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Serous endometrial intraepithelial carcinoma (SEIC) with metachronous umbilical cutaneous, pleural, and peritoneal metastases: Case report and literature review

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Abstract
Serous endometrial intraepithelial carcinoma is most often confined to the uterus, having consequently a favorable prognosis. However, and although this lesion remains limited to the epithelium with no stromal invasion, many cases of extrauterine spread have been reported at time of diagnosis or in a metachronous way. In this work we report the case of a 58-years-old menopausal female with pure serous endometrial intraepithelial carcinoma revealed by vaginal bleeding and pelvic pain with no metastases at exploration. She has undergone total hysterectomy, bilateral salpingo-oophorectomy and bilateral iliac lymph nodes dissection. Six months later, the patient presented with metachronous pleural, peritoneal and cutaneous metastases.

Keywords: *Serous endometrial intraepithelial carcinoma, metastatic disease, case report.*

Introduction

The commonest gynecological cancer in the developed world is endometrial cancer. Serous endometrial intraepithelial carcinoma (SEIC), also called endometrial carcinoma in situ, non-invasive endometrial serous carcinoma, superficial serous carcinoma, minimal uterine serous carcinoma, or serous endometrial intraepithelial neoplasia, is a non-invasive neoplastic lesion of the endometrial epithelium[1]. It predominantly occurs in postmenopausal women[2]. SEIC is most often confined to the uterus, having consequently a favorable prognosis[2]. However, and although this lesion remains limited to the epithelium with no stromal invasion, many cases of extrauterine spread have been reported at time of diagnosis or in a metachronous way[1]. SEIC is therefore not only considered to be a precursor of serous endometrial carcinoma (SEC), but shows a high aggressivity, similar to that of USC[3]. Many hypotheses exist trying to explain occurrence of metastases in cases of SEIC. Among these, dissemination through migration of superficial detached neoplastic cells remains the most

acceptable[4]. Pathological assessment of cases of SEIC finds the same neoplastic cells as in cases of invasive serous endometrial carcinoma[4].

Patient and Observation

Patient Information: We report the case of a 58-years-old menopausal female patient who presented for post-menopausal vaginal bleeding and pelvic pain evolving for a period of 3 months. She had history of hypertension under therapy and diabetes under oral antidiabetics. The patient has a history of benign endocervical polyp resected by hysteroscopy two years ago.

Clinical Findings: Gynecological examination didn't find any bleeding from the cervical Os during speculum examination.

Diagnostic Assessment: Pelvic ultrasounds revealed a suspicious 17mm thickening in the endometrium (Figure 1). Pelvic MRI was also performed, revealing a suspicious endometrial thickening (Figure 2). A thoracic, abdominal and pelvic CT-scan has been also performed revealing no metastatic locations. The patient has then undergone hysteroscopy with endometrial curettage. Pathological assessment has revealed a neoplastic proliferation made of papillae and micro-papillae of markedly atypical cells. The nuclei are enlarged, hyperchromatic and showed irregular contours. The cytoplasm is eosinophilic. Frequent mitoses are observed. The underlying stroma showed no invasion. These findings were consistent with a serous endometrial intraepithelial carcinoma.

Therapeutic interventions: The patient has undergone a total hysterectomy, bilateral salpingo-oophorectomy and bilateral iliac lymph nodes dissection. Microscopic assessment revealed the same intra-epithelial proliferation as shown in the curettage samples (Figures 3). Detailed examination of samples from the uterus specimen has shown no invasion of the endometrial stroma. Lymph nodes were negative for a neoplastic proliferation. Follow-up showed no post-operative complications and decision was to follow the patient up with no indication for post-operative chemotherapy.

