

Case Report

Ovarian malignant mesothelioma with endometrial cyst: a case report and review of literature

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Abstract: Ovarian malignant mesotheliomas are very uncommon and special tumor that occur in women and not associated with asbestos exposure. The preoperative diagnosis is not easy to attain and the outcome after treatment of this disease is uncertain. Here, we report a highly unusual case of malignant ovarian mesothelioma and review the relevant literatures on it. A 39-year-old Chinese woman presented to a local hospital with pelvic pain. Ultrasonography revealed a right adnexal mass which was suspected as endometriotic cyst. The right salpingectomy and multiple biopsies of right ovary were performed via laparoscopy. The final pathologic diagnosis of ovarian malignant mesothelioma with endometrial cyst, epithelia type was made through histologic and immunohistochemical examination. Endometriosis may be the causative factor. To the best of our knowledge, there is no previous case reported before. In order to better define the features of such rare disease and avoid missed diagnosis, we should collect more cases of ovarian malignant mesothelioma and do longer follow-up of the patients.

Keywords: Ovarian malignant mesothelioma, endometrial cyst, immunohistochemistry

Introduction

Malignant Mesotheliomas (MMs) are highly aggressive primary neoplasm of the serosal lining of the pleura, peritoneum, pericardium or tunica vaginalis. It's annual incidence in the United States of approximately 2500 cases per year [1]. As we know, histologic features of mesothelioma cells are sub-divided into epithelial, sarcomatoid, and biphasic tumors. Many of MMS are correlated with asbestos exposure, but ovarian malignant mesotheliomas (OMMs) are not involved. OMMS is a distinctly rare tumor and is poorly described and the knowledge of its natural history is very limited. There are few evidences and statistics about this tumor so that we barely know their clinical features including morbidity, age and prognosis. Preoperative or intraoperative diagnosis has been shown to be difficult, especially the differential diagnosis of primary ovarian epithelial cancer, metastasis from stomach and malignant peritoneum cancer. It is hard to treat this disease appropriately because of its rarity. In this report, we presented a case of OMMS that happened to be found in gynecological opera-

tion. We hope that this information assists doctors in recognizing the diagnosis and treatment of this disease.

Case presentation

Clinical history

A 39-year-old Chinese woman was referred to a local hospital with lower intermittent abdominal pain for a month. She had irregular menstruation for more than one year, and no known asbestos exposure. Clinical examination revealed a right adnexal mass. Other systemic examinations were within normal limits. On examination, her vital signs and CA 125 and carcinoembryonic antigen tumor serum markers were within normal ranges other than CA 199, which was 35.2 $\mu\text{mol/L}$. Urine analysis, chest and abdominal radiographs did not reveal any abnormalities. Transvaginal ultrasonography showed a 41 \times 24 \times 16 cm cyst with no definite solid component. Magnetic resonance imaging (MRI) demonstrated an endometriosis cyst (31 \times 26 \times 24 mm) and the presence of ascites in the lower pelvic. A laparoscopy was

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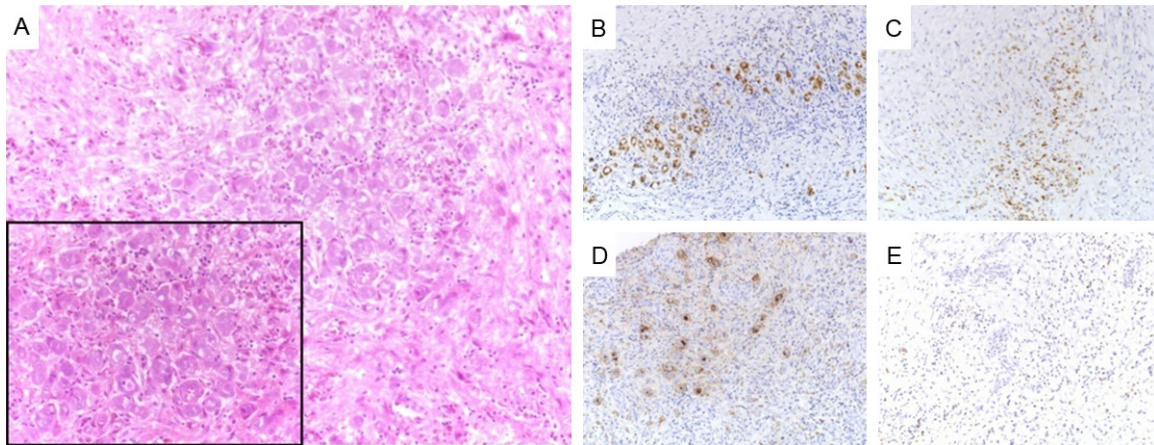


