A case of primary squamous cell carcinoma of the endometrium associated with extensive "ichthyosis uteri"

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Summary

Background: Ichthyosis uteri is an uncommon entity in which the entire endometrium is replaced by stratified squamous epithelium. Though the condition often is considered as benign, dysplastic changes have been reported. *Case:* We describe herein an exceedingly rare case of primary squamous cell carcinoma of the endometrium (PSCCE) associated with extensive ichthyosis uteri with chronic pyometra, who presented with blood-stained vaginal discharge of six-seven months duration. Although repeated endometrial biopsies revealed only strips of stratified squamous epithelium showing moderate to severe dysplastic changes, the tumor markers and magnetic resonance imaging strongly suggested advanced uterine body malignancy. Exploratory laparotomy was performed, and histologic findings of the superficial layer were consistent with ichthyosis uteri; in contrast the lesion of invasive squamous cell carcinoma was located in the deeper layer and lymph nodes. No dysplastic changes of the cervix were noted. *Conclusions:* It is suggested that PSCCE could be associated with pre-existing ichthyosis uteri and deeper biopsies should be performed for the accurate preoperative diagnosis of cases with chronic pyometra.

Key words: Squamous cell carcinoma; Endometrial carcinoma; Ichthyosis uteri.

Introduction

Primary squamous cell carcinoma of the endometrium (PSCCE) is an uncommon entity and has been rarely reported to be associated with ichthyosis uteri, where the entire endometrium is replaced by stratified squamous epithelium, which is originally considered as a benign condition. In this report the authors present the unique clinical and pathological findings of a case of PSCCE in association with extensive ichthyosis uteri.

Case Report

A 66-year-old gravida 2, para 2, healthy woman was referred to our hospital with a several months' history of purulent vaginal discharge with foul odor. Several cytologic examinations of the cervix and endometrium had been performed and classified as negative. She had attained menopause about 15 years before. Endometrial curetting revealed strips of stratified squamous epithelium showing partly well differentiated squamous cell carcinoma, while cervical smear and curetting showed no malignant cells. Magnetic resonance (MR) imaging revealed a well circumscribed intramural mass of predominantly low to intermediate signal intensity on T2-weighted images resembling degenerated leiomyoma and an ill-demarcated mass of mixed signal intensity in the uterine cavity. Extrauterine involvement of the adnexa or pelvic lymph node was suspected. No invasion to the cervix was detected. The patient's tumor marker profile was as follows: SCC (13.7 ng/ml; normal < 1.5 ng/ml), CA 19-9 (29.6 U/ml; normal < 37 U/ml), CEA (4.3 ng/ml; normal < 2.5 ng/ml), CA-125 (25.1 U/ml; normal < 35 U/ml). From these findings, squamous cell carcinoma originating in the endometrium was highly suspected. At exploratory laparotomy, the uterus was remarkably enlarged and densely adherent to the left tube, which was enlarged 3 x 3 x 4 cm. The pelvic peritoneum appeared thick and inflamed. Radical hysterectomy, bilateral salpingo-oophorectomy, pelvic lymph node dissection with pelvic washings and omentectomy were carried out.

Macroscopically, the uterine cavity was markedly distended and filled with foul-smelling purulent keratin debris, and pus occluding the whole entire endometrial cavity (Figure 1). Sectioning revealed stromal invasion of the tumor to almost 100% of the uterine wall thickness with direct invasion to the left fallopian tube. The cervix was examined entirely and showed no gross mucosal lesions. Microscopically, the polypoid mass was covered externally by cornified squamous epithelium and had fibrovascular stroma inside. The entire endometrium was replaced by stratified squamous epithelium showing areas of heavy keratinization, koilocytic changes, nuclear hyperchromasia and moderate increase in nuclear-cytoplasmic ratio indicating low grade dysplastic changes in the underlying ichthyosis uteri (Figure 2). In contrast the invasive squamous cell carcinoma lesion was located in the deeper layer (Figure 3). No dysplastic changes of the cervix were noted. Metastatic lesions measuring 3 x 3 x 2 cm were observed in the left pelvic lymph nodes.

The patient was treated with concurrent chemoradiation therapy. Six months after radiation, SCC level slightly increased, and positron emission tomography and computed tomography suggested recurrence in the small pelvis. She received adjuvant treatment with six courses of weekly carboplatin and paclitaxel administration. She is alive and well with no evidence of disease 22 months after surgery.

