Primary myxoid chondrosarcoma of the uterus: report of a case with immunohistochemical study

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Summary

Chondrosarcoma of the uterus is an extremely rare type of pure heterologous uterine sarcoma. In the present report a case of myxoid chondrosarcoma that occurred in the uterine corpus of a 46-year-old woman is described together with a brief review of the cases of uterine chondrosarcoma previously reported in the literature.

Key words: Chondrosarcoma; Myxoid; Uterus; Sarcoma; Heterologous.

Introduction

Chondrosarcoma of the uterus is an extremely rare type of pure heterologous uterine sarcoma. With the exception of embryonal rhabdomyosarcoma of the cervix, primary uterine sarcomas containing heterologous elements in the absence of epithelial elements are rare neoplasms, usually occurring in elderly women who present with a history of vaginal bleeding, abdominal pain and uterine enlargement [1, 2]. This group of tumors includes pleomorphic rhabdomyosarcoma, chondrosarcoma, osteosarcoma and liposarcoma. The macroscopic and microscopic features of these neoplasms resemble those of their counterparts in other parts of the body. In the uterine corpus an overgrowth of a malignant mixed mullerian tumor (MMMT) must always be ruled out [3], since malignant heterologous components are found in high proportion of the latter tumors.

Clement, in 1978, reported a case of primary uterine chondrosarcoma with leiomyosarcomatous areas and included a review of the literature that revealed 12 previous cases of chondrosarcoma, without glandular elements or other specific heterologous elements, reported since 1854 [4, 5]. A more recent report [6] described a case of a heterologous uterine sarcoma that consisted predominantly of chondrosarcomatous elements with foci of rhabdomyosarcoma.

The aim of the present report is to describe a case of primary myxoid chondrosarcoma of the uterus, and to review briefly previously reported cases of uterine chondrosarcoma.

Case report

A 46-year-old white woman, gravida 3, para 2, was admitted for vaginal bleeding and malaise. Two years earlier she had had diagnostic curettage for another episode of vaginal bleeding, followed by histologic examination that had not revealed any signs of malignancy. Her previous medical history was otherwise unremarkable. Clinical examination revealed an enlarged uterine corpus. Laboratory examination showed severe anemia. Pelvic ultrasound and CT-scan showed a 9 × 8 cm uterine mass. Treatment of anemia with transfusion of whole blood was followed by total abdominal hysterectomy with bilateral salpingo-oophorectomy. The immediate postoperative course was uneventful.

The patient has been regularly re-examined at 3-month intervals. Thirty-six months postoperatively the patient was readmitted due to hematuria. Biopsies of the urinary bladder showed histology similar to the primary tumor. The patient underwent radical cystectomy with urinary diversion. There were no immediate postoperative complications. Postoperative radiotherapy is scheduled to follow.

Pathology

Macroscopic examination of the uterus showed an intramural nodular mass of the corpus uteri, measuring 9 cm in the largest dimension, that was compressing and distorting the uterine cavity. On cut section the tumor had a lobulated nodular appearance and a gelatinous, gray to yellowish-white cut surface. It did not extend to the external surface or to the endometrium. Histologically it was characterized by generally uniform, round or elongated cells with eosinophilic cytoplasm, arranged in cords and strands or in a lace-like pattern, separated by variable amounts of myxoid matrix (Figures 1 and 2). Nuclear pleomorphism was not prominent. The number of mitotic figures varied, with a maximum of 4-5/10 HPF. In some areas cellularity was increased and slight pleomorphism was observed. A single focus of immature cartilage was found. The overlying endometrium showed pressure atrophy.

Intracytoplasmic PAS-positive and diastase-sensitive material (glycogen) was observed. Immunohistochemical examination showed positivity of the tumor cells for vimentin (V9, Biogenex) and S100 protein (polyclonal, DAKO), while stains for cytokeratins (AE1/AE3, Immunon), EMA (E29, DAKO), desmin (D33, DAKO), smooth muscle actin (_sm-1, Novokastra), chromogranin (DAK-A3, DAKO), synaptophysin (snp 88, Menarini) and CD34 (QBEnd/10, Novokastra) were negative. Leu7 (NK-1, Novokastra) was weakly positive. Ki67 (MB67, Neomarkers) labelling index, calculated as the percentage of positive nuclei after counting of 500 cells, varied in places but was always less than 10%.