Figure 1. (A) Hematoxylin and eosin staining of the patient's sample: Epithelia type of Ovarian malignant mesothelioma: Adenomatoid tumors were composed of epithelioid cells that form vacuoles and small tubules, which separated by fibrous stroma; (B-E) Immunohistochemical analysis documented positive expression of calretinin (B), CK5/6 (C), MC (D), while expressions of CEA was negative (E) (A-E. magnification $\times 200$, A $\times 400$ (inlet)).

performed with a pre-surgical diagnosis of endometriosis cyst. At laparoscopy, a blue cyst measuring 4×5 cm was found on the surface of her right ovary, containing bloody fluid. In her pelvis we can see the encapsulated bloody effusion, which was adhered to omentum and the right fallopian tube was suppurative. The left ovary and the uterus were found to be normal. Subsequently the cyst and encapsulated effusion was completely removed, right salpingectomy and multiple biopsies were performed. There are no nodules on the liver, peritoneum, and other abdominal sites on gross inspection in surgery.

Pathological findings and immunohistochemistry

Gross examination revealed that the biopsies specimens sent to our department was a small pile of gray and white tissues, consist of wall of the cyst, ovarian tissue fragments, the right fallopian tube and several pieces of pelvic wall. The samples were paraffin-embedded and 2- μ m thick slides were stained with H&E. Microscopically, the proliferation of fibrous tissue formed cyst wall structure, and local area visible tumor cells arranged loosely. Adenomatoid tumors were composed of epithelioid cells that form vacuoles and small tubules, which separated by fibrous stroma. A few of them secrete mucus. The tumor cells contained abundant eosinophilic cytoplasm, hyperchromatic, bizarre nuclei with prominent nucleoli, mitoses and necrosis were infrequent (**Figure**

1A). Unlike ovarian tissues, we just only found increased inflammatory cell and fibrous tissue in the right fallopian tube and pelvic wall samples. Histological examination revealed the cyst was endometriotic cyst, but ovarian tumor was suspected as malignant tumor. The diagnosis was still not clear at this point, so we decided to do Immunohistochemical examination. In this case, immunohistochemical analysis documented positive expression of Calretinin, MC, CK, CK5/6, Vimentin and WT1, while expressions of CEA, P53, ER, and PR were negative. Although IHC can help in identifying mesothelial cells, none are specific for mesothelioma. calretinin, CK5/6, MC and WT-1 are used collectively for mesothelioma (**Figure 1B-E**). The final diagnosis was Ovarian malignant mesothelioma, epithelia type. The histological pattern was predominantly tubular with mesothelial cells.

Although the patient had no complications and metastasis, the malignancy of this tumor was conformed. So we advised her to have further surgical therapy, but she refused and was discharged in good condition on postoperative day 5, after that, unfortunately, we lost contact with her.

Discussion

Since ovarian malignant mesothelioma (OMM) is seldom observed, the histological diagnosis can often be challenging. Because of its rarity, preoperative diagnosis is difficult, pathogene-