Follow-up and outcome of interventions: Six months later, the patient presented for pleural and peritoneal effusion with apparition of a 4cm cutaneous umbilical nodule. Pathological assessment of the skin nodule (Figure 4) revealed an ulcerated epidermis with underlying dermis containing a carcinomatous proliferation made of papillae, micropapillae and solid nodules. Neoplastic cells showed eosinophilic cytoplasms and enlarged, hyperchromatic, markedly atypical nuclei with frequent mitotic figures (Figures 5). A laparoscopy was also performed in our patient, revealing diffuse peritoneal carcinosis. The biopsy of one of the peritoneal nodules showed infiltration by the same proliferation as demonstrated on skin nodule. In this case, a diagnosis of serous endometrial intraepithelial carcinoma with metachronous pleural, peritoneal and cutaneous metastases has been established. The patient is currently receiving carboplatin and paclitaxel chemotherapy.

Patient consent: The patient family has given informed consent about the publication of this work.

Patient Perspective: The patient's family was pleased with the care she received throughout therapy.

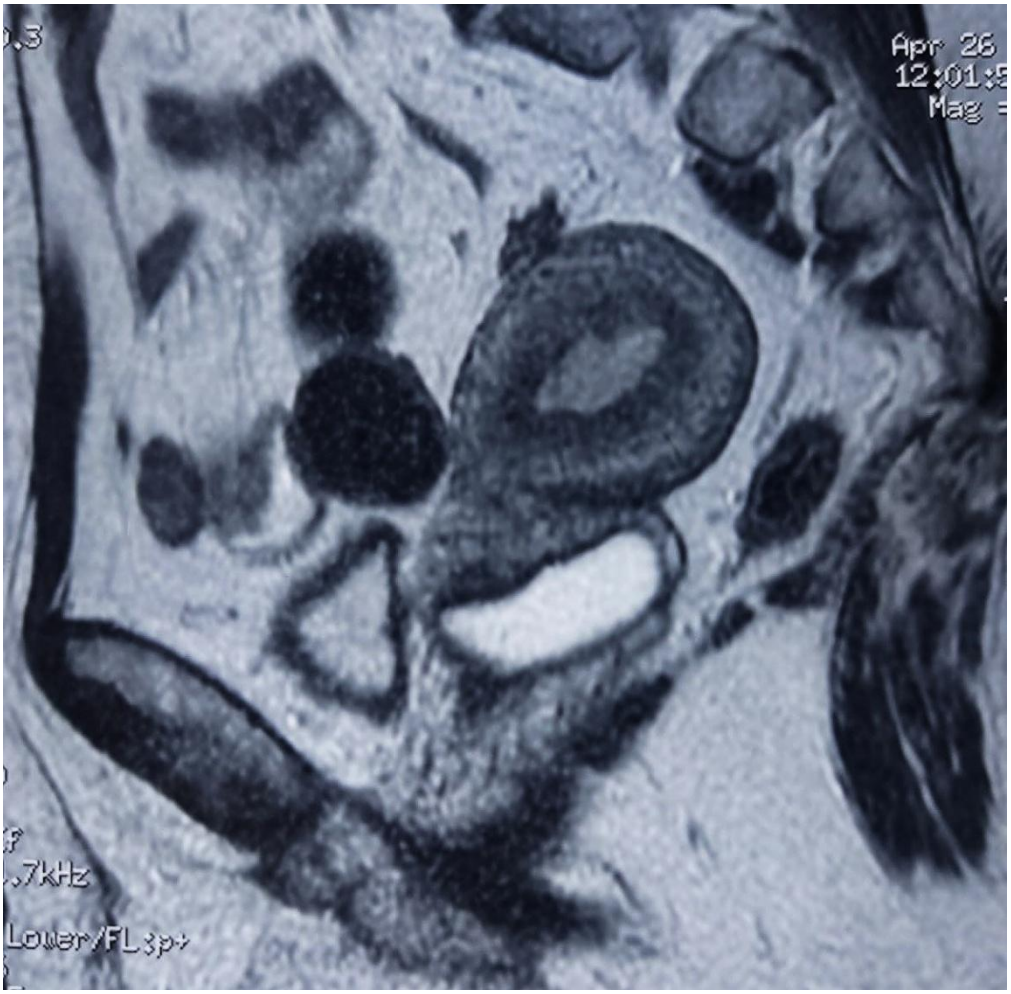

Figure 1: MRI photography showing the endometrial thickening

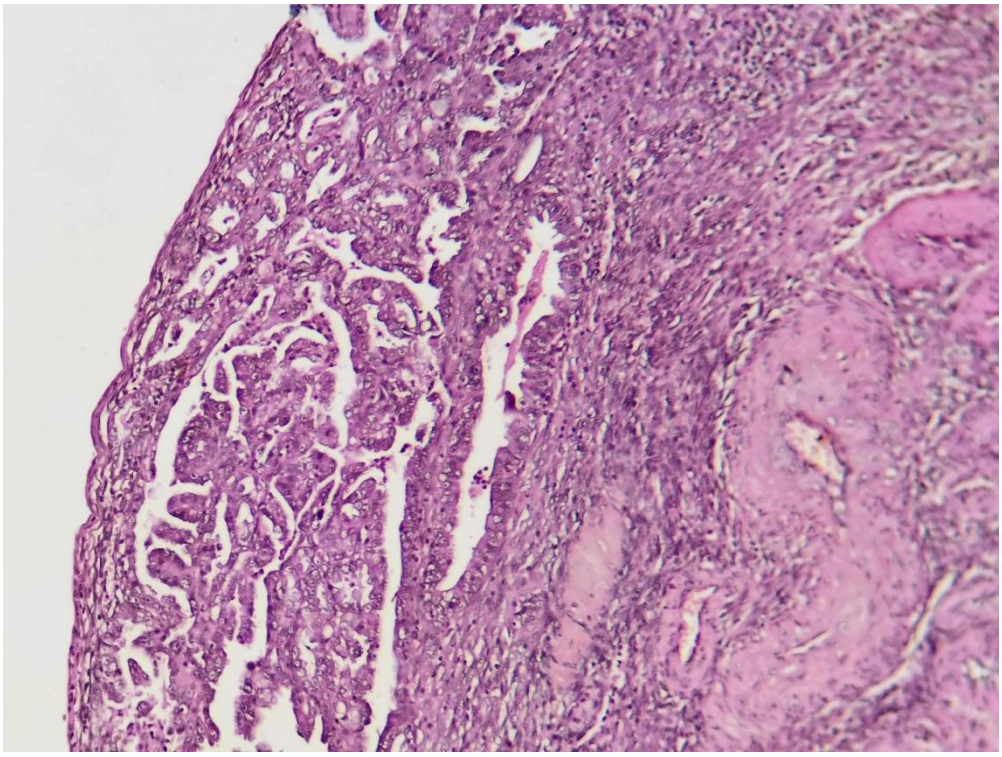

Figure 2: Microphotography showing neoplastic proliferation made of papillae and micro-papillae of markedly atypical cells. (HE; 200X)

