

Lymphoepithelioma-like carcinoma of the vagina

W G McCluggage

Abstract

This report describes a lymphoepithelioma-like carcinoma of the vagina. Although such tumours are well described in the cervix this is only the second report of such a neoplasm at this site. Histology showed a well circumscribed lesion composed of syncytial sheets of epithelioid tumour cells with an intense inflammatory infiltrate, largely consisting of T lymphoid cells. In situ hybridisation and immunohistochemistry for Epstein-Barr virus were negative. A review of the literature reveals that such neoplasms appear to be extremely rare within the female genital tract outside of the cervix.

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Keywords: vagina; carcinoma; lymphoepithelioma-like carcinoma

Lymphoepithelial carcinomas are common tumours within the nasopharynx. Morphologically, they are characterised by large tumour cells with prominent nucleoli usually growing in syncytial sheets and associated with an intense inflammatory infiltrate, chiefly consisting of lymphocytes. Within the nasopharynx, these tumours are usually associated with Epstein-Barr virus (EBV) infection.¹ Similar tumours have been described outside the nasopharynx and have been termed lymphoepithelioma-like carcinomas (LELCs). These rare tumours are most commonly found within the stomach,² salivary gland,³ and lung,⁴ where they are also usually associated with EBV infection. EBV seems to be associated with neoplasms arising in organs of foregut derivation.⁵ In other sites there is generally no association with EBV, although this is not always the case.⁵ LELCs are well described within the uterine cervix,⁶ but only one case has been reported in the vagina.⁷ The aim of this report is to describe a second vaginal example of this rare neoplasm.

Case report

A 90 year old, postmenopausal, white woman presented with vaginal bleeding. There was no past history of gynaecological problems or of malignancy, except for a cutaneous basal cell carcinoma. Vaginal examination revealed a mass in the posterior vagina, which was removed. Postoperative radiological examination of the pelvis and abdomen revealed no abnormality.

Pathological findings

The surgical specimen consisted of a 3.5 cm diameter well circumscribed mass covered by vaginal mucosa.

Histologically, the surface squamous epithelium was focally ulcerated by tumour but showed no dysplastic features. A well circumscribed lesion composed of epithelioid tumour cells was present within the mucosa and subepithelial tissue (fig 1). Tumour cells formed cohesive syncytial sheets without evidence of squamous or glandular differentiation. Tumour cells contained large central nuclei with prominent nucleoli and surrounding abundant eosinophilic cytoplasm (fig 2). There was pronounced nuclear pleomorphism and mitotic figures were easily identified. Vascular invasion was not seen. Associated with the tumour cells there was a pronounced inflammatory cell infiltrate consisting largely of lymphocytes, but also containing plasma cells, histiocytes, and eosinophils (fig 2). These inflammatory cells, in addition to being present within the stroma between tumour cell islands, were intimately intermingled with the epithelioid tumour cells.

Special stains (periodic acid Schiff-diastase and mucicarmine) revealed no evidence of intracytoplasmic mucin. Immunohistochemistry showed strong positive staining of tumour cells with the cytokeratin marker AE1/AE3 (Dako, Ely, UK) but no staining for CD45 (leucocyte common antigen (LCA), Dako). Staining for CD3 (Dako) revealed large numbers of T cells and staining for CD20 (Dako) showed smaller numbers of B cells. There was no staining of tumour cells for the



Figure 1 Low power view showing that the tumour is well circumscribed.

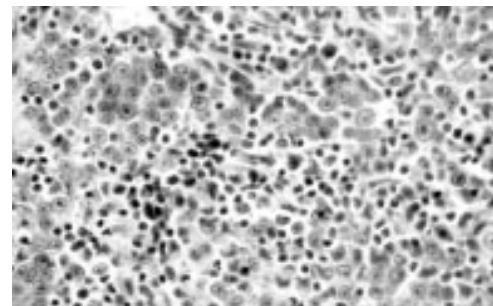


Figure 2 Tumour composed of large epithelioid cells with prominent nucleoli. These are admixed with many inflammatory cells.

