

## A case of extraovarian primary peritoneal carcinoma in an oophorectomized-hysterectomized patient: a diagnostic dilemma

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**SUMMARY:** A case of extraovarian primary peritoneal carcinoma in an oophorectomized-hysterectomized patient: a diagnostic dilemma.

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*Extra Ovarian Primary Peritoneal Carcinoma (EOPPC) is a rare type of adenocarcinoma of the pelvic and abdominal peritoneum. The objective examination and the histological aspect of the neoplasia virtually overlaps with that of ovarian carcinoma.*

*The reported case is that of a 72 year-old patient who had undergone a total hysterectomy with bilateral annessiectomy surgery 20 years earlier subsequently to a diagnosis for uterine leiomyomatosis. The patient came to our attention presenting recurring abdominal pain, constipation, weight loss, severe asthenia and fever. Her blood test results showed hypochromic microcytic anemia and a remarkable increase*

*CA125 marker levels. Instrumental diagnostics with Ultrasound (US) and CT scans indicated the presence of a single peritoneal mass (10-12 cm diameter) close to the great epiploon. The patient was operated through a midline abdominal incision and the mass was removed with the great omentum. No primary tumor was found anywhere else in the abdomen and in the pelvis. The operation lasted approximately 50 minutes. The post-operative course was normal and the patient was discharged four days later.*

*The histological exam of the neoplasia, supported by immunohistochemical analysis, showed a significant positivity for CA 125, vimentin and cytocheratin, presence of psammoma bodies, and cytoarchitectural pattern resembling that of a serous ovarian carcinoma even in absence of primitiveness, leading to a final diagnosis of EOPPC.*

*The patient later underwent six cycles of chemotherapy with paclitaxel (135 mg/m<sup>2</sup>/24 hr) in association with cisplatin (75mg/m<sup>2</sup>). At the fourth year follow-up no sign of relapse was observed.*

**KEY WORDS:** Extraovarian Primary Peritoneal Carcinoma - CA 125 antigen - Immunohistochemistry.

### Introduction

Extraovarian Primary Peritoneal Carcinoma (EOPPC) was first described by Swerdlow in 1959 (1). In 1974, Parmley and Woodruff (2) demonstrated that pelvic peritoneum had the potential to differentiate into a Müllerian type epithelium. In 1977, Kannerstein (3) suggested the importance of distinguishing EOPPC from malignant mesothelioma. EOPPC is a malignancy that spreads widely inside the peritoneal cavity involving mostly the omentum with minimal or no ovarian involvement. Most of the EOPPC reported cases have been of serous histology (4-7); histopathological, immunohistochemical,

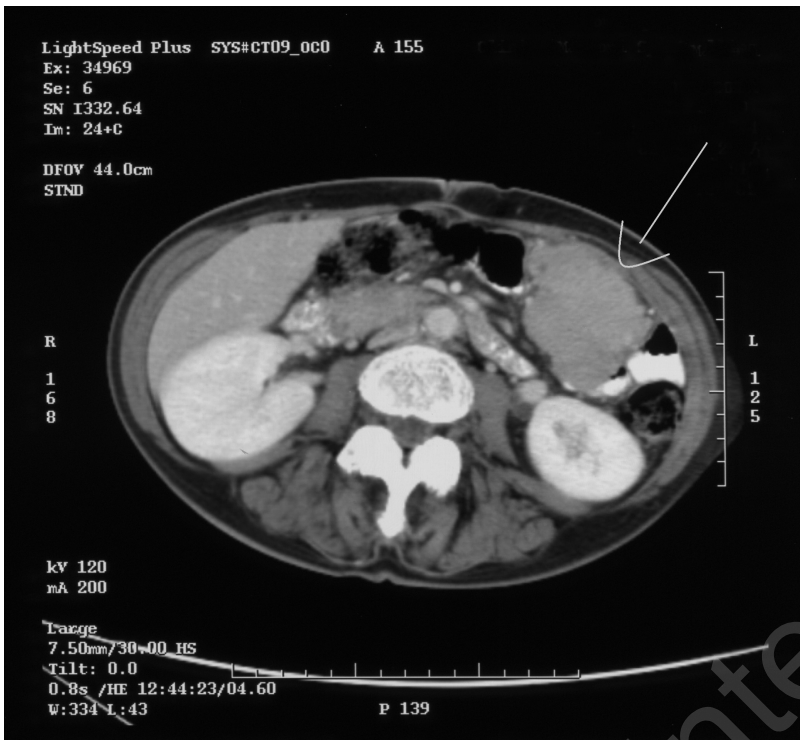
and clinical similarities have been observed with Epithelial Ovarian Cancer (EOC). These similarities in histology and presentation have led to the use of coinciding therapeutic approaches as in primary peritoneal carcinoma: surgical cytoreduction followed by systemic chemotherapy. However, molecular and epidemiologic studies (8, 9) suggest that EOPPC may be a separate entity.

