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CHORIOCARCINOMATOUS DIFFERENTIATION OF ENDOMETRIOID AND MUCINOUS ADENOCARCINOMA OF THE OVARY IN A POSTMENOPAUSAL WOMAN

POSTMENOPOZAL OLGUDA OVERİN ENDOMETRİOİD VE MÜSİNÖZ ADENOKARSİNOMUNDA KORYOKARSİNOMATÖZ DİFERANSİYASYON

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ÖZET

Overin koryokarsinomu, uterin koryokarsinoma göre daha nadir görülür. Bunun yanısıra, over yüzey epitel tümörü ile bir arada görülmesi daha da nadirdir. Burada, 60 yaşındaki postmenopozal kadında bir arada görülen, overin gestasyonel olmayan koryokarsinomu ve miks epitelyal karsinomu olgusundan bahsedeceğiz.

Anahtar Kelimeler: Choriocarcinomatous Differentiation; Endometrioid; Mucinous; Ovarian Cancer

ABSTRACT

Ovarian choriocarcinoma (CC) is very rare compared to uterine CC. Furthermore; ovarian CC coexisting with surface epithelial tumor is very rare. Herein, we report a case of metastatic nongestational ovarian CC in conjunction with mixed epithelial carcinomas in a 60 year old postmenopausal woman.

Key Words: Choriocarcinomatous Differentiation; Endometrioid; Mucinous; Ovarian Cancer

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INTRODUCTION

Choriocarcinoma (CC) is one of the most important neoplasias classified under the heading of gestational trophoblastic diseases. Mostly, it occurs in the uterine body in association with an antecedent pregnancy. The most important diagnostic step is the measurement of serum or urinary human chorionic gonadotropin (hCG) prior to an operation. Nongestational CC located in the ovary is relatively rare and encountered as a part of mixed germ cell tumors (1).

Epithelial tumors are the most common malignant neoplasms in the ovary and nearly 1 of 70 women is affected from this disease (1). But coexistence of ovarian CC with surface epithelial tumors instead of germ cell tumors is very rare and limited with case reports in the literature (1-4).

We report a case of metastatic nongestational ovarian CC in conjunction with mixed epithelial carcinomas; mucinous and endometrioid adenocarcinoma with choriocarcinomatous differentiation.

CASE

A 60-year-old postmenopausal woman, parity 3, was admitted to our hospital with abdominal pain and distention due to an ovarian tumor and ascites. The laboratory data showed high serum levels of CA125: 452 U/mL (< 35 U/ml), CA15-3: 243 U/mL (< 25 U/ml).

In radiological evaluation, thoraco-abdominal computed tomography revealed multiple metastatic lesions in the lower lobes of the lung, a 13 cm solid-cystic adnexal mass, omental cake and severe ascites in the abdominal cavity. Using (18F)-fluoro-2-deoxy-D-glucose (18F-FDG) positron emission tomography (PET) / computed tomography (CT), right adnexal mass with peritoneal dissemination and mediastinal metastasis were observed.

Paracentesis cytomorphological findings were consistent with malignant ascites and peritoneal carcinomatosis. Fractional curettage findings were consistent with microglandular endometrial hyperplasia for the cervix and decidualisation for the endometrium.

The patient was discussed in the tumor board and accepted as advanced epithelial ovarian carcinoma. She was decided to give neoadjuvant chemotherapy and then interval-debulking surgery was planned. 5 cures of neoadjuvant chemotherapy were (carboplatin, paclitaxel) received. Chemotherapy was unable to continue because of persistent neutropenia. After chemotherapy PET and CT findings were regressed, serum levels of CA125 (41 U/mL) and CA15-3 (23.3 U/mL) were decreased. At the first admission, because she was postmenopausal and she was thought to have epithelial ovarian carcinoma, serum b-hCG level was not evaluated. But after neoadjuvant chemotherapy, serum b-hCG level was examined inadvertently and the laboratory data showed high serum level of b-hCG: 1673 mIU/mL (postmenopausal normal, <8,5). Control b-hCG level was also high. Because of this result, a germ cell component of the tumor was suspected before the surgery.

