

FIGO Stage I endometrial carcinoma: evaluation of lung metastases and follow-up

F.L. Labi, S. Evangelista, A. Di Miscia, P. Stentella

Department of Obstetrics and Gynecology, Neonatology Department, Umberto I Clinic, Rome (Italy)

Summary

Purpose: The aim of our study was to evaluate the incidence of lung metastases in the follow-up of women submitted to surgery for endometrial carcinoma, in particular for FIGO Stage I which is the lowest risk stage for this metastatic site. **Methods:** The study was conducted on 210 patients affected by FIGO Stage I endometrial cancer in the years 1990 to 2005 distributed as follows: 35 patients with Stage IA (limited to the endometrium), 150 patients with Stage IB (invasion up to and including half the myometrial thickness), 25 patients with Stage IC (invasion greater than half the myometrial thickness). They underwent follow-up. **Results:** Only one patient out of the group studied has developed lung metastasis six years after surgery. She was staged as FIGO IB (T1b Mx G1). **Conclusion:** We are still following the cases and evaluating the biological behavior of this specific endometrial carcinoma and its reaction to further therapies. We are also looking for possible clinical characteristics in disagreement with those reported in the literature, which would thus make it necessary to reconsider the prognosis and therapy of this stage of disease.

Key words: Endometrial cancer; Lung metastasis; Follow-up; Lung metastasis therapy.

Introduction

The aim of the study was to evaluate the incidence of lung metastasis in the follow-up of women submitted to surgery for endometrial carcinoma, in particular for FIGO Stage I [1, 2], which is the lowest risk stage for this metastatic site [3-5].

According to the studies of the American Cancer Society of the Centers for Disease Control and Prevention and of the Gynecologic Oncology Group we can affirm that endometrial carcinoma is the most common pelvic malignant neoplasia in women [6-8].

It mainly spreads to less than half of the myometrium (Stage IB), over half of the myometrium (Stage IC), endocervical glands (Stage IIA), cervical stroma (Stage IIB), serosa and/or adnexa and/or peritoneum (Stage IIB), vagina (Stage IIIB), pelvic and pre-aortic nodes (Stage IIIC), bowel and bladder mucosa (Stage IVA), distant organs including inguinal and intraabdominal nodes (Stage IVB).

On the basis of the architecture and cytologic atypia, endometrial carcinoma is classified as: well differentiated (G1), moderately differentiated (G2), and poorly differentiated (G3) [9].

The lung is the most frequent site of distant metastasis. The incidence of metastasis varies according to stage and pathology as shown by many studies [3-5] and in particular by a study conducted by a Japanese group which demonstrated that lung metastases due to endometrial cancer FIGO Stage I/G1 have a very low incidence compared to those at a higher stage and with a more aggressive pathology [10].

Materials and Results

Our study was conducted on 210 patients affected by endometrial cancer FIGO Stage I in the years 1990 to 2005 distributed as follows:

- 35 patients with Stage IA (limited to the endometrium);
- 150 patients with Stage IB (invasion up to and including half the myometrial thickness);
- 25 patients with Stage IC (invasion greater than half the myometrial thickness).

All the patients underwent laparotomic surgery in our Institute and more specifically they were submitted to total hysterectomy, bilateral salpingo-oophorectomy, peritoneal washing (with negative results), and lymph node sampling [11-13].

On the basis of substaging and grading, some patients underwent adjuvant therapy [14-18].

Surveillance after treatment was every three months the first and second years, every six months the third year, every six months the fourth and fifth years, and once a year for the following period.

The investigation included a general and gynecologic check-up with vaginal smear, markers, pelvic, kidney and hepatic ultrasounds, lung X-ray (yearly), bilateral mammography (yearly), bone scintigraphy (yearly), abdominal CAT scan (before surgery, 2 years after surgery, and afterwards once a year) [19-21].

Results

Only one patient out of the study group developed lung metastasis six years after surgery. She was staged as FIGO IB (T1b Mx G1).

