Pancreatic Cancer With Ovarian Metastasis: Clinical Features, Diagnosis and Management

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Abstract

Background: To summarize the clinical features, diagnosis and management of pancreatic cancer with ovarian metastasis.

Methods: We retrospectively analyzed the clinical data of patients with ovarian metastases of primary pancreatic cancer who were admitted to our hospital from 01/01/1985 to 04/01/2020.

Results: In total, there were 3757 female pancreatic-cancer patients. 9 of them were diagnosed with ovarian metastasis at an average age of 51.89 (38-69) years. The reason for the patients' visit was generally a mass in the lower abdomen and/or abdominal pain. 7 patients had significantly higher serum CA19-9 levels. 8 patients had pancreatic tumors located in the body or tail; 1 patient, in the pancreatic head. All patients underwent excision of ovarian tumors and resection or biopsy of pancreatic tumors. 6 patients had pancreatic ductal adenocarcinoma (PDAC), 2 had pancreatic cystadenocarcinoma (PCC), and 1 had pancreatic neuroendocrine carcinoma (PNEC), all revealed by the pathological results. Ovarian tumors were assessed by pathology and were consistent with pancreatic metastasis. Currently, 2 patients are still alive (followed until 04/2020). The median survival time for all patients was 7 months (2.9-22 months).

Conclusions: Pancreatic cancer with ovarian metastases is rare and easily misdiagnosed. When ovarian tumors are suspected to be metastatic, elevated serum CA19-9 may indicate that the primary cancer is pancreatic. Enhanced CT can facilitate diagnostic localization. In addition, if the pancreatic tumor cannot be removed, the ovarian tumor should still be resected to reduce the tumor load and improve quality of life.

1 Background

It is well known that pancreatic cancer is the fourth most common cause of cancer-related death and is an extremely infiltrative neoplasm that usually presents with vascular and perineural invasion[1]. Long-term survival is possible only in patients who present with disease diagnosed at the local stage (accounting for only approximately 20% of cases), and radical resection still represents the only hope for a cure. Pancreatic cancer usually metastasizes through the lymphoid system to areas such as the liver, lung, spleen, bone and other organs[2]. However, ovarian metastases in female patients are exceedingly rare in clinical practice.

Pancreatic cancer that has metastasized to the ovaries is found in 4% to 6% of patients at autopsy but is rarely diagnosed clinically[3-5]. Similar cases have been reported in several retrospective studies of nongenital cancers that have metastasized to the ovaries. Pancreatic cancer was identified as the primary malignancy in 2% to 19% of these patients[6-8]. Such patients with an ovarian metastasis generally have no distinguishing clinical symptoms or signs. Most patients are finally diagnosed with primary pancreatic tumors because of pelvic symptoms when they go to the gynecological clinic. It is easy to miss this diagnosis in clinical work, and the true prevalence of the clinical diagnosis, optimal therapeutic protocol, prognosis and survival rates are still not clear. Therefore, we collected and summarized all of the medical records for pancreatic cancer patients with ovarian metastases who were admitted to our hospital from 01/01/1985 to 04/01/2020 to provide a common education and consultation resource for clinical surgeons and gynecologists.

2 Methods

From 01/01/1985 to 04/01/2020, 3757 female patients with pancreatic cancer were admitted to our hospital. Nine of them had been diagnosed with ovarian metastases in which the primary tumor was pancreatic cancer. We collected disease-relevant information, including clinical symptoms, imaging examination, laboratory tests, tumor features, pathological features, surgery and adjuvant treatments. To date, 2 of these patients have remained alive. All patients were followed until death, and the surviving patients were followed until April 2020.

The respective ethics committees approved the collection of these materials. Written informed consent was obtained from the surviving patients. The cases were retrieved from our consultation files. None of these cases have been reported before.

3 Results

3.1 Clinical characteristics

We summarize the clinical characteristics of these 9 patients in Table 1. All patients were female with an average age of 51.89 (range: 38-69) years at the time of discovery of ovarian metastasis). Among these patients, 8 were found to have pancreatic cancer and ovarian metastasis at the same time; 1 patient was first diagnosed with and treated for pancreatic cancer and developed ovarian metastasis 2 years later.

The reason for the patients' visit was generally a mass in the lower abdomen and/or abdominal pain. There were 5 patients with lower abdominal masses and 6 patients with abdominal pain. The lumps were all self-palpable, and the pain was not severe but was a long-term, moderate pain; it was often only after several weeks of pain that the patients came to the hospital. The first diagnostic department was the gynecology department for Patients 1-8, and the primary malignant tumor of the pancreas was found after the gynecological outpatient or inpatient complete examination. Patient 9 was admitted to the oncology outpatient department and was considered to have pancreatic tumor ovarian metastasis after the completion of the examination.

3.2 Imaging and laboratory tests

The optional auxiliary examination of the abdominal pelvic cavity is generally ultrasound or CT scanning. Five patients underwent CT scanning, and 4 patients underwent color ultrasound of the uterus and ovaries at the first diagnosis. Through these tests, ovarian masses were found and suspected to be malignant. The status of ovarian involvement can be assessed before surgery by CT-scan and ultrasound results. Five patients had bilateral ovarian tumors, 3 had only right ovarian involvement and 1 had only left ovarian involvement. According to the CT scanning or PET/CT results, there was no evidence of metastatic liver

cancer in Patients 1-5, and in Patients 6-9, the results were clearly suggestive of metastatic liver cancer. PET/CT results for Patient 8 suggested retroperitoneal lymph node metastasis at the same time. At the first visit, these patients were also tested for serum CA19-9 indicators at the same time. Patients 1-8, except for Patient 6, were negative, and the rest of the patients had noticeably increased serum CA19-9 to varying degrees. The serum level of CA19-9 was high in Patient 9 when she was first diagnosed with a pancreatic tumor (PNEC) but was normal when she was diagnosed with ovarian metastasis 2 years later.