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sis and prognosis are uncertain. MMS was not asbestos related, which is different from peritoneal and pleural MMS. A history of asbestos exposure should not be taken into consideration by the pathologist when diagnosing MMS [6]. So, may be other elements such as chronic inflammation, radiation, organic chemicals, can be causative factors. From this, we deduce the pathogenesis of this tumor may be chronic inflammation led by endometriosis. It was so rare that there were few case reports of patients with malignant mesothelioma in which the initial manifestation was that of an ovarian mass. In their study Clement et al. have reported 9 cases of malignant mesothelioma presenting as ovarian mass with 2 patients having a primary ovarian mass [2]. Mani et al. have described 7 cases of mesothelioma with a primary diagnosis of ovarian cancer [3]. The first case of apparent primary ovarian mesothelioma in the literature according to the author was that reported by Addis and Fox in 1983 of a 67-year-old woman who was found to have a left ovarian tumor at cholecystectomy [5]. As it has been previously described, tumor sizes range from 3 to 15 cm in maximum diameter. Most of them often locate on the ovarian surfaces. The main clinical presentations are chronic or intermittent abdominal or pelvic pain, irregular menstruation or an abdominal or pelvic mass found clinically or radiologically. But in our case, there were no other conspicuous masses except an endometriosis cyst which was confirmed by pathological examination. The patient in our case just only had pelvic pain and irregular menstruation. Clinical examination was almost normal. It was a surgical finding in a patient after the operation with a clinical impression of endometriosis. Furthermore, features seen on H&E-stained sections were not specific enough to lead us to come to right conclusion quickly, for the morphology of the neoplasm is extremely variable and is a major basis for diagnosis dilemma [6]. According to the microscopical presentation of the HE staining, as we found some small tubules and spindle cells, a series of neoplasms must be considered, including, ovarian serous adenocarcinoma, metastasis from gastric or breast cancer, ovarian stromal tumor and so on. In contrast to ovarian MMS, serous adenocarcinoma is often exclusively or predominantly cystic, and cells are not similar to mesothelial cells. Besides, bizarre giant cells, much higher

mitotic rates and numerous psammoma bodies are more frequently seen in serous tumors. Another differential diagnosis is metastasis from gastric or breast cancer such as Krukenberg tumor, of which pathological feature is characterized by the presence of signet ring cells, which are rare in MMS and we cannot find such cells in this tumor. In spite of these differences, these morphologic features are not specific enough and cannot strictly distinguish malignant mesothelioma from primary ovarian or other serous carcinoma. Hence, the definite diagnosis must be established by auxiliary tests, in which immunohistochemistry plays the pivotal role, and is absolutely necessary in the differential diagnosis. In this case, the tumors are immunoreactive for Calretinin, MC, CK, CK5/6, Vimentin and WT1, which are markers for mesothelial cells, is always noted, whereas immunostains for CEA, P53, ER, PR, a-inhibition were negative. Among these markers, CEA is a negative marker for mesothelioma that is commonly expressed in adenocarcinomas. ER and PR positivity most probably indicates a serious carcinoma rather than a mesothelioma, there were no positivity of ER and PR revealed in this case. A-inhibition is often positive in ovarian stromal tumor such as ovarian sex cord, but was negative in this case. These immunophenotypings usually exclude adenocarcinoma and confirm the mesothelial lineage of the neoplasm [7]. Meanwhile, the diagnosis of a primary peritoneal serous adenocarcinoma and diffuse malignant peritoneal mesothelioma also can be excluded for no obvious solid nodules. In the present case, an initial incorrect diagnosis of endometriosis was made, but ultimately was corrected by histologic and immunohistochemical examination. It was a malignant mesothelioma of ovary with an endometriosis cyst. The conventional treatment of this tumor is usually by surgical excision through laparotomy or laparoscopy. In addition to mainly surgical therapy, multiple courses of adjuvant chemotherapy are also recommended if it is necessary [8, 9]. Due to its rarity, we lack of experience for management of this disease and the therapeutic effect of this tumor is not quite sure.

Conclusion

In conclusion, OMMS is a very rare malignancy occurring in the abdomen. Our case report

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highlights the rarity and easily misdiagnosed nature of this neoplasm. As chronic inflammation could lead to MMS, endometriosis may be the most likely factor that causes OMMS in this case. Definitely, the histologic diagnosis is based not only on the appropriate morphology but also on the appropriate immunohistochemistry. Surgery is still the most important method for the patients currently as only the tumor is at its early stage. Follow-up studies after surgery are always needed to further define the etiology of this neoplasm and discover recurrence or any other metastatic lesions which can occur several months or years after the initial diagnosis and treatment. More case series are needed in order to reveal this unknown etiology and it could be beneficial for clinicians treating these patients well.

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Disclosure of conflict of interest

None.

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