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Case report of large malignant pericardial effusion in a post-surgical setting of endometrial mixed carcinoma: A description of unique cytological, histological, and immunohistochemical findings

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Abstract

Appearance of endometrial carcinoma in pericardial effusion is extremely rare. Its major etiological factors include lung cancer, breast cancer, lymphoma, and leukemia. We herein report a case of a large malignant pericardial effusion 7 years after surgery for endometrial carcinoma. A 66-year-old woman who underwent modified radical hysterectomy, bilateral salpingo-oophorectomy, and lymph node dissection for endometrial carcinoma 7 years ago and who had self-interrupted subsequent chemotherapy was presented with vertigo and vomiting. Chest computed tomography revealed pericardial effusion. Cytological examination diagnosed it as adenocarcinoma with psammoma bodies and mitoses. Immunohistochemistry analysis revealed that adenocarcinoma cells were positive for p53, p16, and insulin-like growth factor II mRNA-binding protein-3, but negative for estrogen receptor. Adenocarcinoma cells in pericardial effusion were morphologically and immunohistochemically similar to the serous carcinoma component of the surgical specimen. The appearance of psammoma bodies in cytological examination triggered the diagnosis.

Keywords

Mixed carcinoma, pericardial effusion, cytology, endometrium, psammoma body

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Background

Malignant disease of the pericardium, either primary or metastatic, is known to be the cause of pericardiac effusion.[1,2] The major etiological factors of malignant pericardial effusion include lung cancer, breast cancer, lymphoma, and leukemia, whereas cardiac metastasis from gynecological malignancies is known to be extremely rare. As far as the authors are aware, endometrial mixed carcinoma has never been reported to cause malignant pericardial effusion. Following a diagnosis of endometrioid carcinoma in one of our patients, endometrial cancer surgery was performed. However, 7 years later, a large pericardial effusion occurred, and surgical specimens were reexamined due to detection of serous adenocarcinoma components following cytological examination of the pericardial effusion. This report presents this partial mixed serous adenocarcinoma case.

Case

A 66-year-old woman who underwent modified radical hysterectomy, bilateral salpingo-oophorectomy and lymph node dissection for endometrial carcinoma 7 years ago, and who had self-interrupted subsequent chemotherapy (docetaxel and carboplatin for four courses) was presented with vertigo

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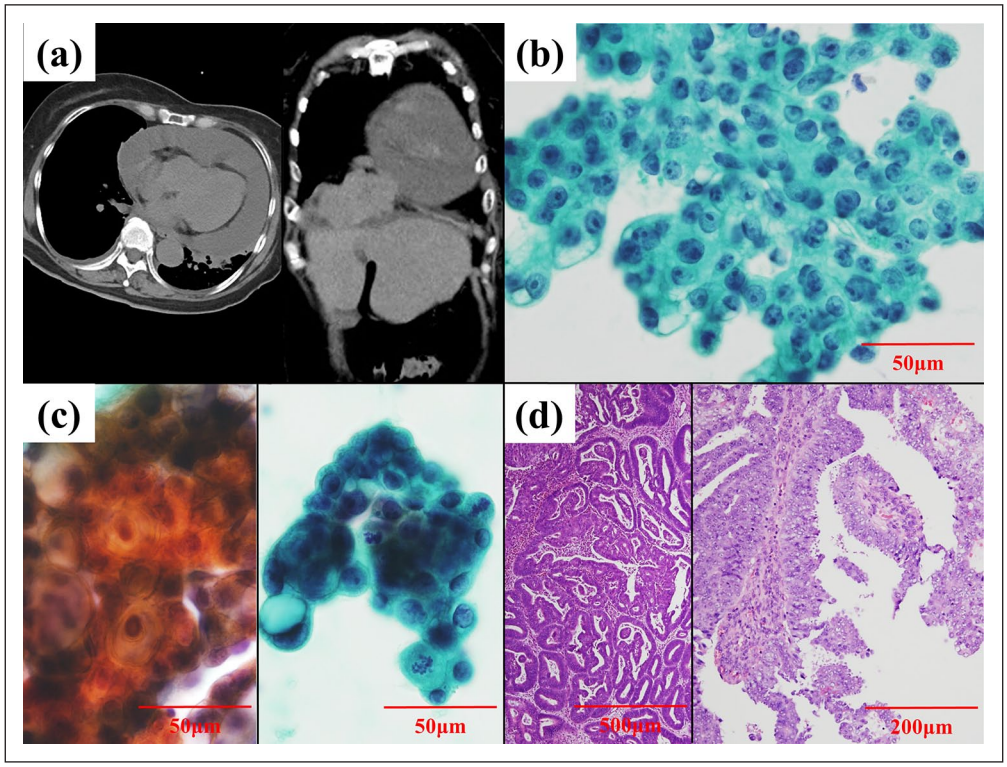

