



Primary Peritoneal Serous Carcinoma Detected by Abnormal Cervical Smear: a Case Report

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Abstract

Primary peritoneal serous carcinoma (PPSC) is a rare malignancy, the clinical characteristics of which resemble ovarian serous carcinoma. We present a rare case of PPSC detected by an abnormal cervical smear, the first one with an absence of ovarian tissue at the time of the initial diagnosis.

A 59-year-old asymptomatic woman presented with glandular atypia on routine Papanicolaou smear. Endocervical and endometrial curettage showed an adenocarcinoma with focal squamous differentiation and uncertain further classification. The patient had a past surgical history of bilateral salpingo-oophorectomy due to endometriosis. Abdominal MRI depicted omental multinodularity, great amount of ascites and possible endometrial tumor. The patient underwent total hysterectomy, omentectomy and biopsies of implants on Douglas pouch. Surgical and histological findings were consistent with primary peritoneal serous carcinoma.

Abnormal pap smear could rarely be suggestive of extrauterine malignancies, such as peritoneal cancer.

Keywords

cervical smear, extrauterine malignancies, glandular atypia, primary peritoneal serous carcinoma,

INTRODUCTION

Primary peritoneal carcinoma is a relatively uncommon neoplasm arising from peritoneal epithelium which was first described by Swerdlow in 1959. Among primary peritoneal malignancies, primary peritoneal serous carcinoma (PPSC) is the most common histologic subtype affecting approximately 0.62/100000 women in US population.¹ Clinical symptoms of PPSC derive predominantly from massive ascites, usually in advanced stage of the disease. Typical preoperative findings indicating PPSC can be elevated Ca-125 levels and depiction of diffuse peritoneal disease, with or without omental involvement, and absence of an ovarian mass.

Only a few cases with atypical presentation of the disease have been described in the literature. The aim of the

present study was to report a case of PPSC diagnosed by a glandular atypia on routine Pap smear, the first one with an absence of ovarian tissue at the time of initial diagnosis.

CASE REPORT

A 59-year-old asymptomatic woman, with previous gynecologic history of bilateral salpingo-oophorectomy due to endometriosis (15 years previously) and two dilatations and curettages (D&C) due to endometrial hyperplasia (1 and 2 years ago, respectively), presented in our outpatient clinic with nuclear atypia of glandular cells found on routine Papanicolaou smear. Previous cervical screening had not detected any pathology. Transvaginal ultrasound depicted an endometrial thickness of 8 mm and free peritoneal fluid,

while mammography was normal. Ca-125 was measured up to 119 U/ml. Endocervical and endometrial curettage was scheduled and pathologic report revealed an adenocarcinoma on the grounds of an endometrial polyp, with focal squamous differentiation. However, the primary origin of the tumor could not be identified.

Abdominal MRI detected omental thickness, free peritoneal fluid and relatively thin endometrium, given the previously performed D&C. The imaging characteristics of the latter indicated a possible endometrial tumor without myometrial and parametrial involvement. Colonoscopy was also performed because of a referred change of bowel habits during the last month; however, the only pathology found was diverticulosis of sigmoid colon.

With a potential diagnosis of endometrial adenocarcinoma, the patient underwent exploratory laparotomy which revealed free peritoneal fluid, extensive omental involvement, multiple adhesions between the small intestine loops, and small implants of the tumor on the pouch of Douglas, as well as the uterine and the bladder serosa. Ovaries and fallopian tubes were not recognized. Perioperative assessment of the upper abdomen did not reveal any further pathology. Total hysterectomy, omentectomy and biopsies of the greater implants on Douglas pouch were performed, resulting in extensive debulking to R1 disease. Small implants < 1 cm in diameter remained in the pouch of Douglas and the bladder serosa.

Histological and immunohistochemical analysis of the specimens revealed no uterine disease. However, extended infiltration of the great omentum consistent with primary peritoneal serous carcinoma was found. Specifically, the neoplasm stained positive for tumor-associated glycoprotein 72 (TAG72), cancer antigen 125 (Ca 125), e-cadherin, HBME, keratin 7 (Ker 7) and negative for keratin 20 (Ker20), Wilms tumor 1(WT1) and cluster of differentiation antigen 15 (CD15), indicating a serous carcinoma. Microscopic lesions of the same tumor were also found in the external cervical surface. Pelvic washings showed metastatic adenocarcinoma. Based on the above findings, the diagnosis was PPSC (Fig. 1).

