Case Report

Huge Peritoneal Malignant Mesothelioma Mimicking Primary Ovarian Carcinoma

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Peritoneal malignant mesothelioma (PMM) is less commonly found in female than male. The most important differential diagnosis of PMM in female patient is primary ovarian carcinoma because of their similar symptoms e.g. dyspepsia, abdominal discomfort from ascites, palpable abdominal mass, etc. However, common clinical presentation of PMM is diffuse spread of peritoneal lesions without dominating tumor mass while primary ovarian tumor usually presents with large pelvic mass and smaller exta-ovarian metastatic lesions. The surgeon may make a provisional intraoperative diagnosis of PMM if both ovaries are clearly identified. Unfortunately, both conditions frequently elicit fibrosis and adhesion that the exact location or the origin of tumor cannot be clearly stated. Histopathologic diagnosis of PMM is also difficult because it has three patterns of histopathology as biphasic tumors composed of epithelial and sarcomatous components or it may be monophasic of either type. When only the epithelial component is found, serous ovarian carcinoma is the important differential diagnosis while the biphasic mesothelioma must be differentiated from malignant mesodermal mixed tumor or carcinosarcoma of the ovary. The pathologist generally requires immunohistochemical study to achieve a correct diagnosis. The clinical feature and detailed histopathologic findings of the patient with PMM will be discussed.

Keywords: *Peritoneal malignant mesothelioma, Ovarian mass, Paclitaxel/carboplatin*

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Peritoneal malignant mesothelioma (PMM) is an uncommon tumor occurring less frequently than its pleural counterpart and is less common in female than male[1,2]. Most cases of PMM presented as diffuse peritoneal lesions, adhesion or non-discrete mass[2-5] and rarely as pelvic nodules or ovarian masses[5-7]. The authors presented an unusual case of PMM that presented as huge pelvic mass accompanying with few peritoneal lesions, mimicking primary carcinoma of the ovary. The diagnosis of PMM was not made pre- and intra-operatively by imaging study or gross findings, respectively, until a thorough microscopic examination revealed an atrophic ovary lying close to the tumor mass.

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Case Report

The patient was a 62-year-old postmenopausal woman, P1-0-0-1, who sought medical consultation for abdominal discomfort which had slowly developed for over two months. No other systemic symptoms or remarkable past medical illnesses were reported. She worked as a housewife in a northeastern agricultural area of the country with no history of asbestos exposure. The only pertinent findings from physical examination were slightly distended abdomen with moderate ascites and ill-defined pelvic mass sized approximately 18 cm in maximal dimension. The mass was rather fixed and without tenderness upon palpation. Pelvic ultrasonography confirmed unilateral right pelvic mass with heterogeneous solid and cystic echogenicity, measured 17.5x11x8 cm, along with moderate amount of ascites. Except for a slightly elevated serum CA 125 (198 mIU/ml), all other laboratory investigations were within normal limits.

An exploratory laparotomy revealed approximately 1,500 cc straw colored ascites and a

solid pelvic tumor measuring 20 cm in diameter in the right adnexal region. The mass had bosselated ventral surface with hypervascularized thin capsule, packed in the cul-de-sac and attached firmly to posterior lower uterus and outer surface of cervix. Cut surfaces of the mass showed light brown soft solid tissue in most areas with scattered foci of cystic changes and necrosis (Fig. 1A, B.). Except two discrete nodules at sigmoid mesocolon and left infundibulopelvic area (measured 1.8 cm and 0.8 cm respectively), no evidences of tumor spreading to the contralateral adnexa, pelvis or abdominal cavity were found upon thorough inspection and manual exploration. Total abdominal hysterectomy, left salpingo-oophorectomy, pelvic and para-aortic lymph node sampling, appendectomy, and resection of the two nodules were subsequently carried out for an intraoperative diagnosis of ovarian carcinoma.

