

Outcome of patients with ovarian metastatic tumors. Report of 83 cases and review

E. Salamalekis¹, P. Bakas¹, K. Sykiotis¹, I. Saloum¹, K. Kontogianni¹, E. Pabameto¹,
A. Pafiti², G. Creatsas¹

¹2nd Department of Obstetrics and Gynecology, ²Histopathology Department, Aretaieio Hospital, University of Athens, Athens (Greece)

Summary

The aim of the study was to review patients with metastatic ovarian tumors in relation to their outcome and clinical characteristics.

Methods: It was a retrospective study including 83 patients with histopathological diagnosis of metastatic ovarian tumor. The examined parameters include age of the patients, origin of the tumor, consistency and appearance of the tumor, histological type and 5-year survival.

Results: The 5-year survival time of patients with metastatic ovarian tumors originating from the genital tract was 14.8% and for metastatic ovarian tumors originating outside the genital tract 5.4%.

Conclusion: The presence of metastatic ovarian tumors should always be included in the differential diagnosis of a pelvic mass. Difficulties in identification of the primary tumor site are present mainly in cases of metastatic tumors from the colon, while metastasis to the ovary from the breast tends to form small nodules in the ovary.

Key words: Metastatic ovarian tumor; Ovarian cancer; Ovarian cyst; Ovarian malignancy; Krukenberg tumor.

Introduction

The incidence of metastatic ovarian tumors varies from 5% of the total ovarian tumors, 10-30% of the total malignant ovarian tumors and up to 61% in histopathological sections of the ovaries [1, 2]. This difference in the incidence of metastatic ovarian tumors could be attributed to differences in collection of the samples (material from cadavers, surgical), performance of histological examination of the ovaries or macroscopic only evaluation and limitation of the study to specific age groups or geographic distribution of some tumors with a tendency to give metastasis to the ovary, e.g., cancer of the stomach [2, 3]. In many cases it is difficult to make a diagnosis of primary or metastatic ovarian tumor before the results of the histopathological examination are available. The differential diagnosis between metastatic ovarian tumors, cancer of the colon and mucinous cystadenocarcinomas is very difficult. Up to 45% of metastatic ovarian tumors from cancer of the colon have been diagnosed primarily as primary ovarian tumors [4, 5]. In cases of breast cancer, microscopic ovarian metastases have been diagnosed after prophylactic oophorectomy, and in up to 63.3% of cases with prophylactic oophorectomy the ovaries have a macroscopically normal appearance [6]. The majority of metastatic ovarian tumors come from the gastrointestinal tract, endometrium, breast and uterine cervix.

In the present study we evaluated the clinical and histopathological characteristics of metastatic ovarian tumors and the overall 5-year survival of the patients.

Material and Methods

This retrospective study took place in the 2nd Department of Obstetrics and Gynecology, University of Athens, Aretaieio Hospital. During the period 1980-2000 1,048 ovarian tumors were managed in our hospital from which 447 were malignant ovarian tumors and 83 were metastatic ovarian tumors. All patients were operated on and the diagnoses were made in the histopathology laboratory of our hospital. The examined parameters include age of the patients, origin of the tumor, consistency and appearance of the tumor, histological type and the 5-year survival. The metastatic ovarian tumors were separated according to their macroscopic morphology – compact with nodular or homogeneous texture and cystic areas while noting the presence of necrosis.

Survival rates were calculated in months from the time of surgical intervention to the date of last known patient status. Survival rates were calculated by the Kaplan-Meier method and statistical comparison of the resulting curves was performed using the long-rank test; p values less than 0.05 were considered statistically significant.

