Case series: Association of cervical lymphoepithelioma-like carcinoma with HPV-16

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Abstract
Lymphoepithelioma-like carcinoma of the cervix is a variant of squamous cell carcinoma. Of all cervical cancer it comprises about 0.7% cases. It differs from the usual squamous cell carcinoma of cervix in its clinical behaviour, morphology and has a better outcome. We report two cases of Lymphoepithelioma-like carcinoma of cervix associated with Human Papilloma Virus-16 in Indian women. They were staged as FIGO Ib1 and Ib2 respectively, and a radical hysterectomy was performed.

Keywords: Human papilloma virus (HPV), Ebstein –Barr virus (EBV)

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Introduction
Lymphoepithelioma-like carcinoma is most common in nasopharynx and has been also reported from stomach, salivary glands and lungs,1 apart from vulva, endometrium, cervix and vagina.2 Hamazaki et al first reported it in 1968.3 Because of lack of lymph node involvement, this type of tumor has shown better clinical outcome.4 In some studies association with Epstein-Barr virus (EBV) and human papilloma virus (HPV) has been found. In Asians EBV has been shown to have a role in initiation of Lymphoepithelioma-like carcinoma.

Case 1
A 42 year old, multiparous woman was admitted with a history of postcoital bleed for the last 6 month. The systemic examination was normal. On perspeculum examination the cervix was hard, bulky and bled on touch. The parametrium and pelvic wall were uninvolved. The cervical punch biopsy suggested Lymphoepithelioma-like carcinoma on histopathological examination. Metastasis workup was normal and FIGO stage was Ib1. Further immunostaining was positive for HPV DNA and negative for EBV. She underwent radical hysterectomy with a normal postoperative convalescence and had no recurrence at 5 years.

Case 2
70 years old, chronic smoker, multipara Indian woman. She had minimal post menopausal bleeding, the systemic examination was normal. On speculum examination the cervix was suspicious which bled on touch. The parametrium and pelvic wall were not involved. Her cervical punch biopsy on histopathological examination also suggested Lymphoepithelioma-like carcinoma. She was HPV DNA positive and EBV was negative. The Computerized Tomography Scan showed no distant metastasis seen and was staged as FIGO Stage Ib2. She underwent radical abdominal hysterectomy. Intra operative and post operative period was uneventful. The patient received radiotherapy in post operative period. On follow up of 3 years she did not have any recurrence.

Discussion
In India cervical cancer is the most common genital cancer in women (80%), with the mean age of presentation between 49 to 54 years. With near universal Pap smear examinations the prevalence of invasive cancers has declined with pre-invasive lesions detection has increased.5

Lymphoepithelioma-like carcinomas are uncommon types of cervical cancers – and considered to be a subtype of poorly differentiated squamous cell carcinomas. The histology typically shows nests of undifferentiated epithelial cells with syncytial growth pattern and lymphocytic infiltrate. It is commoner in Asians as compared to western women.1

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Lymphoepithelioma-like carcinoma showing the squamoid nests with clusters of lymphocytes.

Hasumi et al\(^\text{60}\) have reported more than 41% of cervical Lymphoepithelioma-like carcinoma in women aged less than 40 years. Our Indian patients however were aged 42 years and 70 years respectively.

Although the exact pathogenesis is unknown, but EBV as an etiologic organism has been reported.\(^\text{6}\) Tseng et al reported that 73.3% Asians with cervical lymphoepithelioma-like carcinoma had a positive EBV antibody.\(^\text{7}\) Noel et al\(^\text{8}\) in their study in Caucasians did not detect EBV in patients with cervical lymphoepithelioma-like carcinoma. However they reported HPV-16 and HPV-18 infection in two of the Caucasian patients studied.\(^\text{8}\) Chao et al\(^\text{9}\) reported 12 of 43 patients with cervical lymphoepithelioma-like carcinoma as EBV positive. Of these in Asian women only 48% (12/25) were EBV positive in contrast to 0% of American and Spanish women. This may suggest a racial and geographic influence in the pathogenesis Lymphoepithelioma-like carcinoma. In our cases the results of in situ hybridisation was positive for HPV-16 in both the cases presented.

Van Nagell et al have reported Lymphoepithelial like cervical carcinoma to have less lymphocytic metastasis, less tumor recurrence and a better prognosis as compared to squamous cell and adenocarcinomas.\(^\text{10}\) This was also found to be true in both our cases.

**Conclusion**

Lymphoepithelial like cervical carcinoma is rare with good prognosis. Our series suggest a possible association with HPV-16, and warrants a further study.

**References**