3.3 Tumor characteristics, treatment and follow-up

Pancreatic tumors of Patient 3 were located in the head of the pancreas, and the rest were located in the pancreatic body or tail. All patients underwent surgical treatment, and unilateral or bilateral ovaries and fallopian tubes were removed. The specific surgical modalities and subsequent treatment are shown in Table 1. Pancreatic tumors in Patients 2-9 were found to be unresectable at the time of diagnosis, so they underwent either aspiration biopsy or intraoperative biopsy. The pathological findings were pancreatic ductal adenocarcinoma (PDAC) in Patients 1-6, pancreatic cystadenocarcinoma (PCC) in Patients 7 and 8, and PNEC in Patient 9. Ovarian tumors in all patients were assessed by pathology and were consistent with pancreatic metastasis. The specific pathological types and immunohistochemistry of the ovarian tumors are detailed in Table 2.

We followed all patients to the status of death, and the overall survival time was defined as the period from the first onset of the disease to death. At present, Patients 5 and 6 are still alive, and both follow-up periods ended on 04/22/2020. The median survival time was 7 months (from the onset of the ovarian tumors to death).

4 Discussion

To our knowledge, ovarian metastases of pancreatic cancer are rare and not widely reported. Ovarian metastases commonly originate from malignant tumors of the colorectum, breast, endometrium, stomach, cervix, appendix, etc. However, pancreatic cancer metastasis to the ovaries is quite rare[3, 9-12]. In fact, pancreatic primary tumors account for an estimated 7% of nongenital ovarian metastases[4, 7]. The great majority of these cases are PDAC, with sporadic case reports of metastatic PNEC[13]. We discovered from the Surveillance, Epidemiology, and End Results (SEER) Database that the rate of female pancreatic cancer metastasis was 39.6% in the liver, 15.4% in the lung, 4.4% in the brain and 7.0% in bone between 2010 and 2016. The SEER database does not contain data on ovarian metastasis in pancreatic cancer; however, among the female pancreatic cancer patients of our hospital, the proportion of ovarian metastasis was only 2.39‰ (9/3757). Most were PDAC patients (6/9), and the others were PCC (2/9) and PNEC (1/9) patients.

Pancreatic cancer that first presents as ovarian metastases is extremely difficult to diagnose. Most of these patients were diagnosed as having ovarian neoplasms evidenced by inferior abdominal symptoms and ultrasound/CT examination results. Patients with ovarian metastatic tumors usually complain of abdominal or pelvic pain and abdominal distension (possibly due to ascites). In other cases, ovarian metastases can also manifest as affecting the menstrual cycle or causing vaginal bleeding, even in postmenopausal women[14-16]. Patients in our study were also treated for lower abdominal pain or lumps, with the vast majority diagnosed at gynecological clinics. Among these cases, the vast majority (8/9) of pancreatic tumors were located in the body or tail of the pancreas. Because tumors in the pancreatic body and tail often have difficulty triggering specific clinical symptoms, they are difficult to detect in the early stage. In contrast, pelvic masses make it easier for patients to identify signs and symptoms of compression, discomfort, pain, and a palpable lower abdominal mass.

At the time of the patients' first visit, pelvic CT scanning or ultrasound of the uterus and ovaries may be performed. Pelvic enhanced CT may reveal ovarian masses that are characterized by an uneven and slightly low density, uneven edges, and uneven enhancement (Fig 1). However, CT and ultrasound can often help to locate ovarian lesions but may not accurately identify the nature of ovarian tumors. If the inspection is more comprehensive, there may be additional findings. Most of the time, abdominal enhancement CT can identify pancreatic tumors, which generally exhibit low densities, uneven edges, and an unclear mass shadow in the pancreas (Fig 2). However, in clinical work, some pancreatic surgeons and gynecologists only focus on pancreatic tumors or ovarian neoplasms, respectively, without the benefit of whole abdomen and pelvic enhancement CT, resulting in a missed diagnosis. Theoretically, PET-CT is still the best method to identify metastatic lesions. However, it is still expensive and not routinely performed before surgery. Regarding tumor markers, the sensitive indicator for ovarian tumors is serum CA125, and for pancreatic tumors, it is serum CA19-9. Elevated serum CA19-9 is also a common phenomenon in these patients. This is worthy of the attention of more gynecologists, so that when they endeavor to identify the origin of ovarian tumors, they will also simultaneously screen for digestive tract-related serum tumor markers, especially CA19-9.

The main treatment for pancreatic cancer with ovarian metastases is surgery as soon as possible, with the goal of complete resection. Even if the primary pancreatic cancer is unresectable, resection of the ovarian metastasis is still necessary, as this can not only effectively relieve the clinical symptoms of the patient but also prolong the survival time[17-20]. The median survival time of patients with metastatic ovarian tumors is generally closely related to the primary site of the tumor; in addition, the median survival time is also related to the timing of the diagnosis, whether surgical resection of the metastatic lesions is performed, and other factors[11, 21-25]. All of the patients in our study had their ovarian metastases resected. The median survival of these patients with ovarian metastases was 7 months, suggesting that patients with ovarian metastases did have a poor prognosis.