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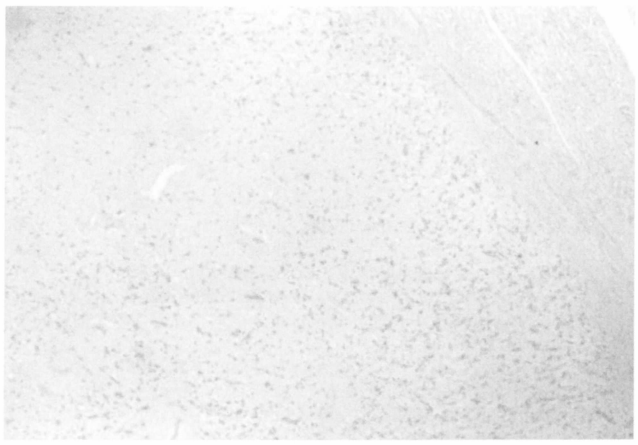

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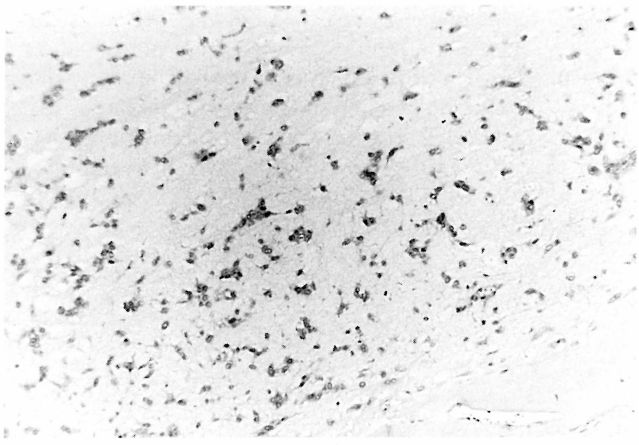

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Figures 1 and 2. — Uniform cells with eosinophilic cytoplasm arranged in cords and strands and separated by myxoid matrix (original magnification x 40, x 100).

The tumor in the wall of the urinary bladder was intramural, measured 4 cm in the largest dimension and showed histologic characteristics similar to those of the initial tumor, except for extensive areas of necrosis (Figure 3). Ki67 labelling index was similar to that of the primary tumor.

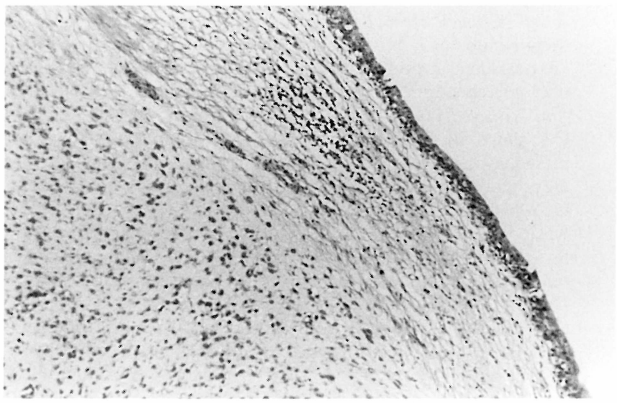

Figure 3. — Metastatic tumor in the wall of the urinary bladder showed histologic characteristics similar to the primary tumor (original magnification x 100).

Discussion

Chondrosarcomas of soft tissue are uncommon tumors and, unlike their skeletal counterparts, are often myxoid in type. The clinicopathologic features of extraskeletal myxoid chondrosarcoma were described by Enzinger and Shiraki in 1972 [7]. It is an uncommon, relatively slow-growing tumor, that occurs mostly in middle-aged adults, primarily in the soft tissues of the extremities. Although the clinical behavior of extraskeletal myxoid chondrosarcoma varies from case to case, this tumor often has a protracted clinical course with a high rate of metastases and local recurrences, resulting in tumor-related death in a high percentage of cases [8, 9]. The majority of extraskeletal myxoid chondrosarcomas have a translocation, t(9;22) (q22;q12), that results in a fusion of the EWS gene and the CHN gene.

