



METASTATIC OVARIAN CANCER

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ABSTRACT

Most of the metastatic ovarian carcinomas are incidental cases found at surgical exploration. Most of them originate from genital system, breasts or gastrointestinal system. In this study; we aimed to analyze the clinical and pathologic features of metastatic ovarian cancers, retrospectively.

In this study, we presented and discussed three cases with metastatic ovarian carcinoma which we encountered in the Department of Obstetrics and Gynecology of Taksim Education and Research Hospital between 2005 and 2007.

These 3 patients had admitted to our clinic with the diagnosis of adnexal mass. One of these had previously undergone mastectomy and chemotherapy was given due to breast cancer. All of the patients were investigated

according to ovarian cancer evaluation protocol. Gastric carcinoma was found in one of the patients. One of the other patients undergone diagnostic laparotomy was diagnosed intra-operatively as colon carcinoma. The diagnosis of the other patient could be determined only after postoperative patho-logical examinations. The ovarian mass in this case was found as metastatic breast cancer.

Keeping in mind that 6 to 27.8 per cent of malignant ovarian masses may be of metastatic in origin; complete and detailed systemic investigation is essential. The possibility that bilateral ovarian masses could be metastatic should be considered and must be referred to an oncology center.

• **Key Words:** Metastatic ovarian cancer, breast neoplasms, gastrointestinal neoplasms *Nobel Med 2010; 6(1): 81-85*

ÖZET

METASTATİK OVARIAN KANSER

Metastatik ovarian kansinonların çoğu cerrahi eksplo-rasyon sırasında tesadüfen rastlanılan olgulardır. Çoğu; genital sistem, meme ve gastrointestinal sistemden kay-naklanır. Bu çalışmada; metastatik over kanseri olguları-nın klinik ve patolojik özellikleri açısından retrospek-tif olarak incelenmesi amaçlandı.

Biz bu çalışmada 2005 - 2007 yılları arasında Taksim Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum Kliniği'ne interne edilen üç metastatik ovarian kansinoma ön tanısı almış olguyu sunduk ve tartıştık.

Bu üç olgu adneksiyal kitle tanısı ile kliniğe kabul edil-miştir. Bir olguya meme kanseri nedeni ile mastektomi yapılmış, ardından kemoterapi almıştır. Tüm olgular ovarian kanser protokolüne göre hazırlandı. Bu hastaların birinde gastrik kansinoma bulundu. Diğer iki hasta ovarian kansinoma ön tanısı ile laparotomiye alındı. Birine

intraoperatif kolon kansinomu tanısı konuldu. Diğer olgunun tanısı ise postoperatif patolojik inceleme sonrası mümkün oldu. Ovarian kitle meme kanseri metastazı idi.

Ovarian kitlelerin %6 ila %27,8'inin metastatik olduğu akılda tutulmalıdır. Bu geniş varyasyon hem meto-dolojiden hem de sekonder tümörün mikroskopik düzeydeki kalıntılarından kaynaklanmaktadır. Over-lerdeki metastatik tümörlerin çoğu Krukenberg tü-mörleri veya mukoselüler tümörlerdir. Ovarian metas-tazlar meme kanseri vakalarında da görülmektedir. Ovarian tümör ön tanılı hastaların preoperatif detaylı tüm vücut incelemesi metastatik overlerin ayırıcı tanısında aydınlatıcıdır.

Bilateral ovarian kitlelerin metastatik olma olasılığı düşünölmeli ve bunlar onkoloji merkezlerine yönlendirilmelidir.

• **Anahtar Kelimeler:** Metastatik over kanseri, meme kanseri, gastrointestinal kanserler **Nobel Med 2010; 6(1): 81-85**

INTRODUCTION

Metastatic ovarian cancers constitute a highly important subgroup of ovarian cancers. These cases are characterized as being symptomatic, with bilateral involvement and poor prognosis.¹ The prevalence of malign ovarian neoplasia has been increasing during the last decades. Ovarian carcinoma constitutes 4 to 5 per cent of all cancer cases in women. Ovarian carcinoma also constitutes 23 to 27 per cent of all gynecologic cancers.² Seven to 10 per cent of malignant ovarian tumors are metastatic.³ Most of them originate from genital system (often from endometrial carcinoma), breast and gastrointestinal system, especially from colon.² This rate may be as high as 20% in some series.⁴ Direct extension or metastasis is seen in only 5 to 6 per cent of the patients and synchronous tumors are found simultaneously in most of the patients. Especially in the patients with endometrioid carcinoma, 1/3 of the patients have both of these cancer; endometrium and ovary. Metastatic carcinoma of the ovaries may be a consequence of direct dissemination, dissemination by blood or lymphatics, or peritoneal implantation.

