

Prikazi bolesnika/  
Case reports

IMMUNOHISTOCHEMICAL DETECTION  
OF UTERINE CERVICAL  
LYMPHOEPITHELIOMA-LIKE  
CARCINOMA (LELC)

IMUNOHISTOHEMIJSKA DETEKCIJA  
LYMPHOEPITHELIOMA-LIKE  
CERVIKALNOG KARCINOMA (LELC)

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*Key words*

Lymphoepithelioma-like carcinoma,  
Karcinom cerviksa, Epstein-Barr-ov  
Virus, Imunohistohemija.

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Lymphoepithelioma-like carcinoma,  
Cervical carcinoma, Epstein-Barr Virus,  
Immunohistochemistry.

*Abstract*

Lymphoepithelioma-like carcinomas (LELCs) have been reported outside the nasopharynx in many sites. Although this distinct neoplasm is a very rare variant of squamous cell carcinoma accounting for only 0.7% of all uterine cervix primary malignant neoplasms, it has become a well-known entity. 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. This relation is suggested, but still controversial. Until now, EBV genome has only been demonstrated in Asian patients with cervical LELC, whereas no reports were submitted about a connection between LELC and EBV in Caucasians, but sporadic appearances of Human Papilloma Viruses (HPV). We report a case of LELC of the uterine cervix in a 64-year-old Caucasian woman from Serbia detected immunohistochemically. Morphologically the undifferentiated carcinoma was accompanied by intense lymphocytic infiltration. Immunohistochemically the tumor expressed epithelial markers. A large proportion of cells expressed proliferative activity.

*INTRODUCTION*

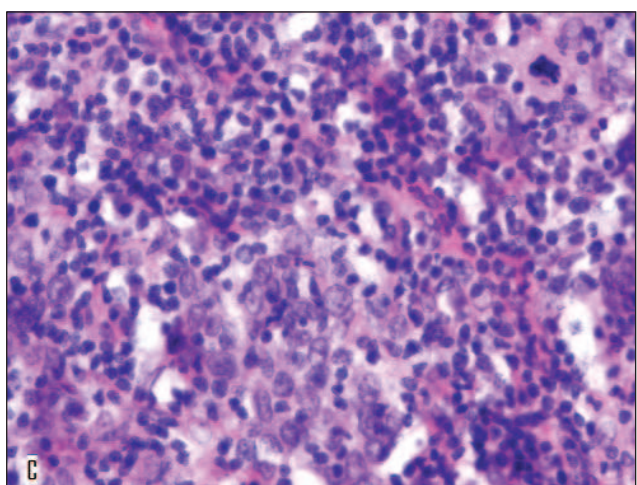
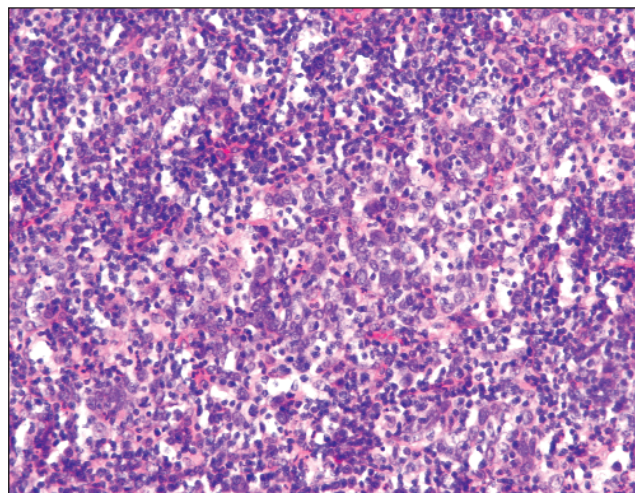
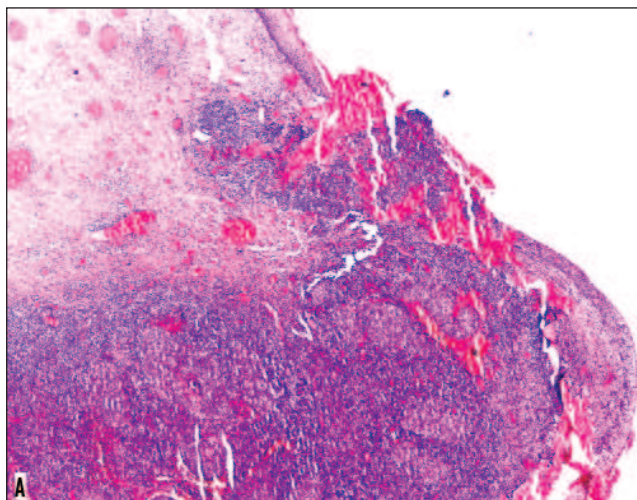
Lymphoepithelioma-like carcinomas (LELCs) have been reported in many sites, including nasopharynx, where it usually occurs, salivary gland, thymus, stomach and uterine cervix. (1,2,3,4). Fortunately, these lesions are responsive to treatment, and patients typically have a favorable prognosis. We report a case of LELC of the uterine cervix detected immunohistochemically.