In some cases of this study, ovarian metastases were revealed to be mucinous tumors. For some pathologists, cases are misdiagnosed as primary ovarian mucinous carcinomas because pancreatic adenocarcinoma can produce large metastatic multicystic ovarian tumors that appear similar to primary ovarian mucinous neoplasms[3]. Ovarian metastases are characterized by multiple cysts containing mucoid material and an external surface lobulated with small gray to pale yellow nodules. Upon microscopic examination, the neoplasms strikingly resemble primary cystic mucinous tumors (Fig 3). They are composed predominantly of mucinous cysts that are usually large and dilated. The stroma between the cysts contains compact aggregates of glands and single glands. An infiltrative pattern with destructive stromal invasion is typically not prominent. Usually, fewer than 3% of primary ovarian carcinomas are mucinous, and most of them are unilateral and at stage I at diagnosis. Therefore, mucinous carcinoma of the ovary may suggest the presence of a nonovarian primary tumor[26, 27]. In addition to morphological characteristics, immunohistochemical markers may be helpful in distinguishing between primary and metastatic

neoplasms of the ovaries[28-31]. Currently, the most commonly used immunohistochemical tumor markers in diagnosing metastatic ovarian tumors are CK20 and CK7[32]. CEA and CA125 may also be routinely examined by the pathology department, but these two markers do not seem to distinguish between primary ovarian and metastatic tumor[33-36].

At present, the mechanism by which pancreatic cancer metastasizes to the ovary remains controversial. Some clinicians consider the metastatic path of pancreatic cancer to the ovary to resemble that of Krukenberg tumors, and the possible sources of ovarian metastases are peritoneal spread, lymphatic spread and hematogenous diffusion[37-42]. The pancreas is a peritoneal interpositional organ. When pancreatic cancer is located in the pancreatic body or tail, the most common lymphatic metastatic pathway is hilar or splenic lymph node metastasis, and the liver tops the list of distant metastatic organs of pancreatic cancer. In addition, by local infiltration, cancer cells may also enter the lymphatic reflux system of the posterior peritoneum. In this study, we found that 5 patients had no evidence of liver metastases when ovarian metastasis was found. Multiple miliary nodules located in the posterior peritoneum were also found during the operation (Fig 4). This suggested that pancreatic cancer cells may have undergone retrograde migration. Pancreatic cancer tissue can mechanically block the lymphatic vessels of the posterior peritoneum; therefore, diffuse pancreatic cancer cells can migrate along this pathway to para-aortic and pelvic lymph nodes, eventually forming an ovarian metastasis. Furthermore, pancreatic cancer spreading to the ovaries usually results in bilateral ovarian metastases, and intraductal cancer emboli are commonly seen in lymphatic vessels by microscopy[43, 44].

Tables

Table 1

Clinical characteristics, treatment methods and follow-up of all 9 patients.

Case No	Age	Abdominal Symptom		Examination at first-time diagnose		CA19-9 (U/ml)	Location of the tumor	Liver metastases	Pathology (Pancreas)	Operation	Adjuvant treatment	Outcor
		mass	pain	CT	Echo							
Pancreatic cancer and ovarian tumor found simultaneously												
1	48	√		√		886	Pancreatictail Left ovary	No	PDAC	Resection of pancreatic body and tail with spleen, appendix; Resection of omentum majus, bilateral accessories, uterus	none	Die
2	43	√	√		√	213.4	Pancreatic tail Bilateralovaries	No	PDAC	Biopsy of pancreatic tumor; Resection of ovarian tumors	chemotherapy	Die
3	58	√			√	63	Pancreatic head Bilateral ovaries	No	PDAC	Biopsy of pancreatic tumor; Resection of bilateral accessories	chemotherapy	Die
4	46		√	√		91	Pancreatic body Bilateralovaries	No	PDAC	Biopsy of pancreatic tumor; Resection of bilateral accessories	none	Die
5	69		√		√	49	Pancreatic tail Right ovary	No	PDAC	Biopsy of pancreatic tumor; Resection of bilateral accessories	chemotherapy radiotherapy	Alive
6	66		√	√		10.9	Pancreatic body Right ovary	Yes	PDAC	Biopsy of pancreatic tumor; Resection ofuterus, bilateral accessories, omentum, appendix	none	Alive
7	38	√			√	3775	Pancreatic tail Bilateralovaries	Yes	PCC	Biopsy of pancreatic tumor; Resection of bilateral accessories	chemotherapy	Die
8	46	√	√	√		12708	Pancreaticbodyandtail Right ovary	Yes	PCC	Biopsy of pancreatic tumor; Resection of rightaccessory	chemotherapy	Die
Pancreatic cancer found firstly												
9	51 53		√	√		266 27.3	Pancreatic body and tail	Yes	PNEC	Biopsy of pancreatic	chemotherapy	Die

	Bilateral ovaries	and liver tumor Resection of bilateral accessories

Table 2
Pathological and immunohistochemical features of ovarian tumors in 9 patients.

