Vulvar malignant pleomorphic adenoma in a patient with lichen sclerosus

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INTRODUCTION

Lichen sclerosus (LS) is a chronic inflammatory skin disease presenting mainly on the anogenital area. The relationship between female genital LS and squamous cell carcinoma (SCC) has been established, with a lifetime risk of 4% to 5% for SCC development on female patients.[1] Vulvar malignant pleomorphic adenoma, also termed *carcinoma ex pleomorphic adenoma*, is a rare tumor, with only 2 cases reported previously.[2,3] The benign counterpart, pleomorphic adenoma (PA), is a commonly diagnosed benign tumor in the salivary glands but may also occur at a variety of other sites. Only about 10 cases of vulvar PA have been reported in the literature.[4] There are no previous reports of PA or malignant PA in a patient with LS. Here we report a third case of vulvar malignant PA, and the first, to our knowledge, in a patient with LS.

Abbreviations used:

LS: lichen sclerosus
PA: pleomorphic adenoma
SCC: squamous cell carcinoma

CASE REPORT

73-year-old woman presented with a slowly growing tumor on the right labia. She had been treated for Dukes C sigmoidal colon carcinoma with resection and postoperative chemotherapy and radiation 11 years earlier. On clinical examination, there was a large tumor hanging from the right labia with a broad base. Evaluation of the diagnostic biopsy suggested a moderately differentiated adenocarcinoma positive for cytokeratin 7 and negative for cytokeratin 20. The immunohistochemical profile did not support the diagnosis of a metastasis from colorectal carcinoma, which was positive for cytokeratin 20 and negative for cytokeratin 7. Partial vulvectomy and right inguinal lymphadenectomy were performed (Fig 1). Sentinel node in the right inguinal area showed a macrometastasis at least 5 mm in size, but nonsentinel nodes were negative. The 6.2-cm right labial tumor had a large degree of morphologic diversity forming glandular and solid structures with some clear cells in a partly fibrous and myxoid stroma. The nuclear pleomorphism was moderate, and only single mitotic figures were seen.

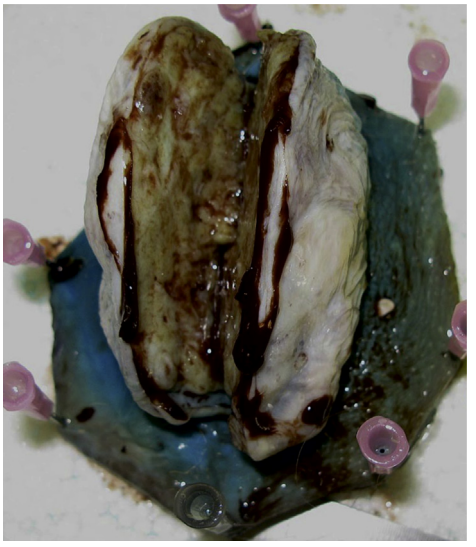

Fig 1. Malignant pleomorphic adenoma of vulva. An exophytic tumor of the vulva was resected with margins.

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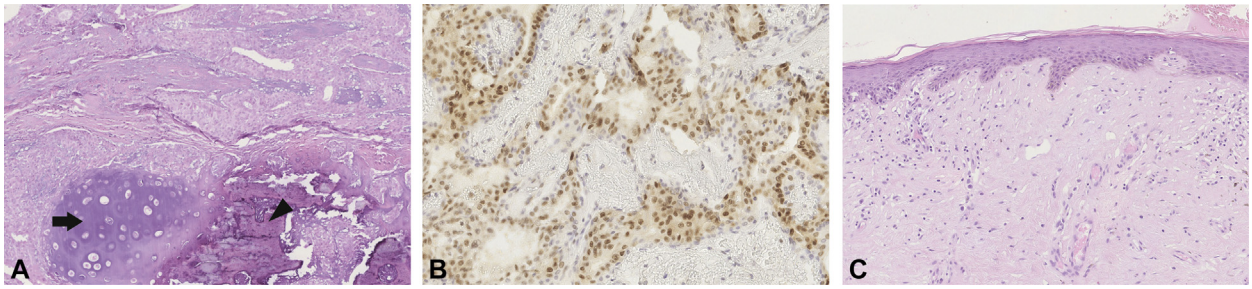

Fig 2. Malignant pleomorphic adenoma of vulva with lichen sclerosus. **A**, Epithelial component with myxoid stroma and metaplastic cartilage (*arrow*) and bone (*arrowhead*). **B**, Epithelial component positive for androgen receptor. **C**, Histologic image of lichen sclerosus at the tumor margin. (**A** and **C**, Hematoxylin-eosin stain; original magnifications: **A**, and **B**, ×20; **C**, ×15.)

