**Case Reports**

# Third stage ovarian carcinoma - case report: the necessity of a multidisciplinary approach to treatment

**E.M. Messalli, C. Scaffa, G. Mainini, M. Rotondi, E. Pecori, L. Cobellis**

*Department of Gynaecologic, Obstetric and Reproductive Sciences*
*Second University of Naples, Naples (Italy)*

**Summary**

Ovarian carcinoma, part of a heterogeneous group of tumours, is the main cause of death by gynaecological neoplasms [1, 2].

The diagnosis, in general, is delayed. Multiorgan diffusion, the necessity of a surgical operation and strong chemotherapy, and the eventual pathology due to patient age are all factors that require a multidisciplinary approach. In fact the case, here reported, refers to a patient who came under our observation for a bilateral ovarian mass discovered casually during an abdominal ultrasound exam carried out for renal colic. Excellent cytoreduction with peritoneal cytology, total abdominal hysterectomy, bilateral salpingo-oophorectomy (Figure 2), bilateral pelvic lymphadenectomy, total omentectomy, removal of nodules from the mesentery, the colon and three nodules in the abdominal wall thickness was executed. The histological report was G3, angioinvasive bilateral ovarian endometrioid adenocarcinoma. Metastasis was found only in one left obturator lymph node out of 17 lymph nodes removed. All of the removed abdominal, mesenteric and intestinal nodules were neoplastic. It is concluded that the complexity of similar cases always requires a multidisciplinary approach as in our case, involving an oncologist, hematologist, surgeon, gynaecologist, radiologist, anaesthesiologist, and nursing staff in the management of third stage ovarian cancer patients to obtain the best treatment thus guaranteeing a higher survival rate and better quality of life.

*Key words:* Ovarian carcinoma; Gynaecological neoplasm; Chemotherapy.

## Case Report

A 67-year-old woman, para 3, with a body mass index (BMI) of 34 was admitted. One sister had died due to a uterine tumour and another to a tumour of another organ. Pathological anamnesis included high cholesterol, hypertension, repeated renal calciuria, appendectomy and laparoscopic cholecystectomy for lithiasis 16 months before the diagnosis.

Gynaecological anamnesis showed menstruation at 11 years and menopause at 49 years. There were no atypical uterovaginal loss. On abdominal palpation, which was difficult due to adipose layer thickness, the gynaecological examination showed two hard swollen areas of the wall. One was umbilical (about 5 cm) and the other (3 cm) was localized in the superior right quadrant of the abdomen. The presence of two adnexal masses was confirmed. They were irregular in shape and consistency, moderately painful, slightly movable, 15 and 6 cm in diameter, and not easily distinguishable from the larger part of the uterus. The cervical exam showed cervicitis.

Pelvic and transvaginal ultrasonography showed a uterus of 82 x 32 x 45 mm. In the right adnexa an anechoic cyst of 136 x 90 mm was localized and in the left, a cyst with the same characteristics (52 x 52 mm). Also the presence of ascites in moderate quantities was identified.

The abdominal CT scan (Figure 1) confirmed the report and the negativity of retroperitoneum nodes. Only CA125 (310.5 U/ml) and CA15-3 (194 U/ml) were raised and were rapidly increasing in a successive preoperatory test. An excellent cytoreduction with peritoneal cytology, total abdominal hysterectomy, bilateral salpingo-oophorectomy (Figure 2), bilateral pelvic lymphadenectomy, total omentectomy, removal of nodules from the mesentery and colon and three nodules in the abdominal wall thickness was executed. The histological report was G3 angioinvasive bilateral ovarian endometrioid adenocarcinoma. Metastasis was found only in one left obturator lymph node out of 17 lymph nodes removed. All of the removed abdominal, mesenteric and intestinal nodules were neoplastic. The staging, however, was pT3cN1 (FIGO IIIc).