Case No	Pathology of ovarian tumors	Grade	CDX2	CK20	CK7	CEA	ER	PR	p53	P16	PAX-8	WT-1	Ki67
1	Metastatic mucinous adenocarcinoma	G2	+	+	+	+	-	-	-				40%
2	Metastatic mucinous adenocarcinoma	G1	+	-	+		-	-	+	-	-	-	20%
3	Metastatic adenocarcinoma	G3		+	-	+	-	-	-				30%
4	Metastatic adenocarcinoma	G1		+	+	+	-	-	-	partial+	-	-	30%
5	Metastatic adenocarcinoma	G2	+	-	partial+		-	-			-		10%
6	Metastatic adenocarcinoma	G2	-	-	+		-	-	-	-	-	-	20%
7	Metastatic mucinous adenocarcinoma	G2	+	+	+	+	-	-	+	-		-	60%
8	Metastatic mucinous adenocarcinoma	G2	-	-	-		-	-	-	-			5%
9	Metastatic pancreatic neuroendocrine tumor	G3	+	+	-	+	-	-	-	-	+		40%

5 Conclusions:

In conclusion, the probability of ovarian metastasis from pancreatic cancer is small; the condition is rare in clinical practice and is difficult to diagnosis early. Most patients develop lower abdominal symptoms at the later stage of the disease. On the basis of our study, we suggest that at the time of discovering ovarian tumors and suspected metastasis, doctors should be more active in screening abdominal and pelvic enhancement CT scans and evaluating serum CA19-9. Additionally, we believe that even if the pancreatic cancer is already unresectable, the ovarian tumors should still be excised, thereby reducing the tumor load and improving quality of life in patients.

6 Abbreviations:

PDAC pancreatic ductal adenocarcinoma

PCC pancreatic cystadenocarcinoma

PNEC pancreatic neuroendocrine carcinoma

SEER Surveillance, Epidemiology, and End Results Database

Declarations:

Ethics approval and consent to participate: This clinical study is a retrospective study. Only the patient's clinical data are collected, and no intervention in the patient's treatment plan will bring no risk to the patient's physiology. Ethics Committee of Peking Union Medical College Hospital allowed us to have this retrospective study.

Consent for publication: We confirm that this work is original and has not been presented or published elsewhere, nor is it currently under consideration for publication elsewhere.

Availability of data and material: The datasets used or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors of this article have no conflict of interest.

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Authors' contributions: WB.W and C.Q contributed to the conception of the study; HT.C and BB.Z contributed significantly to manuscript preparation; ZB.Z, XT.Z, and TH.L performed the data analyses and wrote the manuscript; XD.L helped perform the analysis with constructive discussions. All authors have read and approved the manuscript.

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Reference:

1. Siegel, R.L., K.D. Miller, and A. Jemal, *Cancer statistics, 2019.* CA Cancer J Clin, 2019. **69**(1): p. 7-34.
2. Maitra, A. and R.H. Hruban, *Pancreatic cancer.* Annu Rev Pathol, 2008. **3**: p. 157-88.
3. Hart, W.R., *Diagnostic challenge of secondary (metastatic) ovarian tumors simulating primary endometrioid and mucinous neoplasms.* Pathol Int, 2005. **55**(5): p. 231-43.
4. Young, R.H. and W.R. Hart, *Metastases from carcinomas of the pancreas simulating primary mucinous tumors of the ovary. A report of seven cases.* Am J Surg Pathol, 1989. **13**(9): p. 748-56.
5. Niwa, K., et al., *A case of double cancer (pancreatic and ovarian adenocarcinomas) diagnosed by exfoliative and fine needle aspiration cytology.* Jpn J Clin Oncol, 1988. **18**(2): p. 167-73.
6. Fujiwara, K., et al., *Clinical implications of metastases to the ovary.* Gynecol Oncol, 1995. **59**(1): p. 124-8.
7. Moore, R.G., et al., *Incidence of metastasis to the ovaries from nongenital tract primary tumors.* Gynecol Oncol, 2004. **93**(1): p. 87-91.
8. Yazigi, R. and J. Sandstad, *Ovarian involvement in extragenital cancer.* Gynecol Oncol, 1989. **34**(1): p. 84-7.
9. Baker, P.M. and E. Oliva, *Immunohistochemistry as a tool in the differential diagnosis of ovarian tumors: an update.* Int J Gynecol Pathol, 2005. **24**(1): p. 39-55.
10. Shi, Y., et al., *[Histological classification in 10 288 cases of ovarian malignant tumors in China].* Zhonghua Fu Chan Ke Za Zhi, 2002. **37**(2): p. 97-100.
11. Ayhan, A., et al., *The role of cytoreductive surgery in nongenital cancers metastatic to the ovaries.* Gynecol Oncol, 2005. **98**(2): p. 235-41.
12. Vakiani, E., et al., *Acinar cell carcinoma of the pancreas metastatic to the ovary: a report of 4 cases.* Am J Surg Pathol, 2008. **32**(10): p. 1540-5.
13. Petru, E., et al., *Nongenital cancers metastatic to the ovary.* Gynecol Oncol, 1992. **44**(1): p. 83-6.
14. Kiyokawa, T., R.H. Young, and R.E. Scully, *Krukenberg tumors of the ovary: a clinicopathologic analysis of 120 cases with emphasis on their variable pathologic manifestations.* Am J Surg Pathol, 2006. **30**(3): p. 277-99.
15. de Waal, Y.R., et al., *Secondary ovarian malignancies: frequency, origin, and characteristics.* Int J Gynecol Cancer, 2009. **19**(7): p. 1160-5.
16. Young, R.H., *Ovarian tumors and tumor-like lesions in the first three decades.* Semin Diagn Pathol, 2014. **31**(5): p. 382-426.
17. Ganesh, K., et al., *Clinical and genetic determinants of ovarian metastases from colorectal cancer.* Cancer, 2017. **123**(7): p. 1134-1143.
18. Xu, K.Y., et al., *Clinical analysis of Krukenberg tumours in patients with colorectal cancer-a review of 57 cases.* World J Surg Oncol, 2017. **15**(1): p. 25.
19. Fujiwara, A., et al., *Significance of the resection of ovarian metastasis from colorectal cancers.* J Surg Oncol, 2010. **102**(6): p. 582-7.
20. Falchook, G.S., R.A. Wolff, and G.R. Varadhachary, *Clinicopathologic features and treatment strategies for patients with pancreatic adenocarcinoma and ovarian metastases.* Gynecol Oncol, 2008. **108**(3): p. 515-9.
21. Kim, W.Y., et al., *The role of cytoreductive surgery for non-genital tract metastatic tumors to the ovaries.* Eur J Obstet Gynecol Reprod Biol, 2010. **149**(1): p. 97-101.
22. Jeung, Y.J., et al., *Krukenberg tumors of gastric origin versus colorectal origin.* Obstet Gynecol Sci, 2015. **58**(1): p. 32-9.
23. Jiang, R., et al., *Surgical treatment for patients with different origins of Krukenberg tumors: outcomes and prognostic factors.* Eur J Surg Oncol, 2009. **35**(1): p. 92-7.
24. Kim, H.K., et al., *Prognostic factors of Krukenberg's tumor.* Gynecol Oncol, 2001. **82**(1): p. 105-9.
25. Gagnon, Y. and B. Têtu, *Ovarian metastases of breast carcinoma. A clinicopathologic study of 59 cases.* Cancer, 1989. **64**(4): p. 892-8.
26. McCluggage, W.G. and N. Wilkinson, *Metastatic neoplasms involving the ovary: a review with an emphasis on morphological and immunohistochemical features.* Histopathology, 2005. **47**(3): p. 231-47.
27. Seidman, J.D., et al., *The histologic type and stage distribution of ovarian carcinomas of surface epithelial origin.* Int J Gynecol Pathol, 2004. **23**(1): p. 41-4.
28. Lee, K.R. and R.H. Young, *The distinction between primary and metastatic mucinous carcinomas of the ovary: gross and histologic findings in 50 cases.* Am J Surg Pathol, 2003. **27**(3): p. 281-92.
29. Vang, R., et al., *Immunohistochemistry for estrogen and progesterone receptors in the distinction of primary and metastatic mucinous tumors in the ovary: an analysis of 124 cases.* Mod Pathol, 2006. **19**(1): p. 97-105.

