SPANDIDOS PUBLICATIONS

MOLECULAR AND CLINICAL ONCOLOGY 9: 211-214, 2018

Primary ovarian signet ring cell carcinoma: A rare case report

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Received April 18, 2018; Accepted June 12, 2018

DOI: 10.3892/mco.2018.1653

Abstract. Signet ring cell carcinoma (SRCC) of the ovary is most commonly metastatic from a primary lesion. Primary ovarian SRCC is rare, and the distinction between primary and metastatic SRCC of the ovary may be difficult. We herein present a case of primary SRCC of the ovary in a 54-year-old woman presenting with a right ovarian mass sized 20.5x16.5x11.5 cm. Total abdominal hysterectomy with bilateral salpingo-oophorectomy, partial omentectomy and incidental appendectomy were performed. Upon histological examination, mucinous carcinoma composed predominantly of signet ring cells was observed in the right ovary. The results of immunohistochemical examination included diffuse positivity for cytokeratin (CK)7 and CK20, but the tumor was negative for estrogen receptor, progesterone receptor, caudal type homeobox 2 and Wilms' tumor gene 1. A preoperative computed tomography (CT) scan of the abdomen and a postoperative positron emission tomography-CT scan did not reveal any suspicious extraovarian lesions. Based on the histological and clinicoradiological examinations, this case was diagnosed as a primary ovarian SRCC.

Introduction

Mucinous carcinomas with signet ring cells in the ovary are mostly metastatic lesions from a primary tumor. Particularly when the ovarian carcinoma is predominantly composed of signet ring cells, referred to as signet ring cell carcinoma (SRCC), it is usually designated as a Krukenberg tumor, which is metastatic SRCC that may originate from a number of anatomical sites, most commonly the stomach. Only rare cases of primary SRCC of the ovary have been reported in the literature to date (1-3). The distinction between primary and metastatic SRCC of the ovary has not been well delineated and may be challenging. We herein report the case a patient diagnosed with primary SRCC of the ovary.

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Key words: ovary, signet ring cell carcinoma, mucinous carcinoma, Krukenberg tumor

Case report

A 54-year-old woman was admitted to the Ulsan University Hospital (Ulsan, South Korea) with a palpable firm abdominal mass. The patient exhibited no major symptoms and had no specific past history. The patient underwent an abdominal computed tomography (CT) scan, which revealed a ~20-cm multiseptated cystic and solid mass arising from the right ovary. The abdominal CT scan did not reveal any lesions in the gastrointestinal tract.

The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy, partial omentectomy and incidental appendectomy. The removed right ovary exhibited a sizeable mass, measuring 20.5x16.5x11.5 cm, and had an intact and smooth external capsular surface. On sectioning, the mass contained a multiloculated cystic component filled with mucinous fluid, and eccentric solid components (Fig. 1). The right ovary (4 μm) was fixed in 10% neutral buffered formalin for 12 h at room temperature, and then at 45˚C for 44 min in an automated tissue processor. Subsequently, H& staining was performed using an automated staining system and was processed for 27 min at room temperature. The tissue was analyzed under a light microscope. The left ovary, uterus, cervix and appendix appeared to be normal on macroscopic examination. Histologically, most of the mass was composed of malignant mucinous epithelial cells arranged in predominantly solid and slightly glandular patterns. Characteristically, the tumor predominantly consisted of signet ring cells, particularly in the area of the solid nests, which were arranged in small groups or infiltrated as individual cells (Fig. 2). In some areas, the tumor was lined by benign or borderline mucinous epithelium exhibiting stratification and considerable atypia (Fig. 3). The stroma was generally fibrous and moderately cellular, and focally loose or edematous. There was no evidence of lymphovascular invasion, nodular growth pattern, extracellular mucin or tumor cells on the ovarian surface.

The tumor cells, including the signet ring cells, exhibited diffuse positivity for cytokeratin (CK)7, CK20, alcian blue and mucicarmin (Fig. 4). However, there was no expression of chromogranin, synaptophysin, CD56, caudal type homeobox 2 (CDX2), estrogen receptor, progesterone receptor, or Wilms' tumor gene 1 (not shown, apart from CD56).