*CASE REPORT*

In this paper, we discuss the case of a 64-year-old Caucasian woman, who presented with pelvic pain, who had postcoital bleeding of some months duration. Medical history was noncontributory, cervical cytologic test results were reported as negative 2 years before. At gynecologic examination, there was a fungating tumor, 2 cm in diameter, that occupied the posterior lip of the cervix. Laboratory findings

were within normal limits. A biopsy was performed and histopathology revealed invasive lymphoepithelioma-like carcinoma.

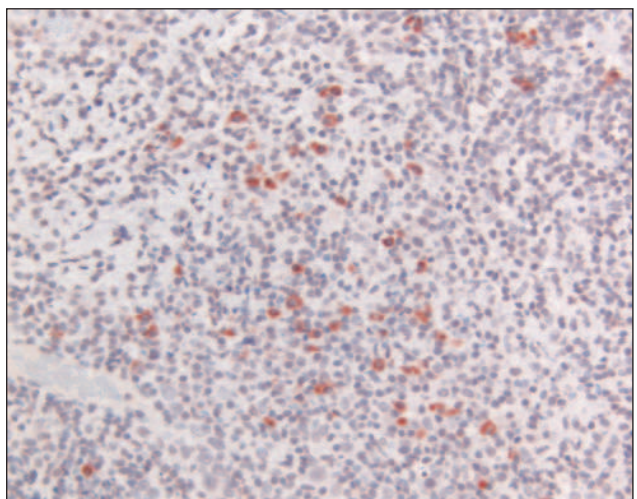
Microscopic examination of the biopsy specimen disclosed a poorly differentiated nonkeratinizing carcinoma composed of cohesive nests surrounded by prominent lymphoplasmacytic infiltrate. No adjacent carcinoma in situ was identified. The depth of invasion was more than 1,5 cm (figure 1A). Small foci of nonkeratinizing carcinoma appeared in the stroma, surrounded by marked inflammatory reaction. There was no evidence of glandular differentiation, keratinization or intercellular bridges (figure 1B). Cells were large and had indistinct cell margins (syncytial-like pattern). Nuclei were vesicular and contained 1 or 2 prominent nucleoli and peripheral chromatin (figure 1C). Immunohistochemistry was performed on paraffin-embedded sections. The tumor cells were strongly positive for Anti-Epithelial



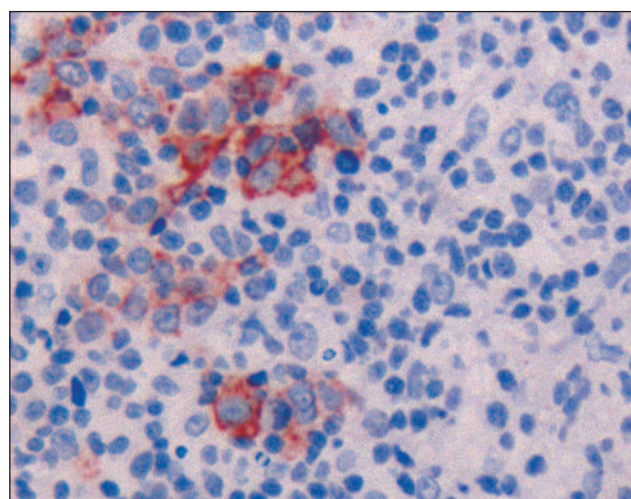
*Figure 1. Characteristic histologic features of lymphoepithelioma-like cervical carcinoma: Ulcerated squamous non-keratinized epithelium can be seen on the surface of the biopsy specimen (figure A).*

*There are pathognomonic partly anastomosing clusters of syncytial epithelioid cells with conspicuous nucleoli set in the background of small lymphocytes (figureB) .*

*High-power view of lymphoepithelioma-like carcinoma. Note syncytial arrangement and prominent nucleoli (figureC). Hematoxylin-eosin, original magnification for A 25x, for B 200x, and for C 400x.*



*Figure 2. Anti EBV-this slide shows patchy EBV neoplastic cells immunoreactivity.*