### Case report

A 72 year-old woman who had undergone surgery, about 20 years earlier, of total hysterectomy with bilateral salpingo-oophorectomy for uterine leiomyomatosis, referred in June 2007 to our Unit for recurrent abdominal pain, constipation, weight loss (Body Mass Index = 17.5), asthenia and fever. Laboratory biochemistry showed hypochromic microcytic anaemia, leucocytosis, increased plasma levels of flogosis markers and a remarkable increase of CA 125 marker (373,2 U/ml vs 0-35 U/ml normal range). Abdominal US scan, magnetic resonance imaging, and CT scan revealed a single solid mass (maxi-

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**Fig. 1 - Abdominal CT scan: high vascularised solid mass with a maximum diameter of 10-12 cm (indicated by the arrow) close to the peritoneum.**

mum diameter 10-12 cm) with high vascularisation close to the peritoneum (Figure 1) and low liquid layer among intestinal loops. Gastroscopy and colonoscopy did not display any neoplasia. Through a midline incision, the solid mass was removed with the great omentum (Figure 2) and washing cytology was performed in the peritoneal cavity. No primary tumour was found anywhere else in the abdomen or in the pelvis. The surgery lasted about 50 minutes. Postoperative course was uneventful. In the fourth postoperative day the patient was discharged. No malignant findings were observed in cy-

tological diagnosis of the washing fluid. At pathology, the irregular tumour mass was well circumscribed, soft, grey-yellow, encapsulated and cm 13x6 in size. The cut section showed the little areas of haemorrhage without necrosis. Microscopically, the tumor was composed of large-round cells with granular cytoplasm and small round nuclei, with abundant lymphoid stroma. Rare psammoma bodies were noted. Initially, the histology was not diagnostically significant. The morphological features as serous papillary carcinoma were consistent with a vascular or mesothelial-derived neoplasia (malignant me-



**Fig. 2 - Intraoperative picture: solid mass with irregular morphology not separable from omentum.**

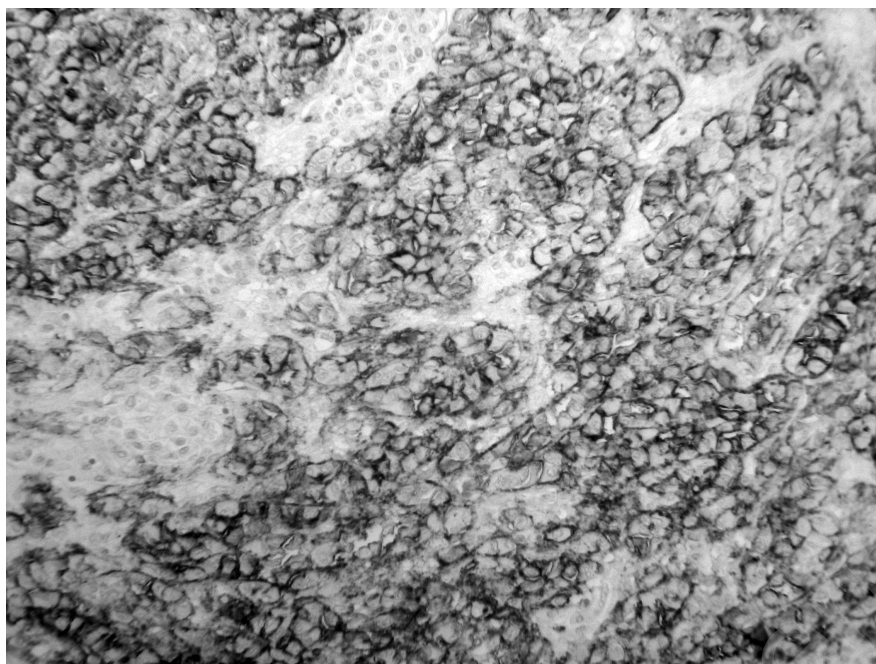


Fig. 3 - Immunohistochemical staining for the CA 125 oncoprotein: the picture shows intense membrane staining in neoplastic cells (magnification x400).

