Five-year survival of a patient with primary endometrial squamous cell carcinoma: a case report and review of the literature

M. Varras[1,*], E. Kioses[2]

[1]*Department of Gynaecology, "George Gennimatas" General State Hospital of Athens*
[2]*Department of Obstetrics and Gynaecology, Medical School, University of Athens, "Alexandra" Hospital, Athens (Greece)*

Summary

Primary endometrial squamous cell carcinoma (PESCC) is an uncommon entity, with fewer than 100 cases reported in the English literature. Survival data for PESCC are not well reported and a precise five-year survival rate for PESCC has not been deternined. This study focuses on the five-year survival of a 61-year-old patient with PESCC and adds information to an area which is not well documented. The patient was treated by hysterectomy with bilateral salpingo-oophorectomy and assigned to FIGO stage Ib. No adjuvant therapy was given. During the 60-month follow-up period, the patient remained free of disease. This outcome suggests that in the early stage of PESCC, surgical treatment alone is adequate to arrest the disease.

Key words: Endometrium; Squamous epithelium; Endometrial carcinoma; Primary endometrial squamous cell carcinoma; Follow-up.

Introduction

Primary endometrial squamous cell carcinoma (PESCC) is an uncommon entity, first reported by Gebhard in 1892 [1]. Since then, fewer than 100 cases have been published in the English literature. In 1928, Fluhmann [2] set up three criteria for establishing the diagnosis: a. No signs of coexisting glandular carcinoma. b. No connection between the endometrial squamous cell carcinoma and the squamous epithelium of the cervix. c. No signs of coexisting primary squamous cell carcinoma of the cervix. In 1975, the WHO added a new criterion: d. There must be clear evidence of squamous differentiation in the tumor, such as intercellular bridges and/or keratin [3].

The prognosis of PESCC is poor compared to endometrial adenocarcinoma, which has a five-year survival rate of 83.5% [4]. The survival rate for PESCC is typically less than 24 months even after complete surgical extirpation, with or without pre- or postoperative irradiation [5]. In 1994, Glaubitz et al [6] reported that only one patient with clinical Stage Ib was known to have survived more than five years.

We present a case of a 61-year-old patient with PESCC who has completed a five-year survival period. The patient was treated by hysterectomy with bilateral salpingo-oophorectomy and assigned to FIGO Stage Ib. No adjuvant therapy was given. During the 60-month follow-up period, the patient remained free of disease. This case was previously discussed by Varras et al in 1997 in a paper describing the pathology of PESCC [7].

Revised manuscript accepted for publication Janaury 16, 2002

Case Report

A 61-year-old nulliparous, postmenopausal, white woman previously in excellent health, presented at Alexandra General Hospital, Department of Obstetrics and Gynaecology of the University of Athens, with a history of one episode of postmenopausal bleeding. Her gynaecological history included an induced abortion and menopause at the age of 51. She had recently had a normal cervical cytological smear. Internal vaginal examination showed the uterus to be anteverted and mobile, and the adnexa were unpalpable. Rectal examination revealed no parametrial involvement. A fractional dilation and curettage showed squamous cell carcinoma of the endometrium, Grade 1 to 2. Preoperative chest X-ray and CT scan of the upper and lower abdomen were clear. Preoperative blood count, biochemical tests and serum levels of tumor markers were within normal limits. The patient underwent a laparotomy on 6th December 1996. Peritomeal washing was taken for cytologic examination and the patient underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy. Also, tissue biopsies from left and right parametrium were taken.

Histopathological examination showed the presence of PESCC Grade 2 with superficial invasion of the myometrium. Fluhman and WHO criteria were fulfilled for the diagnosis of PESCC. Ovaries and tubes showed no evidence of malignancy. No lymph nodes were found in the biopsies from the parametrial tissues. Human papilloma virus (HPV) status was evaluated by *in situ* hybridization using the DNA primers for HPV 6/11, 16/18, 31/35/51. HPV DNA was not detected in the tumor [7]. The stained cytologic smears of the peritoneal washing were negative for malignancy.

The patient was assigned to FIGO Stage Ib, Grade 2 and put on a routine follow-up regime for endometrial carcinoma with clinical examination, pap smear, CT scan of the upper and lower abdomen and chest X-ray. No adjuvant radiotherapy or chemotherapy were given. During the 60-month follow-up period, the patient remained free of disease.

Discussion

Two theories have been offered to explain the pathogenesis of PESCC: the vertical field theory and the squamous metaplasia theory. The vertical field theory implies a local mechanism within the corpus uteri arising from an abnormal population of reverse cells adjacent to the basement membrane. Radical growth eventually replaces normal endometrium by neoplasia and vertical growth invades the myometrim [8, 9]. The squamous metaplasia theory suggests that endometrial squamous metaplasia is a potential precursor of squamous cell carcinoma [10, 11].