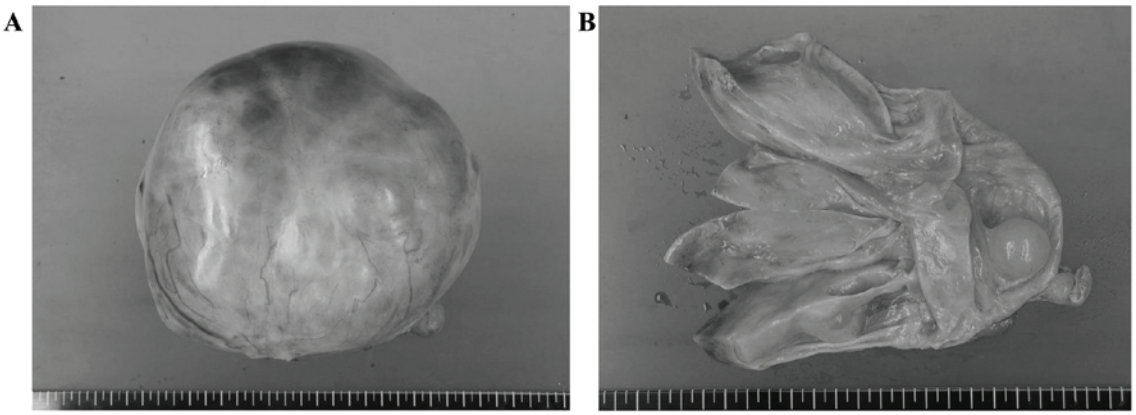

Figure 1. Macroscopic findings. The right ovarian mass exhibited (A) a smooth outer surface and (B) a multiloculated cystic and solid inner composition.

Postoperative positron emission tomography (PET-CT) revealed no residual malignancy and no alternative primary site. The cytology of the peritoneal fluid was negative for malignant cells. Based on these clinicoradiological and histopathological findings, this case was diagnosed as primary SRCC of the ovary. One year after the surgery, a follow-up CT of the abdomen also revealed no evidence of recurrence or an alternative primary site. The patient remains alive and well. These investigations helped exclude other primary foci, and the tumor was definitively diagnosed as primary ovarian SRCC.

Discussion

Primary ovarian mucinous carcinoma comprises 2-3% of ovarian epithelial neoplasms (4). The presence of signet ring cells in an ovarian mucinous carcinoma is usually highly suspicious for a metastatic neoplasm, the primary site of which is most likely in the gastrointestinal tract, referred to as Krukenberg tumor (1,5). In addition to the signet ring cells, other characteristics suggesting a secondary mucinous neoplasm include bilaterality, small size, a nodular element on macroscopic or microscopic examination, prominent histological variation among different areas, destructive invasion or individual cell stromal infiltration, microscopic surface tumor involvement (surface implantations), tumor cells floating in mucin pools, extraovarian extension and considerable lymphovascular invasion, particularly at the ovarian hilum (1,6).

Although the presence of signet ring cells is a key pathological characteristic highly favoring a metastatic rather than a primary neoplasm of the ovary, in the present case the neoplasm was considered to be a primary ovarian tumor due to the following findings: Unilaterality, large size, malignant glands in a fibrous stroma, lack of surface implantations, lack of lymphovascular invasion and no extraovarian spread. Furthermore, the tumor displayed admixed components of benign mucinous cystadenoma and borderline mucinous tumor. The absence of several other characteristics of a metastatic neoplasm and the presence of admixed benign-appearing areas support that this was a primary ovarian neoplasm. Based on these findings, the diagnosis was primary ovarian SRCC.

Immunohistochemistry may be applied as an additional method to help distinguish between primary and metastatic mucinous carcinoma of the ovary. In particular, several primary ovarian mucinous neoplasms display intestinal differentiation and express enteric markers, such as CK20, carbohydrate antigen 19-9, carcinoembryonic antigen and CDX2, at least partially, despite usually maintaining their diffuse CK7 expression (7,8). In the present case, the tumor was diffusely positive for CK20 and CK7, similar to primary ovarian mucinous carcinoma of the intestinal type (8). However, these enteric markers are also variably positive in the majority of upper and lower gastrointestinal adenocarcinomas and pancreatobiliary adenocarcinoma (7). As the immunophenotypes of a primary ovarian mucinous tumor, particularly one containing abundant signet ring cells, and a metastatic mucinous tumor from the stomach, pancreatobiliary tract, appendix, or colorectum, may overlap, immunohistochemical studies may be of limited value in confirming the primary or a metastatic nature of ovarian mucinous tumors. Therefore, the clinical history and radiological findings also have to be carefully reviewed and integrated with thorough gross inspection and histopathological findings to ensure correct diagnosis.

