P R A C E K A Z U I S T Y C Z N E
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Serous peritoneal psammocarcinoma with an aggressive course: a case and review of the literature

Surowiczy piaszczakorak otrzewnej o agresywnym przebiegu: opis przypadku i przeglad literatury

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Abstract

Background. Primary serous peritoneal psammocarcinoma (PSPP) is a rare variant of serous carcinoma characterized by massive psammoma body formation and low-grade cytological features. Patients with serous psammocarcinoma have a protracted clinical course and relatively favourable prognosis, although a more aggressive course of PSPP may occur.

Case presentation: A 52-year-old woman suffering from abdominal pain with ascites and serum CA-125 level substantially elevated underwent an exploratory laparoscopy which revealed bulk disease. The pathology report detected PPSP at the FIGO stage IIIC. The patient received neoadjuvant chemotherapy (3 courses of paclitaxel / pegylated liposomal doxorubicin / carboplatin). Optimal interval debulking surgery was performed as the next step, followed by three courses of adjuvant chemotherapy (paclitaxel / carboplatin). Due to the fact that the patient had residual disease, at the second-look surgery she received consolidation therapy with intraperitoneal and intravenous chemotherapy carboplatin. Eight months after the completion of treatment the patient developed disease recurrence in the peritoneum. Palliative surgery (enterostomy) was performed. Furthermore, the patient received two lines of chemotherapy consisting of cyclophosphamide / cisplatin and then gemcitabine. After twenty five months she developed brain metastases, treated with palliative radiotherapy. The patient died twenty eight months since her primary presentation of PSPP.

Conclusion: PSPP is an infrequent variant of epithelial cancer with favourable prognosis. The disease may, however, take a more aggressive course. Thus, an aggressive therapy is required to postpone the progression.

Key words: **primary serous peritoneal psammocarcinoma** / **psammoma body** / / **interval debulking surgery** / **neoadjuvant therapy** /

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Streszczenie

Pierwotny surowiczy piaszczakorak otrzewnej (PSPSP) jest rzadką odmianą raka surowiczego, charakteryzujący się obecnością licznych ciałek piaszczakowatych oraz niską złośliwością histologiczną. Chore mają względnie korzystne rokowanie, chociaż zdarza się przebieg bardziej agresywny tak jak w prezentowanej pracy.

Opis przypadku: *Chora lat 52 uskarżająca się na bóle brzucha, z cechami wodobrzusza w badaniach obrazowych i znacznie podwyższonym markerem CA 125 została poddana zwiadowczej laparoskopii. Podczas operacji stwierdzono zaawansowaną chorobę nowotworową w jamie brzusznej przy niezmienionych przydatkach. W badaniu histopatologicznym rozpoznano PPSP. W zestawieniu z danymi klinicznymi zaawansowanie określono na IIIC wg klasyfikacji FIGO.*

Chorą zakwalifikowano do neoadjuwantowej chemioterapii (3 kursy Paklitaksel/ Pegylowana Liposomalna Doxorubicyna/ Karboplatyna) a następnie poddano odroczonej optymalnej operacji cytoredukcyjnej, po której zastosowano 3 cykle adjuwantowej chemioterapii (Paklitaksel/ Karboplatyna).

W związku z obecnością minimalnej choroby resztkowej stwierdzonej w trakcie operacji drugiego wglądu, zakwalifikowano pacjentkę do monoterapii karboplatyna (3 cykle) podawaną dootrzewnowo i dożylnie. Po ośmiu miesiącach od zakończenia chemioterapii stwierdzono nawrót choroby nowotworowej w otrzewnej. Z powodu niedrożności przewodu pokarmowego przeprowadzono paliatywną operację z wyłonieniem stomii na jelicie grubym.

Po zabiegu pacjentka otrzymała dwie linie chemioterapii według schematu Cyklofosfamid/ Cisplatyna, następnie monoterapię Gemcytabiną. Po 25 miesiącach od rozpoznania PSPP chorą poddano paliatywnej radioterapii z powodu zmian przerzutowych do mózgu. Pacjentka zmarła 28 miesięcy po zdiagnozowaniu PSPP.