30. Dionigi, A., et al., *Ovarian metastases from colorectal carcinoma. Clinicopathologic profile, immunophenotype, and karyotype analysis.* Am J Clin Pathol, 2000. **114**(1): p. 111-22.
31. Goldstein, N.S., D. Bassi, and A. Uzieblo, *WT1 is an integral component of an antibody panel to distinguish pancreaticobiliary and some ovarian epithelial neoplasms.* Am J Clin Pathol, 2001. **116**(2): p. 246-52.
32. Kondi-Pafiti, A., et al., *Carcinosarcomas of the uterus and ovary: a clinicopathologic and immunohistochemical study of 11 cases.* Eur J Gynaecol Oncol, 2009. **30**(1): p. 93-7.
33. Young, R.H. and W.R. Hart, *Metastatic intestinal carcinomas simulating primary ovarian clear cell carcinoma and secretory endometrioid carcinoma: a clinicopathologic and immunohistochemical study of five cases.* Am J Surg Pathol, 1998. **22**(7): p. 805-15.
34. Lagendijk, J.H., et al., *Tracing the origin of adenocarcinomas with unknown primary using immunohistochemistry: differential diagnosis between colonic and ovarian carcinomas as primary sites.* Hum Pathol, 1998. **29**(5): p. 491-7.
35. Lagendijk, J.H., et al., *Immunohistochemical differentiation between primary adenocarcinomas of the ovary and ovarian metastases of colonic and breast origin. Comparison between a statistical and an intuitive approach.* J Clin Pathol, 1999. **52**(4): p. 283-90.
36. Antila, R., J. Jalkanen, and O. Heikinheimo, *Comparison of secondary and primary ovarian malignancies reveals differences in their pre- and perioperative characteristics.* Gynecol Oncol, 2006. **101**(1): p. 97-101.
37. Miller, B.E., et al., *Colon cancer with metastasis to the ovary at time of initial diagnosis.* Gynecol Oncol, 1997. **66**(3): p. 368-71.
38. Pernot, S., et al., *Signet-ring cell carcinoma of the stomach: Impact on prognosis and specific therapeutic challenge.* World J Gastroenterol, 2015. **21**(40): p. 11428-38.
39. Gore, R.M., et al., *Pathways of abdominal tumour spread: the role of the subperitoneal space.* Cancer Imaging, 2009. **9**(1): p. 112-20.
40. Al-Agha, O.M. and A.D. Nicastri, *An in-depth look at Krukenberg tumor: an overview.* Arch Pathol Lab Med, 2006. **130**(11): p. 1725-30.
41. Takenoue, T., et al., *Krukenberg tumor from gastric mucosal carcinoma without lymphatic or venous invasion: report of a case.* Hepatogastroenterology, 2001. **48**(40): p. 1211-4.
42. Young, R.H., *From Krukenberg to today: the ever present problems posed by metastatic tumors in the ovary. Part II.* Adv Anat Pathol, 2007. **14**(3): p. 149-77.
43. Shiomi, M., et al., *Two cases of histopathologically advanced (stage IV) early gastric cancers.* Tumori, 2001. **87**(3): p. 191-5.
44. Jain, V., et al., *A case of ovarian metastasis of gall bladder carcinoma simulating primary ovarian neoplasm: diagnostic pitfalls and review of literature.* Int J Gynecol Cancer, 2006. **16 Suppl 1**: p. 319-21.