Metaplastic cartilage and bone formation was marked (Fig 2, *A*). A discontinuous capsule surrounded the tumor. Proliferation marker Ki-67 was low (<5 %), and p53 staining was consistent with wildtype *TP53* gene. Further immunohistochemical studies found positive androgen receptor staining (Fig 2, *B*) but stainings for HER-2/neu and estrogen receptor were negative. The histologic study confirmed the diagnosis of grade I malignant PA. In addition, features of LS, including hyperkeratotic thinned epidermis with loss of rete ridges and mild dermal fibrosis with perivascular and dermal lymphoplasmacytic inflammatory cells were noted on the margin of the resected tumor (Fig 2, *C*). The patient had no previous symptoms of LS, and on previous clinical examinations, no findings suggestive of LS had been noted. The patient received postoperative chemotherapy and radiation with paclitaxel. Chest radiograph and abdominal computed tomography showed no signs of metastases. After 8 years, there is no recurrence, but LS is still active.

DISCUSSION

The estimated prevalence of LS is 0.1% and 3% for children and elderly women, respectively.[1] The risk for SCC among patients with LS is increased, with standardized incidence ratio of 33.4.[1,5] Also, the risk of vulvar melanoma among patients with LS is 341 times higher than the risk among women without LS.[6] There are anecdotal reports of basal cell carcinoma and Merkel cell carcinoma developing in patients with LS, but the risk for these malignancies has not been shown to be increased.[1,7]

Pleomorphic adenoma, also known as *benign mixed tumor* or *chondroid syringoma*, is a commonly diagnosed benign tumor in the salivary glands but may also occur at a variety of other sites. It typically presents as a painless, persistent mass. Histologically, PA is an encapsulated tumor consisting of a mixture of epithelial and myoepithelial cells and stromal elements. The epithelial component may form a variety of structures including tubules, ductules, or trabeculae. The pluripotent myoepithelial cells have the capacity to undergo mesenchymal metaplasia to produce the myxochondroid, which is the osseous and cartilaginous ground substance in the stroma that characterizes these.[2] Some markers have been suggested to evaluate the malignant potential of the salivary gland counterpart of the tumor. A report on salivary gland tumors suggests androgen receptor staining as a marker for malignant PA, as the benign tumors stain negative for this marker.[8] However, HER-2/neu, AR, and p53 staining are seen in a subset of histologically benign salivary gland pleomorphic adenomas and, thus, should not be used to predict the carcinomatous nature of the tumor.[9] On the vulva, pleomorphic adenomas have been described as arising from the Bartholin gland, vestibular gland, and cutaneous sweat glands.[4]

Our patient was treated previously for sigmoid colon carcinoma, a recurrence of which was first suspected. However, the location would have been very unusual for a metastasis of sigmoid carcinoma. The cytokeratin expression was suggestive of a new primary tumor, and the tumor histology confirmed the diagnosis of a malignant pleomorphic adenoma. Similarly to a patient described previously,[3] our patient had inguinal lymph node metastases. Interestingly, 4 months after the treatment, the patient described by Gemer et al[3] had a sigmoid adenocarcinoma, which was histopathologically confirmed to be a second primary tumor. All 3 patients described to date have been postmenopausal women.

The margins of the tumor specimen showed typical LS, which had not been diagnosed previously. Most cases of LS are diagnosed in

postmenopausal women. Sometimes LS can be symptom free.[1] Our patient had yearly visits to the gynecology department for 5 years, after which the control visits were transferred to the primary health care. She still has itching and occasional scaling and erosions on perineal area requiring local treatment with topical steroids and emollients.

To our knowledge, this is only the third case of vulvar malignant pleomorphic adenoma reported in literature and the first to occur in a patient with LS. Risk of vulvar malignancies other than SCC should be considered in LS patients. Further studies are needed to evaluate the role of LS in the pathogenesis in these malignancies.

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