The patient was discharged uneventfully on the seventh postoperative day. Given the diagnosis of primary peritoneal serous carcinoma st IIIc, adjuvant chemotherapy with carboplatin-paclitaxel was scheduled.

Supplementary immunochemistry markers were applied to confirm the diagnosis. D2-40 was negative, so in comparison with the negative expression of the marker WT1 peritoneal mesothelioma was excluded (Fig. 2).

DISCUSSION

Primary peritoneal serous carcinoma (PPSC) affects predominantly elderly and postmenopausal women. Although early stages of the disease may be asymptomatic, most patients in advanced stages complain of abdominal distension, abdominal lump, diffuse nonspecific abdominal pain, vomiting, weight gaining and dyspnoea secondary to massive

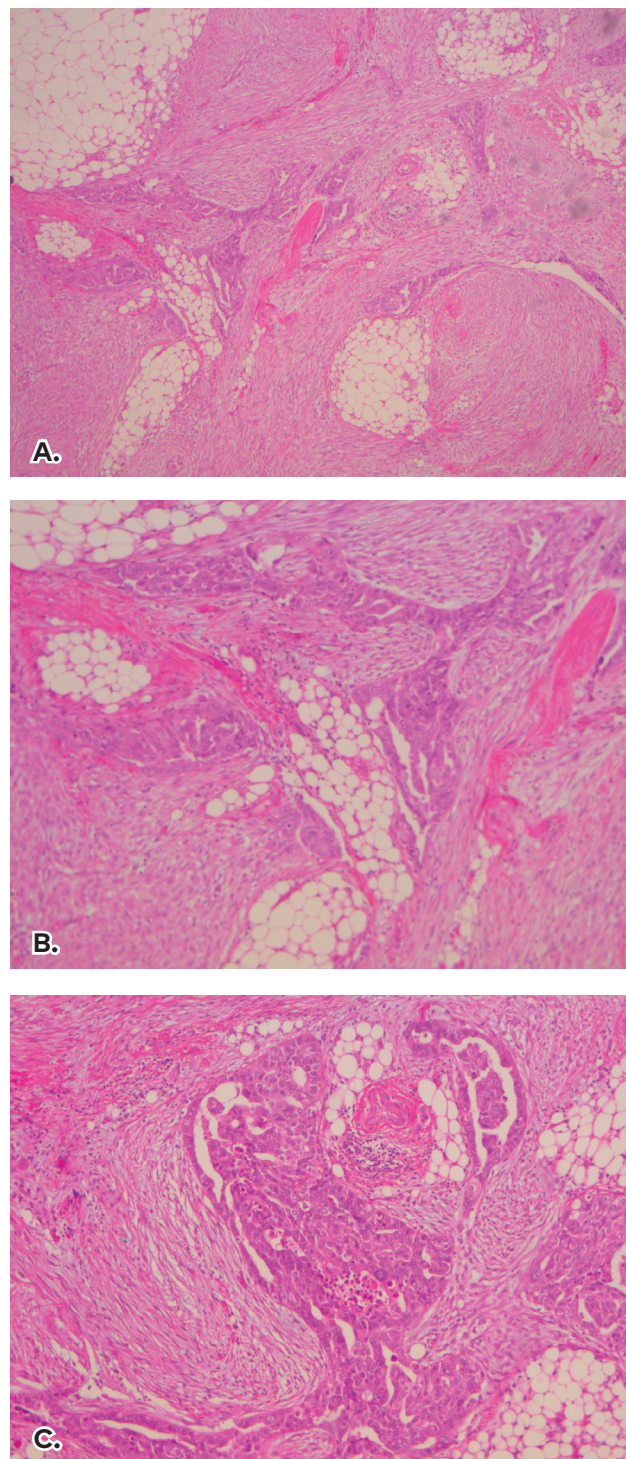


Figure 1. Microscopic findings (×50). Tumor cells characteristic of adenocarcinoma. **A.** HE ×2.5; **B.** HE ×5; **C.** HE ×10.