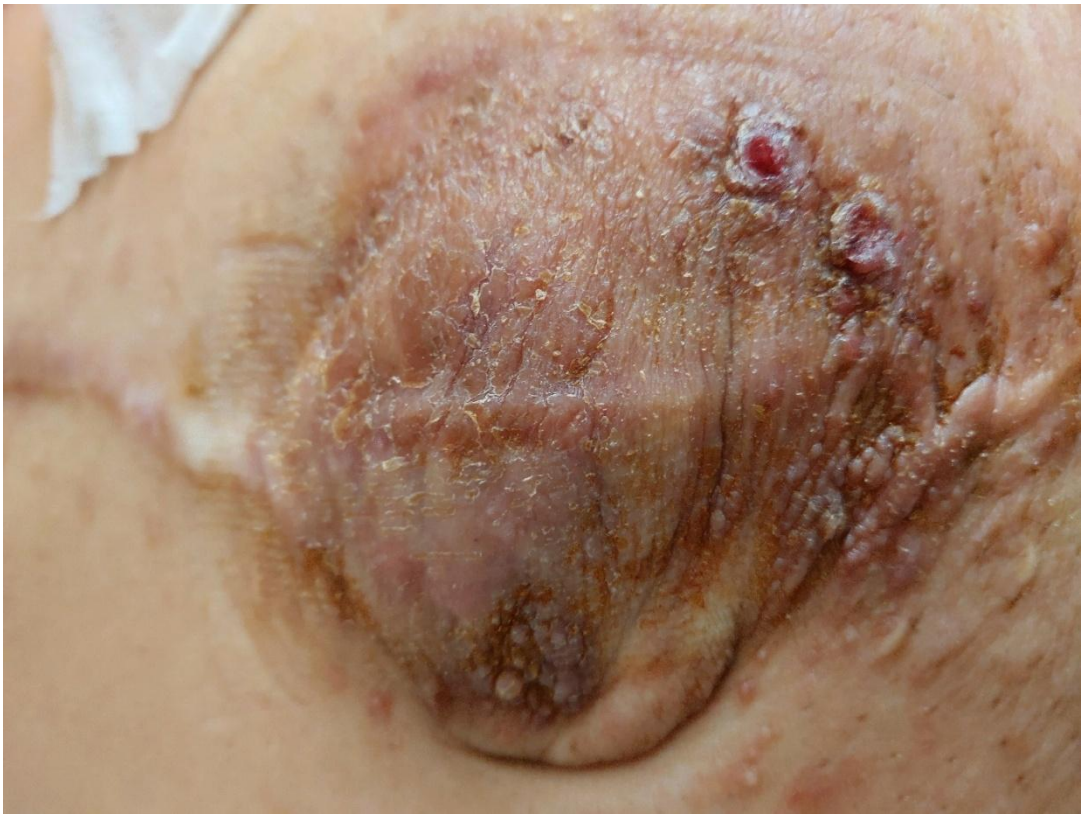

Figure 3: Photography of the 4cm cutaneous umbilical nodule. The skin overlying the lesion was focally ulcerated.