A month after the first surgery, the abdominal ultrasound was negative, CA125 was 101 U/ml and CA15-3 54.9 U/ml. It was not possible to start the planned chemotherapy because of marked leukopenia. A sternal tap was carried out to exclude metastasis. It was identified as haematopoietic cell blockage that needed therapy with erythropoietin and growth factors to boost the white cells.

The first cycle of chemotherapy, according to the usual protocol (carboplatin and taxol), was, however, started three months after the first surgery. The second and third cycles fol-

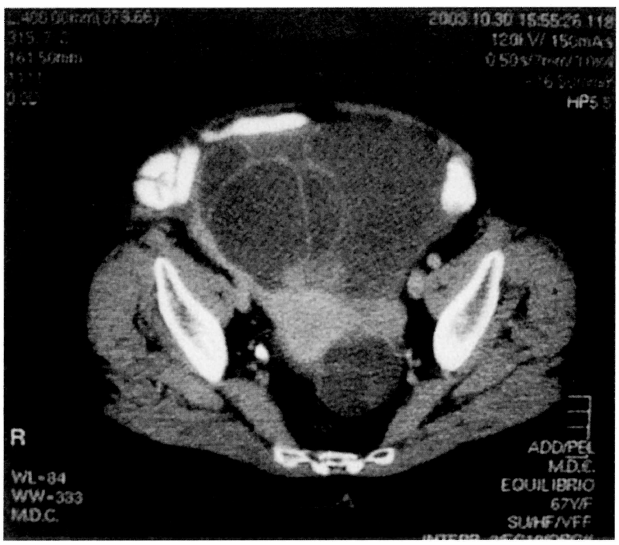


Figure 1. — Presurgical CT.

Revised manuscript accepted for publication March 8, 2005

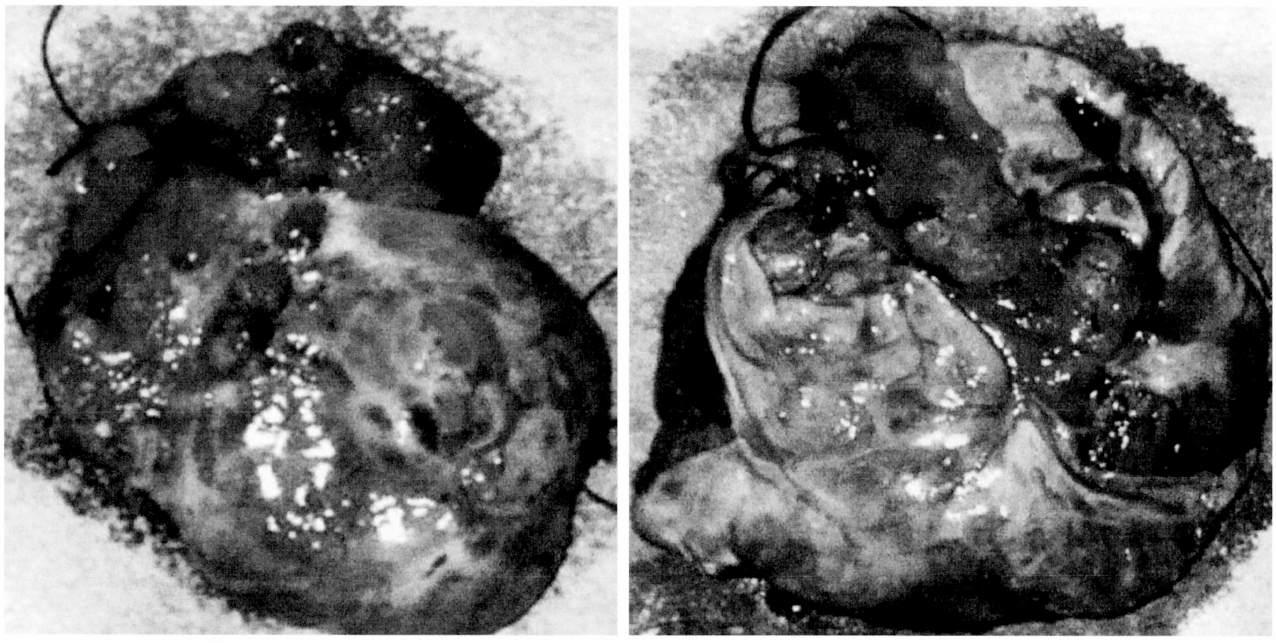

Figure 2. — Left and right ovarian mass.