Figures

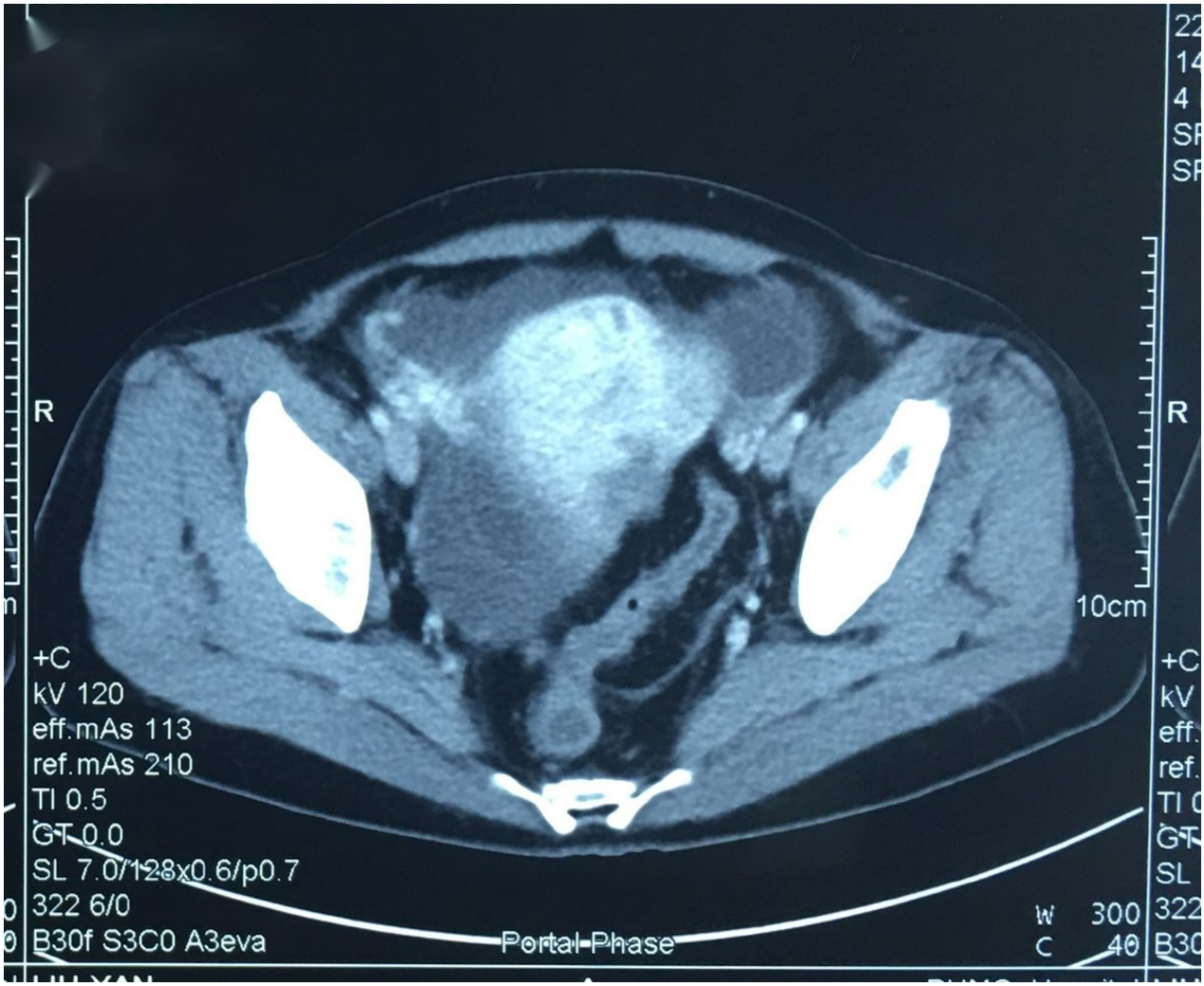

Figure 1

Pelvic enhanced CT showed two masses in the bilateral ovaries, with uneven and slightly low density, uneven edges, and uneven enhancement; the largest sections measured 12.2 x 9.7 cm and 4.9 x 4.4 cm, respectively.

