Primary squamous cell carcinoma of endometrium: A case report

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Summary

A case of primary squamous cell carcinoma of the endometrium (PSCCE) in a virgin treated with surgery - abdominal hysterectomy and bilateral salpingo-oophorectomy, and followed by whole pelvic radiation is presented. The tumor recurred 12 months later and the patient then underwent relaparotomy and excision of recurrent tumor of the pelvis; right hemicolectomy and rectosigmoidectomy were done due to recurrence and metastasis of the primary tumor. After re-operation, six courses of cisplatin and 5-fluorouracil were given intravenously for cytotoxic effects at 3-week intervals. The patient's disease progressed despite therapy, and she died three months after the last cycle or 21 months after the first diagnosis was made.

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

Introduction

Primary squamous cell carcinoma of the endometrium is extremely rare. The disease is usually diagnosed in advanced stage with extensive infiltration of the myometrium and peritoneal cavity. The prevalence of this neoplasm is about 0.1% and its pathogenesis remains obscure [1]. Gebhard first reported primary endometrial squamous cell carcinoma in 1892 [2]. Since then, fewer than 100 cases have been published in the English literature [3].

Case Report

A 66-year-old virgin, nulligravid, nullipara, was admitted to our hospital on February 26, 2002 due to vaginal bleeding of 12 months' duration and pelvic pain and pressure in the small abdomen. Rectal bimanual examination showed an enlarged uterus and normal ovaries. Rectal examination revealed no parametrial involvement. Pelvic ultrasound examination was performed and showed a heterogeneous and enlarged uterine corpus in the middle of the small pelvis measuring 7.4 x 5.5 cm, with a wall thickness of 0.5 cm. A hyperoechoic mass was visualized within the endometrial cavity measuring 4.8 x 2.7 cm. Blood level of serum tumor marker CA-125 was 30.1 kIU/l (normal range 0-35 kIU/l). The general physical examination was unremarkable. The patient took no medications and had no allergies. She had undergone total abdominal hysterectomy and bilateral salpingo-oophorectomy for Stage IC carcinoma of the endometrium. The stained cytological smears of the peritoneal washings were negative for malignancy. Following surgery adjuvant postoperative telegamma radiotherapy to the whole pelvis to a dose of 42.6 Gy was delivered in 20 fractions over five weeks with a planned four-field technique. Pathology revealed a uterus 10.0 x 7.0 x 4.0 cm in size. The serosal surface of the uterus was smooth, and the whole cavity of the uterus was filled with a white, soft, tumor mass. Histologically normal endometrium was not found. In the area where the myometrium was approximately 3.5 cm thick, the tumor invaded 3.2 cm of the myometrium. The tumor was confined to the uterine corpus but tumor invasion of the lymphatic space was seen. The tumor was built of clusters and islands of squamous cells which showed numerous mitotic figures, many atypical. Nuclei were hyperchromatic with nuclear membrane thickening and irregularly arranged chromatin. Immunohistochemical studies demonstrated positive expression of cytokeratin in malignant squamous cells (DAKO, M0821). The cervix was examined entirely and microscopic examination demonstrated benign epithelium with mild chronic inflammation in the stroma. There was no koilocytosis. The ovaries and fallopian tubes were normal. In February 2003, 12 months after the first operation, she was admitted again to our hospital due to vaginal bleeding of two months' duration. Gynecological examination was performed and on the vaginal vault a tumor measuring 2.0 x 2.0 cm was seen, and in the pelvis a solid tumor was palpable. Pelvic ultrasound examination showed a solid tumor in the middle of the small pelvis 4.0 x 4.0 cm in size. A pap smear revealed planocellular carcinoma. Punch biopsies of the tumor demonstrated relapse of squamous cell carcinoma of the endometrium. Pathology revealed and confirmed recurrent primary squamous cell carcinoma. The tumor was built of clusters and islands of squamous cells with hyperchromatic nuclei that showed numerous mitotic figures of which many were atypical. Immunohistochemically the cells were positive on cytokeratin (DAKO, M0821). Repeated analyses of tumor antigens in the blood serum showed CA19-9 and CEA in normal range, but increased levels of CA-125 – 68 kIU/l (normal range 0-35 kIU/l). In February 2003, 12 months after the first operation and irradiation due to recurrence and metastasis of the primary tumor, the patient underwent relaparotomy and excision of the recurrent tumor of the pelvis together with right hemicolectomy and rectosigmoidectomy. After re-operation for recurrence we gave six courses of cis-platin at 85 mg/m^2 x one day and 5-fluorouracil 625 mg/m^2/ day x five days intravenously for cytotoxic effects at 3-week intervals. The patient's disease progressed despite therapy, and she died three months after the last cycle of chemotherapy or 21 months after the original diagnosis.

