Synchronous primary cancers in a woman with scleroderma: a case report

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Summary

Background: Scleroderma is a chronic, multisystem, autoimmune disease. Previous studies have shown an increased risk of malignancy in scleroderma; the most common cancers were lung cancer and breast cancer. *Case:* The patient, a 43-year-old nulliparous premenopausal Greek woman with scleroderma, presented with a history of abdominal pain and atypical vaginal bleeding. She underwent total hysterectomy with bilateral salpingo-oophorectomy, total omentectomy, appendectomy and pelvic lymph node dissection. The histopathology revealed synchronous primary cancers of the endometrium and left ovary. She underwent postoperative chemotherapy and remains well without evidence of disease 25 months after surgery. *Conclusion:* Synchronous primary cancers of the endometrium and ovary are relatively uncommon in the general population. Only a few cases of cancer of the female genital tract in women with scleroderma have been reported in the English literature.

Key words: Synchronous primary cancers; Scleroderma; Endometrial cancer; Ovarian cancer.

Introduction

Scleroderma is a chronic, multisystem, autoimmune disease. Previous studies have shown an increased risk of malignancy in scleroderma [1-3]. The most common cancers were lung cancer and breast cancer [1-3]. Other types of cancers were non-melanoma skin cancer, esophageal cancer, liver cancer and hematopoitic cancers [1, 3]. Only a few cases of cancer of the female genital tract in women with scleroderma have been reported in the English literature [1, 3].

Synchronous primary cancers of the endometrium and ovary are relatively uncommon in the general population [4]. Endometrial and ovarian cancer have several risk factors in common, and on this basis they could occur together in the same woman [5]. The two tumors may have a similar appearance or be of different histologic types.

Perhaps this is the first case worldwide of synchronous primary endometrial and ovarian cancer in a woman with scleroderma.

Case Report

A 43-year-old, nulliparous premenopausal Greek woman presented with a history of abdominal pain and atypical vaginal bleeding. Her past surgical history was unremarkable. She had had scleroderma for the last 21 years. Her family history revealed no evidence of cancer among the first-degree relatives.

On vaginal examination a pelvic mass was palpated. There were no palpable inguinal lymph nodes, and the rest of pelvic examination was normal.

Computed tomography (CT) of the abdomen and pelvis, and abdominal ultrasound (US) revealed an intraabdominal mass of 15.6 x 15 x 12 cm. Preoperative CT of the chest, chest X-ray, intravenous pyelography (IVP), colonoscopy and urethrocystoscopy were normal. Preoperative CA125 was elevated to 426 U/ml.

On exploratory laparotomy, the left ovary was markedly distended, measuring 20 x 15 x 10 cm. Frozen section showed malignancy and the patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy, total omentectomy, appendectomy and pelvic lymph node dissection.

The histopathology revealed synchronous primary cancers of the endometrium and left ovary. The uterine tumor consisted of glandular and villoglandular structures lined by simple to pseudostratified columnar cells, and invaded less than half of the myometrium. The ovarian tumor consisted of glandular and villoglandular structures lined by simple to pseudostratified columnar cells and ruptured the capsule, invaded the left fallopian tube and extended to the omentum. The right ovary was normal. The two carcinomas were positive for vimentin, cytokeratin, epithelial membrane antigen, estrogen receptor, progesterone receptor, CA-125, CA19-9 and B72.3 but CEA negative. The peritoneal washing smear was negative for malignant cells.

The final diagnosis was Stage Ib endometrial carcinoma endometrioid type and Stage IIIc ovarian carcinoma endometrioid type.

The patient underwent postoperative chemotherapy. She received six courses of carboplatinum (AUC 5) and paclitaxel (175 mg/m^2).

She remains well without evidence of disease 25 months after operation.

Discussion

Scleroderma is a chronic, multisystem, autoimmune disease characterized by the presence of excessive deposits of conjunctive tissue components, expressed as fibrosis and structural alterations of the vascular bed. Three factors intervene in the pathogenesis of the disease:

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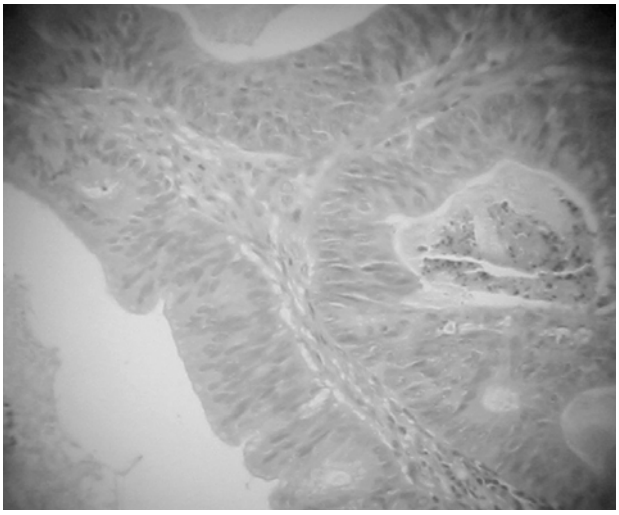

Figure 1. — Endometrial carcinoma of endometrioid type.