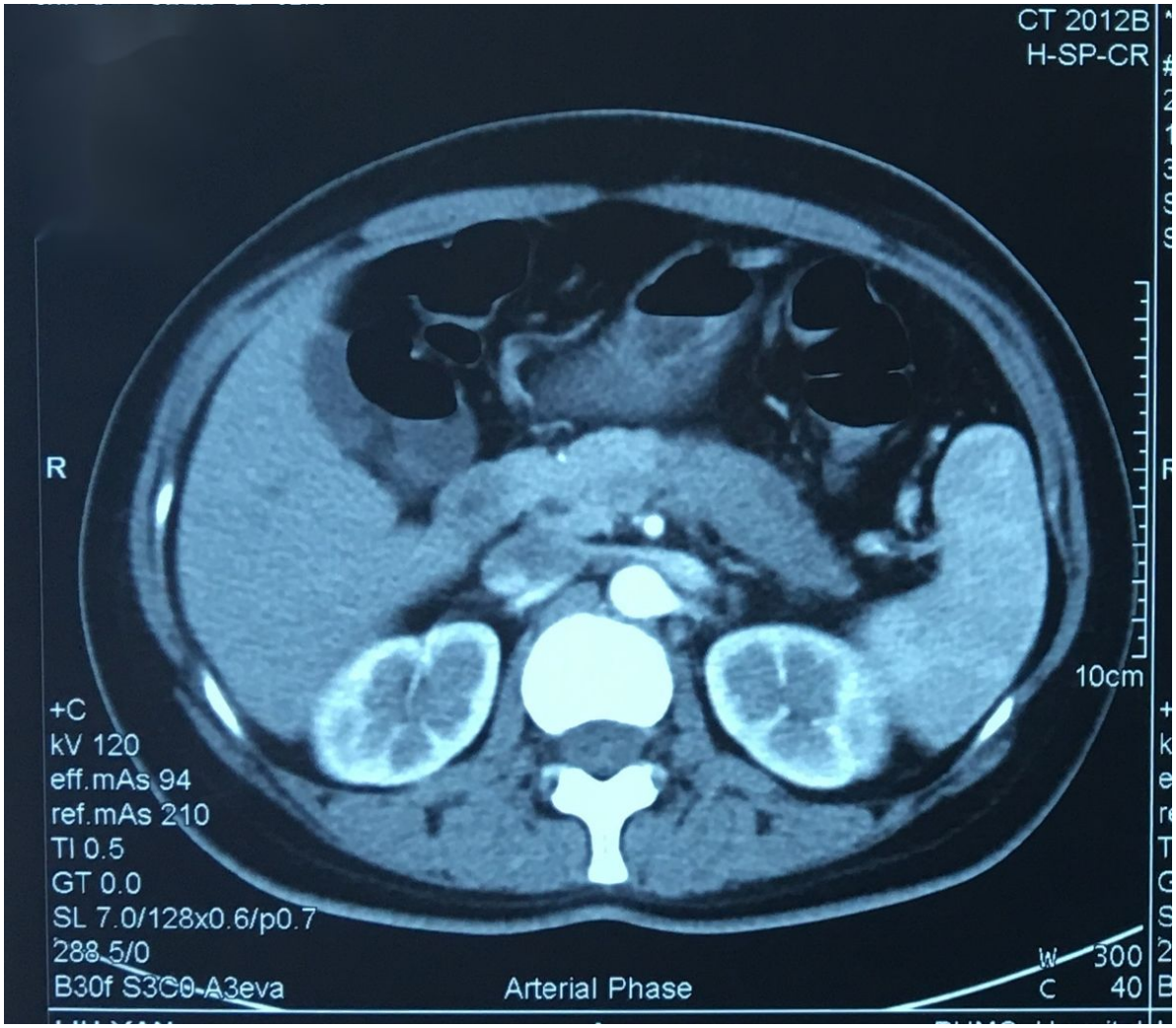

Figure 2

Abdominal enhanced CT showed a low-density mass, which had uneven edges, in the pancreatic body and tail, and the largest cross section was 4.1 x 2.3 cm.