Most of the patients with metastatic ovarian carcinoma are incidental cases found at surgical exploration. Rarely, symptomatic forms of the masses require surgical removal.² Krukenberg tumors constitutes 30-40% of the tumors metastasized to the ovaries. Origin of this tumor may be stomach, colon or gallbladder, but most of them originate from the stomach. A relative decrease

in the incidence of this tumor was observed over the last 2 decades which is correlated with a decrease in the incidence of the gastric carcinoma. Metastatic adenocarcinoma of the colon may involve the ovaries in 1-2% of the cases. They histologically look like the mucinous cystadenocarcinoma of the ovaries.^{5, 6}

In this article, we present 3 cases which had metastatic ovarian cancers originated from different locations like breast and gastrointestinal system. All cases had abdominal symptoms and diagnostic laparotomy had been performed.

CASE REPORT

CASE 1

41 years old, virgin patient was admitted to the emergency department of Taksim Training and Research Hospital presenting with abdominal pain, nausea and vomiting was admitted with prediagnosis of acute abdomen. The patient had previously undergone modified radical mastectomy and left axillary curettage for a tumoral mass in the left breast in May 2000. Pathological examination of the mass was invasive intraductal carcinoma. Yearly follow-up of the patient was normal, and the patient was considered to be an early stage breast cancer patient. Abdominal guarding and suspicious rebound tenderness and a mass extending to the level of the umbilicus were found on physical examination. There was a conglomerate mass →

filling completely the right adnexal region, fossa iliaca and partially crossing to the left side and adhered to the surrounding structures. The left adnexa was normal. There was no ascites.

On sonographic examination; there was an irregular solid mass of 15 cm in diameter with heterogenous echo that extended to umbilicus. In abdominopelvic computerized tomography, mass lesion was found occupying the right half of the pelvis and extending to the level of aortic bifurcation on the midline. It was located in close proximity to the anterior abdominal wall and considered to be originated from the right ovary. Mass was measured 10x7x15 cm in size. Colonoscopy was normal.

Blood biochemistry was normal. CA-125, CA 15-3 and CA 19-9 levels were within normal limits. The patient was operated with diagnosis of right ovarian mass. Small amount of bloody fluid was observed during the exploration. The uterus, the left ovary and fallopian tube were normal. A hemorrhagic necrotized mass of 10x12 cm was observed originating from right ovary and was representing reactive adhesions to the sigmoid colon. Hysterectomy, salpingoopherectomy and appendectomy were performed. Intestinal surface, mesentery of the intestine, subdiaphragmatic surface, the liver and spleen were evaluated as normal. There was no pathologic lymph node in paraaortic regions. Pathology revealed carcinomatous infiltration at the right ovary and the right fallopian tube.

The ovarian tumor was examined comparatively with the breast tumor of the patient. Immune reactivity in tumor cells with GCDFP-15 and CA-125 was not found. The negativity of the patient for CA-125 which is usually positive in patients with ovarian tumors and other morphological findings suggested that the tumor was consistent with metastasis of breast cancer. The patient was referred to the oncology center for chemotherapy.

CASE 2

73 years old, Gravida 5 and Parity 3 patient referred to the outpatient clinic of gynecology department of our hospital with abdominal pain and vaginal bleeding lasting 2 months. A mass was found on physical examination which was filling the pelvis. There was no guarding or rebound tenderness on the abdomen. There was a semisolid mass occupying the small pelvis and extending to the umbilicus.

