

Normal-sized ovarian papillary serous carcinoma: a case report

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Summary

A normal-sized ovarian papillary serous carcinoma is rare. We present the case of a 46-year-old woman with progressive abdominal fullness of one week's duration. The medical evaluation revealed abdominal carcinomatosis with normal-sized ovaries and an elevated serum CA-125 level of 147,365.8 U/ml. Cytoreductive surgery (hysterectomy, bilateral salpingo-oophorectomy, omentectomy, lymphadenectomy, infracolic omentectomy, peritoneal biopsy, washing cytology, and appendectomy) was performed. The histologic examination revealed an ovarian serous papillary carcinoma. Adjuvant chemotherapy was administered. The serum CA-125 level decreased after completion of treatment. Normal-sized ovarian serous surface papillary carcinomas should be kept in mind as an origin of disease in patients who have peritoneal carcinomatosis, which sometimes is a diagnostic dilemma of the disease source. We report this case to emphasize the clinical symptoms and importance of the early and accurate diagnosis of a normal-sized ovarian papillary serous carcinoma.

Key words: Papillary serous carcinoma; Normal sized ovary; Primary ovarian carcinoma.

Introduction

Epithelial ovarian carcinoma is the most lethal gynecologic cancer among women, and accounts for 4% of all malignant tumors in Western countries [1]. In Taiwan, an estimated 600 new cases of epithelial ovarian carcinoma are diagnosed annually, and approximately 350 women will die from the disease [2]. The high mortality rate of epithelial ovarian carcinoma may be partly explained by the difficulty in early diagnosis and the lack of a reliable screening test. The common presentation of epithelial ovarian carcinomas includes an enlarged ovarian tumor and ascites. However, an ovarian carcinoma which presents with a massive amount of ascites without ovarian enlargement is rarely encountered.

In 1989 Feuer [3] first introduced the concept of normal-sized ovarian carcinoma syndrome. A clinical situation occasionally presents in which diffuse metastatic disease of the peritoneal cavity is noted, but the ovaries are of normal size, with or without a fine granularity on the external surface. Normal-sized ovarian carcinoma syndrome has been subdivided into the following categories: mesotheliomas, primary peritoneal carcinoma (PPC), metastatic tumor from another primary origin, and primary ovarian carcinoma.

Among the different subtypes, PPC should be considered first in female patients [4, 5]. Primary epithelial ovarian cancer should be considered next among the differential diagnoses in normal-sized ovarian carcinoma syndrome [5]. Primary epithelial ovarian carcinoma of normal-sized ovary syndrome is a rare neoplasm and is characterized histologically by an exophytic papillary tumor originating from the surface epithelium. Those

patients with primary epithelial ovarian cancers and ovaries of normal size may receive a late diagnosis due to the absence of enlarged ovaries and the resulting poor prognosis. In addition, the biological behavior of normal-sized ovary syndrome might be different from common epithelial ovarian cancer with ovarian enlargement.

We present a case of a papillary serous carcinoma in an ovary of normal size with peritoneal cavity spread in a 46-year-old Taiwanese woman.

Case Report

A 46-year-old gravida 1, para 1, presented with progressive abdominal fullness of one week's duration. The physical examination revealed abdominal distension and shifting dullness; no palpable mass was noted. A bimanual vaginal examination revealed a normal uterus without any adnexal enlargement. Ultrasonography (US) revealed massive ascites and both ovaries were confirmed to be of normal size (Figure 1). Computed tomography (CT) indicated massive ascites with an omental caking (Figure 2). The serum CA-125 value was 147,365.8 U/ml (normal level, < 35 U/ml). The other laboratory tests were normal. On the basis of the clinical examination findings, there was no suspicion of a primary malignancy, such as gastric, pancreatic tail, colon, or chest. An exploratory laparotomy was performed and grossly revealed gray-tan irregular nodules with involvement of the right ovarian surface. Additionally, massive ascites and omental caking were noted. The histopathologic examination of a frozen section showed serous papillary carcinoma of the ovary. The left ovary appeared normal.

Cytoreductive surgery, including a total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, and appendectomy was performed. In addition, pelvic and paraaortic lymphadenectomy and biopsy of the peritoneum were performed. The final histopathologic examination revealed serous papillary carcinoma of the ovary and extra-ovarian metastasis. The final diagnosis was Stage IIIC ovarian serous papillary adenocarcinoma.