Discussion

The case that we report here showed PSCCE in pre-existing extensive ichthyosis uteri with dysplasia. To cor-

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Fig. 1

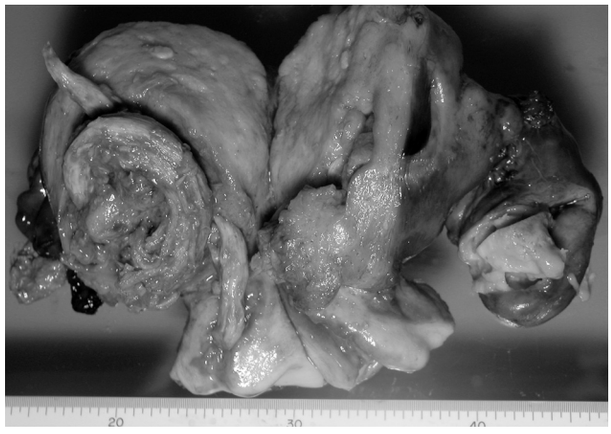

Fig. 2

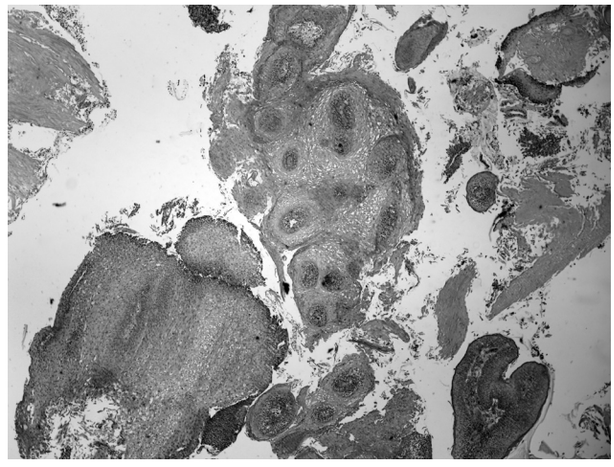

Fig. 3

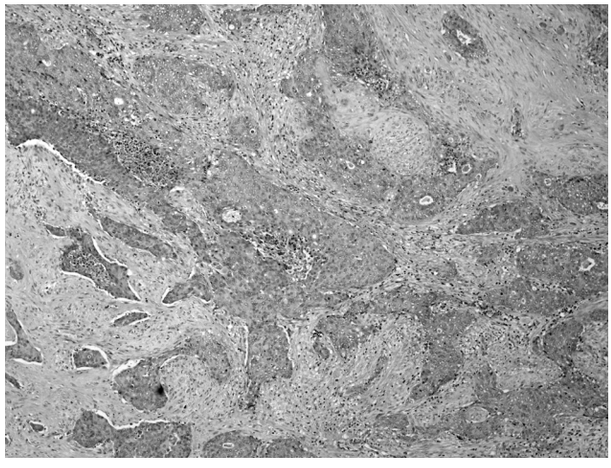

Figure 1. — The uterine cavity was markedly distended and filled with foul-smelling purulent keratin debris and pus occluding the whole entire endometrial cavity.

Figire 2. — The entire endometrium was replaced by stratified squamous epithelium showing areas of heavy keratinization and koilocytic changes.

Figure 3. — The lesion of invasive squamous cell carcinoma was located in the deeper layer.

rectly identify PSCCE, the tumor must satisfy the criteria established by Fluhman and extended by WHO [1]: (a) no coexisting endometrial adenocarcinoma; (b) no connection between endometrial tumor and squamous epithelium of cervix; (c) no coexisting primary squamous cell carcinoma of the cervix; (d) clear evidence of squamous differentiation such as intercellular bridges and/or keratin. Our patient fulfilled these proposed criteria.

Ichthyosis uteri usually lacks any malignant potential. Association of squamous cell carcinoma of the endometrium and ichthyosis uteri is exceedingly rare with few cases reported in the literature. Based on single case reports, various studies have put forth two plausible explanations for histopathogenetic mechanisms responsible for this condition. The first explanation is that a squamous cell lesion of the cervix extends proximally into the endometrium, and colonizes the pre-existing ichthyosis uteri [2, 3]. The second explanation is that squamous cell carcinoma develops within a background of extensive ichthyosis uteri: several investigators report that there is a strong association with cervical stenosis, pyomtra, chronic inflammation and nulliparity, and propose a sequence of change with squamous metaplasia through dysplasia to frank invasive carcinoma [4, 5]. Also in the present case, the patient was a postmenopausal woman who was clinically diagnosed as having pyometra and on histopathlogical examination, extensive ichthyosis uteri with dysplasia and squamous cell carcinoma with areas of multifocal invasion into the myometrium was present. With these reports and from our results, it might be speculated that chronic inflammation of the endometrium plays an important role in the development and progression of PSCCE, in terms of the metaplasia-hyperplasia-dysplasia sequence.

Survival data for PSCCE are scanty. The presence of a malignant squamous cell component in endometrial carcinoma are said to worsen the prognosis [6]. The prognosis of squamous cell carcinoma of the endometrium is related to the stage at diagnosis. In a review of reported cases, 80% of Stage I patients survived whereas survival for patients with Stage III disease was only 20% [7]. Diagnosis of primary squamous cell carcinoma of the endometrium should be considered in a postmenopausal elderly female presenting with pyometra, and deeper biopsies should be performed for an accurate preoperative diagnosis.

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