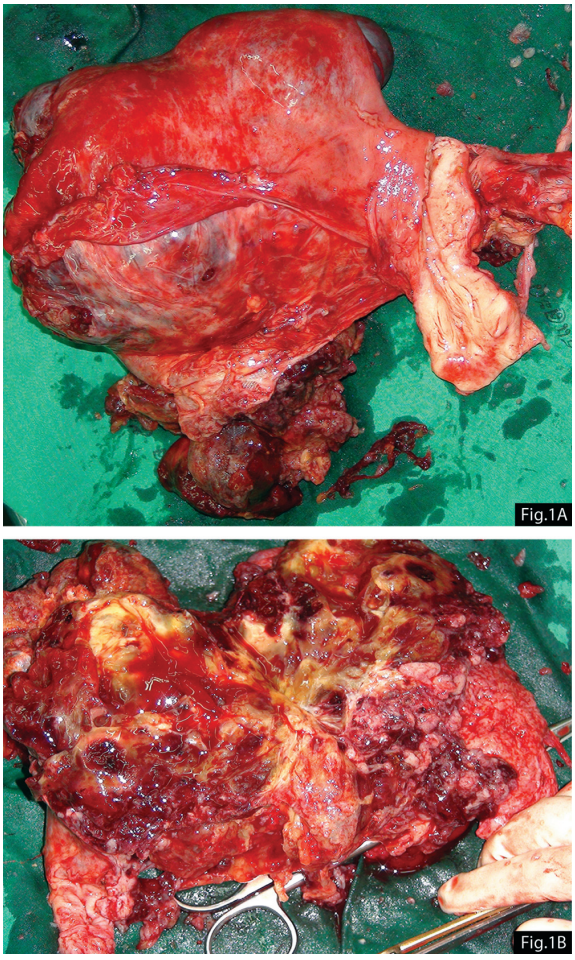

Fig. 1 Gross feature of a large peritoneal mass lying in the right adnexa area (A). The mass was ruptured upon removal. Cut surface (B) showed light brown soft solid tissue in most areas with scattered foci of cystic changes and necrosis.

Microscopically, a well-encapsulated atrophic ovary was demonstrated juxtaposed to the tumor mass without tumor invasion into the ovarian parenchyma (Fig. 2A). The pelvic tumor showed predominantly solid sheet with foci of small slit-like tubules and few fibrous papillary cores. The tumor cells in most parts had features of mesothelial cells: small to medium sized polygonal or cuboidal shape, scanty eosinophilic cytoplasm, small nuclei with mild to moderate atypia, inconspicuous nuclei, and rare mitoses (Fig. 2B). Occasional spindle cell and clusters of cells with moderate to abundant cytoplasm were noted. No lymphovascular invasion was found. Tumor nodules at sigmoid mesocolon and left infundibulopelvic area showed the same morphologic features as the large pelvic tumor. Peritoneal cytology and all other resected tissues were negative for malignancy. Immunohistochemical study was negative with MOC-31 (Dako, monoclonal mouse, MOC-31, 1:300) carcinoembryonic antigen (Dako, polyclonal rabbit, 1:20,000), estrogen receptor (Ventana, SP1, monoclonal rabbit) and inhibin (Serotech, monoclonal mouse, R1, 1:500) and was strong positive with calretinin (Fig. 2C) (DBS, monoclonal mouse, 5A5, 1:100), cytokeratin CK5/6 (Fig. 2D) (Dako, monoclonal mouse, D5/16B4, 1:300), WT1 (Fig. 2E) (Novocastra, monoclonal mouse, WT49, 1:40) and D2-40 (Dako, monoclonal mouse, D2-40, 1:200). A diagnosis of malignant mesothelioma was made.

The patient recuperated well postoperation with a return of CA 125 to normal level at two weeks postoperation. Adjuvant chemotherapy (paclitaxel and carboplatin) was given for six cycles and she was currently doing well without clinical evidence of disease 26 months after diagnosis.

Discussion

Among various clinical manifestations of PMM, the most common finding was diffuse peritoneal lesions in any forms of nodules, granules, papillae, adhesion or non-discrete mass lesions of the pelvic or abdominal viscera[5]. Having a large ovarian mass as a presenting symptom is rarely encountered. Only 18 cases from three previous reports of peritoneal mesothelioma presenting as pelvic or ovarian masses were identified[5-7]. Excluding four cases of benign multicystic mesothelioma, 14 were malignant. Only three out of 14 cases presented as small single pelvic nodule of 1 cm to 4 cm incidentally found