PSPP jest rzadkim podtypem nowotworów nabłonkowych o względnie korzystnym rokowaniu. Choroba ta może mieć jednak agresywny przebieg tak, jak opisano w tej pracy i chorzy ci mogą wymagać intensyfikacji leczenia.

Słowa kluczowe: **pierwotny surowiczy piaszczakorak otrzewnej** / **ciałka piaszczakowate** / **odroczona operacja cytoredukcyjna** / **terapia neoadjuwantowa** /

Background

Serous psammocarcinoma of the peritoneum is a rare variant of epithelial cancer. Histologically, PPSP is characterized by [1] massive psammoma body formation (75%), invasion of peritoneum or intraperitoneal viscera, moderate cytological atypia and mimic serous adenocarcinoma of the ovary. Twenty-three cases of PPSP have been reported in literature [1-13]. Due to the rarity and variable histological criteria, there is no established tumour marker for peritoneal serous psammocarcinoma.

In the following report we present a case of a patient suffering from this rare variant of cancer, confirmed histologically and immunohistochemically. Despite aggressive therapy, the patient had short survival time.

Case presentation

A 52-year-old woman presented with abdominal pain and distension. She was admitted to our Institute due to ascites and serum CA-125 levels elevated to the value of 749 U/ml. The computed abdominal tomography revealed a small cyst (26x23 mm) in the left ovary, a large omental tumour and ascites. Consequently, the patient underwent explorative laparoscopy with oophorectomy and omentum biopsies. Intraoperatory findings showed large tumour mass involving the gastrocolic omentum and dense small bowel adhesions to pancreas and spleen. Both ovaries were normal.

Only a small 23 x 24 mm simple cyst was found during histological examination in the left ovary. The right ovary was normal. In the peritoneum, minimally invasive serous carcinoma cells with moderate cytological atypia, (Figure 1) and massive extensive psammoma bodies, (Figure 2) were detected.

Histopathological diagnosis revealed primary serous peritoneal psammocarcinoma at the FIGO stage IIIC. No estrogen and progesterone receptor was detected immunohistochemically.

Primary serous peritoneal psammocarcinoma cells had CK7-positive, CK19-positive and CK20-negative immunohistochemical phenotype.

The patient received 3 cycles of neoadjuvant chemotherapy consisting of: paclitaxel (175mg/m2 in a 3-hour infusion) / carboplatin (AUC 5) / pegylated liposomal doxorubicin (20mgm^2) every 21 days, in accordance with phase II of the prospective pilot study that is implemented in our institute, described elsewhere [14]. After three courses of such chemotherapy partial response (according to RECIST criteria) was achieved. Optimal interval debulking surgery (≤1cm residual disease) was performed. Technically, the surgery consisted of total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, splenectomy, partial pancreas resection, appendectomy, paraaortic and pelvic lymph node dissections and debulking. The continuation of the therapy involved three courses of adjuvant chemotherapy based on paclitaxel (175mg/m^2) / carboplatin (AUC6). Minimal residual disease in the pathologic examination was found during the second-look operation. At that time, the level of CA125 in the serum was normal. Due to aggressive nature of the neoplasm, intraperitoneal chemotherapy with carboplatin was administered with an installed port. After two courses of chemotherapy the patient was urgently admitted to the hospital with high fever (39.0°C). Apart from high fever, no significant abnormalities were found during clinical examination. The CMV infection was confirmed by positive CMV-IgM in serum. The patient was therefore treated with gancyclovir (325mg i.v. b.i.d. for two weeks). Subsequent abdominal CT scan revealed an enlarged paraaortic lymph node. To determine the nature of this node, PET scan was performed. Paraaortic lymph node enlargement and an additional lesion confined to the liver were found. Therefore, the patient obtained three cycles of consolidating systemic chemotherapy, consisting of carboplatin. At that time the serum level of CA 125 was normal.