Figure 1. Computed tomography, cytological findings of the pericardial effusion, and histological findings of the surgical specimen of endometrium. (a) Computed tomography on admission showed pericardial effusion (left) and a mass measuring 8 cm in size from the pericardium to the liver surface (right). (b) Cytological examination of the pericardial effusion showed the presence of atypical glandular cells with foamy cytoplasm, enlarged nuclei, fine chromatin, and distinct nucleoli (Papanicolaou staining; original magnification, 400×). (c) Psammoma body (left) and mitosis (right) were partly observed in the cytological examination of the pericardial effusion (Papanicolaou staining; original magnification, 400×). (d) The surgical specimen of endometrial carcinoma dissected 7 years earlier had been diagnosed as moderately differentiated endometrioid adenocarcinoma (G2 > G1, pT3pN1cMX, pStageIIIC) (left) (HE staining; original magnification, 40×). On retrospective evaluation of this specimen, a partly included papillary serous carcinoma-like component was identified (right) (HE staining; original magnification, 100×).

and vomiting. At the time the patient was consulted, her consciousness was clear, temperature was 37.2°C, respiratory rate was 24 breaths per min, heart rate was 101 bpm, blood pressure was 114/82 mm Hg, and oxygen saturation was 94% on room air. Echocardiography showed a large accumulation of pericardial effusion, but cardiac wall motion was maintained. Chest computed tomography revealed a large pericardial effusion (Figure 1(a), left) and a mass measuring 8 cm in size from the pericardium to the liver surface (Figure 1(a), right).

Accordingly, pericardiocentesis was performed for treatment. As metastasis of endometrial carcinoma was suspected, we performed cytological examination of the pericardial effusion. Results revealed the presence of many three-dimensional papillary and solid clusters of atypical glandular cells in a background of erythrocytes. Atypical glandular cells were observed to exhibit a foamy cytoplasm, enlarged nuclei, fine chromatin, and distinct nucleoli (Figure 1(b)). Psammoma bodies (Figure 1(c), left) and mitoses (Figure 1(c), right) were also partly observed.

Immunohistochemistry of a cell block of the pericardial effusion showed that adenocarcinoma cells were positive for tumor protein p53 (p53), cyclin-dependent kinase inhibitor 2A (CDKN2A, also known as p16), and insulin-like growth factor II mRNA-binding protein-3 (IMP-3), but negative for estrogen receptor (ER; Figure 2, top line). A surgical specimen from the endometrial carcinoma dissected 7 years earlier had been diagnosed as moderately differentiated endometrioid adenocarcinoma (G2 > G1, pT3pN1cMX, pStageIIIC; Figure 1(d), left). A retrospective evaluation of this surgical specimen showed the partial coexistence of papillary serous carcinoma-like components (Figure 1(d), right). Immunohistochemical staining of the surgical specimen showed that the serous carcinoma-like components were positive for p53 and IMP-3 and partially positive for p16, but negative for ER (Figure 2, middle line). In contrast, the endometrioid carcinoma components were observed to be positive for ER, but negative for p53, p16, and IMP-3 (Figure 2, bottom line). Hence, the endometrial serous carcinoma components were considered to be the origin of the malignant