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S100 protein (Diagnostic Products Limited, Abington, UK) or chromogranin A (Dako). There was no staining of tumour cell nuclei with DO7 (anti-p53) (Novocastra, Newcastle upon Tyne, UK) and staining with MIB1 (anti-Ki-67) (Immunotech, Marseilles, France) showed a proliferation index of approximately 50%.

Immunohistochemical staining with a monoclonal antibody against the EBV latent membrane protein (LMP-1) (Dako) showed no positivity. Likewise, in situ hybridisation showed tumour cells to be EBV encoded early RNA 1 (EBER-1) negative.

Discussion

A review of the literature revealed that this is only the second documented case of LELC arising within the vagina. The previously reported tumour was in an 81 year old woman,⁷ suggesting that at this site these extremely rare neoplasms are usually found in elderly women. LELCs are now well described in the uterine cervix⁶ and, elsewhere in the female genital tract, one such tumour has been described in the vulva⁸ and two in the endometrium.⁹ LELCs have also been described in the stomach,² salivary gland,³ lung,⁴ thymus,⁵ skin, larynx, trachea, renal pelvis, tonsil, middle ear, and urinary bladder. In the breast, medullary carcinoma has been considered a LELC, because it has similar morphological features to these tumours elsewhere. However, recently mammary LELC with distinct histological differences to medullary carcinoma has been described.¹⁰

Lymphoepithelial tumours of the nasopharynx are associated with EBV infection¹ and serological, immunohistochemical, and molecular studies have strongly implicated this virus in the pathogenesis of nasopharyngeal carcinoma, irrespective of geographical distribution or age. In addition to nasopharyngeal lesions, EBV is also associated with LELC of the stomach, salivary gland, lung, and thymus, all foregut derived organs. There is usually no association of EBV with tumours in other organs, although this is not always the case. The association of EBV with LELC appears to be restricted to Asian patients in tumours of the lung and salivary gland, but there is no such restriction with gastric or thymic neoplasms where EBV is found regardless of race.⁵

In most cervical LELCs where EBV studies have been performed, virus has not been identified. This was also true for our case and the previously reported vaginal tumour.⁷ The two endometrial tumours were also negative for EBV.⁹ However, in a study of 15 cervical LELCs in Taiwanese women the detection rate of EBV gene sequences was significantly more frequent than in control cases comprising patients with cervical squamous carcinoma.⁶ In contrast, the detection rate of human papilloma virus (HPV) types 16 and 18 was significantly lower in patients with LELC. It is likely that HPV infection may not be as important in the pathogenesis of cervical LELC as it is in conventional cervical squamous carcinoma. Moreover, it is possible that EBV is implicated

in the development of cervical LELC in the Asian population, where the incidence of this neoplasm is higher than in the West.

In our present case, as in other LELCs, the most likely differential diagnosis is an undifferentiated or anaplastic non-small cell carcinoma with a pronounced inflammatory infiltrate. Morphological features favouring a diagnosis of LELC are syncytial sheets of cells, tumour cells with prominent nucleoli, and an intense inflammatory cell infiltrate intimately admixed with the tumour cells. Lymphoma is also a possible differentiated diagnosis, which is easily solved by immunohistochemical staining with anticytokeratin antibodies and LCA.

LELC of the cervix usually shows a good response to radiotherapy and appears to have a better prognosis than cervical squamous carcinoma, possibly because of the pronounced host reaction to the neoplasm. This makes it important to recognise this histological subtype of cervical carcinoma and not merely categorise it as anaplastic or undifferentiated carcinoma. A favourable prognosis is also a feature of LELC of the nasopharynx, lung, stomach, and breast. Although LELC of the cervix is generally regarded as a variant of squamous carcinoma it is important to make a distinction for the reasons already outlined. As stated previously, the pathogenesis of cervical squamous carcinoma and LELC may be different. In the previously reported vaginal case there was complete regression of the tumour after radiotherapy and there was no evidence of tumour recurrence at six months follow up.⁷ However, because this is only the second reported example of this rare vaginal neoplasm and because no follow up is available in this case, firm conclusions cannot be drawn.

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