

A case of lymphoepithelioma-like carcinoma in the uterine cervix

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Abstract

Lymphoepithelioma-like carcinoma occurring in the reproductive organs is a rare variant of squamous cell carcinoma, and this tumor of the uterine cervix accounts for 0.7% of all primary cervical uterine neoplasms. Associations with Epstein-Barr virus (EBV) and human papilloma virus (HPV) have been demonstrated in some studies. Some investigators suggested that EBV has an important role in the initiation of lymphoepithelioma-like carcinoma in Asian women. Here we report the case of a 45-year-old Japanese woman, gravida 2 and parity 2. She was admitted due to severe atypical genital bleeding caused by uterine cervical cancer. A >60-mm tumor was detected at the uterine cervix, and no distal metastasis or swallowing of lymph nodes was revealed by magnetic resonance imaging and a computed tomography scan. The cervical cancer stage FIGO Ib2 was diagnosed, and a radical hysterectomy was performed for this malignant tumor. The *in situ* hybridization for EBV was negative. HVP infection was strongly suspected because the squamous cell carcinoma was observed macroscopically in the uterine cervix. The prognosis of uterine lymphoepithelioma-like carcinoma is thought to be better than those of other cervical cancer types, but careful follow-up at fixed intervals is recommended. The patient has been followed up for 4 months since her surgery, and no evidence of recurrence has been detected.

Introduction

Lymphoepithelioma carcinoma is most common in the nasopharynx. A similar tumor known as lymphoepithelioma-like carcinoma is generally seen in the stomach, salivary gland, and lung.¹ Lymphoepithelioma-like carcinoma occurring in the uterine cervix is very rare, and was first reported by Hamazaki *et al.* in 1968.² Lymphoepithelioma-like carcinoma of the uterine cervix accounts for only approx.

0.7% of all primary malignant tumors at the uterine cervix, but the clinical outcome of this type of malignant tumor is better than those of other carcinomas occurring in the uterine cervix.³ There are some reports of associations between the pathogenesis of lymphoepithelioma-like carcinoma and Epstein-Barr virus (EBV) and with human papilloma virus (HPV).

Here we present a case of lymphoepithelioma-like carcinoma of the uterine cervix that occurred in a Japanese woman of reproductive age.

Case Report

The patient was a 45-yr-old Japanese woman, gravida 2, parity 2. She consulted a doctor at another hospital because of atypical genital bleeding. The results of the cytology and histology at the previous hospital indicated squamous cell carcinoma. She was admitted to our hospital for treatment of the cervical tumor. On admission, her hemoglobin had decreased to 4.7 g/dL because of severe atypical genital bleeding, and thus a blood transfusion of 12 international units of red cell concentrate/mannitol adenine phosphate (RCC) was administered.

A computed tomography (CT) scan and magnetic resonance imaging (MRI) revealed a tumor (>60 mm) at the uterine cervix (Figure 1). No distant metastatic lesions or enlarged lymph nodes were observed. An internal examination was performed, and the diagnosis of uterine cervical cancer, FIGO stage IB2 was made. We performed a radical abdominal hysterectomy for the uterine cervical cancer as the initial treatment (Figure 2).

The pathological results revealed some tumor parts with intense infiltration of lymphocytes and lesions that looked like lymphoma (Figure 3A,B). Immunostaining was positive for p40 and cytokeratin7 (Figure 3C,D) and negative for vimentin, CD10, and c-caldesmon. A lesion of several sizes of alveolar configuration with cancer pearls as seen in squamous cell carcinoma (Figure 3E) was mixed into the infiltration of lymphocytes. The final diagnosis was thus squamous cell carcinoma with lymphoepithelioma-like carcinoma.

The patient received external beam radiation therapy (50 Gy) according to the 2011 Japanese guidelines for uterine cervical cancer as the treatment after operation. The patient has been followed-up without evidence of recurrence or side effects for four months since her radiotherapy.

Discussion and Conclusions

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Lymphoepithelioma-like carcinoma appearing in the uterine cervix is an uncommon type of uterine cervical cancer. Generally, this type of tumor is thought to be a subtype of poorly differentiated squamous cell carcinoma, histologically characterized by nests of undifferentiated epithelial cells with a syncytial growth pattern infiltrated by a severe lymphocytic infiltrate.