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Discussion

In 1928, Fluhmann set up three criteria for establishing the diagnosis. Strict criteria of primary squamous cell carcinoma of the endometrium (PSCCE) make this tumor exceptional: 1) no coexisting endometrial adenocarcinoma; 2) no connection between the endometrial tumor and the squamous epithelium of the cervix; and 3) no squamous cell carcinoma of the cervix present [4, 5]. In 1975, the WHO added new criteria: There must be clear evidence of squamous differentation in the tumor, such as intercellular bridges and/or keratin [6]. The most frequent presenting symptom is vaginal bleeding. The average duration of symptoms before diagnosis is 11.5 months. Chronic pyometra and nulliparity are predisposing factors [7]. The etiology of PSCCE is unknown. Chronic endometritis, hypovitaminosis A, estrogen deficiency, senile involution, irradiation, chronic irritative processes such as intrauterine devices, and or prolapse are considered pathogenic factors of squamous metaplasia of the endometrial glands. A possible addition to this list is HPV infection. Our patient did not display any of these factors. Invasive squamous carcinoma of the endometrium is rare and is thought to arise by one of two mechanisms: upward spread of a primary cervical lesion or transformation of reserve or "stem" cells located between the glandular basement membrane and the endometrial columnar epithelium [6]. Zidi and co-workers could not demonstrate a pathogenetic role of HPV in squamous metaplasia and they support a theory that favors a sequence of change with squamous metaplasia progressing from dysplasia to invasive carcinoma [6]. Currently, the preferred theory proposes that squamous metaplasia in the endometrium is a precursor to invasive carcinoma. There is no positive correlation between human papilloma virus and PSCCE [8], while another author found HPV (especially types 31-33) and suggested that there may be a pathogenetic role of viruses in the development of PSCCE [1, 9]. Because of the rarity of this entity there is no adequate information about the biological behavior or the prognosis. PSCCE carries a poor prognosis even for Stage I disease as 40% of patients with Stage I disease die within 36 months [10]. Also due to the rarity of PSCCE there is no consensus as to the optimal treatment for this malignancy. Total abdominal hysterectomy with bilateral salpingo-oophorectomy has been the primary treatment [7]. Kennedy *et al.* treated PSCCE with postoperative radiation and cisplatin after abdominal hysterectomy and bilateral salpingo-oophorectomy. The patient has been followed 28 months from the diagnosis and has no evidence of recurrence of cancer. They gave postoperative pelvic irradiation with 15 MV X-rays via a four-field technique (anterior-posterior and opposing lateral fields) to include the obturator, internal iliac, external iliac, and common iliac lymph nodes. Daily fractions of 180 cGy were delivered to a total dose of 5040 cGy. Five courses of cisplatin at 50 mg/m^2 intravenously were given for cytotoxic effects and possible radiosensitzing properties [11]. Adelson and Strumpf also gave cisplatin (50 mg/m^2) IV x one day and 5-fluorouracil (1000 mg/m^2/day) IV x five days for six cycles in a patient who had recurrent and metastatic PSCCE after primary surgery and re-operation for recurrence [12]. Dalrymple and Russell gave adjuvant radiotherapy and chemotherapy - cisplatin, vinblastine, and bleomycin for three courses after surgery, and in comparison to previously reported cases the length of survival for these patients was long [13]. Sorosky and co-workers treated Stage IV primary endometrial squamous cell carcinoma by surgery - total abdominal hysterectomy, bilateral salpingo-oophorectomy and resection of a left parametrial mass were done followed by adjuvant chemotherapy (carboplatin at dose of 250 mg/m^2 for six cycles at 4-week intervals). The patient was free of symptoms eight months after completion of chemotherapy, but during the ninth month post-treatment she acutely developed a small bowel obstruction and underwent explorative laparotomy. Relapse and metastasis of primary squamous cell carcinoma in the peritoneal cavity were confirmed. The patient died three months after re-operation and 17 months after the original diagnosis [10]. Varras and Kioses treated a patient with PSCCE assigned to FIGO Stage IB only surgically - hysterectomy with bilateral salpingo-oophorectomy was done. The patient survived five years. They concluded that in the early stage of PSCCE, surgical treatment alone is adequate to arrest the disease [3].

Conclusion

Our patient was a virgin and we have not confirmed the theory of the role of a virus in development of PSCCE. After the first operation - total abdominal hysterectomy and bilateral salpingo-oophorectomy for Stage IC carcinoma of the endometrium and adjuvant irradiation, the patient was free of symptoms for ten months. Relapse and metastasis of PSCCE was confirmed 12 months after the first operation and she underwent re-operation and adjuvant chemotherapy. In spite of therapy – surgery, irradiation and chemotherapy – she died three months after completion of chemotherapy or 21 months after the original diagnosis, like most patients with this disease.

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