

# Carcinoma of unknown primary site and ectopic pregnancy diagnosed at laparoscopic surgery: a rare coexistence

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## Summary

The authors present a case of carcinoma of unknown primary site detected accidentally during laparoscopic surgery for ectopic pregnancy. A 36-year-old female patient (para 1, gravida 1) was referred to the present hospital with suspected ectopic pregnancy. Transvaginal ultrasound showed a right adnexal mass and echo-free space in the pelvic cavity. Her serum human chorionic gonadotropin level was 7,590 mIU/ml. The authors made a preoperative diagnosis of ectopic pregnancy and performed laparoscopic surgery. The ampulla of the right fallopian tube was enlarged and showed blood clotting. They noticed a white solid mass of size 1 cm on the peritoneum around the right pelvic ligament. Pathologic examination findings of the specimen were consistent with carcinoma. Immunohistochemical stains suggested high-grade neuroendocrine carcinoma. Routine metastatic workup could not reveal the original site. The final diagnosis was carcinoma of unknown primary site. The authors reviewed other case reports on neoplasms coexisting with ectopic pregnancy.

**Key words:** Ectopic pregnancy; Carcinoma of unknown primary site; Neuroendocrine tumor; Laparoscopic surgery.

## Introduction

Ectopic pregnancy is a common gynecological emergency, occurring in 2% of all pregnancies [1]. Ectopic pregnancy is a benign condition; however, in some cases, a coexisting lesion may be found, including an undetected uterine myoma or ovarian tumor. However, neoplasms coexisting with ectopic pregnancy are rare, especially carcinomas. The present authors encountered a patient with carcinoma of unknown primary site detected during laparoscopic surgery for ectopic pregnancy. They reviewed other case reports of neoplasms coexisting with ectopic pregnancy.



Figure 1. — A white-solid mass of sized 1 cm in the peritoneum around the right pelvic ligament.

## Case Report

A 36-year-old female patient (para 1, gravida 1) was referred to the present hospital with suspected ectopic pregnancy. Her last menstruation was six weeks prior. Her past medical history was non-specific. On examination, her vital signs were within normal limits. Physical examination showed that the abdomen was soft, flat, and not tender. On a bimanual examination, the uterus was normal in size without pain. No mass was palpable. Transvaginal ultrasound revealed a right adnexal mass and echo-free space in the pelvic cavity. Her serum hCG was 7590 mIU/ml, and her hemoglobin was 8.2 g/dL.

The authors made a preoperative diagnosis of ectopic pregnancy and performed laparoscopic surgery. There was a small amount of blood effusion in the pelvic cavity. The ampulla of the

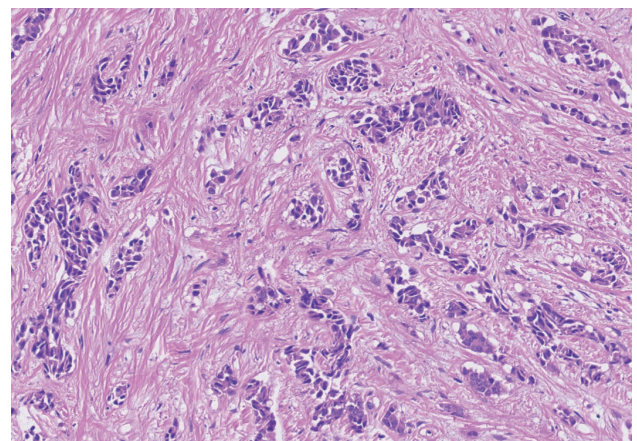


Figure 2. — Tumor composed of nest, and trabeculae with extensive areas of fibrous tissues.

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Table 1. — Cases of ectopic pregnancy and coexisting neoplasms.

Reference	Year	Age	Surgery	Location of neoplasm	Pathology
(carinoma)					
Carapeto <i>et al.</i> [9]	1978		Salpingectomy	Fallopian tube	Tubal carinoma (serous papillary carcinoma)
Jin <i>et al.</i> [8]	2013	35	Salpingectomy	Fallopian tube	Tubal carinoma (serous papillary carcinoma)
Kucukozkan <i>et al.</i> [10]	1992	33	TAH, RSO	From conua to broad ligament and retroperitoneal space	Gestational choriocarcinoma
Rotas <i>et al.</i> [11]	2007	35	Salpingectomy	Cornua of uterus	Gestational choriocarcinoma
Present case		36	Salpingectomy	Peritunium	Carcinoma of unknown primary site
(benigin mass)					
Verras <i>et al.</i> [7]	2007	32	Salpingotomy	Fallopian tube	Extraskelatal chondoroma
Mondal [6]	2010	27	Salpingectomy	Fimbrial end	Adenofibroma

TAH: total abdominal hysterectomy, RSO: right salpingoophrectomy.

right fallopian tube was enlarged and showed blood clotting. Her uterus, left ovary, and left fallopian tube seemed normal. The authors noticed a white solid mass of size 1 cm on the peritoneum around the right pelvic ligament (Figure 1). They performed right salpingectomy and resected the small mass on the peritoneum. The postoperative course was not eventful.

