

# Gastrointestinal system-derived secondary gynecologic tumors: 10 years experience at a single center

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## Abstract

**Aim:** To perform a retrospective review of gynecologic malignancies originating from gastrointestinal system (GIS).

**Material and Methods:** The study included 35 patients who underwent surgery at Gaziantep University, Faculty of Medicine, Department of Gynecology and Obstetrics from January 2007 to December 2017 and were diagnosed with secondary gynecological malignancies originating from GIS. The patients' age, primary tumor, metastatic tumor localization and size were recorded. The malignancies were classified based on origin, as those arising from the colon, appendix, pancreas, stomach, peritoneum, and those of an unknown origin.

**Results:** The mean age of the patients was 50.8 years (min: 24, max: 98) and the mean tumor diameter was 9.8 cm (min: 2 cm, max: 23 cm). Malignancies originating from the colon were most common secondary gynecologic malignancies. The primary tumor was localized at the colon in 21 patients (60%), stomach in eight (22.8%), and in the pancreas in one patient, appendix in one patient, peritoneum in one patient (2.8%). The origin of the primary tumor could not be determined in three patients (8.5%). Of the malignancies originating from the colon (n=21), 16 (76.1%) metastasized to the ovaries, four (19%) to the vagina, one (4.7%) to the cervix, while all tumors originating from the stomach, peritoneum, pancreas, appendix and those derived from the GIS without specific origin metastasized to the ovaries. Of the ovarian metastases, 26 (86.6%) were bilateral while four (13.3%) were unilateral.

**Conclusion:** Female genital system is among the substantial targets of metastasis of GIS-derived tumors. Metastatic tumors have a more aggressive behavior. Metastatic tumors must be distinguished from primary tumors as treatment modalities differ in these tumors. A multidisciplinary approach should be employed in the diagnosis, management and follow-up of cases, and the genital system should be screened carefully during both preoperative assessment and postoperative follow-up in patients with primary GIS malignancies.

**Keywords:** Metastatic Tumor; Gynecologic Tumor; Gastrointestinal System.

## INTRODUCTION

Genital system metastases from extra-genital tumors are rare. The gastrointestinal system (GIS) and the breasts are the most common extra-genital organs metastasizing to the genital system (1). Extra-genital system tumors most commonly metastasize to the ovaries (75.8%) and vagina (13.4%) (1).

Comprising an important subgroup of ovarian neoplasms which cause several problems in diagnosis and management, ovarian metastases are well-known by both clinicians and pathologists. The remaining secondary tumors of the genital system are rarely seen and may readily be overlooked during routine practice (2). The majority of metastatic tumors are carcinomas, particularly

adenocarcinomas, and other tumor types are extremely rare (2). Metastatic tumors of the gynecologic system are seen in younger ages than primary gynecologic tumors and have a more aggressive course. Therefore; diagnosis, treatment and follow-up require great care.

In our study, we aimed to demonstrate the distribution of GIS-derived secondary gynecologic malignancies in a tertiary healthcare hospital and to emphasize the need for a multidisciplinary approach in the treatment and diagnosis of these tumors.

## MATERIAL and METHODS

The study included 35 patients who underwent surgery at Gaziantep University, Faculty of Medicine, Department

**Received:** 14.09.2018 **Accepted:** 08.10.2018 **Available online:** 16.10.2018

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of Gynecology and Obstetrics from January 2007 to December 2017 and were diagnosed with GIS-derived secondary gynecological malignancy in their pathological examination. The study was approved by the Clinical Trials Ethics Committee of Gaziantep University (2018/99).

The patients' age, primary tumor, the localization and size of metastatic tumor were recorded. The malignancies were classified based on origin, as those originating from the colon, appendix, pancreas, stomach, and peritoneum, and those of an unknown origin.