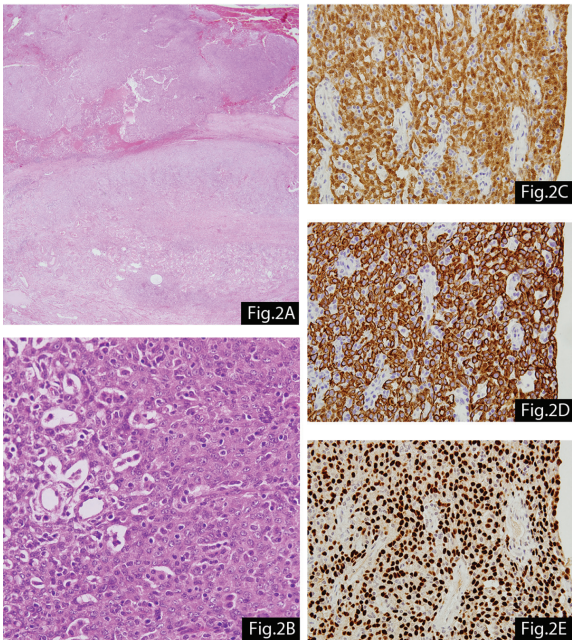

Fig. 2 (A) Histopathology revealed an ipsilateral encapsulated atrophic ovary (lower) lying juxtaposed to the tumor mass (upper) separated with a cleft-like space without tumor involvement into the ovarian parenchyma (12.5x). (B) The tumor cells arranging in solid sheet (right side) with foci of small slit-like tubules (left side) had small to medium sized polygonal or cuboidal shape, scanty eosinophilic cytoplasm, small nuclei with mild to moderate atypia, inconspicuous nuclei, and rare mitoses (400x). (C-E) Immunohistochemical study revealed strong positivity for calretinin (C, 200x), cytokeratin CK5/6 (D, 200x) and WT1 (E, 200x).

intraoperation without other peritoneal lesion[5] while the other 10 cases showed 3 cm to 15 cm cystic or solid and uni- or bilateral ovarian masses accompanied by diffuse peritoneal implants[6,7]. The last case presented as a 10-cm pelvic mass adjacent to ovary with two additional sites of lesions[5].

The patient with PMM had an unusual presentation of a huge pelvic mass, however, with limited small foci of peritoneal diseases. This clinical manifestation generally leads a surgeon and a pathologist to have a diagnosis of primary ovarian tumor. Thus, the tentative primary diagnosis was a primary ovarian carcinoma (based on gross findings) and subsequently primary ovarian malignant mesothelioma (when histopathologic and immunohistochemical study revealed its nature). From limited available data from only a few cases reported to date[6,8-10], the primary ovarian mesothelioma tended to have striking ovarian enlargement having tumor infiltrating most of the parenchyma with limited peritoneal lesions[2,6]. The present feature was different from secondary ovarian involvement by the PMM that usually have infiltration of tumors confined to the serosa or superficial cortex with more extensive extraovarian lesions[2,6]. Nevertheless, bearing in mind that primary ovarian mesothelioma is very rare, and no residual ovarian tissue was identified in the tumor mass. The pathologist performed extensive sectioning and meticulous microscopic study when an atrophic ipsilateral ovary uninvolved by the tumor was identified, leading to a final diagnosis of PMM.

Due to their rare incidences and various microscopic appearances of PMM, the differential diagnosis was extensive[6,11]. Microscopic features of PMM are those features of malignant mesothelioma wherein 75 to 85% had only epithelial component, 15 to 22% were mixed, and only 3% was purely sarcomatoid[2,3]. Sheets of epithelial or epithelial-like cells may be papillary, tubular, or solid[2-4,6,8]. In any cases wherein the epithelial component dominated, serous carcinoma was the important differential diagnosis while tumors with biphasic features of epithelial component and spindle cell sarcomatoid appearance, malignant mesodermal mixed tumor or carcinosarcoma of the ovary must be excluded. One distinct feature of serous adenocarcinoma and epithelial component of carcinosarcoma are generally of poorly differentiated carcinoma exhibiting high nuclear grade with numerous mitotic figures while that of the PMM frequently exhibits only mild or moderate degree of morphologic atypia with grade 1 or grade 2 nuclear features[2,6]. Mitotic figures were infrequent with less than four mitotic figures per high power field[2,6]. Most areas of tumor in the present case had solid sheet of polygonal or cuboidal cells with small tubular or glandular-like formation and papillary cores. Only sparse areas showed spindle cell or sarcomatous component. The bland microscopic findings of tumor cells in the present case had resemblance to mesothelial cells, with mild to moderate nuclear atypia, with inconspicuous nuclei, and occasional mitosis. These characteristics favor towards malignant mesothelioma rather than the two aggressive serous or carcinosarcoma.

Panels of special histochemical and immunohistochemical stains are generally required to differentiate PMM from other ovarian carcinoma[3,4,12]. Positive studies of cytokeratin, calretinin, WT1, and

D2-40 but negativity for MOC-31, CEA, and ER in the presented patient indicated mesothelial nature of the tumor[11-13]. Appraising all microscopic including IHC findings, a final diagnosis of peritoneal malignant mesothelioma was made.