Results

The incidence of metastatic ovarian tumors was 7.9% (83/1,048) of the total ovarian tumors and 18.5% (83/447) of the total malignant ovarian tumors. Mean patient age was 59.2 years (range 26 to 76 years old). The origin of metastatic ovarian tumors from neoplasms of the genital tract was as follows: endometrium 22% (18/83), uterine cervix 8% (7/83), uterine corpus 7%

(6/83), and fallopian tubes 4% (3/83). The origin of metastatic ovarian tumors from neoplasms outside the genital tract was as follows: stomach 21.6% (18/83), breast 15.5% (13/83), colon 14% (12/83), pancreas 2.4% (2/83), lung 1.2% (1/83), appendix 1.2% (1/83), kidney 1.2% (1/83), and one case of unknown origin.

In relation to localization of the metastatic ovarian tumors, out of 83 cases there were 48 cases with bilateral development (57.8%), 24 in the right ovary (28.9%) and 11 in the left ovary (13.3%). Eight cases of metastatic ovarian tumors presented as primary tumors from the stomach (4 cases), colon (3 cases), and breast (1 case). The diameter of the metastatic ovarian tumors ranged from 1 to 24 cm with a mean diameter 6.6 cm. The smallest size was from metastatic tumors of the breast and the largest size from metastatic tumors of the colon with the biggest tumor having a weight of 1,580 grams.

In relation to the macroscopic morphology, 78.3% of the metastatic ovarian tumors were compact with a global or kidney shape and with cystic areas in less than 5% of the tumor. The external surface was smooth, nodular in 34 cases and irregular in 31 cases. Eight cases had findings of necrosis. Eighteen cases were cystic tumors with origin from the gastrointestinal tract and mainly from the colon.

Fourteen cases (16.9%) had the characteristic morphology of Krukenberg tumors with diffuse development of cancer cells (signet-ring type) and substrate of connective tissue. There were no signet-ring type cells in any other case of metastatic ovarian tumor. Of Krukenberg tumors 85.7% (12/14) originated from the stomach.

Survival of patients with metastatic ovarian tumors included 34 cases with metastatic tumors from the genital tract: eight cases were excluded due to lack of information. Ten patients lived for more than five years and four of them for more than ten years. Four patients lived for four years, six patients for three years, one patient for two years, three patients for one year and two patients for six months.

Of 49 cases with metastatic tumors outside the genital tract 14 cases were excluded due to lack of information. Five patients lived more than five years and two of them more than ten years. One patient lived for four years, three patients lived for three years, three patients lived for two years, 13 patients lived for one year, ten patients lived for six months.

Median survival time after surgical removal of the metastatic ovarian tumors with origin from the genital tract was 48 months (Table 1, Figure 1), while with origin

Table 1. — *Survival time and proportion after surgical removal of metastatic ovarian tumors originating in the genital tract.*

Survival time	Survival proportion	Standard error
6 months	92.6%	0.048
12 months	81.5%	0.070
24 months	77.8%	0.078
36 months	55.6%	0.081
48 months	40.7%	0.081
60 months	14.8%	0.041

Median survival time was 4 years.

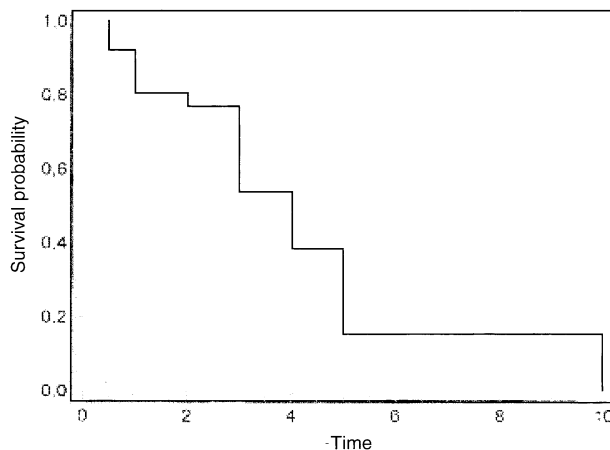


Figure 1. — Kaplan-Meier survival curve of patients with metastatic ovarian tumors originating in the genital tract.

outside the genital tract it was 12 months (Table 2, Figure 2). There was a statistically significant difference in the comparison of survival curves between the two groups ($p < 0.05$).

