Endometrial carcinosarcoma with osteoclast-like giant cells

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Summary

We encountered a case of endometrial cancer with a poorly differentiated epithelial component, accompanied by a compact proliferation of atypical spindle cells and osteoclast-like giant cells. Immunohistochemically, the epithelial component was EMA and prekeratin positive with vimentin-positive spindle cells, whereas the osteoclast-like giant cells were strongly immunoreactive for CD68. The description of osteoclast-like giant cells adds to the knowledge of endometrial carcinosarcoma tumor biology.

Key words: Endometrium; Carcinosarcoma; Osteoclast-like giant cells.

Introduction

Giant cell tumor of bone is a primary osteolytic tumor characterized by the formation of osteoclast-like giant cells. Tumors of the female reproductive organs have only exceptionally been reported to contain osteoclast-like giant cells, whereas these cells have regularly been reported in extraskeletal soft tissues including the pancreas, liver and thyroid. By definition, carcinosarcoma consists of an admixture of malignant epithelial and mesenchymal cells. Depending on the mesenchymal cell type, the tumor is considered homologous or heterologous. In descending order, heterologous tumors contain one or more of the following elements: rhabdomyoblasts (rhabdomyosarcoma), cartilage (chondrosarcoma), osteoid bone (osteosarcoma), liposarcoma and melanocytes [1, 2]. To the best of our knowledge, the occurrence of endometrial carcinosarcoma with osteoclast-like giant cells remains unreported in endometrial carcinosarcoma.

Materials and Methods

Sections were stained with hematoxylin and eosin. Immunohistochemical reactions, by use of the avidin-biotin-peroxidase complex method, were performed on sections of the formalin-fixed, paraffin-embedded tissue using antibodies against EMA, prekeratin, vimentin, CD68, Ki67 and p53. Appropriate positive control samples were run concurrently for all antibodies tested. Clinical information was obtained from clinical and surgical notes.

Case Report

A 57-year-old woman presented with postmenopausal bleeding and endometrial biopsy suggested endometrial carcinosarcoma. Apart from hypertension, otosclerosis and a stomach ulcer, her medical history was without particularities. Total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy and pelvic lymph node dissection were performed for non-metastatic endometrial carcinosarcoma. Subsequently, the patient was included in a phase II trial and adjuvant chemotherapy was administered.

Pathologic findings

A detailed analysis of the endometrial biopsy showed the presence of three different components. One component consisted of endometrioid glandular and cribriform structures, delineated by atypical cells that were characterized by large irregular and vesicular nuclei and an eosinophilic cytoplasm. Multiple mitoses were present. This poorly differentiated epithelial component was accompanied by a compact proliferation of atypical spindle cells (Figure 1A) and osteoclast-like giant cells (Figure 2). The mesenchymal component was also highly mitotically active with many abnormal mitotic figures. An overview of the immunohistochemical results is presented in Table 1. Immunohistochemical study of the tumor showed strong EMA (Figure 1B) and prekeratin immunoreactivity of the epithelial component, whereas the mesenchymal component stained for vimentin (Table 1). Both components were moderately or strongly positive for p53 and Ki67 (Table 1). The osteoclast-like giant cells were strongly immunoreactive for CD68 (Figure 3).

Pathologic examination of the uterus revealed only a residual focus of poorly differentiated endometrial carcinoma without myometrial invasion. There was no cervical extension, and the adnexae, omentum, peritoneal biopsies from the paracolic gutters, Douglas and bladder as well as 25 lymph nodes were without metastatic disease. The surgical stage was pT1a N0.

Table 1. — *Results of immunohistochemical studies in the different cellular components of endometrial carcinosarcoma with osteoclast-like giant cells.*

Antibody	Carcinoma	Sarcoma	Osteoclast-like giant cells
EMA	+++	+	–
Prekeratin	+++	–	–
Vimentin	–	++	+
CD68	–	–	+++
P53	+++	++	–
Ki67	++	+++	–

+++, strongly positive; ++, moderately positive; +, weakly positive; –, negative.