Revised manuscript accepted for publication February 25, 2010

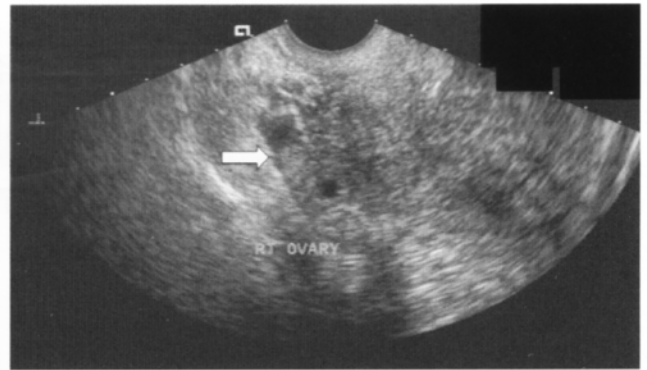
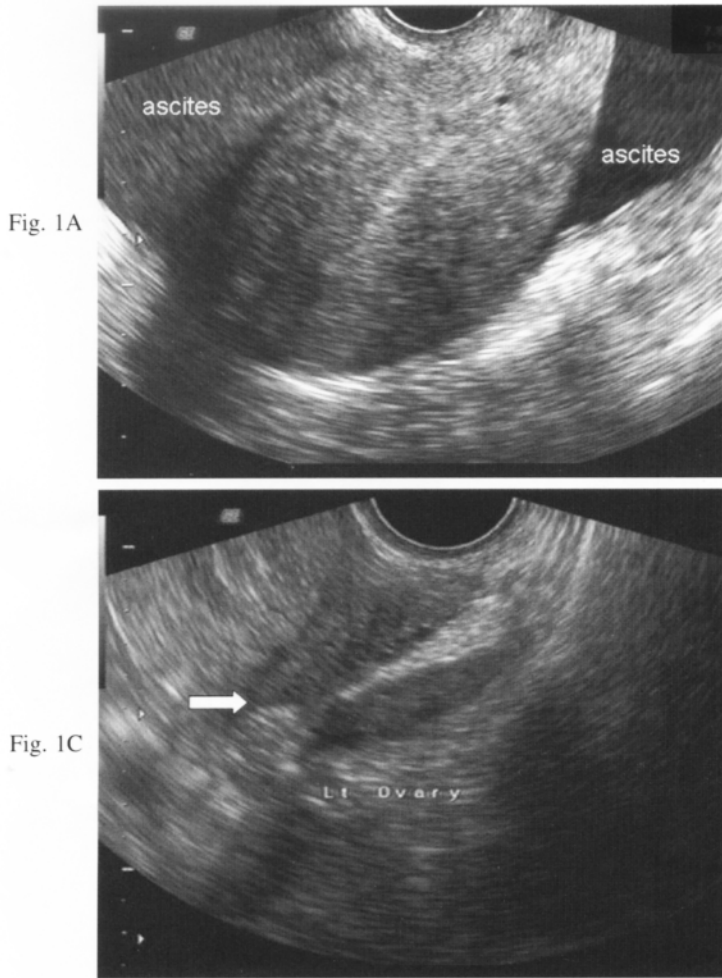


Fig. 1B



Fig. 2

Figure 1. — Pelvic ultrasonography. A) Massive ascites. B) Right ovary (arrow) is confirmed to be of normal size. C) Left ovary (arrow) is confirmed to be of normal size. Figure 2. — Computed tomography of the lower abdomen. Large omental caking, infiltration (arrow), and massive ascites.

The patient received adjuvant chemotherapy consisting of carboplatin (area under the concentration curve = 5) and taxol (175 mg/m²). The serum CA-125 level decreased after completion of treatment.

Discussion

Epithelial ovarian carcinomas are believed to originate from the surface epithelium covering the ovary. The most common symptoms of epithelial ovarian carcinomas include abdominal distention and pain. Some patients are asymptomatic. Therefore, the most common presentation is a large ovarian mass at the time of diagnosis. However, normal-sized ovarian carcinomas with disseminated peritoneal spread are rare and this primary epithelial ovarian cancer has been classified as a normal-sized ovarian carcinoma syndrome.