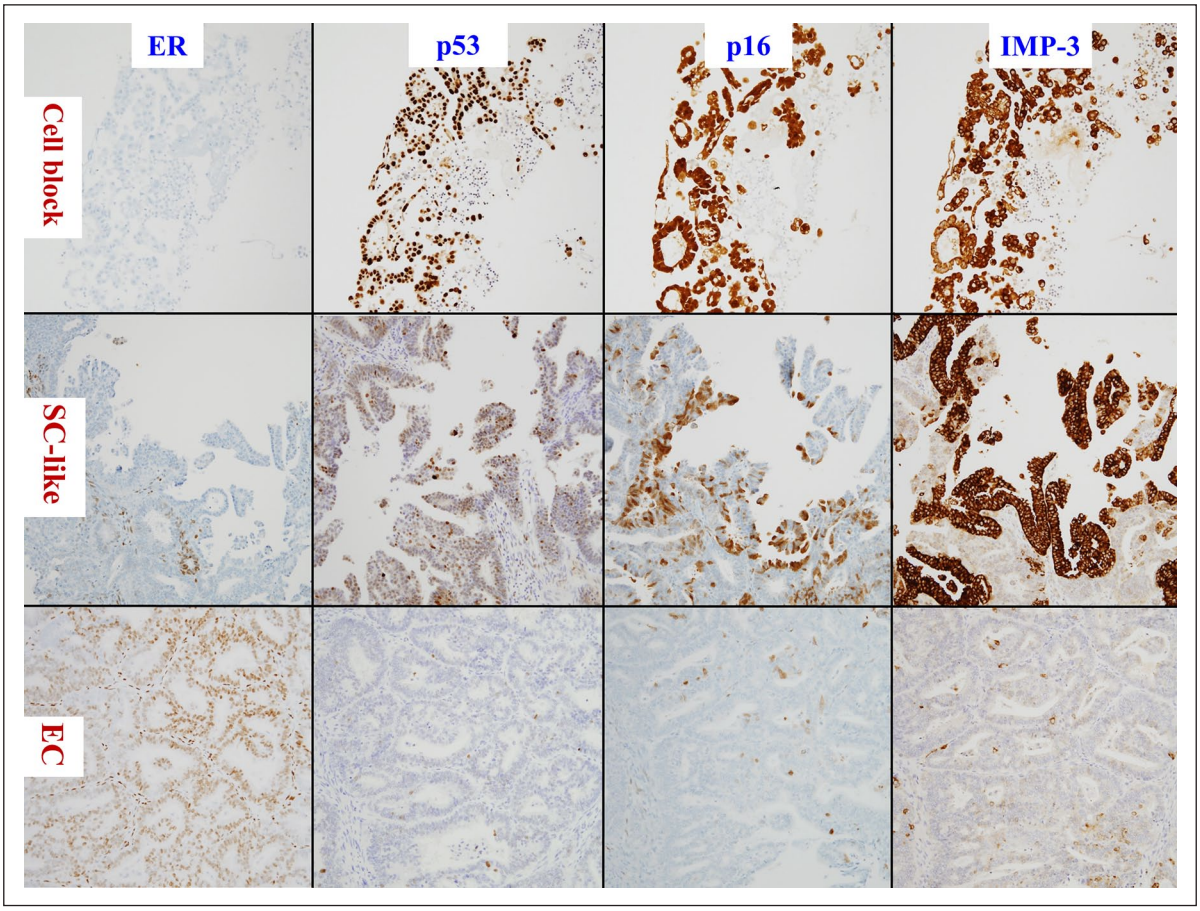

Figure 2. Immunohistochemical staining of a cell block of the pericardial effusion (top line), serous carcinoma (SC)-like components (middle line), and endometrioid carcinoma (EC) components (bottom line) of the surgical specimen dissected 7 years earlier. Staining of the cell block of the pericardial effusion revealed that adenocarcinoma cells were positive for p53, p16, and IMP-3, but negative for ER. The SC-like components were positive for p53 and IMP-3 and partially positive for p16, but negative for ER. In contrast, the endometrioid carcinoma components were positive for ER but negative for p53, p16, and IMP-3.

pericardial effusion. After relapse was confirmed through cytodiagnosis, a single dose of 500 mg carboplatin and 260 mg paclitaxel was administered to the patient. However, 20 days after administration, the patient suffered decreased blood pressure, labored breathing, and pleural fluid accumulation. The overall condition of the patient gradually worsened thereafter, and she passed away 30 days after administration. Clinically, the cause of death was considered to be carcinomatous pericarditis, but no autopsy was performed following the wishes of the family.