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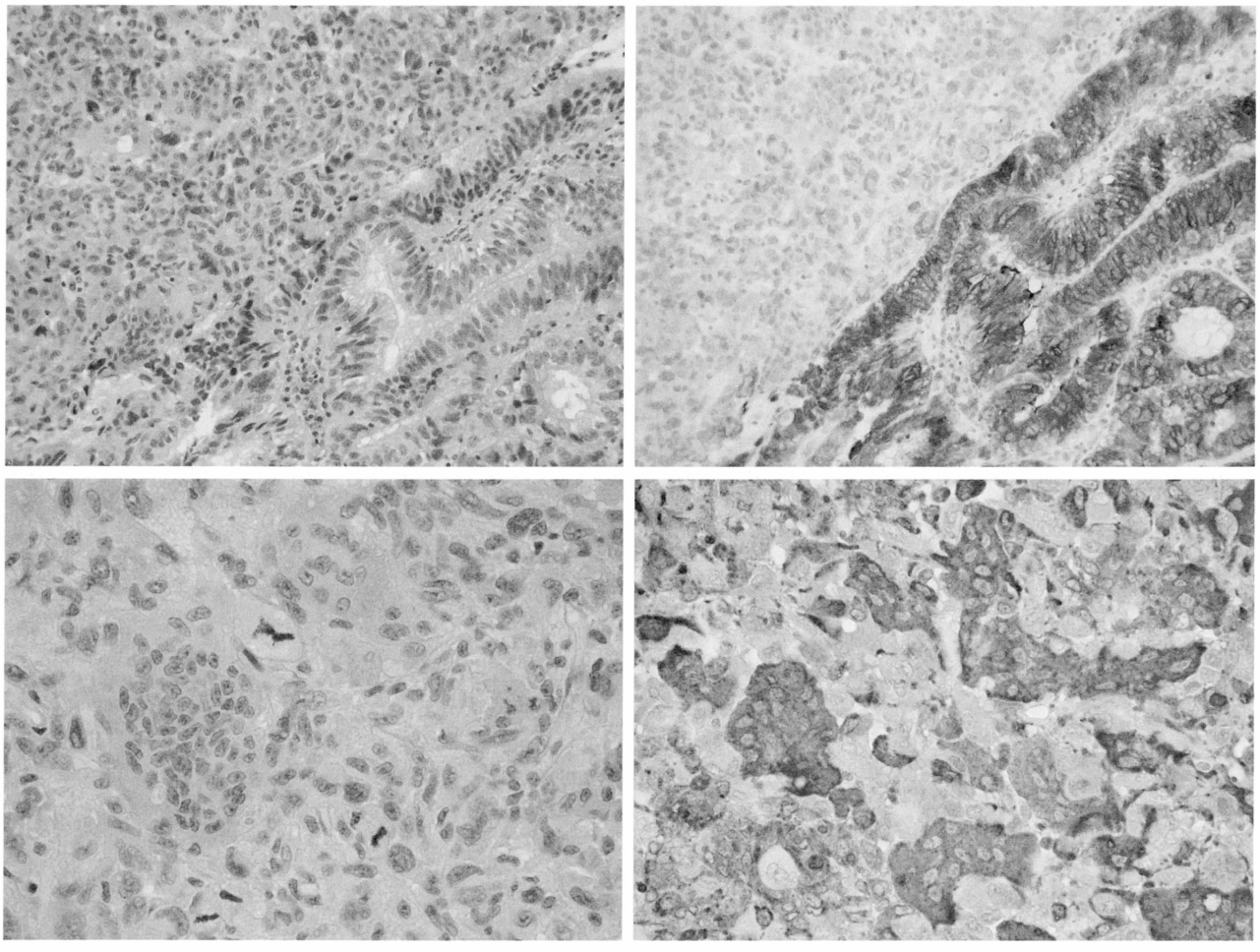

. 1a Fig. 1b

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Figure 1. — A) Carcinosarcoma, with the two components side-by-side. B) Immunohistochemical staining for EMA strongly decorates the carcinoma cells. Some spindle cells of the sarcomatous component are weakly positive. The osteoclast-like giant cells are negative.
Figure 2. — Sarcomatous component. Atypical mononuclear spindle cells are intermingled with osteoclast-like giant cells. The spindle cells show numerous mitotic figures, many of which are abnormal.
Figure 3. — The osteoclast-like giant cells stain strongly positive with CD68.

Discussion

The pathobiology of endometrial carcinosarcoma has inspired many researchers during the last 15 years and carcinosarcomas are currently regarded as metaplastic endometrial carcinomas. Consequently, the designation *endometrial* carcinosarcoma corresponds best to its tissue origin and should be used instead of *uterine* carcinosarcoma.

Osteoclast-like giant cells have been described in endometrial adenosquamous carcinoma and uterine leiomyosarcoma. The recognition of a previously unreported cell type adds to the knowledge of tumor biology in metaplastic endometrial cancer. The observation of a strong expression of a marker of osteoclasts (CD68) in combination with the cellular morphology corresponds best to an osteoclast-like phenotype in the current case of endometrial carcinosarcoma.

The origin of these osteoclast-like cells can be twofold. Since metaplasia to cells otherwise not encountered in the uterus is known to occur in metaplastic endometrial cancer, one could hypothesize that endometrial-derived cells possess the potential for osteoclastogenesis. Similar to metaplasia towards rhabdomyosarcoma, chondrosarcoma, osteosarcoma and liposarcoma, endometrial cancer cells might have the potential to dedifferentiate into osteoclastoma. Alternatively and most probably, the presence of osteoclast-like giant cells should be viewed as an excessive form of stromal reaction. Strong arguments for the latter hypothesis have been provided in osteoclast-like giant cell tumors of the pancreas [4]. Mutations of K-*ras* are common early genetic events in tumorigenesis of the pancreatic ductal epithelium and have been analyzed after microdissection in different cell types in pancreatic cancer. Osteoclast-like giant cells were positive for the histiocytic marker CD68 but lacked mutations of K-*ras,* in contrast to the presence of mutations in ductal carcinoma cells and pleomorphic large cells [4]. Therefore, osteoclast-like giant cells are considered to be non-neo-

plastic and of mesenchymal origin. The observation that in our case p53 and Ki67 were immunohistochemically positive in the carcinoma and sarcoma component but negative in the osteoclast-like giant cells is in concordance with this hypothesis.

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