Several other factors have been discussed as being influential in the development of PESCC. HPV has been strongly implicated in squamous neoplasms of the lower genital tract and also has been identified in the squamous component of endometrial adenocarcinoma [9, 12]. In our case using DNA primers for HPV 6/11, 16/18 and 31/35/51, HPV DNA was not detected in the tumor [7]. Six additional cases have been reported where HPV was not detected by *in situ* hybridization [6, 9, 13, 14]. It seems, therefore, that there is not any association between PESCC and HPV infection and thus HPV is unlikely to be a carcinogenic factor in the development of PESCC. Smoking has also been implicated as a co-carcinogen in squamous cell cervical carcinoma [9]. Although our patient did not have a smoking history, her exposure at home and work is not known. Radiation therapy has been associated with the late development of malignant endometrial tumors, but it is unknown if this increased risk exists for PESCC [9]. Five cases of PESCC with a prior history of pelvic radiation therapy have been published [9, 15, 16, 17]. Squamous metaplasia of the endometrium has been observed in association with senile involution, oestrogen or vitamin A deficiency, tuberculosis, and irradiation or chronic irritative processes such as intrauterine devices or prolapse [6]. The relationship between squamous metaplasia of the endometrium and PESCC remains controversial [14]. Some investigators consider squamous metaplasia as precancerous PESCC, based on their frequent coexistence [10, 11]. However, in a review by Im et al of 34 cases of PESCC, squamous metaplasia was clearly documented in only 11 cases, suggesting that endometrial squamous metaplasia is not a definitive precursor of PESCC [14]. Pyometra is associated with PESCC in approximately 31% of cases [8]. Pyometra, however, could be the result of obstruction of the internal cervical os by the tumor rather than the cause of the malignancy [18]. Our patient had no history of pelvic radiation therapy, squamous metaplasia of the endometrium or pyometra.

In a review of 64 cases of PESCC by Goodman *et al.* [19] the average age of the patients was 67 years. The presenting signs and symptoms of the disease included: 1. Postmenopausal bleeding in 68% (44/64). 2. Vaginal discharge in 28% (18/64). 3. Pain in 17% (11/64). 4. Weight loss in 6% (4/64). 5. Pelvic mass in 6% (4/64). 6. Brain metastases in 1.5% (1/64). Our patient was 61 years old, slightly younger than the average, and presented with the most common sign, postmenopausal vaginal bleeding.

Survival data for PESCC are not well reported [5] and a precise five-year survival rate for PESCC has not been determined. The existing PESCC data, while incomplete, does suggest a much worse prognosis than adenocarcinoma despite similar treatment [5]. However in a review of 64 PSECC cases, Goodman et al [19] found that all the patients with surgical Stage I tumors had survived for the period they were followed up, suggesting that a tumor that is confined to the uterus, regardless of the grade and depth of myometrial invasion, has a good prognosis. This observation was affirmed by our case. In contrast, all five patients with Stage IV disease, and most patients with Stage III disease, died despite adjuvant therapy. Adjuvant therapy in PESCC is still controversial. Some authors consider PESCC to be radioresistant [17, 20, 21] and chemotherapy is not commonly used [9]. Adelson and Stumpf reported no response to cisplatin and infusional 5-fluorouracil [22], while Sorosky et al reported a complete clinical response to carboplatin where the patient was symptom free for nine months postchemotherapy [9].

In conclusion, we have presented a case of PESCC FIGO Stage Ib who survived in a disease-free state for five years after being treated with hysterectomy and bilateral salpingo-oophorectomy, but no adjuvant therapy. This outcome suggests that in the early stage of PESCC, surgical treatment alone is adequate to arrest the disease. In addition, our patient's biopsy revealed no evidence of HPV DNA supporting the conclusion that HPV is not a carcinogenic factor in the development of PESCC.

Acknowledgments

The authors would like to thank the colleagues in the Pathology Department of "Alexandra" General Hospital of Athens (Greece) for the microscopic examination of the surgical specimens.

References

[1] Gebhard C.: "Ueber die vom oberflächenepithel ausgehenden carcinomformen des uteruskörpers sowie über den hornkrebs des cavum uteri". *Z. Geburtschilf. Gynakol.*, 1892, *24*, 1.

[2] Fluhman C. F.: "Squamous epithelium in the endometrium in benign and malignant conditions". *Surg. Gynecol. Obstet.*, 1928, *46*, 309.

