



Case Report

Lymphoepithelioma-Like Carcinoma of the Uterine Cervix - Reporting Three Rare Clinical Cases with Lymph Node Metastasis

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Abstract

Objective: Lymphoepithelioma-like carcinoma of the uterine cervix is a rare subtype of squamous cell carcinoma (SSC) and it is more common in Asia-5.5%, than in Europe-0.7%. It is considered that LELC is associated with Epstein-Barr virus (EBV) infection in Asian and with Human papilloma virus (HPV) or no infection in Caucasian patients. Compared to the common cervical cancer LELC affects younger women, its outcome is better and it has to be with a lower frequency of regional lymph node metastasis and recurrence.

Case report: We present three cases of LELC with lymph node metastasis and a follow-up of the patients. The diagnosis was confirmed histologically. All three cases have been examined Immunohistochemically for assessment of the viral status for both EBV and HPV. Two of them died from the cervical cancer and one is still alive without evidence of recurrence. The results of the immunohistochemical study showed that two of them were negative for both viruses and one was positive only for EBV.

Conclusion: Our data shows that the immunohistochemical results for the viral status cannot be used as a predictive factor as opposed to the lymph node status and lymphovascular space invasion (LVSI).

Keywords

Lymphoepithelioma-like cervical carcinoma; Lymph node metastasis; Prognosis; Virus status

Introduction

Lymphoepithelioma-like carcinoma (LELC)-was firstly described as a neoplasm of the nasopharynx, tonsils, stomach, lungs, salivary glands and the thymus [1-4]. It was firstly reported in the uterine cervix by Hamazaki [5]. It has been proposed that cervical LELC may be related to Epstein-Barr virus (EBV) infection, since it occurs in LELC arising at other locations [6]. This is a rare tumor with small incidence-5,5% in Asians and even less-0,7% in Caucasians. It affects mostly younger women and it is suggested to be associated by EBV in the Asian population and with Human papilloma virus (HPV) or no infection in Caucasian patients. The LELC has better prognosis

than the common cervical cancer such as squamous cell carcinoma and adenocarcinoma [7].

Case Report

We present three cases of women, diagnosed with lymphoepithelioma-like carcinoma. The diagnosis was confirmed histologically. They were operated in the Clinic of Gynecologic Oncology, University Hospital "Dr. G. Stranski"-Pleven, Bulgaria for a period of 9 years (2007-2016). The patients have been examined routinely-histologically and immunohistochemically - for assessment of the viral status, with monoclonal antibodies against EBV/HPV by DAKO protocol. We used Mo a Hu Papillomavirus (HPV), Clone K1H8 and FLEX Monoclonal Mo a Epstein-Barr Virus, LMP, Clone CS.1-4.

Case 1: A 67 year old woman, gravida 3, para 2 was admitted in the Clinic of Gynecologic Oncology because of postmenopausal bleeding that had started several weeks ago. Because of this she had went to gynecologist, who performed a biopsy of the uterine cervix. The result from the biopsy was squamous epithelium with atypical zones and plenty of atypical mitoses. There were parts that contained necrosis.

The general physical examination was normal. She was in good general health, with no other diseases, except diabetes type II, which was well maintained. She had never undergone any kind of surgical procedure up to this point. On pelvic examination the cervix had an exophyte lesion 0.5/0.5 sm, which was located close to the cervical canal. The upper part of the cervix was bulky and harder than the rest. All other pelvic organs were without pathology.

Radical hysterectomy with bilateral adnexectomy and total pelvic lymph node dissection was performed. The final pathological result was: LELC with Lymphovascular space invasion (LVSI). The total number of lymph nodes was 31, with 2 micro metastasis on the right hemipelvis- one from the obturator group nodes and the other from internal iliac lymph nodes. The rest of the surgical specimen and the regional lymph nodes showed no evidence of malignancy. The patient was staged according to the TNM grading system- T1b1pN1M0. Immunohistochemistry did not detect any viral presence. The patient was treated with post-operative TGT (50 Gy). She died from the disease 6 months after the diagnosis.