ascites. Elevated Ca-125 levels and scan findings consistent with ascites, omental involvement, and parietal peritoneal nodules without ovarian pathology may indicate PPSC. Given that PPSC shares the same clinical presentation with primary ovarian serous carcinoma and the two entities are indistinguishable immunohistochemically, the Gynaecology Oncology Group has set specific criteria in order to set the diagnosis of PPSC. Apart from ovarian serous carcino-

ma, PPSC is crucial to be distinguished from other primary peritoneal cancer subtypes, such as malignant mesothelioma, pseudomyxoma peritonei and clear cell carcinoma of peritoneum, as well as from secondary peritoneal carcinomatosis or inflammatory peritoneal diseases such as actinomycosis. Standard management includes cytoreductive surgery combined with pre/postoperative platinum-based chemotherapy. Hyperthermic intraperitoneal chemotherapy (HIPEC) is also suggested. Given the diffuse spread of the carcinoma in omental, peritoneal and serosal surfaces, an optimal debulking is not always possible to be achieved.²

Apart from the typical presentations mentioned above, some uncommon presentations have also been reported in

the literature. An asymptomatic, abdominal skin lesion that led to the diagnosis of PPSC was described by Cowan et al. in 1995.³ Another patient was diagnosed as having PPSC by a video-assisted thoracoscopic surgery due to bilateral pleural masses⁴, while three cases of PPSC⁵⁻⁷ and one of serous peritoneal psammocarcinoma⁸ were diagnosed by abnormal cytology (**Table 1**). We report the fourth case of PPSC detected by abnormal cervical cytology, which is the first one with an absence of ovarian and tubal tissue at the time of the diagnosis.

Concerning the pathogenesis of PPSC, accumulating evidence suggests that most extrauterine high-grade serous carcinomas originate from the fimbriated end of the fallo-