In the present case, diffuse CK7 and CK20 positivity and CDX2 negativity were helpful in excluding the possibility of colorectal or appendiceal primaries (1), whereas negativity for chromogranin, synaptophysin and CD56 help exclude other primary ovarian mucinous tumors that may comprise signet ring cells, such as goblet cell carcinoid.

Possible primary lesions in the female genital tract, such as the cervix, and in the appendix were excluded following total abdominal hysterectomy, bilateral salpingo-oophorectomy and incidental appendectomy and examination of the resected specimens. No other lesions in the gastrointestinal tract were identified on abdominal CT. Consequently, primary ovarian SRCC was diagnosed. The remaining point of argument in this case is that a small occult primary neoplasm in other organs, most commonly in the stomach or appendix, may have been missed. However, postoperative PET-CT and follow-up CT 1 year after surgery showed no residual malignancy or alternative primary site. Taking into consideration the histopathological findings, these radiological evaluations support the exclusion of another primary focus, and the tumor was definitively confirmed as a primary ovarian neoplasm.

In conclusion, we herein described a rare case of primary ovarian SRCC. The distinction between primary and metastatic

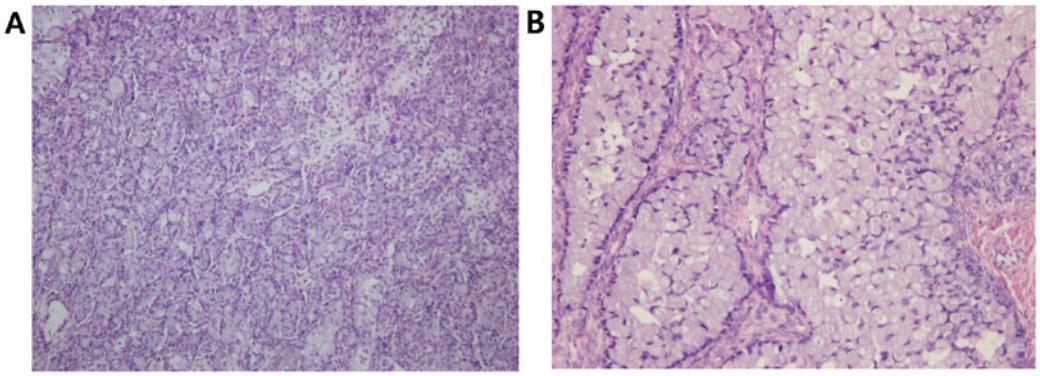

Figure 2. The tumor predominantly consisted of signet ring cells, particularly in the area of solid nests [hematoxylin and eosin staining; magnification, (A) x100 and (B) x200].

