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Multimodal oncosurgery approach to treat peritoneal carcinomatosis in a patient with occlusive ovarian carcinoma

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Summary

Background: This paper aims to present a "pattern" of oncosurgery solution in a case generally considered unrecoverable: intestinal occlusion in case of ovarian carcinoma and carcinomatosis. *Case Report:* A 62-year-old female patient with ascites, carcinomatosis, unresectable pelvic tumour, and intestinal obstruction suffered a five-step oncosurgery "model": three surgical interventions overlapping chemotherapy administered via the systemic and intraperitoneal route: Step 1: colostomy and partial omentectomy; Step 2: five courses of systemic chemotherapy supported by granulocyte colony-stimulating factor; Step 3: radical surgery - total hysterectomy, bilateral adnexectomy, pelvic lymphadenectomy, omentectomy, appendectomy, pelvic peritonectomy, and hyperthermic intraperitoneal chemotherapy; Step 4: consolidation systemic chemotherapy consisting of three more similar cycles; Step 5: closure of the colostomy. Nine months after the beginning of treatment, the patient is with no evidence of disease. *Conclusions:* The association of surgical and oncologic treatment and the use of hyperthermic intraperitoneal chemotherapy (HIPEC) technology can solve some of these complex cases.

Key words: Peritoneal carcinomatosis; Occlusive ovarian cancer; Hyperthermic intraperitoneal chemotherapy.

Introduction

Ovarian cancer is a clinical entity with an increasing incidence among genital cancers in Romania. It is the first death cause of genital malignancies worldwide [1], presenting the particularity of increased tropism of the peritoneal serous in case of peritoneal carcinoma and paucity of clinical complaints, most of the cases being detected at this stage. A positive aspect of most of the ovarian cancers is represented by chemosensitivity, which makes it susceptible to systemic oncology therapy and local hyperthermic intraperitoneal chemotherapy (HIPEC). In 1980 Spratt *et al.* demonstrated for the first time the effectiveness of hyperthermic intraperitoneal chemotherapy (HIPEC) in the treatment of ovarian peritoneal carcinomatosis, observations extended and continued by Sugarbaker in the 1990s [2]. Initiated in June 2013, the HIPEC program of the present Hospital totals 15 of such procedures, ten of them being used to treat ovarian cancers with peritoneal carcinomatosis.

Case Report

The history of a 62-year-old patient began nine months ago with lower abdominal pain, enlarged volume of the abdomen, and bowel disorders. She was evaluated and operated in a Romanian emergency hospital where she was diagnosed with inoperable ovarian tumour, “frozen pelvis”. This case was considered to be beyond therapeutic resources and indication for chemotherapy irrelevant, reason why biopsy sampling was also considered useless. The patient was sent to the present hospital. At the time, ten days postoperatively, the patient was still hospitalized without bowel movement and experienced incoercible vomiting and general malaise.

The first abdominal pelvic CT performed on admission showed bowel obstruction in the lower quadrant, ovarian tumour that invaded the rectosigmoid junction (emphasized distension of the entire digestive tract and hydro-air levels, preperforative cecum), and produced peritoneal carcinomatosis with ascites, peritoneal nodules, and “omentum cake” aspect. Pelvic adenopathy (obturator, presacral, and external iliac region up to 15 mm) (Figure 1).

On admission, the laboratory using the PCR technique detected an inflammatory syndrome of 6.6 mg/dl (normal values (NV) below 0.5), neutrophilic leukocytosis 12,600 /mmc, hypoalbuminemia (2.4 g/dl) with hypoproteinemia (5.6 g/dl), unmarkedly elevated nitrogen retention with urea 27.7 (NV under 18), creatinine within normal limits (0.47), due to catabolic syndrome with muscle atrophy. The tumor markers showed increased level of CEA 4.9 (NV under 3.8 ng/ml) and CA 125 840U / ml.

It was decided that a minimal surgical intervention should be performed for the purpose of clearance and biopsy sampling (Step 1): relaparotomy, the Maydl rod colostomy at the level of the sigmoid colon preceded by the evacuation of intestinal contents through a small incision performed at the level of the future stoma, patchy resection of the omentum for biopsy, and cytoreductive purposes.