lowed at a distance of a month for the same problems and an echocardiographic report of a well compensated dilatative cardiomyopathy.

Before the third cycle CA125 (99.8 U/ml) was stable while CA15-3 (161.3 U/ml) showed a constant increase in respect to the postsurgical values. The clinical exam showed a polycyclical swollen area of about 7 cm, fairly mobile, corresponding to the left inguinal area. Removal of the inguinal mass was proposed but not accepted. About a month after, other clinical tests were carried out and both ultrasound and PET/CT showed an area of rapid tumoural growth that needed second-line chemotherapy with Doxorubicin cloridrate (40 mg/m$^2$). Also this therapy was ineffective (CA125 363 U/ml; CA15-3 203 U/ml) and again complications arose from the general condition of the patient who died after nine months from the diagnosis and the first surgery.

## Discussion

Ovarian carcinoma is characteristically found in 50-75 year-old women. Progression is often with few symptoms so it is called "the silent killer" [3].

Lack of a valid precocious diagnosis and the underhand spread explain the delayed diagnosis of the disease and its high mortality rate. Also in this case, the tumour spread was silent so that the symptoms were diagnosed as renal lithiasis and gallbladder pathology. The diagnosis, in fact, was occasional during an abdominal ultrasound executed for renal colic.

Often family predisposition or a true genetic makeup is found in anamneses like in this case. Among the several risk factors, age and race are without a doubt pertinent, while among the protective factors, the number of pregnancies and breast feeding, slightly affected this patient. As always, the gynaecological exam was fundamental in the initial diagnosis and clinical staging since the abdominal palpation (even more difficult in obese patients) allowed us to identify the presence of nodes in the wall which were not identified in the successive CT scan. This exam, however, has a complementary role in the study of ovarian masses because, in general, it adds little to ultrasound diagnosis of ovarian pathology, while it is surely important for retroperitoneum evaluation [4].

The markers CA125 and CA15-3 were useful because their elevation and rapid increase raised clinical suspicion further [5].

Once the diagnosis of a suspected Stage III ovarian neoplasm was made, explorative laparotomy for peritoneal cytology, hysterectomy with bilateral oophorectomy, cytoreduction (possibly excellent with a small residual tumour of about 0.5 cm) [6], lomboaortic and pelvic lymphadenectomy, omentectomy and appendyectomy were carried out. Today, these are considered the guidelines of therapy [1] although not all surgeons agree on the use of lymphadenectomy and strong cytoreduction [6], as it puts the patient at risk because of greater and more difficult exeresis without assured improvement in quality of life. In these cases, easier treatments according to many authors [7, 8], could be debulking the main masses followed by adjuvant chemotherapy and secondary surgical cytoreduction. In our case lomboaortic lymphoadenectomy was not performed because of the retroperitoneum negativity to palpation, the preoperatory tests and the patient's obesity. Thus the patient was classified as having non evident disease (NED) at the end of the first cytoreductive surgery. This was also confirmed by a rapid decrease in CA125 and CA15-3 values.

As in the case of our patient, variations in markers are often more useful in the evaluation and management of follow-up [9]. A more reliable prognostic index of disease gravity could be the value of CA 15-3 because an increase is linked to lower survival rate, as in this case [5].

The metastasis in the abdominal wall thickness was covered by the parietal peritoneum which was seemingly healthy. The position suggested implants in the area of the

trocar insertions during the previous laparoscopic cholecystectomy carried out 16 months before the current diagnosis.