Discussion

Teresa has reported that lung, breast, and hematologic cancers account for 38%, 23%, and 18% of cases of malignant pericardial effusion, respectively.[3] The remaining 21% of cases of effusion have been shown to be secondary to adenocarcinoma of unknown primary source, thymoma, ovarian carcinoma, mesothelioma, testicular carcinoma, osteogenic sarcoma, and gastrointestinal tract and genitourinary tract malignancies.[3] The appearance of endometrial carcinoma in pericardial effusion is known to be extremely rare.

Previous cases of malignant pericardial effusion have occurred after hysterectomy for endometrial carcinoma, such as serous carcinoma,[4–6] clear cell carcinoma,[7] poorly differentiated endometrial adenocarcinoma,[2,8] and carcinosarcoma.[9] Most of these cases showed other sites of metastasis, including the pericardium. However, there was no other recurrence, except for pericardium in a single case.[6] The long recurrence interval was a defining characteristic of that case, which was similar to our own case. To our knowledge, none of the previous case reports mentioned the reasons behind the accumulation of pericardial fluid, but we believe that the pericardial effusion in our case was due to the pericardial infiltration of the metastatic mass from the pericardium to the liver surface.

In the World Health Organization (WHO) classification of Tumors of Female Reproductive Organs, mixed carcinoma is defined as a mixed endometrial carcinoma composed of two or more different histological types of

endometrial carcinoma, at least one of which belongs to the type II category. In addition, the behavior of these tumors has been reported to correlate with the highest-grade component, and a serous component of as little as 5% in a mixed carcinoma might adversely influence the outcome.[10] According to Quddus et al.,[11] in clinicopathological examinations of stage I mixed-type carcinomas with serous carcinomas or clear cell carcinomas as a minor component, survival time was observed to be shorter for patients with mixed-type carcinoma than for those with pure endometrioid carcinoma. In the research of Li et al.[12] as well, when mixed-type endometrioid carcinoma contained serous components, prognosis was found to be significantly worse. As such, the presence or absence of serous carcinoma has been considered as an important factor in predicting prognosis. Li et al.[12] divided relapse cases into groups based on whether the relapse occurred in the pelvic cavity or distant sites and investigated the incidence of pure endometrioid carcinoma, serous carcinoma, and mixed-type carcinoma, but there was no significant difference observed in the observed frequency of the relapse site based on tissue type.

In our case, most of the tumors were endometrioid carcinoma, but cytological examination of the pericardial effusion with immunohistochemistry revealed the presence of serous carcinoma components. A retrospective evaluation of the surgical specimen revealed partial serous carcinoma-like components, which were considered to have metastasized to the pericardium. Under the current definition, our case might be considered as a case of mixed carcinoma. Of note, the cytological examination in our patient led to the diagnosis of endometrial mixed carcinoma. If serous carcinoma components had been discovered upon closer examination at a point in time in the past when diagnostics on samples from primary endometrial cancer surgery were being conducted, this would have enabled a more accurate prognosis of the main tumor to be expressed to the patient. Accordingly, this might have prevented the patient from deciding to terminate her treatment from the perspective of poor prognosis. Therefore, it is made apparent that if there are suspicions of serous components within an endometrioid carcinoma, additional immunohistochemical examinations should be performed.

In the present patient, adenocarcinoma cells were observed to appear with psammoma bodies in the pericardial effusion. Although papillary thyroid carcinoma is a differential diagnosis for a malignant tumor with psammoma bodies, this entity was excluded based on clinical information and cytomorphology. Adenocarcinoma cells in the pericardial effusion were shown to be morphologically and immunohistochemically similar to the serous carcinoma-like components of the surgical specimen. These results supported the notion that serous carcinoma-like components could appear in pericardial effusion.

Conclusion

We encountered a case in which cytological examination of pericardial effusion led to the diagnosis of endometrial mixed carcinoma. The appearance of psammoma bodies triggered the diagnosis. The detailed examination of the mixed carcinoma components that defined the prognosis was considered important.

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Author contributions

S.M., A.S., and Su.Y. participated in the conception of the idea and writing of the manuscript. S.M., A.S., T.S., Su.Y., K.M., N.K., and So.Y. performed the clinical investigation and pathological/immunohistochemical examination. All authors have read and approved the final manuscript.

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

Consent for publication

Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

Availability of data and materials

The data set supporting the findings and conclusions of this case report is included within the article.

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