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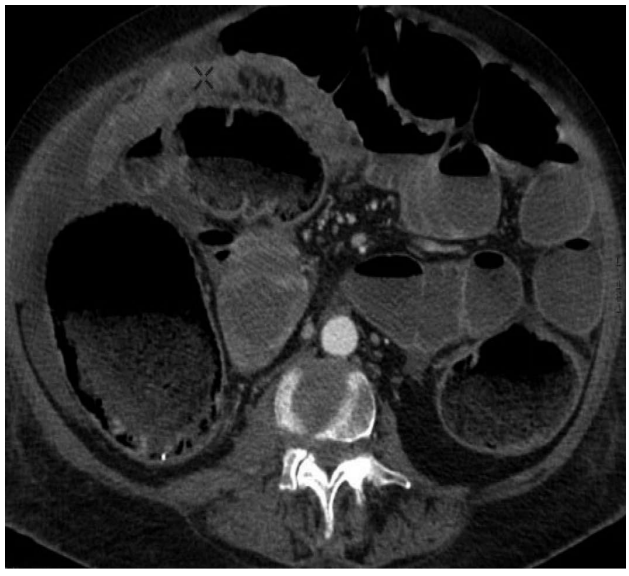

Figure 1. — Hydro-air levels, ascites, peritoneal nodules, and omental cake.

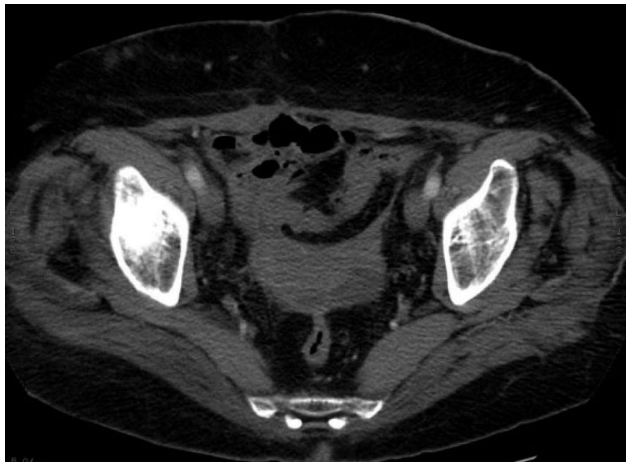

Figure 2. — Inhomogeneous left ovarian cystic tumour formation in contact with the sigmoid colon.

Postoperative evolution was uneventful, the patient was discharged five days postoperatively. The pathological examination revealed: ovarian origin peritoneal and epiploic metastasis of serous carcinoma.

The second step (October 2013 - February 2014) consisted of systemic chemotherapy, five courses of paclitaxel 175 mg/m^2, and carboplatin AUC 5 in 21-day cycles with good clinical and haematological tolerance supported by granulocyte colony-stimulating factor (GCSF), with a very good clinical and imagistic response (normalized tumour markers, nearly complete imaging response) (Figure 2).

Stage 3 (March 2014) consisted of radical surgery combined with HIPEC, five months after the initial surgery. A total hysterectomy with bilateral adnexectomy, pelvic lymphadenectomy, omentectomy, appendectomy, peritonectomy, and HIPEC by using 100 mg of cisplatin at 41- 42 ˚C for 90 minutes under general orotracheal anaesthesia were all performed. The total duration of the intervention was 370 minutes. Note that after the patient responded to systemic chemotherapy, ovarian tumour invading the rectosigmoid junction disappeared, thus the rectosigmoid resection was no longer needed and the lateral colostomy on the sigmoid colon was preserved.

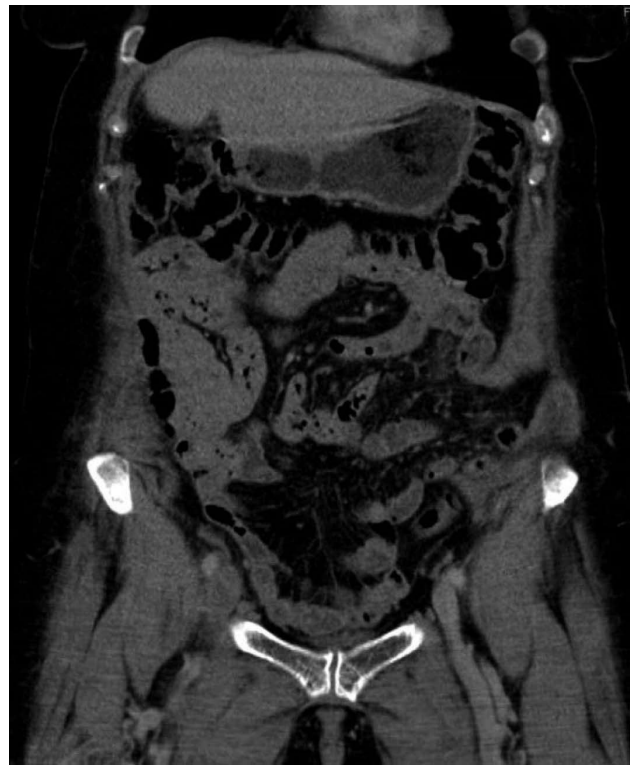

Figure 3. — Coronal CT without any signs of abdominopelvic tumor.