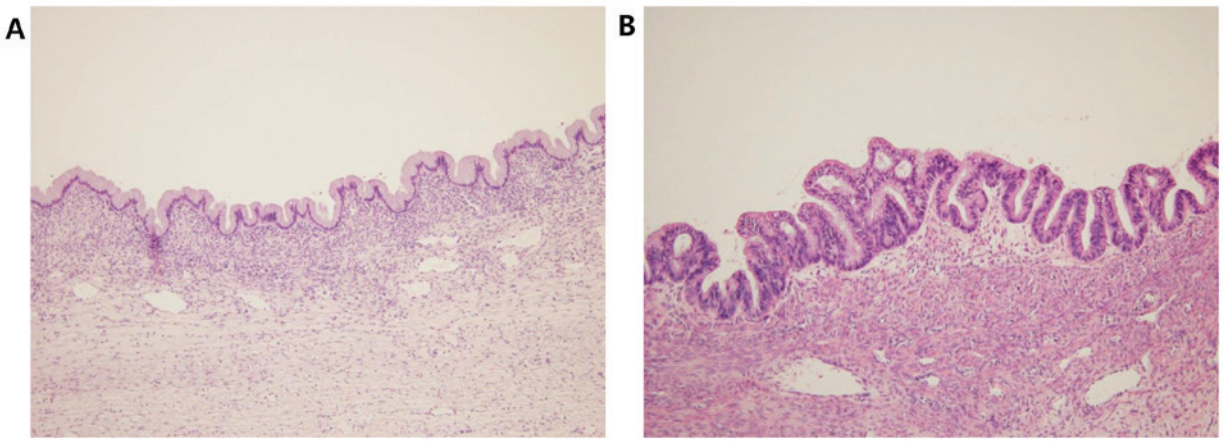

Figure 3. In some areas, the tumor exhibited mucinous epithelium consistent with (A) benign or (B) borderline tumor (hematoxylin and eosin staining; magnification, x100).

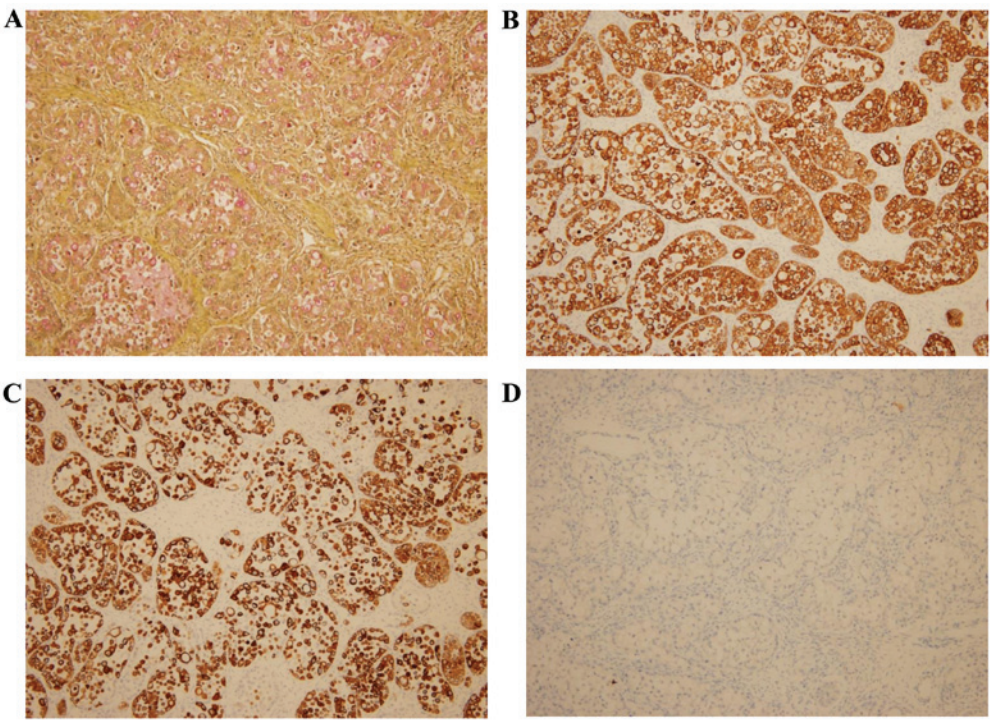

Figure 4. Immunohistochemical examination. The tumor exhibited diffuse strong positivity for (A) mucicarmin, (B) cytokeratin (CK)7 and (C) CK20 (magnification, x100). (D) The tumor was negative for CD56 (magnification, x100).

ovarian mucinous carcinomas, particularly those consisting of predominantly signet ring cells, has not been well delineated. All aspects of the pathological evaluation and clinical correlations are crucial for correct diagnosis. The aim of this case report was to remind pathologists to consider primary ovarian SRCC as a differential diagnosis when they encounter ovarian tumors with a major signet ring cell component.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

Not applicable.

Authors' contributions

HJ and KR performed the histological examination. JH and KB wrote the manuscript and KB supervised the study throughout. All the authors have read and approved the final version of this manuscript.

Ethics approval and consent to participate

Written informed consent was obtained from the patient prior to surgery.

Patient consent for publication

Written informed consent was obtained from the patient regarding the publication of the case. details and associated images.

Competing interests

The authors have no competing interests to disclose.

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