Chondrosarcoma in the uterus usually appears as a heterologous component of MMMTs, in which it is admixed with epithelial and usually other stromal elements. MMMTs are the most common form of uterine malignant mesenchymal and mixed epithelial tumors, which account for less than 5% of malignant tumors of the uterine corpus [10] and may also occur in other parts of the female genital tract [11]. When chondrosarcoma occurs as a component of a MMMT, it is usually seen as one or more microscopic foci [12]. Uterine tumors composed predominantly or entirely of chondrosarcoma are exceedingly rare [4-6].

The development of primary pure heterologous uterine sarcomas might be explained by the presence of multipotential cells residing in the myometrium and being capable of differentiating into myocytes, endometrial stromal cells and perhaps other elements [13]. It has also been suggested that primary pure heterologous sarcomas may arise from primitive embryonal cell rests or from complete stromal overgrowth of a MMMT [6, 14].

Thirteen cases of uterine chondrosarcomas have been previously reported in the literature [4 and references therein, 5]. The age of the patients varied from 36 to 66 years. The patient in the present case was 46 years old at the time of initial diagnosis. The mean age of these cases is 52 years and the median age 54 years, which is lower than that of MMMTs [10]. The most common symptom was abnormal vaginal bleeding, as in the present case; less common symptoms were abdominal pain, dysuria and vaginal discharge. The uteri were enlarged in almost all previously reported cases, but spread of the tumor beyond the uterus was not observed. In ten cases the neoplasms appeared to arise from the endometrium, while in three cases they were considered to be of myometrial origin, as in the present case. In Clement's review of chondrosarcomas the tumors were well or moderately differentiated, but generally merged with more cellular, non-specialized sarcoma [4]. Tumors containing areas

referred to as fibrosarcoma, spindle cell or round cell sarcoma, and pleomorphic sarcoma were not excluded from the above study. The tumor of that report varied from well to poorly differentiated. It should be noted that myxoid areas were commonly described in the previously reported cases. In the present case the tumor exhibited characteristics of myxoid chondrosarcoma in all histological sections examined, with some areas of increased cellularity.

Tumor entities in the histological differential diagnosis include mainly MMMTs, myxoid leiomyosarcoma and myxoid liposarcoma. The possibility of metastatic chondrosarcoma must also be ruled out by clinical and laboratory examination of the patient. Extensive sampling of the tumor is necessary in order to rule out the presence of epithelial elements and therefore a MMMT. Immunohistochemical stains for cytokeratins and epithelial membrane antigen may facilitate the recognition of sparse epithelial elements, although in rare cases extraskeletal myxoid chondrosarcomas have been reported to exhibit positivity [8, 9]. In the present case positivity for vimentin and S100, and negativity for epithelial markers and markers of myoid differentiation were consistent with the diagnosis.

In the few previously reported cases of uterine chondrosarcoma with follow-up information, with the exception of a patient who was alive and well eight months postoperatively and another patient who died two days postoperatively, all seven patients died from recurrence or metastatic disease in a period of four to 23 months after initial diagnosis and treatment. Eight of the patients underwent some form of hysterectomy and one was treated only by curettage. The malignant behavior of uterine chondrosarcoma in the above cases does not differ significantly from other types of pure heterologous uterine sarcomas [2, 14]. The case reported by Kofinas *et al.* [6] resulted in death of the patient from metastatic disease 13 months post-therapy. In the present case the interval between surgery and appearance of metastasis was relatively longer, probably similar to the behavior of extraskeletal myxoid chondrosarcoma of soft tissue.

In summary, an extremely rare case of pure primary chondrosarcoma of the uterus is reported with a brief review of cases previously described in the literature. The tumor in the present case exhibited histologic features of myxoid chondrosarcoma and metastasized three years after surgery. This course is more similar to extraskeletal myxoid chondrosarcoma than other types of pure heterologous uterine sarcoma.

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