The patient, 55 years old with negative anamnesis for risk factors, underwent a total hysterectomy with bilateral salpingo-oophorectomy, removal of the vaginal cuff and pelvic lymphadenectomy. Peritoneal washing was negative. The pathologic diagnosis was highly differentiated G1 endometrial adenocarcinoma. Follow-up was totally

Revised manuscript accepted for publication April 19, 2007

negative up to the sixth year, when a routine lung X-ray followed by a CAT scan showed bilateral lung metastasis.

The patient was submitted to various hormonal therapies without results [22-24]. A second-line treatment included chemotherapy with cisplatinum [25-28] up to volume reduction of the metastasis followed by bilateral lung metastasectomy [29]. She had been free of disease for six months when she developed a new bilateral lung metastasis. The patient is now in treatment with aromatase inhibitor.

Discussion

According to the clinical history of the patient who developed metastasis, we can assert that this case, based on the biological behavior, was an endometrial sarcoma rather than an endometrial carcinoma:

- family and personal history were negative for risk of developing endometrial adenocarcinoma;
- the first symptom of the patient was an episode of metrorrhagia lasting 12 hours two years after menopause, typical of uterine sarcoma rather than of endometrial carcinoma which causes abnormal bleeding;
- atypical incidence of recurrence (after 6 years), response to hormonal treatment (negative) and surgery of recurrence (recurrence of metastasis six months afterwards).

Conclusion

Two different pathologists reexamined the histological samples to exclude a wrong evaluation between endometrial adenocarcinoma and sarcoma.

We are still following the case and evaluating the biological behavior of this specific endometrial carcinoma as well as its reaction to further therapies.

We are also investigating possible eventual clinical characteristics not in agreement with those reported in the literature, which would make it necessary to reconsider the prognosis and therapy of this stage of disease.