Generally, the mean age of patients with common uterine cancer is from 49 to 54, but that of patients with lymphoepithelioma-like carcinoma occurring in the uterine cervix appears to be younger. Hasumi *et al.*⁴ reported that more than 41% of patients with uterine lymphoepithelioma-like carcinoma were less than 40 years old. In addition, it was reported that uterine lymphoepithelioma-like carcinoma is more common in Asian women compared to West women.¹

The fundamental pathogenesis of lymphoepithelioma-like carcinoma is unknown, but many reports have suggested that EBV has an important role as a causative agent.³ Tseng *et al.*⁵ reported that 73.3% (11/15) Asian women with lymphoepithelioma-like carcinoma occurring in the uterine cervix were positive for the antibody of EBV.⁵ However, the positive ratio of those patients in Caucasian women in the West is probably lower. Noel *et al.*⁶ reported that EBV had not been detected in Caucasian women with lymphoepithelioma-like carcinoma as of 2001. In their review of uterine lymphoepithelioma-like carcinoma reports, Chao *et al.*⁷ reported that 12 of 43 patients with uterine lymphoepithelioma-like carcinoma were

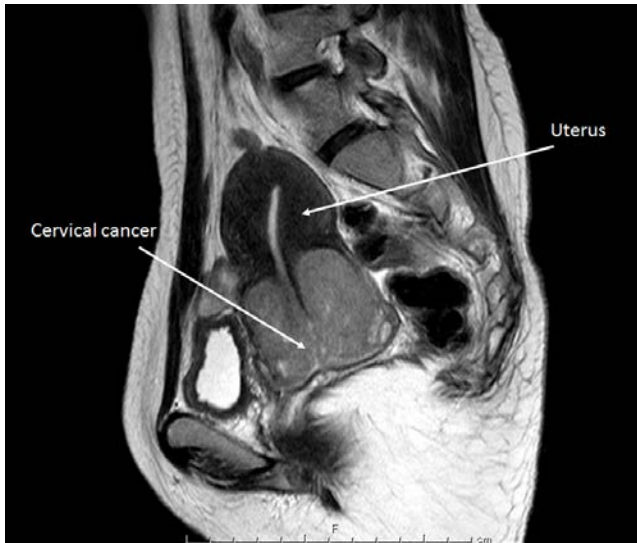


Figure 1. T2-weighted image of magnetic resonance imaging (MRI) showing the >60-mm tumor at the uterine cervix of the patient, a 45-year-old Japanese woman. No infiltration to a cardinal ligament or enlarged lymphocyte was detected in this MRI.

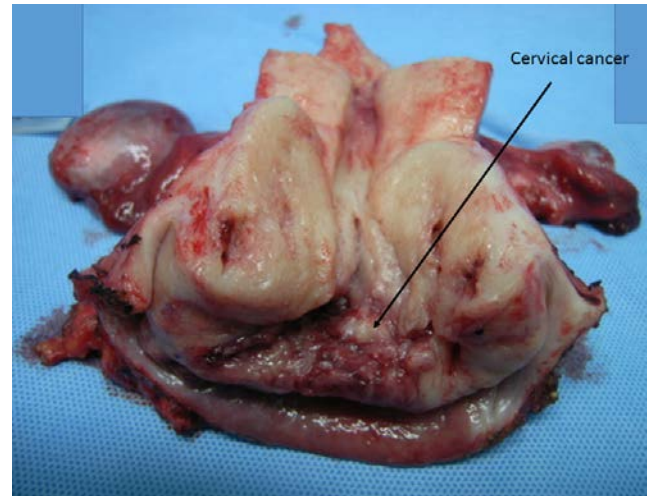


Figure 2. Carcinomatous and necrotic tissue is visible at the uterine cervix. An adequate margin of the vaginal wall and cardinal ligament were removed by the radical hysterectomy.

positive for EBV. However, they found that if only the cases of Asian women are examined, 48% (12/25) of the women with uterine lymphoepithelioma-like carcinoma were positive for EBV, whereas 0% of the 9 patients of American and Spanish descent were positive for EBV. Thus racial and geographic factors might influence the pathogenesis of lymphoepithelioma-like carcinoma.⁷ In the present case, the result of the in situ hybridization for EBV was negative.

Some researchers have reported that HPV may be associated with lymphoepithelioma-like carcinoma. HPV is well recognized as an etiological factor in the pathogenesis of uterine cervical cancer. Noel *et al.*⁶ reported that HPV-16 and HPV-18 infection was detected in two Caucasian women with lymphoepithelioma-like carcinoma in the uterine cervix. Bais *et al.*⁸ reported that HPV-16 and HPV-45 infection was present in their patient.

