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CASE REPORT

Simultaneous Bilateral Occurrence of a Mixed Mesodermal Tumor and Cystadenocarcinoma in the Ovary

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The mixed mesodermal tumor is a very uncommon malignancy. The aggressiveness of this lesion is illustrated by extremely poor prospects for afflicted patients: postoperative survival is usually shorter than 24 months. According to the literature, malignant mixed tumor of the ovary is rather rare and its occurrence with other malignancy is exceptional. We report here a case of a 62-years old woman with serous cystadenocarcinoma in the right ovary and a heterologous malignant mixed mesodermal tumor in the left one. Both tumors expressed cytokeratins, while only the mesodermal tumor expressed S-100 and focal NSE. (Pathology Oncology Research Vol 10, No 2, 117–120)

Keywords: malignant mixed mesodermal tumor, ovary, simultaneous occurrence

Introduction

The mixed mesodermal tumor is a very uncommon malignancy. The aggressiveness of this lesion is illustrated by extremely poor prospects for afflicted patients: postoperative survival is usually shorter than 24 months. Infrequent occurrence and indistinctive symptomatology make preoperative recognition of this tumor difficult. Diagnostic imaging (MRI, in particular) is almost entirely relegated to monitoring the efficacy of postoperative chemotherapy. In the pelvis, this tumor typically develops in the uterus and only a single case of its simultaneous occurrence with primary malignancy of another organ has been published. According to the literature, malignant mixed tumor of the ovary is rather rare and its joint occurrence with another malignancy (serous cystadenocarcinoma) of the contralateral ovary is exceptional.

Case report

A 62-years-old female patient has been admitted for flatulence and dyspepsia, associated with a substantial increase of abdominal circumference. Apart for appendectomy and tonsillectomy, her history was unremarkable and did not contain previous complaints on ill health. The patient had no pregnancies and has had never taken oral contraceptives. Ten years earlier, curettage had been performed for metrorrhagia, but no specific abnormality was identified by histology. On admission, bimanual examination revealed that the pelvic cavity was filled by a mobile, cystic mass, which was inseparable from the uterus and extended upwards to the level of the umbilicus. In agreement with physical findings, ultrasound examination depicted an amorphous, multilocular, cystic lesion bulging from the pelvis up to the umbilicus. The cyst was presumed to originate from the right half of the pelvis. Irregular thickening of its wall and multiple foci of echogenic, intraluminal growth suggested malignancy. Low-resistance flow was detected in the wall of the cyst. Appraisal of the uterus and left adnexal structures was not possible. Abdominal ultrasound, chest x-ray, and routine laboratory work-up (blood test and urinalysis) were normal, but a marked elevation of Ca-125 level (241 IU/ml) was found.

Surgical exploration was performed through lower median access. A large tumor (220x180x180 mm) of the right ovary was removed along with the contralateral ovary (45x40x30 mm and exhibiting exophytic growth) and the uterus of normal size. The greater proportion of the omentum was also excised in view of the presumably malignant process. No signs of peritoneal dissemination were visible in the abdominal cavity (on serosal surfaces of the gut and omentum) and no metastases were palpable in the liver.

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Tumor cells could not be identified by cytology in the lavage fluid used for rinsing the abdominal cavity.

Postsurgical treatment comprised six sessions of combined cytotoxic chemotherapy (30 mg bleomycin, 50 mg adriablastin and 25 mg cisplatin) administered at 4-week intervals. The patient was symptom-free during this period and no changes have been ascertained in her gynecologic status compared to postoperative (negative) findings. Follow-up ultrasound did not delineate abnormalities above the uterine stump; Ca-125 level decreased to 47 IU/ml.

