Debulking Surgery for High-grade Serous Endometrial Cancer with Disseminated Peritoneal Lesions

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Abstract. Endometrial cancer is one of the most common malignancies in postmenopausal women with good results in terms of survival, especially when diagnosed in early stages. However, prognosis significantly worsens when disseminated lesions are found. We present the case of a 60-year-old patient who presented with diffuse abdominal pain and weight loss. The patient was diagnosed with endometrial cancer with disseminated lesions and successfully submitted to debulking surgery. At two-year follow-up, the patient presents no recurrent disease.

Endometrial cancer, one of the most common gynecologic malignancies, usually affects postmenopausal women (1). The most commonly reported sign consists of postmenopausal vaginal bleeding, which, most often, determines further investigation. In such a case, the patient is usually diagnosed in early stages of the disease, submitted to surgery with curative intent and reports an excellent result in terms of survival (2-4). However, in certain cases, vaginal bleeding is not seen, with the patient presenting diffuse abdominal pain, weight loss or asthenia. As a result, a longer period of time will pass between the onset of the symptoms and the moment of establishing the right diagnosis. Therefore, the patient will be diagnosed when disseminated lesions are already present with, unfortunately, a poorer outcome. It has been widely demonstrated that, while patients diagnosed in early stages of the disease report a 5-year survival of up to 85%, cases diagnosed in advanced stages will report a 5-year survival rate of less than 15%. Another significant prognostic factor in patients with endometrial cancer was shown to be the histopathological subtype; while cases diagnosed with type I endometrial cancer (endometroid tumors) report a favorable prognosis, women diagnosed with type-II endometrial cancer (serous cell tumors or clear cell tumors) will experience a poorer outcome. However, it seems that applying the principles of debulking surgery can significantly improve the outcomes of these cases (5, 6).

Case Report

A 60-year-old, nulliparous patient presented with diffuse abdominal pain, asthenia and weight loss. The preoperative imaging studies revealed the presence of a diffuse endometrial thickening in association with the presence of diffuse peritoneal thickening, mesenteric nodules and ascites. The patient was submitted to endometrial biopsy that revealed the presence of a high-grade endometrial serous carcinoma. After the specific preoperative preparation, the patient was submitted to debulking surgery, a total hysterectomy with bilateral adenexectomy, total colectomy, partial cystectomy with cystoraphy, pelvic, para-aortic lymph node dissection, total omentectomy, pelvic, parietal and left diaphragmatic peritonectomy, with a R0 resection being achieved (Figures 1-3). The terminal ileum was exteriorized in terminal right ileostomy. The postoperative course was uneventful, with the patient being discharged in the fifth postoperative day. The urinary catheter was removed in the 21th postoperative day. Histopathological and immunohistochemical studies revealed the presence of a high-grade serous endometrial carcinoma with three pelvic positive nodes. The patient was submitted to six cycles of adjuvant chemotherapy. Three months after ending the adjuvant treatment, she was submitted to a control computed tomography scan that revealed absence of recurrent disease. Therefore, the continuity of the digestive tract was

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re-established through a side to side ileo-rectal anastomosis. At 2-year follow-up, the patient is free of any recurrent disease.

Discussion

Advanced-stage endometrial cancer is associated with significantly poorer outcomes when compared to early stage of disease. However, it has been demonstrated that the principles of debulking surgery, that have been widely implemented as gold standard in advanced stage ovarian cancer, can be successfully applied with good results in terms of survival in advanced stage endometrial cancer as well (7-11).

One of the most relevant studies that evaluated the role of debulking surgery in the presence of peritoneal carcinomatosis for advanced stage endometrial cancer originates from Jerome Delotte, published in 2014 (4). The study was conducted on 13 patients submitted to debulking surgery combined with hyperthermic intraperitoneal chemotherapy between January 2001 and January 2013. Among these cases, resection of digestive segments was needed in three cases, while other visceral resections, such as partial cystectomy, atypical hepatectomy, splenectomy or diaphragmatic dome resection, were performed in other eight cases. The completeness of cytoreduction (CC) was defined by the dimension of the largest residual nodules as follows: CC=0, no macroscopic residual nodules; CC=1, residual nodules <2.5 mm; CC=2, residual nodules between 2.5 mm and 25 mm; and CC=3, residual nodules >25 mm. After ending the debulking process, the CC score was 0 for eight patients, 1 for three and 2 for two. The authors reported a median disease-free survival of 11.4 months and a median overall survival of 19.4 months. Among these cases, two patients were diagnosed with type-II endometrial cancer; in the first case, the CC score was 0, the time to relapse was 4 months, with the patient being deceased at the end of the study, while, in the second case, the CC score was 1, with the patient being alive and without recurrences after 1.56 months of follow-up (4).

Another study conducted on the survival impact of cytoreduction for advanced-stage endometrial cancer comes from Alagkiozidis et al. (12). The authors included 168
patients submitted to debulking surgery for advanced-stage endometrial cancer between 1984-2009, with 105 of them being submitted to complete cytoreduction. Among cases in which suboptimally debulking surgery was performed, the most common sites of residual disease included the pelvic area (in 61% of cases), mid-abdomen (in 35% of cases) and upper abdomen (in 35% of cases). As for the histopathological subtype, the serous or clear-cell adenocarcinomas were reported in 32% of patients. The authors reported a median time to death of 13 months among suboptimally debulked patients, significantly lower when compared to those in whom complete cytoreduction was achieved (and who reported a median overall survival rate of 25 months). In univariate analysis, there was no significant difference in terms of survival in regard to race, histopathological type or tumor grade, while, in multivariate analysis, the risk of death was significantly correlated with the presence of residual disease and initial stage at diagnosis. When it comes to the survival analysis in regard to the histopathological subtype, the authors demonstrated that the histopathological subtype did not impede the feasibility of complete cytoreduction. Patients with type I endometrial cancer and no residual disease reported a median survival of 36 months, while those with incomplete debulking reported a median survival of 21 months; in the meantime, patients with type II endometrial cancer -the serous subtype- reported a median overall survival of 22 months when complete cytoreduction was performed and only 12 months for incompletely debulked patients. Moreover, the authors demonstrated that patients submitted to surgery after 2000 benefited more often from radical procedures and experienced a better outcome when compared to those submitted to surgery before 2000 (12). The strength of the study was related to the demonstration of the benefits of debulking surgery for type II endometrial tumors; the authors clearly demonstrated that type II tumors can be also submitted to debulking surgery with good results in terms of survival.

A similar study, which was focused on the effectiveness of debulking surgery for serous endometrial carcinomas, comes from Thomas et al. (13). In this study, the authors included 125 patients diagnosed with stage IIIC-IV uterine papillary serous carcinomas; patients submitted to complete cytoreduction experienced a median overall survival of 51 months, significantly higher when compared to those submitted to optimal cytoreduction (but with residual disease) who experienced a median overall survival of 14 months or to those submitted to incomplete cytoreduction (who reported an overall survival rate of 12 months). Moreover, the same study underlined the fact that performing radical surgical procedures in order to achieve a R0 resection did not affect the overall survival rate (13). A similar conclusion was also revealed by Memarzadeh et al.’s study that included 43 patients with stage IIIC and IV uterine papillary serous carcinomas, demonstrating, in this way, the effectiveness of cytoreductive surgery in improving both the progression-free and overall survival of these patients (14).

**Conclusion**

Although type-II endometrial cancer has been considered for a long time as an aggressive biological subtype, recent studies demonstrated that cytoreductive surgery can be safely applied and associated with a significant benefit in terms of survival even if multiple visceral resections are needed.

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