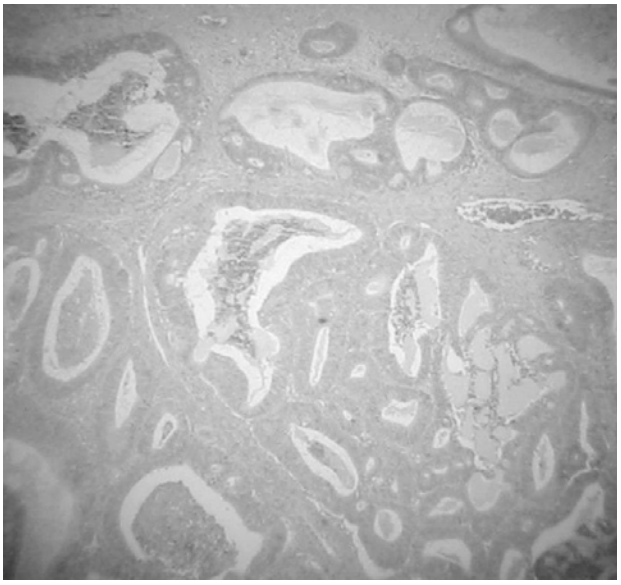

Figure 2. — Ovarian carcinoma of endometrioid type.

alterations in collagen synthesis, vascular alterations and immunologic anomalies. Previous studies have shown an increased risk of malignancy in scleroderma [1-3].

All subtypes of scleroderma are associated with an increased risk of malignancy, but differences in risk have been found between them. Patients with diffuse scleroderma had the highest relative risk of malignancy. In contrast, patients with limited or other forms of scleroderma had similar increased relative risks [1].

The most common cancers were lung cancer and breast cancer [1-3]. Other types of cancers were non-melanoma skin cancer, esophageal cancer, liver cancer and hematopoitic cancers [1, 3]. Only a few cases of cancer of the female genital tract in women with scleroderma have been reported in the English literature [1, 3].

One disease may increase the risk of the other, either as a direct complication or as a result of the treatment given. Alternatively, the two disorders may share common risk factors [2].

Perhaps patients with scleroderma have a more fragile genome, and prior genetic damage may predispose to both scleroderma and cancer [1].

It has been hypothesized that the immunologic alterations produced in the pathogenesis of scleroderma could be related to the development of cancer [1].

It is possible that the use of immunosuppressive agents in patients with scleroderma might have predisposed them to develop cancer [1, 2].

Perhaps the response of the uterine corpus, fallopian tubes, and the ovarian epithelium as a morphologic unit could explain the development of synchronous endometrioid tumors in different components of the mullerian system, when simultaneously subjected to carcinogens [4].

Endometrial and ovarian cancer have several risk factors in common, and on this basis they could occur together in the same woman [5]. Hormonal causes may be involved in the pathogenesis. Future studies are needed to further evaluate the role of estrogen in these synchronous primary cancers of the endometrium and ovary [6].

The empirical criteria for identification of synchronous primary cancers include either different histologic types (major criterion) or all of the following minor criteria: 1. both tumors confined to primary sites, 2. no direct extension between tumors, 3. no lymphovascular tumor emboli, 4. no or only superficial myometrial invasion, and 5. no distant metastasis [4]. According to this criteria, the present case was synchronous primary cancers.

Patients with synchronous primary cancers tended to be 10-20 years younger than their counterparts with endometrial or ovarian carcinoma [8]. The median age at diagnosis is 50 years [6, 7]. The women had distinct clinical characteristics including young age, obesity, premenopausal status and nulliparity [6].

Independent prognostic factors for synchronous primary cancers seem to be age, stage of ovarian cancer, grade of endometrial cancer, and adjuvant therapy [9].

Treatment of choice for early-stage synchronous primary cancers is total abdominal hysterectomy with bilateral salpingo-oophorectomy, total omentectomy, appendectomy and pelvic lymph node dissection. In advanced stage, patients require more aggressive management with adjuvant chemotherapy or radiotherapy after surgery [4, 10].

The two tumors may have a similar appearance (usually endometrioid but sometimes papillary, clear cell, or mucinous) or be of different histologic types [7, 8].

Patients with synchronous primary endometrioid tumors of the endometrium and ovary (endometrioid/endometrioid) had a better median overall survival than those with non-endometrioid or mixed histologic subtypes [6, 4]. The Gynecologic Oncology Group (GOG) found that patients had an overall good prognosis with a 5-year survival of 86% and 10-year survival of 80% [7].

The reason for the better median overall survival for these patients is not intuitively obvious [7]. Perhaps this may due to the detection of patients at earlier clinical stage and lower graded disease state [10].

Conclusion

The reason for the better median overall survival for our patient is not intuitively obvious, and may be due to the detection of the cancer in early-stage and low-grade disease state. We have no information on tumor behavior, response rate to standard therapy, or natural history of synchronous primary cancers in scleroderma patients.

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