After chemotherapy, total abdominal hysterectomy, bilateral salpingoophorectomy, lymph node dissection, omentectomy and appendectomy were performed. High serum level of b-hCG didn't decrease after operation. Postoperative serum levels of tumor markers, one week after the surgery were BhCG: 1639 mIU/mL, CA125: 47 U/mL, CA15-3: 28,6 U/mL. Pathological examination revealed two distinct histological types; adnexal mucinous and endometrioid adenocarcinoma with choriocarcinomatous differentiation in both ovaries. The tumor sizes were 5 cm in the right adnexa and 4 cm in the left adnexa. It was possibly shrinked with chemotherapy effect. Epithelial carcinoma metastasis was observed in peritoneal biopsies and omentum. Simple endometrial hyperplasia without atypia and a couple of calcified fibroids were examined in the uterus. The tumor metastasis was observed in the uterine serosa. Histological grade of the tumor was 3. In the microscopic evaluation of the ovaries, besides classical endometrioid adenocarcinoma areas, syncytiotrophoblastic cells with eosinophilic cytoplasm and wide nuclei with dense chromatin pattern were observed. With immunohistochemical stains, these cells were positive for b-hCG stain (Figure 1).

As a result of this report, tumor board decision was adjuvant chemotherapy with BEP regimen (bleomycin, etoposid, cisplatin) for the patient (bleomycin 30 mg on day 2; etoposid 100 mg/m^2 on day 1-2; cisplatin 20 mg/m^2 on day 1-5 every 28 days). She received first dose of the chemotherapy 4 weeks after the operation but before the first dose, b-hCG level raised to 4591 mIU/ml. At the present time, the patient received second cycle of chemotherapy and struggling with severe neutropenia.

DISCUSSION

The co-exiestence of CC and other neoplasias have been reported mainly with the female genital tract (6-8) and rarely with carcinomas of the esophagus (9), bladder or renal pelvis (10,11), stomach (12), rectum (13), lung (14), and breast (15). Syncytiotrophoblastic cells produce b-hCG in CC wherever the tumor located.

In most of the cases, CC coexisting with other tumors, b-hCG levels decreased after operation. During the follow up b-hcg levels increased again when tumor