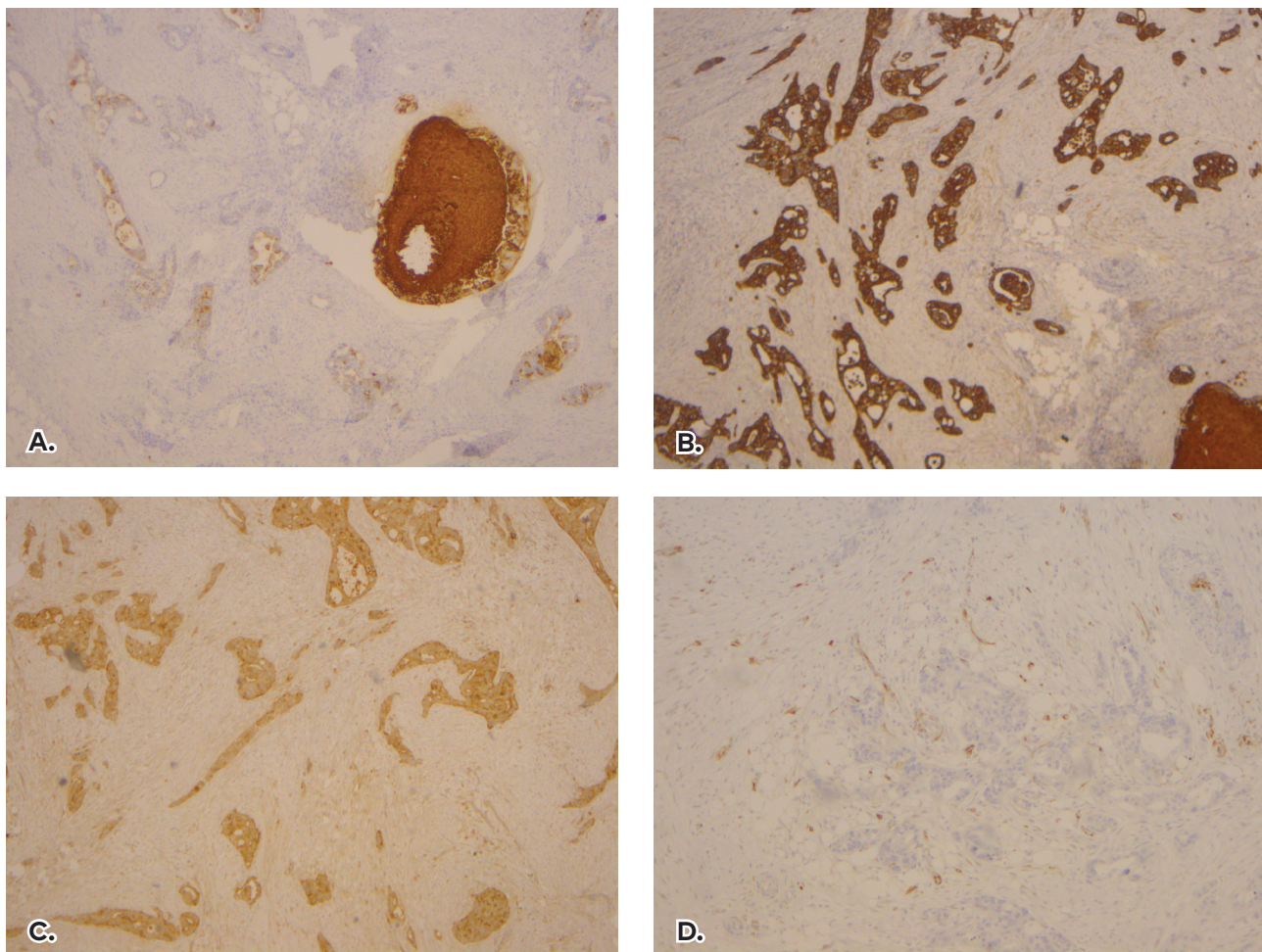


Figure 2. Adenocarcinoma markers. **A.** Marker TAG72: positive; **B.** marker CK7: positive; **C.** marker CEA: positive; **D.** marker WT1: negative.

Table 1. Clinical and laboratory findings

	Age	Symptoms	Pap smear findings	Final histological report
Olsen TG, et al. ⁵	76	Asymptomatic	Severe glandular dysplasia	Primary peritoneal carcinoma
Wright JD, et al. ⁶	Postmenopausal	Vaginal bleeding	Adenocarcinoma cells	Primary peritoneal carcinoma
Riboni F, et al. ⁸	70	Asymptomatic	Neoplastic cells with psammoma bodies	Peritoneal serous psammocarcinoma
Wang H, et al. ⁷	49	Asymptomatic	High grade adenocarcinoma	PPSC

pian tubes. Serous tubal intraepithelial carcinoma is a precursor lesion of the fallopian tubes that has been found in many cases of both primary ovarian and peritoneal serous carcinomas and is considered to be the source of a significant proportion of these diseases. Based on the latter theory, it is of great interest that our patients had a history of bilateral salpingo-oophorectomy 15 years before the diagnosis of PPSC. Possible illustrations have been reported in the literature in order to explain the development of PPSC in the absence of fallopian tubes, predominantly in BRCA mutation carriers with a history of a prophylactic bilateral salpingo-oophorectomy and they include: i) the presence and the metastasis of the precursor lesion in the peritoneum before the salpingo-oophorectomy, ii) remnant ovarian or tubal tissue postoperatively, and iii) primary origin of peritoneal cancer.⁹

Pap smear is typically used to detect either pre-invasive or invasive cervical disease. Schnatz PF et al. performed a metanalysis of 24 studies including 2389206 Pap smears, 0.29% of which revealed glandular cells of undetermined significance (AGUS). Out of these AGUS revealing smear tests, 5.2% were proved to be consistent with malignancy. The most common malignancies were endometrial adenocarcinoma (57.6%), cervical adenocarcinoma (23.6%), ovarian and fallopian tube carcinoma (6.4%), squamous cell carcinoma of the cervix (5.4%), and other (6.9%), indicating thus that an abnormal test pap could also be suggestive of extra-uterine malignancies.¹⁰

Specifically, ovarian, fallopian tube, gastrointestinal and breast tumors seems to be the most common of the carcinomas detected by an abnormal test pap¹¹, while less common primary tumors such as melanoma¹², renal cell and urothelial carcinoma¹³ have also been reported. Six cases of serous borderline carcinoma of the ovary with abnormal glandular cells and/or psammoma bodies on the smear test have also been discussed in the literature.¹⁴

The first case of extrauterine malignancy detected by an abnormal smear test was reported by Frech in 1946, when malignant glandular cells were found in the Pap smear test of a patient with serous papillary carcinoma of the ovary.¹⁵

Efflux of the neoplastic peritoneal cells through the genital track, secondary cervical metastasis and the possible origin of PPSC from serous tubal intraepithelial carcinoma could explain the presence of malignant cells in a pap smear. Cervical metastasis, although, occurs rarely because of the limited blood flow and lymphatic drainage of the cervix, as well as its high content of fibrous tissue.

To sum up, abnormal cytology could rarely be suggestive of an extrauterine malignancy, such as PPSC. We raise the awareness of such a rare entity.