The specimen was sent for pathologic examination, and the diagnosis of the small mass was carcinoma. Microscopically, the tumor was composed of nests and trabeculae with extensive areas of fibrous tissue. The individual cells were small to intermediate in size and had scanty cytoplasm. The nuclei were oval or round, and hyperchromatic with absent or inconspicuous nucleoli (Figure 2). They were stained for CAM 5.2, neuron-specific enolase, synaptophysin, chromogranin A, and AE1:AE3. They were not stained for CK7, CK20, CK903, and vimentin. These pathological examinations suggested well-differentiated neuroendocrine carcinoma. The authors conducted a systemic examination including CT/MRI, upper and lower endoscopy, and PET-CT; however, it did not reveal the original site of the mass. The final diagnosis was carcinoma of unknown primary site. The patient declined to receive adjuvant chemotherapy and was managed as an outpatient.

## Discussion

Carcinoma of unknown primary site is a relatively common disease, accounting for 4–5% of all invasive cancers [2]. From a pathologic viewpoint, carcinoma of unknown primary site can be classified into different types, including adenocarcinoma, squamous cell carcinoma, neuroendocrine carcinoma, and poorly differentiated tumors. The final diagnosis of the present case was neuroendocrine tumor (NET).

NETs are epithelial neoplasms with predominant neuroendocrine differentiation, arising in most regions of the body, mostly in the foregut, midgut, or hindgut. The study of 35,618 cases of NETs during 31 years in the United States Surveillance, Epidemiology, and End Results (SEER) registry showed the clinical aspects of NETs [3]. The primary sites significantly varied according to sex and races. In female patients, the primary site was the lung, stomach, and appendix; in contrast, male patients were more likely to have the tumor in the thymus, duodenum, and pancreas. Among NETs, tumors of unknown primary

site account for 13% in the SEER registry and 10.9% in another study [4]. As multiple organs are involved, a variety of criteria have been developed, including the lungs, thymus, and pancreas. Although several criteria seem be confusing, there are common points of view in classifying NETs: well differentiated (low and intermediate grade) and poorly differentiated (high grade). These differences lead to clinical prospects. Well-differentiated tumors, also termed as low-grade tumors, contain typical carcinoid or islet cell tumors. In contrast, poorly differentiated tumors, or high-grade tumors, contain small-cell carcinoma and large-cell NET in the lung. In the study of 82 cases of NETs of unknown primary site, 69.5% were well-differentiated tumors, 3.7% were poorly differentiated tumors, and the others were not classified [4].

The clinical aspects of NETs of unknown primary site differ between well-differentiated and poorly differentiated cases. Well-differentiated NETs of unknown primary site are often slowly progressive. In the SEER registry, the median survival of NETs of unknown primary site was 124 months. The treatment should be similar to that given for typical carcinoids [5], and can include local therapies, octreotide, and single-agent chemotherapy. In contrast, poorly differentiated NETs of unknown primary site have poor prognosis. The median survival was 10 months in the SEER registry. Aggressive treatment similar to that given for small-cell lung carcinoma, including platinum-based combination chemotherapy, is needed.

Ectopic pregnancy is a common gynecological emergency. In most cases, preoperative examination depends on serum hCG and transvaginal ultrasound, and the medical team makes the decision in performing emergency surgery. Thus, compared with other gynecological surgeries, imaging examination including CT/MRI is lacking. An unsuspected lesion is sometimes found during surgery, such as a uterine myoma or an ovarian tumor.

Ectopic pregnancy with a coexisting neoplasm is rarely found on laparoscopic or pathological evaluations. Nevertheless, there are some case reports on neoplasms associated with ectopic pregnancy (Table 1) [6–11]. In the case of

benign neoplasms, Mondal reported a case of adenofibroma coexisting with ectopic pregnancy [6]. He noticed a firm tumor located at the fimbrial end of the same fallopian tube. Similarly, extraskelatal chondroma was reported by Varras *et al.* [7]. They detected “a whitish mass” within the same fallopian tube during salpingostomy, and pathological evaluation revealed extraskelatal chondroma. Regrading malignant masses, tubal malignancy was reported by two authors [8, 9]. Tong *et al.* did not detect a mass during laparoscopic surgery; however, final pathological examination confirmed tubal carcinoma associated with tubal pregnancy in the same fallopian tube [8]. Two cases of gestational choriocarcinoma were found associated with ectopic pregnancy [10, 11]. Kucukozkan *et al.* detected trophoblast-like tissue extending into the right broad ligament and the retroperitoneal space involving the hypogastric artery during laparotomy for ectopic pregnancy. They performed total hysterectomy and right salpingo-oophorectomy. Pathological examination revealed choriocarcinoma associated with ectopic pregnancy [10]. The present authors performed a computerized MEDLINE search. The search terms chosen were “laparoscopic surgery,” “ectopic pregnancy,” and “carcinoma of unknown primary site.” MeSH terms were also used. No report was found. To their knowledge, this case report is the first to describe a carcinoma of unknown primary site associated with ectopic pregnancy.

At present, laparoscopic surgery is the standard treatment in gynecological surgery. Moreover, laparoscopy for ectopic pregnancy has been frequently performed in clinical situations. As mentioned above, because ectopic pregnancy requires emergency surgery, the preoperative evaluation lacks imaging examinations. It is important for gynecologists to observe the abdominal cavity carefully during laparoscopic surgery, especially in emergency laparoscopy. Furthermore, pathological evaluation of an unsuspected mass is also important.

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