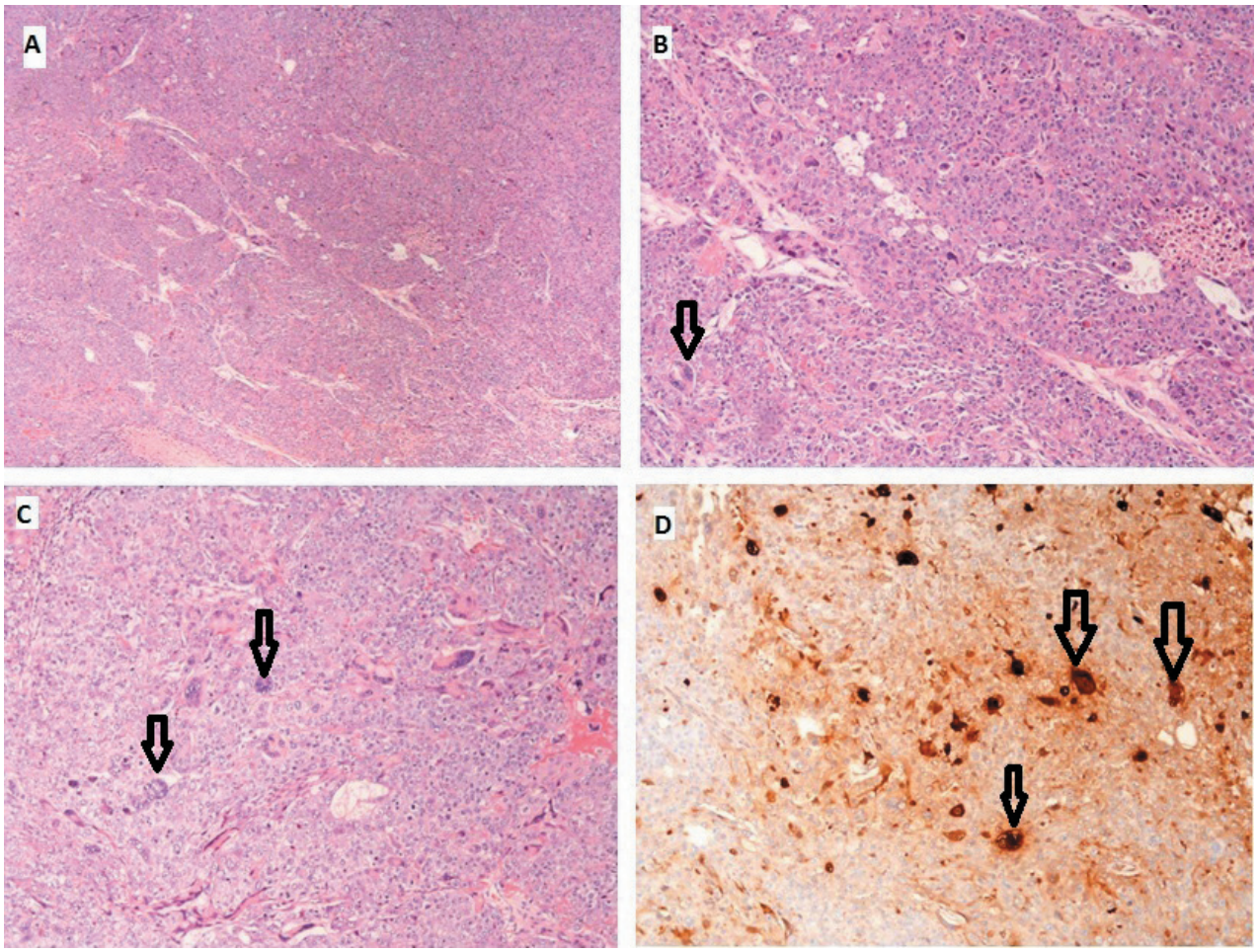

Figure 1 • A. Endometrioid adenocarcinoma of the ovary. (x40) **B.** Presence of the syncytiotrophoblastic cells (arrows). (x100) **C.** Choriocarcinomatous differentiation areas (arrows). (x100) **D.** Immunohistochemical staining of b-hCG positive cells (arrows). (x100)

relapsed. In our case, CA125 level returned to normal after neoadjuvant chemotherapy but the level of b-hCG did not change neither after the neoadjuvant chemotherapy nor after the operation. Additionally, serum b-hCG level increased after the operation before starting the adjuvant chemotherapy. Thus we can speculate that the lung lesions or other distant metastatic lesions may also include choriocarcinomatous component. Adjuvant chemotherapy was started and follow up will be done with CA125 and b-hcg levels.

Hirabayashi et al reviewed previous cases very well in their report (1). Similar to previous cases, our patient was also postmenopausal who is 60 years of age. In three of five cases, CC was present with mucinous neoplasms, the other were present with poorly differentiated adenocarcinoma and endometrioid & small cell adenocarcinoma. In our case, CC was present with endometrioid and mucinous adenocarcinoma of the ovary. The main different aspect of our case was that she received neoadjuvant chemotherapy before the operation. She was misinterpreted as a pure epithelial ovarian neoplasm in the admission without examining serum b-hCG level and received chemotherapy according to epithelial ovarian neoplasm protocol. The most important message of this report is that tumor marker aspect of serum b-hCG should never be forgotten in postmenopausal women. If we had had examined b-hCG at the fist admission, patient could be operated primarily or the chemotherapy regimen could be prepared after a biopsy compatible with a CC protocol.

In previous reports, luteinisation in the ovaries was observed due to the increased b-hCG secretion in choriocarcinomatous differentiation of the ovarian tumor (1). In our case, luteinisation was not detected in the ovary, probably due to the effect of neoadjuvant chemotherapy. But decidualisation in the endometrial biopsy, which performed before neoadjuvant chemotherapy, could be the sign of luteinisation of ovaries.

As seen in previous cases, CCs coexisting with surface epithelial tumor were highly malignant and most

of the reported patients showed a rapid tumor progression with metastatic disease. 4 of 5 previous patients died because of the disease in a period of 6 days to 15 months. Our patient had been just operated and still receiving chemotherapy at the present time. But the progression in b-hCG levels just after the operation before the chemotherapy showed that this disease was also aggressive.