We did not check the existence or non-existence of HPV infection in the present case, because the lesion of squamous cell carcinoma was mixed with that of lymphoepithelioma-like carcinoma, and thus HPV infection was strongly suspected in this case.

Several researchers reported that the prognosis of lymphoepithelioma-like carcinoma is better than those of other types of cervical cancer such as common squamous cell carcinoma and adenocarcinoma.^{4,8} Van Nagell *et al.*⁹ reported that uterine lymphoepithelioma-like carcinoma has less lymphocytic metastasis and tumor recurrence compared to common uterine cancers such as common squamous cell carcinoma and adenocarcinoma. Moreover, Hasami *et al.*⁴ found that the 5-year survival of

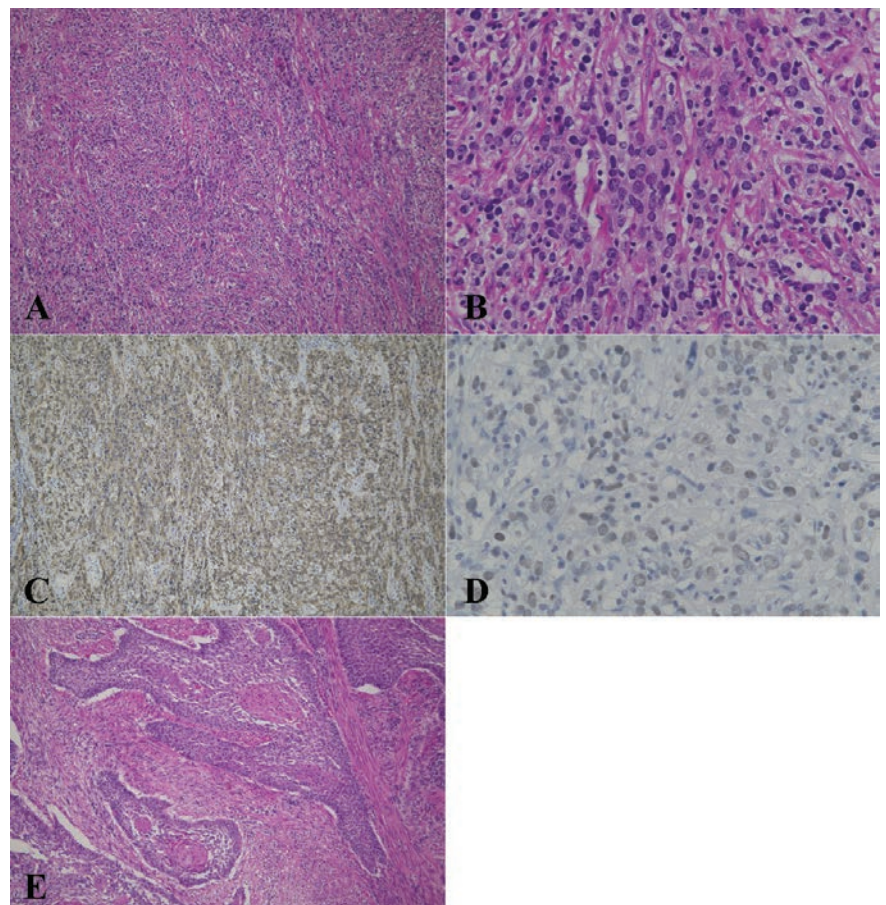


Figure 3. An intense infiltration of lymphocytes is seen. The lesions looked like lymphoma. A) Hematoxylin and Eosin staining (H&E), 100. B) H&E $\times 400$. The immunostaining for cytokeratin7 and P40 was positive. This result microscopically suggested lymphoepithelioma-like carcinoma. C) H&E, $\times 40$; D) H&E, $\times 100$. A lesion with several sizes of alveolar configuration with cancer pearls, which was diagnosed as squamous cell carcinoma of the keratinizing type. E) H&E, $\times 100$.

patients is also better in uterine lymphoepithelioma-like carcinoma compared to other squamous cell carcinomas. In this present case, even though the tumor size was >60 mm, we did not microscopically detect vascular or lymphovascular invasion, infiltration of vaginal wall or cardinal ligament, or metastasis to lymph node. Only 4 months have passed since the initial treatment, so the patient has been strictly followed-up at our hospital. We have reported a rare case of lymphoepithelioma-like carcinoma of the uterine cervix, stage Ib2, FIGO. The patient was treated with a radical hysterectomy and chemotherapy, paclitaxel and carboplatin, 6 cycles. This type of tumor tends to have a good clinical outcome, but we have been following the patient carefully.

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