Laboratory findings were not significant. Tumor markers were within normal limits except CA-125 (124 u/ml) which was elevated. On transvaginal ultrasonography,

the uterus was atrophic and the endometrium was pencil-line. There was a solid mass 10x10 cm in diameter containing mostly solid components anteriorly and rarely demonstrating cystic appearance with heterogenous echo and irregular borders on the right side of the uterus. There was no mass in the left adnexal region. There was widespread fluid in cul de sac. On abdominal tomography there were several hypodense foci (metastasis) the biggest of which was 11 mm in diameter on the subdiaphragmatic surface of the liver. A cystic mass lesion with lobulated borders occupying the right side of the pelvis, demonstrating septal and peripheral contrast enhancement and showed mural nodules and multiple septations with thick walls (ovarian tumor?). This mass was observed to be in close proximity with the sigmoid colon on two CT sections. Widespread fluid formation was observed in the abdomen.

On double contrast colon roentgenograms, contrast material and air passage to the proximal of the rectosigmoid junction was interrupted. Irregularity, mucosal destruction and filling defects of polypoid appearance were observed on the adjacent rectum mucosa. Pathology of rectoscopic biopsy samples showed chronic inflammatory edematous mucosa of mild activity showing focal cystic hyperplasia.

On laparotomy, there was 1500 cc fluid in the abdomen. A multicystic mass 25 cm in diameter containing serous fluid and originated from the right ovary was observed with irregular margins showing adhesions with the right side of the abdomen, the omentum and posterior side of the broad ligament. Multiple metastases of which the biggest was 2 cm on the liver were observed, excised and sent to frozen section. The result was malignancy. Hysterectomy and bilateral salpingoopherectomy was performed. This was followed by low anterior resection and end-to-end anastomosis. No post-operative complication developed. The patient was referred to the radiation oncology service after discharge. Pathology revealed carcinoma metastasis in the right ovary (frozen section). The capsule was intact. Moderately differentiated adenocarcinoma with serosa infiltration was seen in the large intestine. Surgical margins were intact. Tumor diameter was 3 cm. According to Dukes Classification (Astler Collier Modification) the stage was B2. Angiolymphatic invasion was seen. No tumor was observed in the lymph nodes (2 nodes were obtained). Lesion of the liver was adenocarcinoma metastasis. Tumor cells were observed in the ascitic fluid. Considering the morphological characteristics and immunohistochemical CEA positivity of the tumors in the ovary, large intestine and the liver, it was concluded that the tumor in the ovary was colon tumor metastasis. →

CASE 3

36 years old, Gravida 6 and Parity 6 patient was admitted to gynecology department of our hospital with abdominal pain, distension, nausea, vomiting and indigestion with a prediagnosis of bilateral ovarian tumor with the finding of ascites in the abdomen. The patient had distension and abdominal pain for 5 months and indigestion for 3 months.

The abdomen was quite distended due to the presence of ascites. Cul de sac was irregular and rectal mucosa was intact. The corpus was palpated to be larger than normal in the massive free ascitic fluid. Its margins could not be observed. Implantation metastasis was present in the cul de sac. There was a semisolid mass located in the right adnexal region and extending to the umbilicus. There was also a second semisolid mass on the right side which was located in the right pelvis and smaller than the left one.

On biochemistry, abnormal findings were as following; leukocyte was 12.500 μ l, erythrocyte sedimentation rate was 33 mm/hr, AST 77 u/l (high), ALT 72 u/l (high), ALP 475 u/l (high), total protein 5.8 g/dl (low), and albumin was 2.6 g/dl (low). Tumor markers were CEA: 5.34 u/ml (high), CA-125: 342 u/ml (high). On vaginal sonography; the right adnexa was about 20 cm in diameter and a solid mass containing some cystic areas was observed. The left adnexa was 7 cm in diameter and a semicystic mass was observed. Multiple biopsy samples were taken from the corpus of the stomach on gastroscopy. The ascites was exudative. No atypical cells were seen in cytologic examination. On pathology, signet ring cell carcinoma was reported. Then the case considered as Krukenberg tumor. She was referred to oncology center.