Treatments for PMM consist of surgery to remove tumors, biologic or immunotherapy, chemotherapy, and radiation therapy. Prognosis of PMM varied from a few months to several years. Some authors proposed PMM of sarcomatous or biphasic type (compared with the papillary/epithelioid or multicystic type) was poor prognostic factors[14]. These clinico-pathologic characteristics feature should be carefully evaluated in each case to collect more data on this uncommon tumor.

In conclusion, with an unusual presentation and a wide range of microscopic morphology, careful gross and microscopic examination including immunohistochemical study should be carried out to make a correct diagnosis regarding the primary site and nature of the tumor. When the optimal chemotherapy has not yet been identified, paclitaxel and carboplatin as in epithelial ovarian cancer may be one effective regimen.

Potential conflicts of interest

None.

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มะเร็งเยื่อบุช่องท้อง (peritoneal malignant mesothelioma) ขนาดใหญ่ที่คล้ายคลึงกับมะเร็งรังไข่ปฐมภูมิ

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มะเร็งเยื่อบุช่องท้อง (peritoneal malignant mesothelioma) เป็นโรคที่พบในเพศหญิงได้น้อยกว่าเพศชาย ข้อวินิจฉัยแยกโรคที่สำคัญที่สุดของมะเร็งเยื่อบุช่องท้องในผู้ป่วยหญิง คือ มะเร็งรังไข่ปฐมภูมิ (primary ovarian carcinoma) เนื่องจากมีอาการคล้ายคลึงกัน เช่น ท้องอืด แน่นท้องจากการที่มีน้ำในช่องท้อง (ascites) หรือ คลำได้ก้อนในท้อง เป็นต้น อย่างไรก็ตาม อาการแสดงของมะเร็งเยื่อบุช่องท้องมักจะตรวจพบก้อนกระจายอยู่ทั่วไปตามเยื่อบุผิวในช่องท้อง (diffuse peritoneal spread) โดยไม่มีก้อนขนาดใหญ่เด่นชัด ในขณะที่มะเร็งรังไข่ปฐมภูมิ มักจะมีก้อนในช่องเชิงกรานขนาดใหญ่และมีก้อนมะเร็งขนาดเล็ก ๆ ที่กระจายไปนอกรังไข่ แพทย์ผู้ผ่าตัดอาจจะสามารถให้การวินิจฉัยเบื้องต้นในระหว่างผ่าตัดได้ถ้าพบมะเร็งกระจายในช่องท้องโดยที่เห็นรังไข่ปกติทั้ง 2 ข้าง อย่างไรก็ตาม ทั้ง 2 ภาวะนี้มักจะกระตุ้นก่อให้เกิดพังผืดในช่องท้องทำให้แพทย์ไม่สามารถระบุตำแหน่งหรือ ต้นกำเนิดของก้อนมะเร็งได้ชัดเจน การวินิจฉัยทางจุลพยาธิวิทยาของมะเร็งเยื่อบุช่องท้องก็เป็นเรื่องยากเนื่องจากมะเร็งเยื่อบุช่องท้องอาจมีลักษณะทางจุลพยาธิสภาพได้ 3 แบบ คือ biphasic โดยมีทั้งส่วนที่เป็นเยื่อบุผิว (epithelial) และที่เป็นเนื้อเยื่อเกี่ยวพัน (sarcomatous) หรือ อาจพบเพียงลักษณะใดเพียงลักษณะหนึ่ง (monophasic) ในกรณีที่พบแต่ส่วนที่เป็นเยื่อบุผิว การวินิจฉัยแยกโรคที่สำคัญ คือ มะเร็งรังไข่ชนิด serous carcinoma ในขณะที่ถ้าพบมะเร็งแบบ biphasic การวินิจฉัยแยกโรคที่สำคัญ คือ malignant mixed mesodermal tumor หรือ carcinosarcoma โดยทั่วไป พยาธิแพทย์มักจะใช้การย้อมอิมมูนโนเคมิสทรีเพื่อช่วยให้สามารถให้การวินิจฉัยได้ถูกต้อง รายงานนี้จะนำเสนออาการทางคลินิกของผู้ป่วยรวมทั้งสิ่งตรวจพบทางพยาธิสภาพต่าง ๆ ของมะเร็งเยื่อบุช่องท้อง