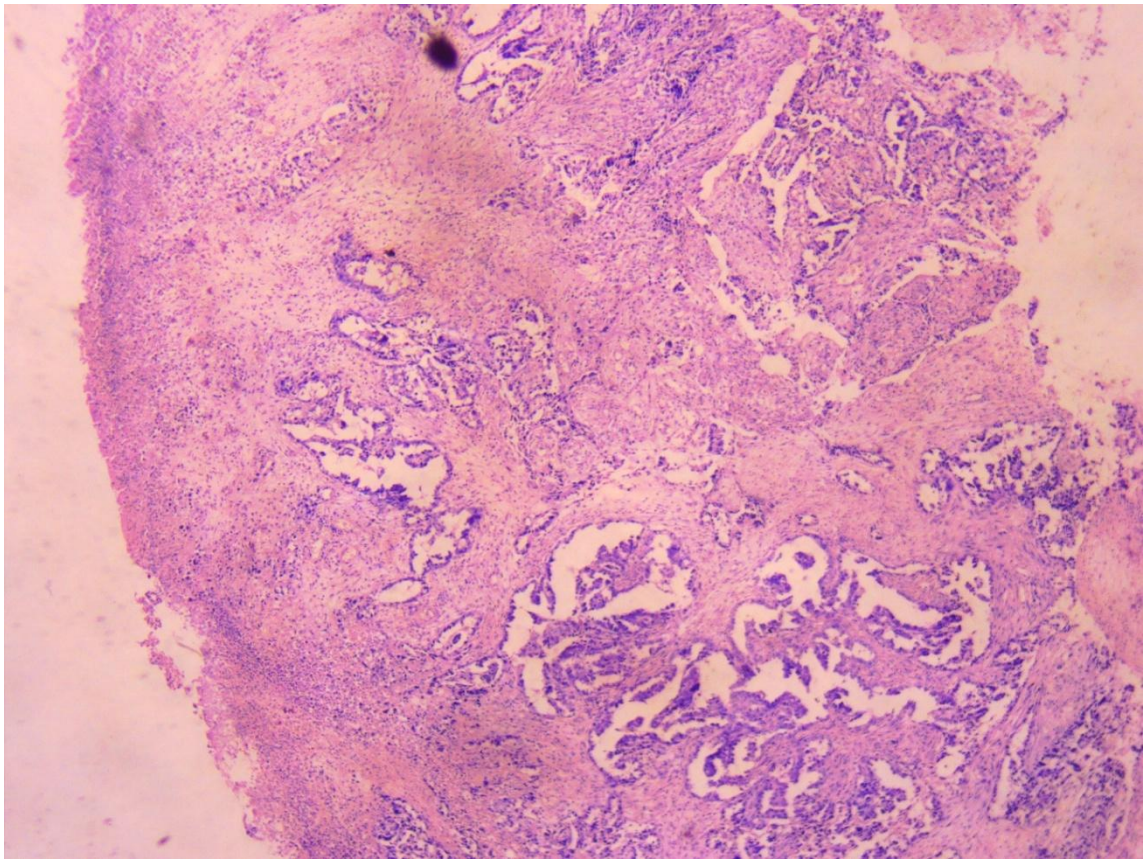

Figure 4: Microphotography from the cutaneous nodule sample showing underlying dermis containing a carcinomatous proliferation made of papillae, micropapillae and solid nodules. (HE, 100X)

Discussion

SEIC predominantly occurs in postmenopausal women in form of postmenopausal bleeding[2]. No risk factor could have been identified for development of SEIC, therefore there are no precautions that can diminish the risk of its occurrence[5]. On the radiological level, endometrial thickening or even polypoid lesion could be seen through pelvic ultrasounds. CT-scan is useful for detection of extrauterine dissemination[3]. Diagnosis is established through pathological assessment showing markedly atypical cells, confined to the endometrial epithelium, without invasion of the endometrial stroma. Since the lesion can be very focal, diagnosis can be challenging on biopsy and therefore certainty is insured with pathological assessment of the uterine wall[6].

Neoplastic cells often show many mitotic figures and apoptotic bodies. A hobnail appearance can also be observed. The architecture can be papillary and may contain micro-papillae as observed in our case, on both primary and metastatic sites.

On the immunohistochemical level, the most reported useful antibodies are anti-Ck7, anti-p53, and anti-estrogen receptors antibodies[7]. The overexpression of p53 has been noticed in many cases, associated to negativity for estrogen receptors. There are currently no reported factors enabling prediction of the SEIC. Occurrence of metastases in cases of SEICs is a well-documented phenomenon although no definite mechanism could be established[4]. Cases of metachronous metastasis of SEIC have been reported in the literature. Some have had a considerable delay between initial diagnosis and occurrence of metastases until up to 8 years in one case report.[8] 3 years was the reported delay in another case report[9].

One of the existing theories about occurrence of metastases in cases of pure forms of SEIC is spread of the neoplastic cells directly into the uterine cavity, then through the uterine tubes to reach the pelvic cavity[4]. The lack of data about this neoplasia is due to many factors namely: Rarity of pure forms of SEIC that are not associated to an invasive endometrial serous carcinoma and the existence of many given names for this entity[4].

On the therapeutic level, the most described primary treatment is surgical staging[4]. In a study about this neoplastic pathology in The Netherlands, no certainty about management was reported because of its rarity[4]. This same study has shown through a survey, that no consensus about neither the surgical nor adjuvant therapy exists[4]. The guideline of the National Comprehensive Cancer Network in the USA for example, doesn't use a separate section for treatment of patients with pure SEIC[10]. Since it is still not certain if SEIC can give secondary pelvic or paraaortic/paracaval lymph nodes metastases, therefore indication for lymph node dissection is not yet established in cases of pure SEIC[4].

Conclusion

Serous endometrial intraepithelial carcinoma is therefore not only a precursor of serous endometrial carcinoma but shows a high aggressivity, similar to that of USC with a real risk of metastases occurrence.

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