Case 2: A 47 year old woman, gravid 2, para 2 had postcoital genital bleeding. A biopsy of the uterine cervix was taken- small cell squamous carcinoma of the uterine cervix. She was then admitted to the Clinic of Gynecologic Oncology. Her general condition was normal, she had no other diseases. The pelvic examination showed enlarged uterus in AVF position-m.l. IV and presence of an exophyte lesion 5/5sm, protruding from the cervix. The other pelvic organs were normal.

Radical hysterectomy with bilateral adnexectomy and total pelvic lymph node dissection was performed. Hystopathological results showed LELC of the uterine cervix with ulcerations. One of the iliac lymph nodes from the right hemipelvis had diffuse metastasis. The rest of the surgical specimen showed no evidence of malignancy. The result from the peritoneal cytology showed typical mesotel cells with degenerative changes. The staging is pT1b2pN1M0. Her viral status was negative from the immunohistochemistry. The patient was

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advised to undergo postoperative TGT but she refused this treatment. She remains disease-free 8 years after the diagnosis.

Case 3: A 40 year old woman, gravida 2, para 2 had genital bleeding and she went to a gynecologist. A biopsy was taken- squamous cell carcinoma. She was admitted in the Clinic of Gynecologic Oncology for a surgical treatment. She was in good general health, with data for chronically bronchitis. The gynecological examination showed an exophyte cervical lesion 3/3sm, which was bleeding in touch. The other pelvic organs were without of abnormalities. She underwent Robot assisted radical hysterectomy with bilateral adnexectomy and total pelvic lymph node dissection. The histopathologic result showed LELC of the uterine cervix, with ulcerations, hemorrhages and LVSI. A metastasis from the carcinoma was found in one of the right lymph nodes. The rest of the surgical specimen and the regional lymph nodes showed no evidence of malignancy. Later the presence of EBV in the tumor site was detected via immunohistochemistry. She underwent postoperative TGT but died 35 months years after the diagnosis.

Discussion

LELC of the uterine cervix is a rare variant of squamous cell carcinoma. First it was classified in the group of low differentiated squamous cell carcinomas. The tumor size can vary from no visible lesion to a large exophytic mass and histopathological; it is characterized by syncytial like aggregates of undifferentiated tumor cells with indistinct cytoplasmic margins, vesicular nuclei with prominent nucleoli and lack of glandular or squamous differentiation [8]. This typical appearance helps separate LELC from other squamous cell carcinomas [9]. In the female genital tract it has been reported in the vulva, vagina, uterine cervix and endometrium [10].

This type of cervical cancer is very rare and it is more common in Asia, when compared to Europe-5.5%/0.7% [11]. There is a difference between the patient's ages in both continents- 55-77 for Asians and 21-58 for the Caucasians. Hasumi [11] reported that more than 41% of patients with cervical LELC were less than 40 years old [12].

It is important to point out that compared to the common cervical cancer LELC affects younger women, its outcome is better and it has to be with a lower frequency of regional lymph node metastasis and recurrence [7,11-13]. Although generally LELC is said to have a better prognosis, this cannot be confirmed by our three cases. The patient from Case 1 was older than the average age, in which the disease is diagnosed. She had done TGT, as well as the patient from the third case, but despite that, they both died from cancer. The patient from Case 2 is still alive with no TGT, and this could be due to the radical surgery. The general difference between the first and the third case is presence of LVSI. It is easy to see that the presence of metastasis or even, micrometastasis has a bad prognostic value in patients with cervical cancer especially with LVSI. Our data shows that the immunohistochemistry results for the viral status cannot be used as a predictive factor-the EBV positive patient died; so did one of the virus-negative women. It would be good if more data is collected, concerning the viral status. The lymph node status and LVSI can be used as prognostic factors of LELC. Last but not least, the role and mechanism of the viral status is unclear up to this point. In lung LELC, up regulation of bc2 has been suggested [14]. Researchers found up regulation of p53 in nasopharyngeal and gastric LELC [15,16]. We need to process more data, so we can see where the role of EBV stands in the pathogenesis and the prognosis of LELC.

Conclusion

In conclusion, LELC of uterine cervix is a rare but distinct tumor

that is interesting for both clinicians and pathologists. The prognostic factors are not yet fully determined. Neither the tumor size, not the viral status could be used as a prognostic factor but probably lymph node metastasis and especially LVSI could. It is crucial that more data, concerning the viral status will be gathered and processed.

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