In our case, the tumor was histologically identical to serous papillary carcinomas originating from the surface epithelium of normal-sized ovaries. Embryologically, serous surface papillary carcinoma of the ovary is assumed to originate from the ovarian epithelium and the peritoneal mesoderm that potentially could become Mullerian ducts or from the malignant degeneration of

nests of ovarian tissue remnants in the peritoneum [6]. Serous surface papillary carcinoma of the ovary is a rare neoplasm found in women that is characterized histologically by an exophytic papillary tumor originating from the surface epithelium of the ovary. The characteristic growth pattern of this carcinoma of the ovary is characterized by peritoneal seeding; with only surface involvement of the ovaries, both ovaries are likely to be of normal size [7-9]. However, the clinical presentation and histologic appearance of this disease are quite similar to other malignant ovarian neoplasms and it has a great tendency to spread externally [10].

The peak incidence of epithelial ovarian carcinoma is 50-60 years of age. A previous study reported that the mean age of patients with PPC was 64 years (range, 56-69 years), and the median age of patients with ovarian serous carcinoma was 52 years [5]. Additionally, ovarian cancer has been associated with nulliparas, low parity, and infertility. A reduction in risk by as much as 40%-60% among multiparas has been reported consistently [11, 12]. However, Choi *et al.* [5] described all the patients in both groups (PPC and papillary serous carcinoma in ovaries of normal size) to be multiparas [5].

Serum CA-125 level is useful in distinguishing benign from malignant adnexal masses, following the response to treatment of ovarian cancer, and monitoring tumor recurrence. In one report, when the serum CA-125 level was > 1000 U/ml, 89% of patients had gynecologic cancer, 7% had non-gynecologic cancers, and 3% had benign conditions [13]. In a case series report, the serum CA-125 level was reported to be elevated in all patients with normal-sized ovarian papillary serous carcinoma; moreover, in most patients, the level was > 200 U/ml [14]. We believe that a highly elevated serum CA-125 level is a critical indicator that suggests the possibility of serous surface papillary carcinoma of the ovary. Therefore, CA-125 levels are useful for estimating the response of cytoreductive surgery or chemotherapy and monitoring tumor recurrence.

Several reports have described the most characteristic CT features of serous surface papillary carcinomas of the ovary as mesenteric or omental involvement, ascites, peritoneal thickening, and normal-appearing ovaries [15-17]. The MRI findings of papillary serous carcinomas in ovaries of normal size in the current study were similar [5]. Therefore, primary ovarian carcinoma should be included in the differential diagnosis of patients with diffuse peritoneal seeding and ovaries of normal size. In assessing cases of serous surface papillary carcinoma of the ovary it is important to distinguish between this carcinoma and peritoneal carcinomatosis from another primary malignancy. On serial imaging, the small foci of malignancy may not be identified, and some cases of gastrointestinal malignancy can be overlooked. Therefore, the absence of a visible primary tumor cannot always suggest the possibility of serous surface papillary carcinomas of the ovary or exclude the possibility of peritoneal carcinomatosis from another primary malignancy.

The treatment results and prognosis for patients with serous surface papillary carcinoma of the ovary remains controversial. A recent report showed that serous surface papillary carcinoma of the ovary responded completely to initial cytoreductive surgery followed by platinum-based chemotherapy [8]. Another report presented evidence of long-term survival of patients with serous surface papillary carcinomas of the ovary [18]. In patients treated with adjuvant paclitaxel and platinum for Stage III/IV epithelial ovarian carcinoma, the clinical complete response rate and progression-free survival have been reported to be 54% and 18 months, respectively [5]. Our patient was treated aggressively with cytoreductive surgery and adjuvant chemotherapy.

In conclusion, it is difficult to establish a preoperative diagnosis in patients with normal sized ovarian carcinoma syndrome. Therefore, serous surface papillary carcinoma of the ovary should be kept in mind as a possible diagnosis in patients with extensive peritoneal carcinomatosis, relatively normal-sized ovaries, and a highly elevated serum CA-125 level. In the case of patients with serous surface papillary carcinoma of the ovary, cytoreductive surgery followed by adjuvant chemotherapy is recommended. We emphasize the importance for clinical gynecologists to be familiar with normal-sized ovarian carcinoma syndrome in order to make an early and correct diagnosis.