Because postoperative evolution was uneventful, the patient was discharge on 5th postoperative day. The post-chemotherapy pathological results showed microscopic bilateral ovarian and lymphatic and epiploic implants of ovarian serous adenocarcinoma ypT3a ypN1 ypMx (two positive left obturator lymph node metastases out of 26).

Step 4 consisted of consolidation chemotherapy (March - May 2014) started two weeks post-operatory and comprised of three courses of paclitaxel 175 mg/m^2 and carboplatin AUC 5 in 21-day cycles, the last CT scan showing no tumour deposits in the abdomen (Figure 3).

Step 5 (June 2014) was represented by the closing of the lateral colostomy and, thus, achieving the desired functionality of surgery, besides the oncological one: R0 resection, bowel movement restored, and complete social reintegration. Currently, nine months postoperatively, the patient is asymptomatic, there are no signs of recurrence, and oncological treatment is no longer required. The patient is only followed up by the oncology clinic. The evolution of tumour markers is shown in Table 1.

Discussion

Traditionally, patients with ovarian cancer and peritoneal carcinomatosis are considered to have a terminal disease,

Table 1. — *The evolution of tumour markers.*

Data	CA 125 (NV < 35 UI /ml)	CEA (NV < 3.5 ng/ml)
30.09.13 Hospitalization	840.8	4.9
16.10.13 Initializing chemotherapy	963.4	
13.11.13	371.6	
11.12.13	86.4	
06.01.14 HIPEC	23.62	
03.02.14	14.05	
24.03.14	20.56	
14.04.14	13.59	
05.05.14 Final chemotherapy	10.21	

beyond therapeutic solutions, the vast majority undergoing surgical procedures or palliative cancer therapy. The multimodal oncosurgery approach combined with HIPEC has proven to be an extremely efficient alternative, with a median tumour-free period between ten to 57 months and five-year survival rate in different series of patients between 12% and 66%. Thus peritoneal carcinomatosis deriving from ovarian cancer nowadays is considered a loco-regional disease [2].

Standard chemotherapy is the combination of paclitaxel 175 mg/m^2 and carboplatin AUC 6-5 administered intravenously every three weeks (level of evidence IA) [3]. Usually they are administered in six cycles. This combination is equally efficient but it is more toxic and less convenient to administer. Epithelial ovarian cancers present high risk of recurrence, therefore postoperative chemotherapy is recommended for all patients in FIGO Stages II-IV [3].

The only HIPEC program in Romania is operated in the present hospital, ovarian cancer being the most frequent indication, ten of 15 cases of HIPEC performed in the present authors' surgery department address this type of disease.

Regarding operation timing, HIPEC can be applied in five moments of the natural evolution stages of an ovarian cancer as established by Helm *et al.* [2]: 1) primary treatment; 2) debulking after initial chemotherapy; 3) consolidation after achieving a complete pathological response confirmed by second-look laparotomy; 4) first-time recurrence; 5) safeguard therapy [2].

Regarding the used cytostatic therapy, the present authors opted for the Konigsrainer 2011 protocol with cisplatin 50 mg/m^2 for 90 minutes with closed abdomen vis-a-vis the Deraco (cisplatin 40 mg/l plus doxorubicin 15 mg/l) and Elias protocol (oxaliplatin 460 mg/m^2) [4-6].

The internationally attained results of aggressive cytoreductive surgery associated with HIPEC in current cancer treatment, makes us believe that in the near future this will become "standard of care" in ovarian cancer cases aggravated by peritoneal carcinomatosis.

Conclusions

The article aims to change the attitude of the medical world towards the treatment of ovarian cancer aggravated by peritoneal carcinomatosis, from an exclusively oncological palliative therapy, to a multimodal oncosurgery aggressive therapy, combined with HIPEC targeting the prolongation of disease-free period and survival rate. The timing of HIPEC is essential and systemic neoadjuvant chemotherapy plays an important role in obtaining the desired R0 resection and its consolidation.

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