Some authors report 58% of metastases from the trocar if only the skin is sutured while this percentage decreases to 2% if the abdominal wall is sutured layer by layer [10]. The study of these authors however, refers to metastases after laparoscopy in patients already affected by ovarian tumours generally in the ascitic phase [11, 12]. In our case laparoscopic cholecystectomy was carried out 16 months before the diagnosis. Carlson *et al.* reported a similar case of metastasis of serous papilliferous ovarian carcinoma Stage IIIC found 16 months after the initial surgery in the area of the trocar used seven months before this surgery for the same cholecystectomy operation [13]. In this case it is possible that at the time of laparoscopy the ovarian tumour was already present, but not known, and with exfoliant cells present in the abdominal cavity, thus the tumour was in the initial stage, undiagnosed, but already capable of freeing tumourous cells into the peritoneum.

The successive therapy foresaw adjuvant chemotherapy (with carboplatin and taxol) but was delayed due to strong myelodepression which made it necessary to use drugs to stimulate the medulla both before and during the therapy. The usefulness of these drugs is, above all, conditioned by a few possible negative effects [14], which increase the death rate and deep vein thrombosis. A solution to the problem could be, therefore, to investigate the action of erythropoietin on apotosis and angiogenesis [15].

Another unique characteristic of our case was the evidence of metastasis in the left inguinal lymph nodes manifested by palpable painful swollen areas during the adjuvant chemotherapy. Similar cases are however rare [16]. According to McGonigle *et al.*, inguinal ovarian metastasis happens only after blockage of lymphatic drainage due to tumour emboli with consequent lymphatic backward flux to the inguinal lymph nodes [17]. In our case this could be the consequence of ligament blockage due to utero-adnexal exeresis and the pelvic lymphadenectomy.

Another hypothesis is that asymptomatic metastasis could have already been present in the left inguinal lymph nodes because the only lymph node metastasis was found on the same side in an obturator lymph node.

Regarding lower survival rate some authors do not agree on the link between the endometrioid histotype that represents about 2% of epithelial carcinomas [1, 18]. The reported cases showed however several negative prognostic factors, some specific, as the poor differentiation and vessel invasion, others unspecific, such as myelodepression which delayed the chemotherapy and dilatative cardiomyopathy that resulted in difficulties for the second-line chemotherapy.

Finally the management problems that occurred during the treatment of this patient were many and varied: myelodepression, dilatative cardiomyopathy, the choice of chemotherapy, secondary debulking, and removal of the inguinal lymph nodes and definitely, but not last, the condition and the wishes of the patient and her family with resulting psychological considerations.

We report this case, once again to confirm that the complexity of similar cases always requires a multidisciplinary approach, involving in the management of third stage ovarian cancer patients an oncologist, haematologist, surgeon, gynaecologist, radiologist, anaesthesiologist, and nursing staff to obtain the best treatment thus guaranteeing a longer survival rate and better quality of life.

## References

[1] Benedet J.L., Haker N.F., Ngan H.Y.S.: "Staging classifications and clinical practice guidelines of gynaecologic cancers". *Int. J. Gynecol. Obstet.,* 2000, *70,* 207.

[2] Hoskins W.J.: "Surgical staging and cytoreductive surgery of epithelial ovarian cancer". *Cancer*, 1993, *71,* 1534.

[3] Goff B.A., Mandel L.S., Melancon C.H., Muntz H.G.: "Frequency of symptoms of ovarian cancer in women presenting to primary care clinics". *JAMA,* 2004, *291,* 2705.

[4] Forstner R., Hricak H., Occhipinti K.A., Powell C.B., Frankel S.D., Stern J.L.: "Ovarian cancer: staging with CT and MR imaging". *Radiology,* 1995, *197,* 619.