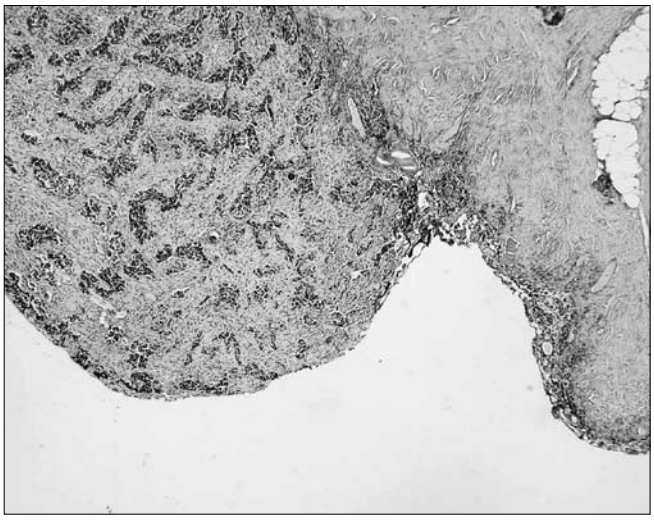

Figure 1. Primary peritoneal serous psammocarcinoma, 40x. Glandular cells minimally invade peritoneum stroma.

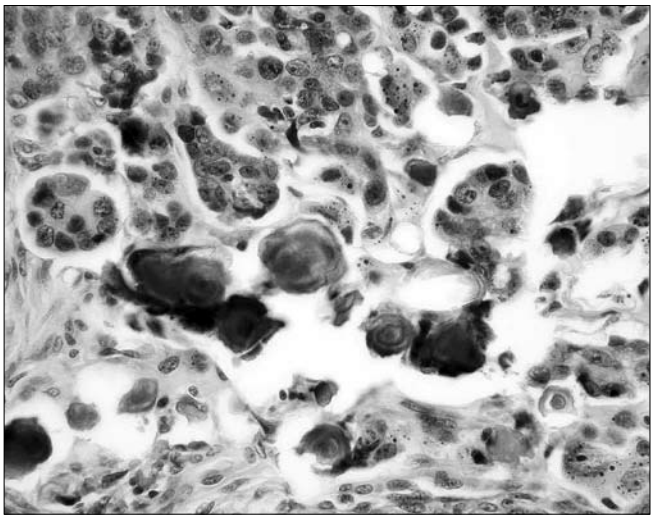

Figure 2. Primary peritoneal serous psammocarcinoma, 400x. Histological examination revealed that neoplastic epithelium has been replaced by psammoma bodies.

Seven months after the last cycle of the consolidating chemotherapy, increasing CA 125 levels were observed (from 46U/ml to 116U/ml). The control CT scan revealed stable enlarged paraaortic lymph node (largest diameter of 23mm). Another PET scan revealed lesions within the peritoneum and in the paraaortic lymph nodes. In the seventeenth month of the PPSP course, bowel obstruction occurred. Enterostomy as palliative surgery was performed. Subsequently, the patient received four courses of salvage chemotherapy consisting of cyclophosphamide (750mg/m^2) and cisplatin (75mg/m^2). She achieved stable disease according to the RECIST criteria and CA 125 level with subsequent progression seen after further four months. Therefore, she received two courses of salvage therapy with gemcitabine (1250mg/m^2) on 1st, 8th and 15th day during a 28-day cycle. In the course of this treatment unresectable brain metastases with clinical presentation appeared. The patient was irradiated with the dose of 2000cGy for the whole brain. The patient died of disease progression, 28 months after the PPSP was diagnosed.

Discussion

PSPP is a very rare variant of peritoneal cancer. The case history presented above indicates this malignant disease with good prognosis may indeed have an aggressive course. The patient obtained a very aggressive, cytotoxic treatment: neoadjuvant, adjuvant, consolidating and salvage chemotherapy. Due to recurrences, she received two lines of chemotherapy with salvage gemcitabine regimens. During the therapy a CMV infection occurred and it required medication with gancyclovir. The patient survived twenty eight months after the diagnosis of PSPP.

Both the epithelium of the ovary and the mesothelium of the peritoneum have the same embryonic origin. Mesenchymal cells are able to give rise to epithelial organs through mesenchymal-epithelial transition that is crucial for the development of a primary carcinoma. [15] It is histologically indistinguishable from primary epithelial ovarian carcinoma, and its diagnosis requires differential diagnosis between mesothelioma and ovarian cancer. Immunohistochemistry is useful in distinguishing ovarian cancer from peritoneal mesothelioma [16].