Different mechanisms have been suggested to explain the co-exiestence of carcinoma and choriocarcinoma so far. Multidirectional tumor cell differentiation from a common stem cell and de-differantiation of epithelial cells into choricarcinoma are the most possible mechanisms (6). Oliva et al. and Jiménez-Heffernan et al. noted the presence of areas of gradual transition of cystadenoma into the choriocarcinomatous elements (2,3). We also recognized similar areas in our case and we are in the same line with the other reports that dediferantiation of epithelial cells is the more possible way in our case.

The case is reported for its rarity and to describe its importance in clinical practice. Although it is vey rare, in postmenopausal women ovarian CC can be seen with epithelial ovarian neoplasms. CC can be diagnosed by the measurement of serum or urinary human chorionic gonadotropin (hCG) prior to an operation and it should be never forgotten that hCG should also be examined in postmenopausal women as a tumor marker.

Conflict of Interest: The authors declare that there is no conflict of interest.

REFERENCES

1. Hirabayashi K., Yasuda M., Osamura Y., Hirasawa T., Murakami M. Ovarian nongestational choriocarcinoma mixed with various epithelial malignancies in association with endometriosis. Gynecologic Oncology 2006;102:111–117
2. Oliva E, Andrada E, Pezzica E, Prat J. Ovarian carcinomas with choriocarcinomatous differentiation. Cancer 1993;72:2441–6.
3. Jiménez-Heffernan JA, Perna C, Martinez A, Casinello J, Cuevas J. Coexistent ovarian mucinous cystadenocarcinoma and ovarian choriocarcinoma. Arch Gynecol Obstet 2002;266:235–7.
4. Ozaki Y, Shindoh N, Sumi Y, Kubota T, Katayama H. Choriocarcinoma of the ovary associated with mucinous cystadenoma. Radiat Med 2001; 19:55–9.
5. Kurman RJ, Norris HJ. Malignant mixed germ cell tumors of the ovary. A clinical and pathologic analysis of 30 cases. Obstet Gynecol 1976; 48:579–89.
6. Yamada T, Mori H, Kanemura M, Ohmichi M, Shibayama Y. Endometrial carcinoma with choriocarcinomatous differentiation: a case report and review of the literature. Gynecol Oncol 2009;113:291-294.
7. Akbulut M, Tosun H, Soysal ME, Oztekin O. Endometrioid carcinoma of the endometrium with choriocarcinomatous differentiation: a case report and review of the literature. Arch Gynecol Obstet 2008;278:79-84.
8. Horn LC, Hanel C, Bartholdt E, Dietel J. Serous carcinoma of the endometrium with choriocarcinomatous differentiation: a case report and review of the literature indicate the existence of 2 prognostically relevant tumor types. Int J Gynecol Pathol 2006;25:247-251.
9. Patil S, Ramakrishna KA, Rao SG et al. Choriocarcinoma - a rare association with squamous cell carcinoma of esophagus. Indian J Gastroenterol 2006;25:42-43.
10. Dennis PM, Turner AG. Primary choriocarcinoma of the bladder evolving from a transitional cell carcinoma. J Clin Pathol 1984;37:503-505.
11. Grammatico D, Grignon DJ, Eberwein P et al. Transitional cell carcinoma of the renal pelvis with choriocarcinomatous differentiation. Immunohistochemical and immunoelectron microscopic assessment of human chorionic gonadotropin production by transitional cell carcinoma of the urinary bladder. Cancer 1993;71:1835-1841.
12. Yoon JH, Kim MS, Kook EH et al. Primary gastric choriocarcinoma: two case reports and review of the literatures. Cancer Res Treat 2008;40:145-150.
13. Verbeek W, Schulten HJ, Sperling M et al. Rectal adenocarcinoma with choriocarcinomatous differentiation: clinical and genetic aspects. Hum Pathol 2004;35:1427-1430.
14. Chen F, Tatsumi A, Numoto S. Combined choriocarcinoma and adenocarcinoma of the lung occurring in a man: case report and review of the literature. Cancer 2001;91:123-129.
15. Erhan Y, Ozdemir N, Zekioglu O et al. Breast carcinomas with choriocarcinomatous features: case reports and review of the literature. Breast J 2002;8:244-248.