After her discharge from hospital, the patient has not returned for the scheduled follow-up visits. Three months after the last chemotherapy session, she was readmitted with hyperpyrexia (body temperature >39 C) and blood-tinged, foul-smelling vaginal discharge. The source of the latter was a fragile-putrid tumor mass, filling the vaginal fornix. The properties of the discharge suggested a recto-vaginal fistula. The tentative diagnosis of local recurrence was confirmed by ultrasound, which showed a 74x72-mm mass of inconsistent echogenic pattern above the uterine stump. The patient was discharged home after a week on palliative treatment, which had improved her general condition. Four weeks later, emergency readmission was necessary for suspected ileus, marked enlargement of abdominal circumference, vomiting, and foul-smelling vaginal discharge. The decrepit patient died after 6 days of supportive therapy (fluid- and protein-replacement, vitamins, parenteral nutrition). The following diagnoses were established by autopsy: cachexia, metastasizing malignancy of the ovarium, retroperitoneal lymph node metastases, fatty degeneration of the myocardium, pulmonary edema, and left ventricular failure. Neoplastic growth that filled the pelvis and infiltrated paraaortic lypmh nodes and the rectum was identified by histology as malignant mixed mesodermal tumor.

Histological findings

The tumor of the right ovary (19x13x9 cm) has the appearance of a multilocular sac, filled with yellowish, serous fluid. Firm, grayish-white growths of 1 to 3 cm in diameter are visible on the inner surface of the sac. Light microscopy of hematoxyline-eosine stained specimens reveals cystic, neoplastic proliferation with solid glandular regions. The tumor consists of moderately polymorphic cells resembling cuboidal epithelium. The cytoplasm of tumor cells is of medium width and of eosinophilic hue. The nuclei are rotund to oval, asymmetrical in shape and contain irregular chromatin. Hyperchromic nuclei and dividing cells are visible in relatively great numbers. Mucus production cannot be demonstrated by PAS-staining. Accordingly, the histological diagnosis was poorly differentiated serous cystadenocarcinoma *(Figures 1, 2)*.

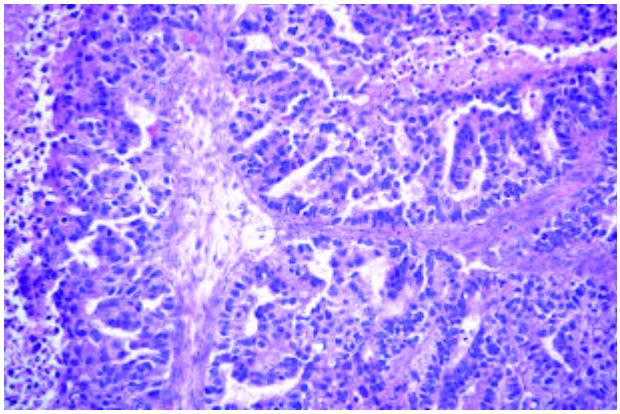

Figure 1. *Papillary serous carcinoma of the right ovarium. Papillary structures are covered by polymorphic cuboidal tumor cells. Necrosis is present. HE, 200x*

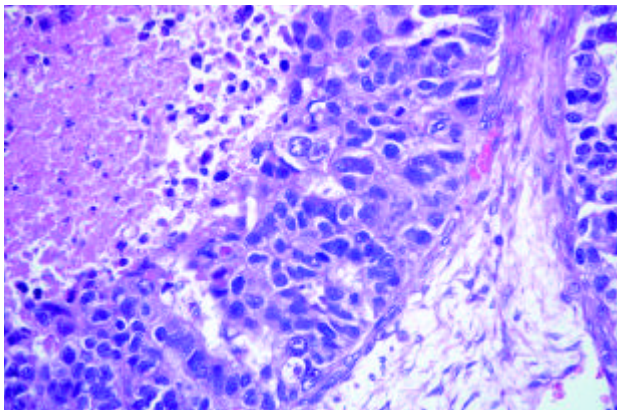

Figure 2. *Higher magnification of the papillary serous carcinoma, aborted slit like glandular structures are present within the tumor. HE, 400x*