DISCUSSION

Five to six percent of abdominal mass undergone exploratory laparotomy due to ovarian tumor are metastatic in origin.^{2, 7, 8} In oophorectomy specimens performed in metastatic breast tumors, involvement rate of 20 to 30% has been found. Sixty percent of them are bilateral. It has been reported that ovarian involvement is less in earlier stages of cancer.⁹ Ovarian metastasis in patients with breast cancer as pelvic mass or ascites develops within 5 years after the primary treatment.¹⁰ In our patient, ovarian metastasis developed from the breast cancer 2 years later than the primary treatment. Secondary ovarian lesions can be clinically seen as bilateral, noncystic and originating from the lobular carcinoma of the breast.¹¹ In our patient there was a unilateral and solid metastatic mass originated from the intraductal carcinoma of the breast. Metastases

of the breast cancer into the ovaries are seen sonographically as bilateral solid mass. These metastases are seen in 4th stage of the disease.¹² The diagnostic method of choice in ovarian metastasis of breast cancer is transvaginal ultrasonography.^{13, 14} But this is not sufficient in differential diagnosis. Sensitivities of CA-125 and CA15-3 are low.¹¹ As a matter of fact, CA-125 and CA15-3 values were normal in the patient presented here. Exploratory laparotomy was performed in our patient due to prediagnosis of ovarian tumor. Hysterectomy with bilateral salpingoopherectomy was performed. Differential diagnosis of metastatic as well as primary tumors of the ovaries may be determined by monoclonal antibodies.¹¹ Our patient was also considered to have breast cancer metastasis as a result of pathologic and immunohistochemical examination.

Colon adenocarcinoma constitutes 37-45% of all metastatic ovarian tumors.⁷ Harcourt and Dennis reported that the first complaint of 3% of female patients with colorectal carcinoma was ovarian mass. 45% of metastatic ovarian tumors of colon cancers were considered to be primary ovarian tumors.¹⁵ Endometrioid type of colon adenocarcinomas resembles epithelial ovarian cancer. Colon cancer is the most difficult to differentiate from others among the metastatic ovarian tumors. Also in our patient the differential diagnosis was not possible and the patient had undergone to exploratory laparotomy. Hysterectomy and bilateral salpingoopherectomy was performed. Low anterior resection and end-to-end anastomosis was also performed after it has been observed that the tumor was colonic in origin. Necessity of prophylactic oophorectomy in the patients previously diagnosed as colorectal adenocarcinoma is still uncertain. Scully-Richardson estimated that oophorectomy should be done in 1-2% of the patients with gastrointestinal cancer¹⁶ although the effect of oophorectomy on the survival has not been proved. However the morbidity is higher in the metastatic cases. Macroscopic metastases to the ovaries are poor prognostic finding in colonic carcinoma. Liver metastasis, if present, decreases the median survival time from 20.1 months to 8.1 months in the cases of colonic carcinoma metastasized to ovaries.¹⁷⁻¹⁹

Among the tumors originated from the gastrointestinal system and metastasized to the ovaries is Krukenberg tumor; it is an adenocarcinoma with signet ring cell. Our patient had also widespread mucosal irregularities and thickening of the fundus and corpus of stomach and biopsy samples were taken from these sites. Histological characteristic of this tumor is signet-ring cells filled by the mucine in cellular matrix of the ovarian stroma.^{5, 10, 21} This characteristic distinguishes this tumor from other adenocarcinomas. If there was a role of →

CA-125 in differential diagnosis of the primary ovarian cancer or metastatic ovarian carcinoma originated from the gastrointestinal system was investigated, it has been found to be positive in 84.5% and 4% of the patients, respectively.²² CA-125 values were high in both patient presented here.

Consequently, CA-125 monoclonal antibody may be used in differential diagnosis of ovarian cancer.²³⁻²⁵ Patients who have ovarian metastasis of other sites of cancer could admit to hospital with symptoms of intra-abdominal mass even with acute abdominal symptoms and this could be independent from the principal site of cancer. Detailed evaluation should be done preoperatively for correct differential diagnosis of metastatic or non metastatic ovarian tumors. Probability about different origins of ovarian mass should be

evaluated particularly. In our article we presented three cases with cancer of primary breast and gastrointestinal system emerged with ovarian metastasis.

CONCLUSION

Metastatic ovarian tumors constitute 6-27.8% of all malign ovarian masses.¹⁴ This wide variation results from both methodology and the fact that secondary tumor remains at microscopic level.

Most of the metastatic tumors in the ovaries are Krukenberg tumor or mucocellular tumors. Ovarian metastases are seen also in women with breast cancer. Preoperative detailed whole body investigations of the patients prediagnosed as ovarian tumor is informative in differential diagnosis for the metastatic ones.



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