Table 2. — *Survival time after surgical removal of metastatic ovarian tumors originating outside the genital tract.*

Survival time	Survival proportion	Standard error
6 months	73.0%	0.062
12 months	37.8%	0.057
24 months	29.7%	0.067
36 months	21.6%	0.058
48 months	18.9%	0.060
60 months	5.4%	0.020

Median survival time was 1 year.

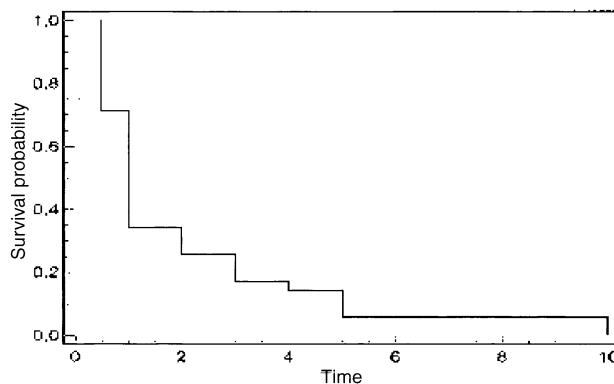


Figure 2. — Kaplan-Meier survival curve of patients with metastatic ovarian tumors originating outside the genital tract.

Discussion

The incidence of metastatic ovarian tumors with post-operative histopathological diagnoses in the present study was 18.6%. It has been reported that 4.4% of women who died from malignant tumors were found to have ovarian

metastases at necrotomic examination [7] and 25% of cases with breast cancer that underwent prophylactic oophorectomy had ovarian metastasis [6]. The incidence of metastatic ovarian neoplasms in relation to total malignant ovarian neoplasms has been reported from 21.1% [8] to 28% [9] which is in accordance with our findings. Our material did not include cases of prophylactic oophorectomy for breast cancer. The origin of metastatic ovarian neoplasms in our study was as follows: gastrointestinal tract 42%, breast 15.5%, and genital tract 41%. The reported distribution of origin for metastatic ovarian neoplasms varies from 47% for the gastrointestinal tract (stomach 18%, colon 29%) breast 31% and genital tract 18% [9] to 74% for the gastrointestinal tract (stomach 61%, colon 13%) and breast 13% [10]. It appears that the most common origin for metastatic ovarian neoplasms is the gastrointestinal tract and the most common organ is the stomach.

The mean age of the patients in this study was 59.2 years with a range from 26 to 76 years old. This finding appears to be higher compared to previous reports but it could be attributed to the increased incidence of metastatic ovarian neoplasms from the genital tract in older ages. Localization of the tumors tends to be bilateral and is attributed to lymphogenic dissemination of breast cancer and neoplasms of the upper abdomen [2, 6]. In the present study there was no correlation between macroscopic morphology of metastatic ovarian neoplasms and the origin of the tumor, although metastasis from the breast had a tendency to create small nodules in the ovary. The term Krukenberg tumor has been used for metastatic ovarian neoplasms, but in this study Krukenberg tumors were defined as metastatic ovarian tumors with diffuse development in ovarian tissue with mucous-containing cells (signet-ring) [12]. The incidence of Krukenberg tumors was 16.9% (14/83) and 85.7% originated from the stomach (12/14). The reported incidence of Krukenberg tumors with origin from the stomach varies from 70% [13] to 94% [14]. The prognosis of metastatic ovarian tumors is generally poor and the majority of patients die the first year after the initial diagnosis [11, 12].

In the present study the median survival time of patients with metastatic ovarian tumors originating from the genital tract was 48 months and for metastatic ovarian tumors originating outside the genital tract it was 12 months; there was a statistically significant difference. The 6, 12, 24, 36, 48 and 60-month survival time of patients with metastatic ovarian tumors originating from the genital tract and for metastatic ovarian tumors originating outside the genital tract is shown in Tables 1 and 2, respectively. The reported 5-year survival time of patients with metastatic ovarian tumors originating from the genital tract is 47% and for metastatic ovarian tumors originating outside the genital tract 19% [8].