## RESULTS

The mean age of the patients was 50.8 years (min: 24, max: 98) and the mean tumor diameter was 9.8 cm (min: 2 cm, max: 23 cm). Malignancies originating from the colon were most common secondary gynecologic malignancies. The primary tumor was localized at the colon in 21 patients (60%), stomach in eight patients (22.8%), pancreas in one patient, appendix in one patient and peritoneum in one patient (2.8%). The origin of the primary tumor could not be determined in three patients (8.5%) as follow-up was not performed in our hospital for these patients (Table 1).

Primary Tumor	N, %	Secondary Tumor
Colon	21 (60%)	Ovaries 16 (76.1%)
		Vagina 4 (19%)
		Cervix 1 (4.7%)
Stomach	8 (22.8%)	Ovaries
Pancreas	1 (2.8%)	Ovaries
Appendix	1 (2.8%)	Ovaries
Peritoneum	1 (2.8%)	Ovaries
Unknown origin	3 (8.5%)	Ovaries

Of the malignancies originating from the colon (n=21), 16 (76.1%) metastasized to the ovaries, four (19%) to the vagina and one (4.7%) to the cervix, while all tumors originating from the stomach, peritoneum, pancreas, appendix and those derived from the GIS without specific origin metastasized to the ovaries (Table 1). The ovaries were the most common genital organs to which the malignancy metastasized from the GIS (n=30; 85.7%). The vaginal metastasis rate was 11.4% (n=4), whereas the cervical metastasis rate was 2.8% (n=1). No metastasis to the uterus, vulva or fallopian tubes was detected.

Of the ovarian metastases, 26 (86.6%) were bilateral while four (13.3%) were unilateral. The pathological diagnosis was adenocarcinoma in the majority of metastatic tumors (n=27; 77.1%).

## DISCUSSION

The metastasis of extra-genital tumors to the female genital system is rare and has a poor prognosis (1). It is important to distinguish primary tumors from metastatic tumors in order to guide the treatment. The misinterpretation of a metastatic tumor as a primary one may result in inappropriate and incomplete treatment.

The GIS is one of the systems that frequently metastasize to the genital system. In a review by Güngördük et al., it was suggested that approximately half of the metastases in the genital system originate from the GIS. Of the metastases in the genital system, 40% originate from the colon and rectum, whereas 8-10% originate from the stomach and about 5% from the appendix (1). In our study, it was found that 60% of the genital system metastases originated from the colon, whereas 22.8% originated from the stomach and 2.8% from the appendix. We think that the higher percentage of metastases resulted from the smaller number of patients in our study.

In the above-mentioned review, it was reported that the organs most frequently involved in extra-genital metastasis were the ovaries (75.8%), vagina (13.4%), uterus (4.7%), cervix (3.4%), vulva (2.0%), and the fallopian tubes (0.7%). Similarly, in our study, the ovaries were the genital organs which were the most common target of metastasis (n=30; 85.7%). The vaginal metastasis rate was 11.4%, whereas the cervical metastasis rate was 2.8%. No metastasis to the uterus, vulva or fallopian tubes was detected.

Metastatic vulva cancer comprises about 5-8% of all vulva cancers (3). Adenocarcinoma is very rare and is generally manifested in metastatic vulva tumors. Among extra-genital organs, vulvar involvement by metastases most frequently originates from an intestinal adenocarcinoma and the labium majora is the most commonly involved metastasis site (4). However, in our study, no case with vulva metastasis was found among 35 patients. We think that the limited number of patients in our study is the major factor in this result.

Primary vaginal cancer accounts for about 0.3% of female genital system cancers (5). Vaginal metastasis is more frequently seen than primary vaginal tumors and metastatic tumors comprise approximately 75% of all vaginal tumors (6). In our study, the rate of metastatic vaginal tumors was found to be 11.4%.

The cervical metastasis rate of extra-genital organs is approximately 3.4% (7). Similarly, the cervical metastasis rate was found to be 2.8% in our study. The frequency of adenocarcinoma is 0.4-11.7% among the histology of all cervix cancers, while it is 21-56% among metastatic cervix cancers (8,9). In our study, there was one patient with cervical metastasis, whose histology was adenocarcinoma.