The tumor of the left ovary (5.5x3x1.5 cm) contained a small focus of normal ovarian tissue. The microscopic appearance of the lesion is markedly dissimilar to the contralateral one. The histologic picture is extremely variegated and is characterized by the simultaneous presence of malignant epithelial and mesenchymal structures. The stroma is cellular and fibrous; cells are small with rotund or elongated (spindle-shaped) hyperchromic nuclei. Proliferating cells are seen in abundant numbers. Sporadic loosening and myxomatous degeneration of the stroma is visible with elongated (stelliform or triangular) mesenchymal tumor cells. Other regions contain islets of malignant chondrocytes, resembling immature hyaline cartilage. The epithelial component comprises glands of highly diverse shape and width. The glands are constituted by tumor cells resembling cuboidal or cylindrical epithelium and having hyperchromic nuclei of irregular shape. Based on these features the histological diagnosis was heterologous malignant mixed mesodermal tumor *(Figures 3, 4)*.

The uterus was of normal size and without abnormality; the resected part of the omentum was also free of neoplastic involvement.

Immunhistochemical studies were performed on both tumors in order to identify their origin. Antibodies against cytokeratine, S-100 protein, neuron-specific enolase (NSE), vimentin, desmin, smooth muscle actin, neurofilament, glial filament, and chromogranin were used for this purpose. Tumor cells constituting the serous cystadenocarcinoma exhibited intense cytokeratine positivity, whereas non-malignant stromal cells present in minor proportions were vimentin positive – all other histochemical reactions were negative. The epithelial component of the contralateral tumor was similarly characterized by marked cytokeratine positivity; the epithelium of several narrow glands reacted with antibodies against S-100 protein. Stromal cells were positive for vimentin, desmin and smooth muscle actin. Small clusters of cytokeratine positivity were also ascertained with occasional reaction to antibodies against NSE and S-100 protein. Cartilaginous islets gave a strong immunhistochemical reaction with antibodies against S-100 protein. No reactions were observed with antibodies against neurofilaments, glial components, or chromogranin.

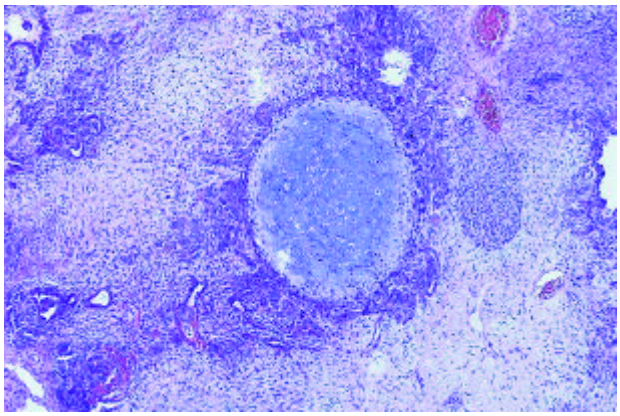

Figure 3. *Matured and immatured tissue components are present within the left ovarium. In the center there is a small nodule of hyaline cartilage surrounded by epithelial and connective tissue. HE, 100x*

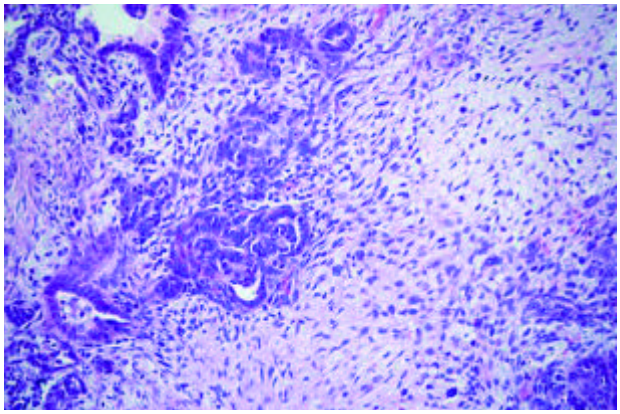

Figure 4. *Malignant epithelial component within immature myxoid connoctive tissue. HE, 200x*