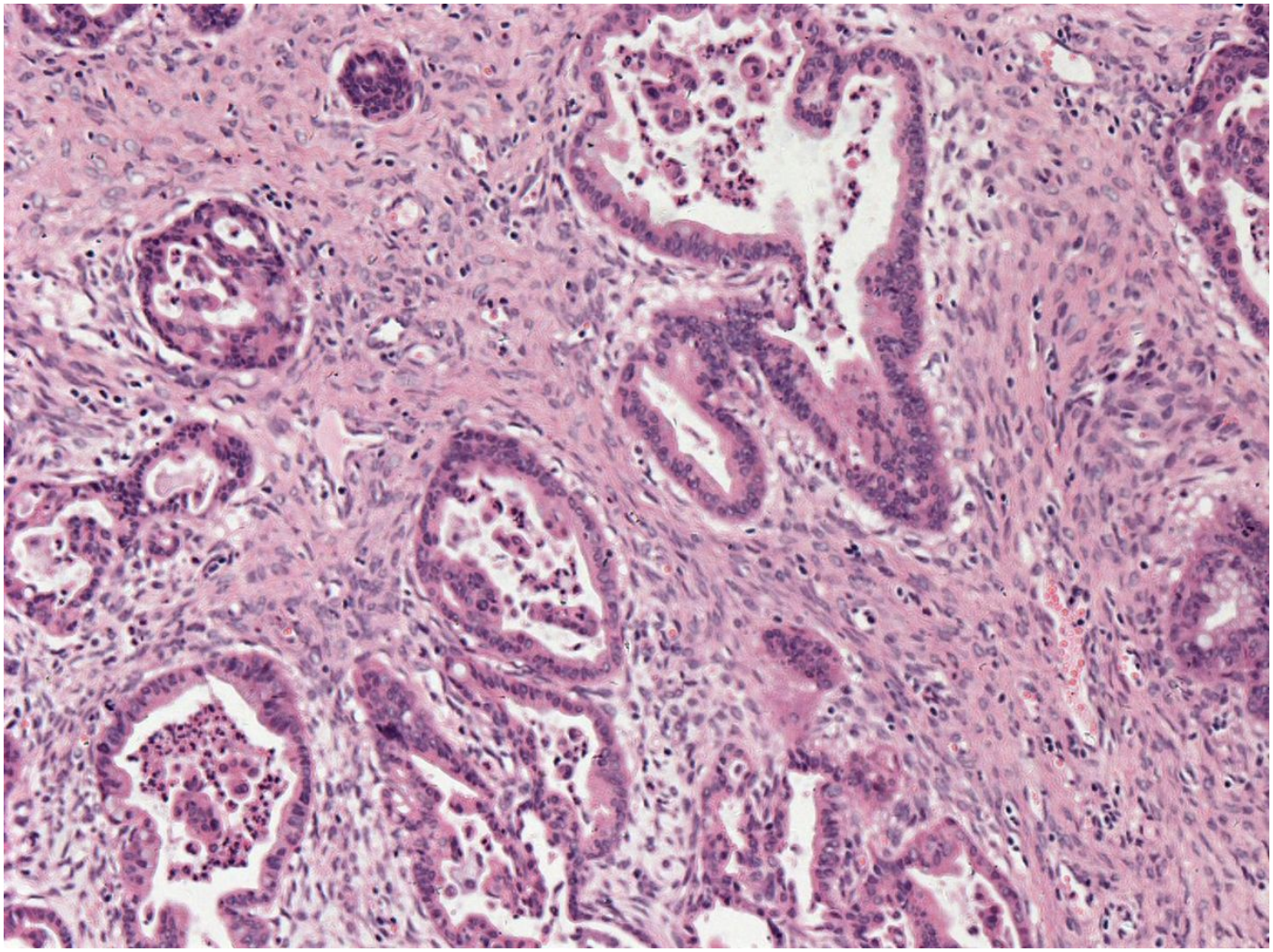

Figure 3

Hematoxylin-eosin staining of the metastatic ovarian tumors.

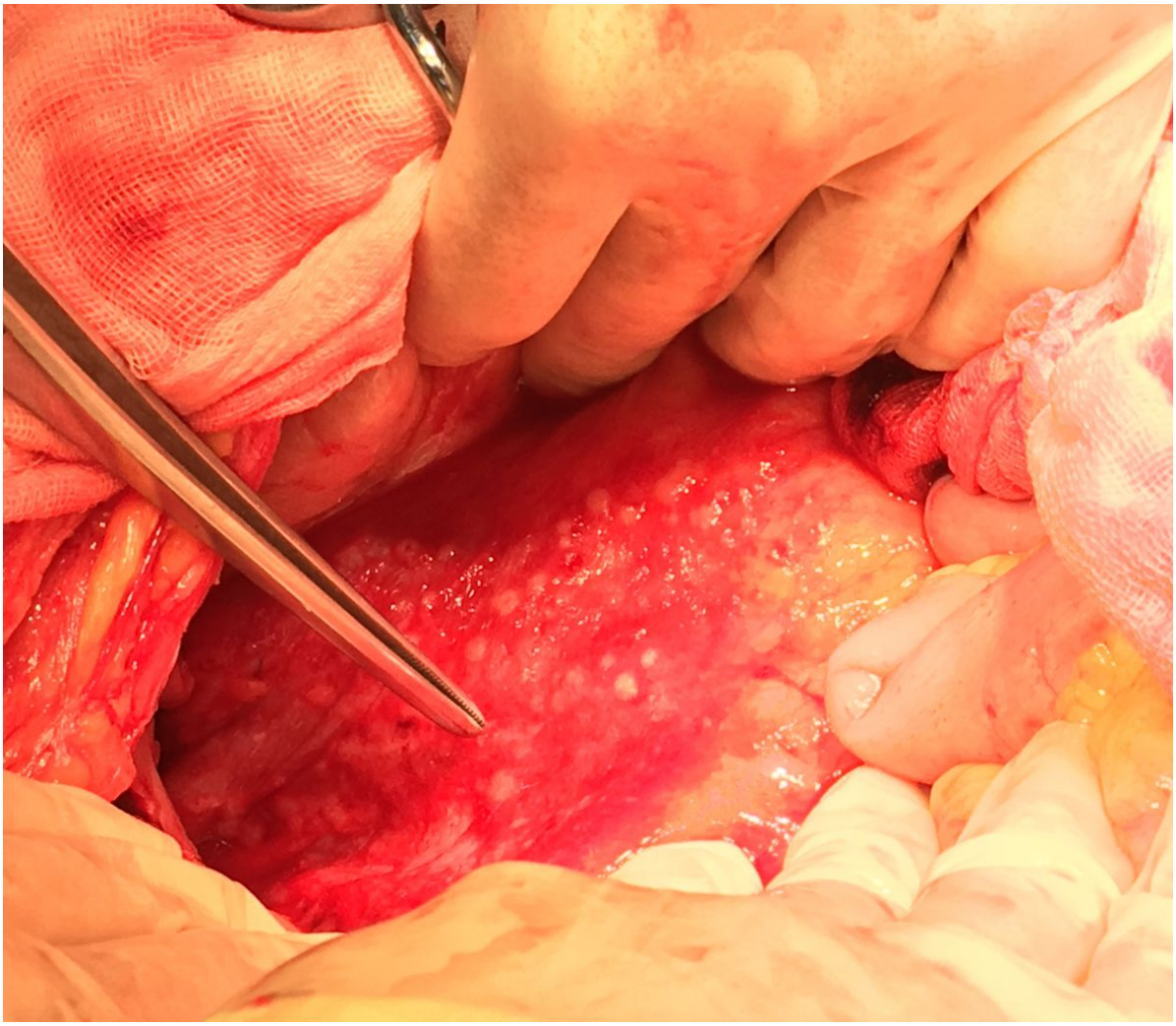

Figure 4

During the operation, many scattered metastatic nodules were observed to be present on the patient's peritoneum (indicated by forceps), and the size of these nodules ranged from 3-5 mm.