*Figure 3. Immunohistochemical detection of Anti-EMA: Selected immunohistochemistry depicts squamous epithelial origin of neoplastic cells in clusters contrasting darker cells representing dense lymphoplasmatic infiltration (original magnification 200x).*

Membrane antigen (EMA). p63 protein as homologue of the p53 protein, being a powerful marker for squamous differentiation, was diffusely expressed, which excluded a glandular or neuroendocrine differentiation. Anti-p53 protein was expressed as well. Tumor cells also expressed a high proliferative rate i.e. Ki 67(MIB 1) of more than 80% positive tumor nuclei. Neoplastic cells were negative for HMB45 and Desmin. The inflammatory background contained many Leukocyte Common Antigen (LCA) positive cells.

Immunohistochemical detection of the Anti-EBV latent membrane protein was positive (figure 2).

#### DISCUSSION

Lymphoepithelioma carcinoma of the uterine cervix is a rare entity outside the nasopharynx with only a few reports concerning the clinical outcome following treatment (1,2). It is an uncommon neoplasm that usually occurs in Asian patients (3), whereas 73% of the Taiwanese women studied

by Tseng et al. harbored EBV in the neoplastic cells (5,6). The outcome has been better than in cases of the usual squamous cell carcinoma of the cervix. Therefore, it is essential to consider only those poorly differentiated tumors as such that fulfill strict morphologic criteria: negative lymphoid markers, indistinct cytoplasmic margins, vesicular nuclei with prominent nucleoli, and, in the opinion of most authors, absence of glandular or squamous differentiation (1,2). LELC is described to have prevalence for Asian women (in whom EBV has been demonstrated). Caucasian women have a low prevalence of cervical LELC with no infection of the EBV and sporadic appearances of Human Papilloma Virus (HPV) (7,8). The histologic and EBV results of the uterine cervical LELC were similar to the classic nasopharyngeal lymphoepithelioma. Our case contains clues supporting the concept of the relation between cervical LELC and the presence of EBV, though a definite confirmation by the Polymerase Chain Reaction (PCR) is recommendable. Immunohistochemically the tumor expressed EMA, which proved epithelial squamous origin of the neoplastic cells (figure 3) as well as p63, which is preferentially expressed in basal nuclei and immature cervical squamous epithelium

and p53 which showed focal nuclear positivity in neoplastic cells. Large proportion of tumor cells, more than 80%, expressed MIB-1 (Ki-67). The accompanying, marked lymphoplasmocytic stromal infiltration showed LCA positivity, whereas tumor cells were LCA negative (figure 3).

### CONCLUSION

Lymphoepithelioma-like carcinoma is a rare variant of squamous cell carcinoma of the uterine cervix. This is the first case of LELC of the uterine cervix in Caucasian woman from Serbia that was detected immunohistochemically. We present LELC in order to bear in mind the possibility of LELC whenever confronted with poorly differentiated carcinoma rich in lymphoplasmocytic infiltration regardless of the anatomic site.

*ACKNOWLEDGEMENT: The authors would like to thank to mr sc.med.dr Predrag Peric for his unselfish, time consuming full support and cooperation .*

### Apstrakt

Lymphoepithelioma-like karcinoma (LELC) je opisan na brojnim lokalizacijama pored nazofarinksa. Iako ova jedinstvena neoplazma predstavlja jedan veoma redak oblik skvamoznocelularnog karcinoma koja se sreće u samo 0,7% svih slučajeva primarnih malignih neoplazija materice, reč je o jednom u međuvremenu dobro poznatom entitetu. Pretpostavlja se da postoji povezanost između cervikalnog LELC i infekcije Epstein-Barr-ovim virusom (EBV) jer se pojavljuje u slučajevima LELC sa incidencijom na drugim lokacijama. Dotična udruženost je nasumična, premda još uvek kontroverzna. Do sada je EBV-ov genom bio dokazan kod azijskih pacijentkinja sa cervikalnim LELC, dok ne postoje izveštaji o povezanosti LELC-a i EBV-a kod belkinja, gde se nailazi samo na sporadično prisustvo Human Papilloma Virus-a (HPV). Naš izveštaj tiče se jednog imunohistemijski dokazanog slučaja LELC kod jedne 64-godišnje belkinje srpskog porekla.

Morfološki je to bio nediferentovani karcinom praćen intenzivnim limfocitnim infiltratom. Imunohistohemijski, tumor je ekspresirao epitelne markere. Tumorske ćelije pokazuju visoku proliferativnu aktivnost.

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