Discussion

Malignant serous tumors are common neoplasms, contributing 40 to 50 per cent of all ovarian malignancies and usually occurring in the age group between 45 and 65 years. This tumor originates from the superficial germinal epithelium and can grow to a highly variable size (from microscopic to that a man's head). Typically, it is cystic, multilocular and filled with watery, serous or occasionally blood-tinged fluid. Its outer surface is smooth, whereas the inner may exhibit papillary growth. In well-differentiated tumors, microscopy reveals papillary structures with an axis of immature mesenchymal connective tissue – the latter bearing slightly polymporphic, cuboidal tumor cells. Small, calcified deposits ('psammoma bodies') are extremely common in these tumors. The papillary character is inversely related to the extent of dedifferentiation, which is associated with increasing irregularity and polymorphism of tumor cells. Eventually, when the papillary pattern has been lost, tumor cells are seen crammed together in clusters or bundles, with occasional appearance of glandular structures. The prognosis of the tumor is dependent on the level of differentiation and clinical stage.

Malignant mesodermal tumors are extremely uncommon lesions (less than 1 per cent of ovarian malignancies). Although this type of lesion has been described in the young,[1] it is almost exclusively seen in postmenopausal women – the mean age of patients is 64.5 years.[2,3,4,5] This neoplasm is thought to originate from the rudiment of the Mullerian duct. It is also known as carcinosarcoma, because it is jointly constituted by malignant epithelial and mesenchymal components. The latter can be homologous or heterologus, depending on the presence or absence of a similar tissue (e.g. smooth muscle, connective tissue, etc.) within the ovary. Heterologous elements most commonly comprise bone, cartilage, striated muscle, or adipose tissue. Epithelial components may include serous, mucinous, endometrial or epithelial elements – usually seen as glandular structures. The stroma is often a chaotic medley of epithelial and mesenchymal cells, with a hypercellular sarcomatous component. The cells have small, round or spindle-shaped nuclei (with a great proportion of hypercromic forms) and exhibit extensive mitosis. Chondrosarcoma is the most common heterologous sarcomatous component. Immunohistochemical work-up reveals EMA and cytokeratine positivity of epithelial elements and occasionally, a proportion of stromal cells. Sarcomatous regions are positive also to vimentin and focal positivity to myoglobin, S-100, NSE, actin, and desmin can

occur. Similar to this case, the positive reaction of epithelial components to antibodies against S-100 protein has already been described earlier.

The occurrence of a malignant mixed mesodermal tumor in the ovary implies an ominous prognosis for the patient. Treatment consists of surgical extirpation (or palliative resection to reduce tumor mass) followed by cytotoxic chemotherapy and – depending on the stage of the tumor – pelvic irradiation.[5] Unfortunately, survival only seldom exceeds 2 years despite complex antitumor therapy.[6] In our case the patient was 62 years old and her survival was 13 months. Preoperative recognition is difficult owing to the lack of clinical manifestations. MRI is the most suitable imaging modality for this purpose, although it is indispensable only for the appraisal of chemotherapeutic efficacy. When performed on this indication, however, it proves extremely reliable and thereby supersedes second-look laparotomy.[7]

The simultaneous occurrence of malignant mixed mesodermal tumor with other neoplasms is unusual. Only sporadic reports have been published on the joint occurrence of its primary endometrial occurrence with ovarian adenocarcinoma[8] or ipsilateral benign ovarian teratoma.[9]

Conclusion

Our case is remarkable for the presence of two distinct types of malignancy in the ovaries of the same patient. One of these neoplasms, malignant mixed mesodermal tumor is extremely uncommon and no reports on its simultaneous occurrence with another ovarian tumor of different origin can be identified in the literature.

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