Primary ovarian cancer can be excluded by the following criteria: (1) both ovaries must be of normal size; (2) the extraovarian involvement must be greater than the involvement on the surface of the ovary; (3) the ovarian component must be less than 5x5 mm within the ovary or confined to the ovarian surface; and (4) the cytological characteristics must be of the serous type [17].

Psammoma bodies are microscopic, laminated, calcinated, calcified and extracellular bodies. The mechanism of psammocarcinoma body formation remains unclear and it has been suggested that psammoma bodies arise as products of neoplastic and histiocytic cellular degradation.

Gilks et al. [1] proposed some morphological criteria for the diagnosis of peritoneal psammocarcinoma when the following microscopic features were present: destructive invasion of peritoneal viscera in extraovarian cases; no more than moderate cytological atypia; no areas of solid epithelial proliferation except for occasional nests with no more than 15 cells in diameter; at least 75% of papillae and nests associated or completely replaced by psammoma body formation.

Twenty-four cases of PPSP have been reported in the literature to date [1-13] and they may help define the clinical and pathological features of this neoplasm. The features have been depicted in Table 1.

To sum up, an average patient age at clinical presentation of the disease was 54 (95% CI, 47-61 years). Common symptoms and signs of the disease included: abdominal pain, pelvic mass, distension, nausea and vomiting. The most frequent stage at the primary diagnosis was FIGO stage III, with the exception of the two cases described by Weir et al. [4]. The optimal surgical debulking as the mainstay was performed in 19 out of 24 described cases. One patient underwent conservative surgery and our patient underwent optimal interval surgery with primary neoadjuvant chemotherapy. Nine patients were treated with adjuvant chemotherapy based on platinum analogues, and one with pelvic and abdominal radiation therapy.

Our patient received consolidation intraperitoneal chemotherapy with carboplatin. Follow-up data were available in 20 out of 24 cases.

Table I. Peritoneal serous psammocarcinoma: clinical features.

Authors	Age (years)	Presenting symptoms or signs	Surgery	Chemotherapy / radiotherapy	FIGO stage	Follow up
Gilks et al. [1]	58	abdominal swelling	supracervical hysterectomy, BSO	NA	IIIB	< 1 year
Gilks et al. [1]	55	abnormal Pap smear	TAH/BSO, omentectomy	NA	IIIA	NED: 10 years
Gilks et al. [1]	48	menometrorrhagia, pelvic mass	TAH/BSO, omentectomy	NA	IIIB	< 1 year
Chen et al. [7]	59	midline pelvic mass	cyst aspiration, TAH/BSO, omentectomy	NA	IIIA	1 year
Chen et al. [7]	71	abdominal pain, distension, anasarca	laparoscopy, laparotomy, biopsy	cyclophosphamide / carboplatin – three cycles	IIIB	DOD: < 1 year
Mc Caughey et al. [8]	27	psammoma bodies in Pap	TAH/BSO, omentectomy	none	IIIA	NED: 8 years
Mc Caughey et al.[8]	45	lower abdominal and pelvic pain	TAH/BSO, cauterization, biopsies	whole abdominal and pelvic radiation therapy	IIIA	< 1 years
Whitcomb et al.[5]	59	abdominal pain, nausea, vomiting	TAH/BSO, omentectomy, debulking,	NA	IIIC	NED: 2 years
Molpus et al.[6]	58	increasing abdominal girth, progressive shortness of breath	TAH/BSO, omentectomy, debulking	none	IIIC	PFS: 4 years; AWD: 8 years
Munkarah et al.[2]	27	abdominal pain	conservative surgery: LSO, omentectomy, appendectomy, debulking; secondary debulking surgery after chemotherapy.	cyclophosphamide / cisplatin – 6 cycles	IIIC	NED: 6,5 years
Weir et al. [4] - a report of 7 patients	Average – 48 years (range 42-73 years)	incidental (in 3/7 patients, pelvic mass (in 3/7 patients), abdominal pain (1/7 patients)	2 patients: TAH/BSO, omentectomy, 2 patients: BSO, omentectomy, 1 patient: USO, omentectomy, 1 patient: myomectomy, 1 patient: omentectomy	one patient – taxol / carboplatin one patient – cisplatin / cyclophosphamide	no data	data were available in 3 out of 7 cases. NED at 1.4, 3.8, 8.3 years
Lehner et al. [9]	37	spotting, abdominal pain	exploratory laparoscopy, TAH/BSO, omentectomy, lymphadenectomy	carboplatin / cyclophosphamide – 6 cycles	IIIB	NED: 2 years
Poggi et al. [3]	66	abdominal pain, nausea, vomiting	BSO, omentectomy, debulking / the patient had previously undergone TAH for symptomatic leiomyomata uteri	NA	IIIB	PFS: 1,5 years
Piura et al. [10]	67	abdominal pain, girth, weakness	TAH/ BSO, omentectomy, debulking	paclitaxel / cisplatin – 6 cycles	IIIC	NED: 1,3 years
Bilgin et al. [11]	46	heavy menstrual bleeding, lower abdominal mass	TAH/BSO, omentectomy, lymphadenectomy	paclitaxel / carboplatin – 6 cycles	NA	NED: 5,5 years
Akbulut et al. [12]	67	abnormal vaginal bleeding, abdominal- pelvic pain	TAH/BSO, omentectomy, lymphadenectomy, debulking	adjuvant: cyclophosphamide cisplatin - 9 cycles second line: paclitaxel / carboplatin – 6 cycles Rth palliative	IIIC	PFS: 5 years, AWD: 6 years
Koumoun-dourou et al. [13]	83	incidental, large bowel obstruction symptoms	TAH/BSO, omentectomy, left colectomy, debulking	NA	III	NED: 4,4 years
presented	52	abdominal pain, distension	exploratory laparoscopy; interval debulking surgery: TAH/BSO, omentectomy, splenectomy, partial pancreas resection, paraaortic and pelvic lymphadenectomy, debulking; third-look operation	neoadjuvant: 3 cycles of paclitaxel / pegylated liposomal doxorubicin / carboplatin; adjuvant: 3 cycles of paclitaxel / carboplatin; consolidation: 3 cycles of carboplatin i.p. / i.v.	IIIC	PFS: 8 months; DOD: 2,3 years