[5] Schutter E.M.J., Davelaar E.M., van Kamp G.J., Verstraeten R.A., Kenemans P., Verheijen R.H.M.: "The differential diagnostic potential of a panel of tumor markers (CA 125, CA 15-3, and CA 72-4 antigens) in patients with a pelvic mass". *Am. J. Obstet. Gynecol.,* 2002, *187,* 385.

[6] Griffiths C.T., Parker L.M., Lee S., Finkler N.J.: "The effect of residual mass size on response to chemotherapy after surgical cytoreduction for advanced ovarian cancer: long-term results". *Int. J. Gynecol. Cancer,* 2002, *12,* 323.

[7] Saia P., Creasman W.: "Epithelial ovarian cancer". Clinical Gynecologic Oncology. 6th edition, N.Y., Mosby, 289, 2002.

[8] Maggioni A., Maneschi F., Mangioni C., Landoni F., Scambia G., *et al.*: "Randomized trial of lymphadenectomy (LY) vs. sampling (SA) or resection of bulky nodes (RBN) as primari surgical procedure in early epihtelial ovarian cancer". *Int. J. Gynecol. Cancer,* 1999, *9,* 43.

[9] Fioretti P., Gadducci A., Ferdeghini M., Prontera C., Malagnino G., Facchini V. *et al.*: "The concomitant determination of different serum tumor markers in epithelial ovarian cancer: Relevance for monitoring the response to chemotherapy and follow-up of patients". *Gynecol. Oncol.,* 1992, *44,* 155.

[10] Van Dam P.A., DeCloedt J., Tjalma W., Buytaert P., Becquart D., Vergote I.B.: "Trocar implantation metastasis after laparoscopy in patients with advanced ovarian cancer: Can the risk be reduced?". *Am. J. Obstet. Gynecol.,* 1999, *181,* 536.

[11] Kruitwagen R.F.P.M., Swinkels B.M., Keyser K.G.G., Doesburg W.H., Schijf C.P.T.: "Incidence and effect on survival of abdominal wall metastases at trocar or puncture sites following laparoscopy or paracentesis in women with ovarian cancer". *Gynecol. Oncol.*, 1996, *60,* 233.

[12] Morice P., Viala J., Pautier P., Lhomme C., Duvillard P., Castaigne D.: "Port-site metastasis after laparoscopic surgery for gynecologic cancer. A report of six cases". *J. Reprod. Med.,* 2000, *45,* 837.

[13] Carlson N.L., Krivak T.C., Winter W.E., Macrì C.I.: "Port site metastasis of ovarian carcinoma remote from laparoscopic surgery for benign disease". *Gynecol. Oncol.*, 2002, *85*, 529.

[14] Leyland-Jones B.: "Breast cancer trial with erythropoietin terminated unexpectedly". *Lancet Oncol.,* 2003, *4*, 459.

[15] Brower V.: "Epoetin for cancer patients: a boon or a danger?". *J. Nat. Cancer Inst.,* 2003, *95,* 1820.

[16] Scholz H.S., Lax S., Tamussino K.F., Petru E.: "Inguinal lymph node metastasis as the only manifestation of lymphatic spread in ovarian cancer: A case report". *Gynecol. Oncol.,* 1999, *75,* 517.

[17] McGonigle K.F., Dudzinski M.R.: "Endometrioid carcinoma of the ovary presenting with an enlarged inguinal lymphnode without evidence of abdominal carcinomatosis". *Gynecol. Oncol.,* 1992, *45*, 225.

[18] Mangioni C., Bonazzi C., Colombo N., Epis A., Landoni F., Vasena L. *et al.* : "Pathologic complete responses in advanced epithelial ovarian cancer: prognostic factors for long-term survival". In: Conte P.F., Ragni N., Rosso R., Vermorken J.B., eds. Multimodal Treatment of Ovarian Cancer. New York, Raven Press 1989, 271.

Address reprint requests to:
M. ROTONDI, M.D.
Via G. Mazzini, 5
80059 Torre del Greco (NA) Italy