The ovaries are a rare target for the metastasis of malignant tumors. Although ovarian carcinomas and GIS carcinomas can be morphologically similar, which may be challenging for differential diagnosis, discriminating between them is crucial due to considerable differences in treatment protocols, metastasis characteristics, response to chemotherapy and prognostic features (10).

The incidence of metastatic ovarian tumors were reported as 4.4% to 29.4% (11). Metastatic ovarian tumors account for 6-7% of all adnexal masses detected in pelvic examination

about 70% of ovarian metastases are bilateral (12). In our study, of the ovarian metastases, 26 (86.6%) were bilateral while four (13.3%) were unilateral. The histopathology of primary ovarian tumor and metastatic ovarian tumor is similar. Therefore distinctions can be difficult (13). Differentiating between primary and metastatic malignant ovarian tumors is important due to the distinct treatment approaches. Ovarian metastasis of extra-genital organs has a poor prognosis. The ovaries are one of the most common metastatic sites for gastrointestinal tumors. In a study including 255 non-genital ovarian metastases, 57% were identified as GIS-derived malignancies (14). Ovarian metastasis may present findings before or at the same time as the primary GIS tumor. Krukenberg tumors are the GIS tumors that most commonly metastasize to the ovaries and comprise 4% of all metastatic ovarian tumors. Although Krukenberg tumors most frequently originate from the stomach, they may also originate from the intestines, appendix, breast, pancreas or the urinary system (12). In our study, 26 (86.6%) of the ovarian metastases were bilateral.

In colon cancer, metastasis to the female genital system is rare and the most common targets of metastasis are the ovaries (71.4%) and the vagina (19.6%) (14). Similarly, in our study, of the tumors originating from the colon, 16 (n=21/35) metastasized to the ovaries and four (19%) metastasized to the vagina. Colorectal cancers comprise about 11-45% of ovarian metastasis (12). In our study, ovarian metastasis had occurred in 30 patients and 16 (53.3%) of these originated from the colon. Approximately 28-35% of colorectal cancers present with ovarian metastasis before the primary cancer (12). The age of onset is younger in metastatic ovarian tumors than primary tumors. This is related to the greater blood supply at younger ages. Therefore, the GIS must be evaluated in case of bilateral ovarian tumors at younger ages.

In cases with unilateral (right) ovarian mass, it should be kept in mind that metastasis may occur from the appendix (15). The ovarian metastasis rate is approximately 59-88% in appendix tumors. Therefore, a right hemicolectomy and bilateral salpingo-oophorectomy is recommended during treatment (12). A bilateral salpingo-oophorectomy should be added to the surgical treatment if not already performed in cases where the pathology is reported as tumor of the appendix. Most appendix tumors metastasizing to the ovaries are of mucinous type. Ovarian tumors are mostly bilateral and large in diameter (16). In our study, ovarian metastasis originating from the appendix was identified in one patient, whose tumors were bilateral and 8 and 9 cm in diameter, respectively. The fact that ovarian and appendix tumors were typically synchronous, that they were histologically the same, that the ovarian tumor was bilateral, and that the right ovary was particularly involved suggests that the tumor spread from the appendix.

## CONCLUSION

A considerable proportion of the metastatic sites of GIS-derived tumors are in the female genital system. Metastatic tumors have a more aggressive behavior. Metastatic tumors must be distinguished from primary tumors as treatment modalities differ in these tumors.

For these reasons, a multidisciplinary approach should be employed in the diagnosis, management and follow-up of cases, and the genital system should be screened carefully during both preoperative assessment and postoperative follow-up in patients with primary GIS malignancies.

*The study was presented as a oral presentation at the 1st Gastrointestinal Research Congress*

*Competing interests: The authors declare that they have no competing interest.*

*Financial Disclosure: There are no financial supports*

*Ethical approval: The study was approved by the Clinical Trials Ethics Committee of Gaziantep University (2018/99).*

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