Abbreviations: TAH – total abdominal hysterectomy, BSO – bilateral salpingo-oophorectomy, USO – unilateral salpingo-oophorectomy, LSO – left salpingo-oophorectomy, NA – not administered, NED – no evidence of disease, DOD – death of disease, PFS – progression free survival, AWD – alive with disease, i.p. – intraperitoneal, i.v. – intravenously.

The clinical outcome without recurrence of the disease was noted in 19 out of 20 patients and the follow-up was from 8 months to 10 years (mean 3.6 years).

These data suggest a more favourable event-free survival in serous type described previously by Dubernard et al. [18], with a 3-year survival rate (29% in a group of 37 patients). Additionally, there is a possibility that PPSP may have an aggressive presentation, as described by Poggi et al. [3] in their report. In such cases chemotherapy appears to be of clinical importance in the treatment of such an aggressive variant of PSPP.

Conclusion

Based on a small number of cases, it is reasonable to conclude that peritoneal psammocarcinoma is a rare serous tumour, characterized morphologically by invasiveness, low-grade cytologic features and abundant psammoma body formation. Prognostic factors suggest that this neoplasm has more favourable prognosis when comparing to usual serous carcinomas. Nevertheless, our findings and others [3] have shown that PSPP may have a more aggressive course as well.

Consent

Written informed consent for publication of this case report and any accompanying images was obtained after the death of the patient from her next of kin (husband).
A copy of the written consent is available for review by the Editor-in-Chief of this journal.

List of abbreviations

PSPP: primary serous peritoneal psammocarcinoma;
FIGO: International Federation of Gynecology and Obstetrics;
RECIST: Response Evaluation Criteria in Solid Tumours;
AUC: area under the curve;
CMV: Cytomegalovirus.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

LB, AG-B, MG, RS and WB participated in the patient care process. LB and GW performed the literature review and drafted the manuscript. PW made pathological diagnosis and histological pictures. MG, WB, RS and CS assisted in the review of the literature and in revising the manuscript. All authors read and approved the final manuscript.

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Written informed consent for the publication of this case report and any accompanying images was obtained from the next of kin of the patient.

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