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References

- [1] Greenlee R.T., Murray T., Bolden S., Wingo P.A.: "Cancer Statistics 2003". *Can Cancer J. Clin.*, 2003, 50, 7.
- [2] Lin H., Changchien C.C.: "Management of relapsed/refractory epithelial ovarian cancer: Current standards and novel approaches". *Taiwan J. Obstet. Gynecol.*, 2007, 46, 379.
- [3] Feuer G.A., Shevchuk M., Calanog A.: "Normal-sized ovary carcinoma syndrome". *Obstet. Gynecol.*, 1989, 73, 786.
- [4] Ransom D.T., Patel S.R., Keeney G.L., Malkasian G.D., Edmondson J.H.: "Papillary serous carcinoma of the peritoneum. A review of 33 cases treated with platin-based chemotherapy". *Cancer*, 1990, 66, 1091.
- [5] Choi C.H., Kim T.J., Kim W.Y., Ahn G.H., Lee J.W., Kim B.G. *et al.*: "Papillary serous carcinoma in ovaries of normal size: A clinicopathologic study of 20 cases and comparison with extraovarian peritoneal papillary serous carcinoma". *Gynecol. Oncol.*, 2007, 105, 762.
- [6] Lauchlan S.C.: "The secondary Mullerian system". *Obstet. Gynecol. Surv.*, 1972, 27, 133.
- [7] Mills S.E., Andersen W.A., Fechner R.E., Austin M.B.: "Serous surface papillary carcinoma: a clinicopathologic study of 10 cases and comparison with Stage III-IV ovarian serous carcinoma". *Am. J. Surg. Pathol.*, 1988, 12, 827.
- [8] Strnad C.M., Grosh W.W., Baxter J., Burnett L.S., Jones H.W. 3rd, Greco F.A. *et al.*: "Peritoneal carcinomatosis of unknown primary site in women: a distinctive subset of adenocarcinoma". *Ann. Intern. Med.*, 1989, 111, 213.
- [9] Altaras M.M., Aviram R., Cohen I., Cordoba M., Weiss E., Beyth Y.: "Primary peritoneal papillary serous adenocarcinoma: clinical and management aspects". *Gynecol. Oncol.*, 1991, 40, 230.
- [10] Kuwashima Y., Uehara T., Kurosumi M., Shiromizu K., Matsuzawa M., Kishi K.: "Pathological aspects of normal-sized ovarian carcinoma". *Eur. J. Gynecol. Oncol.*, 1996, 17, 17.
- [11] Hankinson S.E., Colditz G.A., Hunter D.J., Willett W.C., Stampfer M.J., Rosner B. *et al.*: "A prospective study of reproductive factors and risk of epithelial ovarian cancer". *Cancer*, 1995, 76, 284.
- [12] Risch H.A., Marrett L.D., Howe G.R.: "Parity, contraception, infertility, and the risk of epithelial ovarian cancer". *Am. J. Epidemiol.*, 1994, 140, 585.
- [13] Topalak O., Saygili U., Soyuturk M., Karaca N., Batur Y., Uslu T. *et al.*: "Serum pleural effusion, and ascites CA-125 levels in ovarian cancer and nonovarian benign and malignant diseases: a comparative study". *Gynecol. Oncol.*, 2002, 85, 108.
- [14] Kim H.J., Kim J.K., Cho K.S.: "CT Features of serous surface papillary carcinoma of the ovary". *Am. J. Roentgenol.*, 2004, 183, 1721.
- [15] Furukawa T., Ueda J., Takahashi S., Higashino K., Shimura K., Tsujimura T. *et al.*: "Peritoneal serous papillary carcinoma: radiological appearance". *Abdom Imaging*, 1999, 24, 78.
- [16] Stafford-Johnson D.B., Bree R.L., Francis I.R., Korobkin M.: "CT appearance of primary papillary serous carcinoma of the peritoneum". *Am. J. Roentgenol.*, 1998, 171, 687.
- [17] Chopra S., Laurie L.R., Chintapalli K.N., Valente P.T., Dodd G.D. III.: "Primary serous carcinoma of the peritoneum: CT-pathologic correlation". *J. Comput. Assist. Tomogr.*, 2000, 24, 395.
- [18] Chen K.T., Flam M.S.: "Peritoneal papillary serous carcinoma with long-term survival". *Cancer*, 1986, 58, 1371.

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