon, accounting for 1% to 2% of all uterine neoplasms.[1] They are frequently classified as either homologous, referring to tumors that consist of tissue normally found within the uterus, or heterologous, implying those with tissue foreign to the uterus.[1] Pure heterologous osteosarcomas in the uterus are distinctly rare, with published references limited to case reports.[2] In our case, the absence of a skeletal osteosarcoma, which was determined by complete medical assessment, indicated that the tumor was not a metastasis from a neoplasm of the bones. The main clinical features of osteosarcomas originating in the uterus are vaginal bleeding, abdominal pain, and uterine enlargement.[3] The mean age of patients is 64 years, and most of them are perimenopausal or postmenopausal at the time of diagnosis.[4]

Osteosarcoma is a mesenchymally derived malignant tumor that by definition produces osteoid and/or bone. Implicit in this definition is the fact that tumor cells themselves produce the osseous matrices and that the osseous matrices must be neither reactive nor metaplastic. Other elements, such as malignant cartilage or malignant fibrous tissue, may or may not be produced. Its histogenesis in the uterus is still a subject of controversy. It is known that there are multipotential cells residing in the myometrium that are capable of differentiating into myocytes, endometrial stromal cells, and other elements.[3] Malignant change in one of these cells could explain the development of a primary osteosarcoma in the uterus. This hypothesis is attractive, since focal neural and muscular differentiation, as observed in the present case, are frequently present.[5] Other possibilities include a monomorphic differentiation from a malignant mixed mullerian tumor (MMMT) or a malignant change in a focus of osseous metaplasia, which are frequently seen in uterine muscular neoplasms.[3]

Although the uterus is an uncommon site for primary osteosarcomas, the histologic features are characteristic enough to allow a diagnosis without special stains.[4] The differential diagnosis includes above all the heterologous MMMT with bone formation. The distinction is made by the presence of an epithelial component, which is seen in the MMMT but not in the osteosarcoma. Extensive sampling for the search for epithelial elements is very important, since osteosarcomas are more aggressive and have a worse outcome than the MMMT with bone formation.[5] Indeed, uterine osteosarcomas are very aggressive neoplasms with a mean survival time of 8.5 months.[5] Treatment modalities include hysterectomy either followed or not followed by bilateral salpingo-oophorectomy, radiation therapy, and/or chemotherapy.[4]

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