REFERENCES

1. Liao CL, Chow S, Chen LM, et al. Trends in the incidence of serous fallopian tube, ovarian, and peritoneal cancer in the US. *Gynecol Oncol* 2018; 149(2): 318-23.
2. Iavazzo C, Vorgias G, et al. Primary peritoneal serous papillary carcinoma: clinical and laboratory characteristics. *Arch Gynecol Obstet* 2008; 278(1): 53-6.
3. Cowan LJ, Roller JJ, Connelly PJ, et al. Extraovarian stage IV peritoneal serous papillary carcinoma presenting as an asymptomatic skin lesion – a case report and literature review. *Gynecol Oncol* 1995; (3): 433-5.
4. Suh JH, Kim YH, Chang ED. Primary papillary serous carcinoma of the peritoneum diagnosed by video-assisted thoracoscopic surgery: report of a case. *Surg Today* 2008; 38(8): 743-6.
5. Olsen TG, Nycum LR, Graham RL, et al. Primary peritoneal carcinoma presenting on routine Papanicolaou smear. *Gynecol Oncol* 2000; 78(1):71-3.
6. Wright JD, Horowitz NS, Rader JS. Primary peritoneal carcinoma presenting as adenocarcinoma on a Pap smear. A case report. *J Reprod Med* 2002; 47(11): 933-5.
7. Wang H, Chen PC. Primary serous peritoneal carcinoma presenting first on a routine Papanicolaou smear: a case report. *Acta Cytol* 20120; 54(4): 623-6.
8. Riboni F, Giana M, Piantanida P, et al. Peritoneal psammocarcinoma diagnosed by a Papanicolaou smear; a case report. *Acta Cytol* 2010; 54(3): 311-3.
9. Iavazzo C, Gkegkes I, Vrachnis N. Primary peritoneal cancer in BRCA carriers after prophylactic bilateral salpingo-oophorectomy. *J Turk Ger Gynecol Assoc* 2016; 17(2): 73-6.
10. Schnatz PF, Guile M, O'Sullivan DM, et al. Clinical significance of atypical glandular cells on cervical cytology. *Obstet Gynecol* 2006; 107(3): 701-8.
11. Grupta D, Balsara G. Extrauterine malignancies. Role of Pap smears in diagnosis and management. *Acta Cytol* 1999; 43(5): 806-13.
12. Giordano G, Gnetti L, Pilato FP, et al. The role of cervical smear in the diagnosis and management of extrauterine malignancies metastatic to the cervix: three case reports. *Diagn Cytopathol* 2010; 38(1): 41-5.
13. Allison DB, Olson MT, Maleki Z, et al. Metastatic urinary tract cancers in pap test: Cytomorphological findings and differential diagnosis. *Diagn Cytopathol* 2016; 44(12): 1078-81.
14. Tepeoglu M, Ozen O, Ayhan A. Ovarian serous borderline tumor detected by conventional Papanicolaou smear: a case report. *Acta Cytol* 2013; 57(1): 96-9.
15. Frech HC. Adenocarcinoma of the ovary diagnosed by vaginal smear. *Am J Obstet Gynecol* 1949; 57(4): 802-4.

Первичная перитонеальная серозная карцинома, обнаруженная в аномальном цитологическом мазке: клинический случай

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Абстракт

Первичная перитонеальная серозная карцинома (ППСК) представляет собой редкое злокачественное новообразование, клинические характеристики которого аналогичны таковым у серозной карциномы яичников. Мы представляем редкий случай ППСК с дефицитом ткани яичника во время первоначального диагноза аномального цитологического мазка.

59-летняя бессимптомная женщина с железистой атипией при рутинном цитологическом мазке. Эндоцервикальный и эндометриальный кюретаж выявил аденокарциному с очаговой плоскоклеточной дифференцировкой и неопределённой классификацией. Больная в прошлом имела в хирургическом анамнезе двустороннюю сальпингоофоректомию вследствие эндометриоза. МРТ брюшной полости показала мультинодулярность предсердий, большое количество асцитической жидкости и возможную опухоль эндометрия. Больная подверглась тотальной гистерэктомии, оментэктомии и биопсии Дугласова пространства. Хирургические и гистологические данные соответствуют первичной перитонеальной серозной карциноме.

Аномальный цитологический мазок редко может указывать на внематочные злокачественные новообразования, такие как рак брюшины.

Ключевые слова

первичная перитонеальная серозная карцинома, цитологический мазок, железистая атипия, внематочные злокачественные новообразования.