[3] Paulsen H., Taylor C.: "International histological classification of tumors No. 13. Histological typing of female genital tract tumors No. 13". *World Health Organization.* Geneva, 1975.

[4] Abeler V. M., Kjorstad K. E.: "Endometrial adenocarcinoma with squamous cell differentiation". *Cancer*, 1992, *69*, 488.

[5] Kennedy A. S., De Mars L. R., Flannagan L. M., Varia M. A.: "Primary squamous cell carcinoma of the endometrium: A first report of adjuvant chemoradiation". *Gynecol. Oncol.*, 1995, *59*, 117.

[6] Glaubitz M., Kupsh E., Günter H. H., Lellé R. J., Kühnle H.: "Primary squamous cell carcinoma of the endometrium. Case report and review of the literature". *Eur. J. Gynaec. Oncol.*, 1994, *15*, 37.

[7] Varras M. N., Kioses E., Diakomanolis E., Papaspirou R., Sotiropoulou M., Charalambidis V., Deligeoroglou E., Koukoulomatis P., Michalas S.: "Primary squamous cell carcinoma of the endometrium". [in Greek] *Adol. Gynecol. Reprod. Menop.*, 1997, *9*, 311.

[8] Pritzker J., Anselmo M. T., Veridiano N. P., Tancer M. L.: "Squamous cell carcinoma of the endometrium. A case report". *J. Reprod. Med.*, 1992, *37*, 194.
[9] Sorosky J. I., Kaminski P. F., Kreider J., Podczaski E. S., Olt G. J., Zaino R.: "Endometrial squamous cell carcinoma following whole pelvic radiation therapy: Response to carboplatin". *Gynecol. Oncol.*, 1995, *57*, 426.
[10] Seltzer V. L., Klein M., Beckman E. M.: "The occurrence of squamous metaplasia as a precursor of squamous cell carcinoma of the endometrium". *Obstet. Gynecol.*, 1977, *49 (1, Suppl.)*, 34.
[11] Baggish M. S., Woodruff J. D.: "The occurrence of squamous epithelium in the endometrium". *Obstet. Gynecol. Surv.*, 1967, *22*, 69.
[12] Kealy W. F., Annis P. G., Barry J. A., Hogan J. M.: "Adenoacanthoma of the endometrium†: Morphological changes induced by human papilloma virus". *J. Clin. Pathol.*, 1990, *43*, 554.
[13] Jeffers M. D., McDonald G. S. A., McGuinnes E. P.: "Primary squamous cell carcinoma of the endometrium". *Histopathology*, 1991, *19*, 177.
[14] Im D. D., Shah K. V., Rosenshein N. B.: "Report of three new cases of squamous carcinoma of the endometrium with emphasis in the HPV status". *Gynecol. Oncol.*, 1995, *56*, 464.
[15] Hopkin I. D., Harlow R. A., Stevenw P. J.: "Squamous carcinoma of the body of the uterus". *Br. J. Cancer.*, 1970, *24*, 71.
[16] Menezer J.: "Primary squamous cell carcinoma of the endometrium". *Harefuah*, 1975, *89*, 169.
[17] Simon A., Kopolovic J., Beyth Y.: "Primary squamous cell carcinoma of the endometrium". *Gynecol. Oncol.*, 1988, *31*, 454.
[18] White A. J., Buchsbaum H. J., Macasaet M. A.: "Primary squamous cell carcinoma of the endometrium". *Obstet. Gynecol.*, 1973, *41*, 912.
[19] Goodman A., Zukerberg L. R., Rice L. W., Fuller A. F., Young R. H., Scully R. E. "Squamous cell carcinoma of the endometrium: A report of eight cases and review of the literature". *Gynecol. Oncol.*, 1996, *61*, 54.
[20] Gedikoglu G., Demirel D., Gunhan O., Finci R.: "Endometrial squamous cell carcinoma". *Acta Obstet. Gynecol. Scand.*, 1991, *70*, 619.
[21] Orhon E., Ulgenalp I., Baser I., Dilek S., Pabuccu R.: "Primary squamous cell carcinoma of the endometrium". *Eur. J. Cancer*, 1991, *27*, 946.
[22] Adelson M. D., Strumpf K. B.: "Squamous cell carcinoma of the endometrium presenting as peritonitis with small bowel obstruction". *Gynecol. Oncol.*, 1992, *45*, 214.

Address reprint requests to:
M. N. VARRAS, M.D., Ph.D.
Obstetrician - Gynaecologist
Consultant in Obstetrics and Gynaecology
Platonos 33, Politia (Kifisia)
14563 Athens (Greece)