The difference in prognosis between metastatic ovarian tumors originating from the genital tract and those originating outside the genital tract could be attributed to the finding that in many cases of metastatic ovarian tumors

originating from the genital tract bilateral oophorectomy was performed at the time of initial operation, having only microscopic ovarian metastases. However in cases of metastatic ovarian tumors originating outside the genital tract, bilateral oophorectomy was performed at a second procedure mainly because of enlarged ovaries, thus there was a significant time interval with undetected ovarian metastasis which could have adversely affected the prognosis. Additionally, lymph node metastasis is frequently seen in patients with metastatic ovarian tumors of gastrointestinal origin and it appears that retrograde lymphatic spread is a likely route for metastasis [14].

Metastatic ovarian tumors present a tendency for bilateral development, mainly as compact tumors with the origin more frequently from the stomach, endometrium and breast. Many of them appear as primary ovarian tumors. The presence of metastatic ovarian tumors should always be included in the differential diagnosis of a pelvic mass. Difficulties in identification of the primary tumor site are present mainly in cases of metastatic tumors from the colon, while metastases to the ovary from the breast tend to form small nodules in the ovary.

References

- [1] Holtz F., Hart W.R. *Cancer*, 1982, 50, 2438.
- [2] Janovski N.A., Paramandlem T.L.: "Ovarian tumors". In: "Major Problems in Obstetrics and Gynecology". Saunders Co., 1973.
- [3] Young R.H., Path F.R.C., Scully R.E.: "Metastatic tumors of the ovary". In: "Blausteins Pathology of the Female Genital Tract". 4th edition, Springer-Verlag, 1994, 939.
- [4] Ulbright T.M., Roth L.M., Stehman F.B. *Cancer*, 1984, 53, 1164.
- [5] Yakushiji M., Tazaki T., Nishimura H., Kato T.: "Krukenberg tumors of the ovary: a clinicopathological analysis of 112 cases". *Acta Obstet. Gynecol. Jpn.*, 1987, 39, 479.
- [6] Lumb G., Mackenzie Dh.: "The incidence of metastases in adrenal glands and ovaries removed for carcinoma of the breast". *Cancer*, 1959, 12, 521.
- [7] Fox H., Langley F.A. In: "Tumors of the Ovary". London, Heine-mann, 1976, 300.
- [8] Hashimoto N.Y., Yamamoto T., Kamiura S., Seino H., Ohira H., Sawai K. *et al.*: "Metastatic ovarian tumors: A review of 64 cases". *Gynecol. Oncol.*, 2003, 89, 314.
- [9] Webb M.J., Decker D.G., Mussey E.: "Cancer metastatic to the ovary, factors influencing survival". *Obstet. Gynecol.*, 1975, 45, 391.
- [10] Horie K., Konishi I., Fujii S., Kozasa H., Noda Y., Okamura H., Mori T.: "A clinical study of metastatic ovarian tumors". *Obstet. Gynecol.*, 1986, 38, 435.
- [11] Woodruff J.D., Novak E.R.: "The Krukenberg tumor study of 48 cases from the ovarian tumor registry". *Obstet. Gynecol.*, 1960, 15, 351.
- [12] Johanson H.: "Clinical aspects of metastatic ovarian cancer of extragenital origin". *Acta Obstet. Gynecol. Scand.*, 1960, 39, 681.
- [13] Hale R.W.: "Krukenberg tumors of the ovaries: a review of 81 records". *Obstet. Gynecol.*, 1968, 32, 221.
- [14] Chang T.C., Changchien C.C., Tseng C.W., Lai C.H., Tseng C.J. *et al.*: "Retrograde lymphatic spread: A likely route for metastatic ovarian cancers of gastrointestinal origin". *Gynecol. Oncol.*, 1997, 66, 372.

Address reprint requests to:
E. SALAMALEKIS, M.D.
Assoc. Prof. in Obstetrics and Gynecology
Alexandras avenue 108
11472 Athens (Greece)