References

- [1] Gastaldi A., Bianchi U.A. *et al.*: "Surgical staging in endometrial cancer". Proceedings of the International Meeting of Gynecologic Oncology, SOG, Padua, 1985.
- [2] Creasman W.T.: "FIGO stage 1988 revision". *Gynecol. Oncol.*, 1989, 35, 125.
- [3] Kilgore L.C., Partridge E.E., Alvarez R.D., Austin J.M., Shingleton H.M., Moojin F. *et al.*: "Adenocarcinoma of the endometrium: survival comparisons of the patients with and without pelvic node sampling". *Gynecol. Oncol.*, 1995, 56, 29.
- [4] Connel P.P., Rotmensch J., Waggoner S., Mundt A.J.: "Significance of adnexal involvement in endometrial carcinoma". *Gynecol. Oncol.*, 2003, 74, 74.
- [5] Lutman C.V., Havrilesky L.J., Cragun J.M., Secord A.A., Calingaert B., Berchuck A. *et al.*: "Pelvic lymph node count is an important prognostic variable for FIGO Stage I and II endometrial carcinoma with high-risk histology". *Gynecol. Oncol.* 2006 Jan 5; [Epub ahead of print].
- [6] Parazzini F., La Vecchia C., Bocciolone L., Franceschi S.: "The epidemiology of endometrial cancer". *Gynecol. Oncol.*, 1991, 41, 1.
- [7] Jemal A., Murray T., Ward E. *et al.*: "Cancer statics 2005". *Cancer J. Clin.*, 2005, 55, 10.
- [8] Purdie D.M., Green E.: "Epidemiology of endometrial cancer". *Best Pract. Res. Clin. Obstet. Gynecol.*, 2001, 15, 341.
- [9] Amant F., Moerman P., Neven P., Timmerman D., Van Limbergen E., Vergote I.: "Endometrial cancer". *Lancet*, 2005, 366, 491.
- [10] Otsuka I., Ono I., Akamatsu H., Sunamori M., Aso T.: "Pulmonary metastasis from endometrial carcinoma". *Int. J. Gynecol. Cancer*, 2002, 12, 208.
- [11] Santin A.D., Bellone S., O'Brien T.J., Pecorelli S., Cannon M.J., Roman J.J.: "Current treatment options for endometrial cancer". *Expert Rev. Anticancer Ther.*, 2004, 4, 679.
- [12] Leijon T., Rosenberg P., Boeryd B.: "Total abdominal hysterectomy and bilateral salpingo-oophorectomy. A sufficient treatment for patients with low risk endometrial carcinoma". *Int. J. Gynecol. Oncol.*, 1997, 7, 376.
- [13] Zorlu C.G., Simsek T., Ari E.S.: "Laparoscopy or laparotomy for the management of endometrial cancer". *JSLs*, 2005, 9, 442.
- [14] Creutzberg C.L., van Putten W.L., Koper P.C. *et al.*: "Surgery and postoperative radiotherapy versus surgery alone for patients with stage-I endometrial carcinoma". *Lancet*, 2000, 355, 1404.
- [15] Cengiz M., Singh A.K., Grigsby P.W.: "Postoperative vaginal brachytherapy alone is the treatment of choice for grade 1-2, stage IC endometrial cancer". *Int. J. Gynecol. Cancer*, 2005, 15, 926.
- [16] Chen S.S.: "Operative treatment in Stage I endometrial carcinoma with deep myometrial invasion and or grade 3 tumor surgically limited to the corpus uteri". *Cancer*, 2000, 63, 1834.
- [17] Mangioni C., DePalo G., DelVecchio M.: "Surgical pathologic staging in apparent Stage I endometrial cancer". *Int. J. Gynecol. Cancer*, 2003, 3, 373.
- [18] Patterson E. *et al.*: "Management of stage I carcinoma of the uterus". *Obstet. Gynecol.*, 1992, 59, 755.
- [19] Kew F.M., Cruickshank D.J.: "Routine follow up after treatment for a gynaecological cancer: a survey of practice". *Int. J. Gynecol. Cancer*, 2006, 16, 380.
- [20] Bouros D., Papadakis K., Siafakas N., Fuller A.F. Jr.: "Patterns of pulmonary metastasis from uterine cancer". *Oncology*, 1996, 53, 360.
- [21] Bouros D., Papadakis K., Siafakas N., Fuller A.F. Jr.: "Natural history of patients with pulmonary metastases from uterine cancer". *Cancer*, 1996, 78, 441.
- [22] Barakat R.R., Bundy B.N., Spirtos N.M., Bell J.G., Mannel R.S.: "A prospective randomized double-blind trial of estrogen replacement therapy vs placebo in women with Stage I or II endometrial cancer: a GOG study". *Gynecol. Oncol.*, 2004, 78 (abstract 1).
- [23] Agboola O., Grunfeld E., Coyle D., Perry G.: "Cost and benefits of routine follow-up after curative treatment for endometrial cancer". *CMAJ*, 1997, 157, 879.
- [24] Morice P., Levy-Piedbois C., Ajaj S., Pautier P., Haie-Neder C., Lhomme C. *et al.*: "Value and cost evaluation of routine follow up for patients with clinical Stage I/II endometrial cancer". *Eur. J. Cancer*, 2001, 37, 985.
- [25] Morrow C.P., Bundy B.N., Homesley H.D. *et al.*: "Doxorubicin as an adjuvant following surgery and radiation therapy in patients with high-risk endometrial carcinoma, Stage I and occult Stage II: a GOG study". *Gynecol. Oncol.*, 1990, 36, 166.
- [26] Seltzer V., Vogl S., Kaplan B.: "Adriamycin and cis-diamminedichloroplatinum in the treatment of metastatic endometrial adenocarcinoma". *Gynecol. Oncol.*, 1984, 19, 308.
- [27] Fleming G., Brunetto V., Cella D., Look K.Y., Reid G.C., Munkarah A.R. *et al.*: "Phase III trial of doxorubicin plus cisplatin with or without paclitaxel plus filgrastim in advanced endometrial carcinoma: a GOG study". *J. Clin. Oncol.*, 2004, 22, 2159.
- [28] Hoskins P., Swerton K., Pike J., Wong F., Lee N.: "Paclitaxel and carboplatin, alone or with irradiation, in advanced or recurrent endometrial cancer: a phase II study". *J. Clin. Oncol.*, 2001, 19, 4048.
- [29] Campagnutta E., Giorda G., De Piero G. *et al.*: "Surgical treatment of recurrent endometrial carcinoma". *Cancer*, 2004, 100, 89.

Address reprint requests to:
S. EVANGELISTA, M.D.
Vico Leone, 1 - Pignataro Int.mna
03040 Frosinone (Italy)
e-mail: evan.simo@libero.it