sothelyoma); but the immunohistochemical analysis did not give clear indications; the cells were positive for EMA and pancyokeratine-pool, but negative for either vascular (FLI-1, CD31, FVIII) or mesothelial biomarkers (calretin). Thereby, the diagnosis was of secondary lesion of an undifferentiated neoplasia of probable epithelial origin. The immunohistochemical study showed, tumor cells were diffusely and strongly positive for CA 125 (Figure 3), vimentin, and pan-cytokeratin, and focally positive for EMA; LCA, desmin, S-100, CD34, smooth muscle actin, CD117, HMB45, TTF-1, calretinin, cytokeratin7, cytokeratin 20, cytokeratin 5/6 were negative in neoplastic cells. The percentage of positive tumor cells for ki-67 was about 5%. Thus, the CA125 positivity, calretinin negativity and the absence of primary ovarian tumor diagnosed the EO PPC. In postoperative period, the patient received a first-line chemotherapeutic treatment with paclitaxel (135mg/m<sup>2</sup>/24 hr) and cisplatin (75 mg/m<sup>2</sup>) in combination for six cycles. Serum CA125 level decreased until complete normalization at postoperative day 30. Positron emission tomography-computed tomography conducted after the operation gave no abnormal cluster images. No evidence of relapse was found at a fourth year follow-up.

## Discussions

The Extraovarian Primary Peritoneal Carcinoma is a rare adenocarcinoma that arises from the peritoneum lining of the pelvis and abdomen. There are currently two theories explaining the pathogenesis of EO PPC. Some authors suggest that embryonic germinal cell rests surviving along the gonadal embryonic pathway malignantly transform into EO PPC (10). Others contend that field carcinogenesis occurs, within the coelomic epithelium lining in the abdominal cavity and the ovaries (germinal epithelium), displaying a common response to an oncogenic stimulus (11). In addition, it has

been hypothesized that exposure of the peritoneal surface to components of semen is important in the etiopathogenesis of primary peritoneal carcinoma and the closely related sporadic epithelial ovarian cancer (12). Occasionally, the clinical presentation is indistinguishable from that of advanced-stage epithelial ovarian cancer; patients usually present with nonspecific abdominal symptoms and ascites, reported in approximately 85% of cases. Most reported cases of EO PPC have been in women, usually elderly. In literature there are only two reported cases in males (13, 14), there are none in ovariectomized women and rarely, as presented in our case, the tumor appears as a single solid mass without ascitic fluid (15). Surgical exploration reveals widespread involvement of omentum with minimal or no ovarian involvement and rarely invasion into other abdominal or pelvic organs; Theodosopoulos et al. (16) have observed, over ten years, five cases of EO PPC with invasion of large bowel mimicking colonic obstruction. To achieve a uniform assessment of the outcomes and to differentiate EO PPC from ovarian papillary serous adenocarcinoma, the Gynaecologic Oncology Group has set the following diagnostic criteria (17). The diagnosis of EO PPC is typically made by exclusion after both operative and pathological assessment. The management of patients with EO PPC is similar to that of patients with epithelial ovarian cancer, and consists of cytoreductive surgery followed by multi-agent cisplatin based chemotherapy (18). Several chemotherapeutic regimens have been used with varying degrees of success (19). Most reported combinations have included platinum com-

pounds, often in conjunction with antimicrotubule agents. Paclitaxel with platinum compounds have been introduced into chemotherapeutic regimens for EO PPC. In report of a prospective, randomized trial comparing cyclophosphamide and cisplatin (PC) with paclitaxel and cisplatin (PT), McGuire and others reported improved clinical response rates (63 and 79%, respectively). The progression-free survival also differed significantly (13.8 m with PC and 17.9 m with PT). This group reported the mature data from this trial which also documented a significant difference in overall survival (24 m versus 38 m respectively) (20). In the first report describing the use of the combination of paclitaxel (135mg/m<sup>2</sup>) and cisplatin (50 to 75 mg/m<sup>2</sup>), given for six cycles in four EO PPC patients, Menzin (21) showed a complete surgical response in one patient and a partial surgical response in the others.

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## Conclusion

The patient described in the present report is a rare case of EO PPC in an ovariectomized woman, characterized by a single solid peritoneal mass and absent ascites. Patients with EO PPC should be reported separately from those with ovarian carcinoma but should be treated in a similar fashion. A correct diagnosis and timely management of this unusual histologic entity can result in long-term disease-free survival of the patient.

## Conflict of interest

The paper was not financially supported and no financial relationships exist between the authors. No conflict of interest exists.