Adenoid cystic carcinoma of Bartholin's gland: A case report

M. Krašević[1], *M.D., Ph.D.*; **H. Haller**[2], *M.D., Ph.D.*; **Z. Iternička**[1], *M.D.*; **I. Valstelić**[2], *M.D.*; **N. Matejčić**[2], *M.D., Ph.D.*

[1]*Department of Pathology,* [2]*Department of Obstetrics and Gynecology, University of Rijeka, Rijeka (Croatia)*

Summary

Objective: A case of adenoid cystic carcinoma (ACC) of the Bartholin's gland in a 34-year-old woman with unusual presentation and early recurrence is reported.

Methods: Clinical and histologie features were recorded. Immunohistochemical stains and cell-cycle analysis by flow cytometry technique on paraffin-embedded tumor tissue were performed.

Results: The tumor presented as a painful nodule in the episiotomy scar three months after delivery. Initial treatment included only wide local excision. Six months later local recurrence occurred despite clear surgical margins. Histologically a predominant "classic" cribriform growth pattern was identified. Immunoreactivity in tumor cells supported dual epithelial-myoepithelial differentiation. Estrogen and progesterone receptors were negative. The DNA histogram revealed a diploid stemline and a low S-phase fraction.

Conclusion: ACC of the Bartholin's gland is a rare malignant tumor with great propensity for local recurrence. The optimal therapeutic approach has not been established due to the lack of well-defined prognostic parameters.

Key words: Adenoid cystic carcinoma; Bartholin's gland; Immunohistochemistry; Flow cytometry; Steroid receptors.

Introduction

Adenoid cystic carcinoma (ACC) of the Bartholin's gland is a rare, but distinctive type of primary vulvar malignancy. The tumor has a protracted [1], but malignant clinical course, with a propensity for local recurrence. Distant metastases may appear as late as 16 years after the initial diagnosis [2].

A case of a young woman with ACC of the Bartholin's gland is reported with respect to clinical, histological, immunohistochemical and cell-cycle characteristics of the tumor.

Case Report

A 31-year-old white, gravida 2, para 2 woman underwent excision biopsy of a painful "granuloma" located on the left part of the vaginal introitus in the mediolateral episiotomy scar in February 1999. The patient noted a firm nodule approximately three months after the second delivery in 1996. She began to experience discomfort and pain during intercourse in 1998. Nine and seven years earlier marsupialization of left and right Bartholin's gland abscesses, respectively, was performed.

The histologic examination revealed adenoid cystic carcinoma (ACC) originating in the Bartholin's gland. Initial treatment included only wide local excision. The surgical margins were free of tumor. Six months later local recurrence developed, subsequently managed by hemivulvectomy and ipsilateral lymph node dissection. In addition, the patient received radiotherapy. Chest X-ray was normal. Thirteen months after the treatment of recurrence the patient is well, without evidence of disease. The primary lesion measured 1.3 cm in diameter. Histologically, the Bartholin's gland was replaced by poorly circumscribed tumor composed of small basaloid cells arranged predominatly in a cribriform pattern. Tubular structures formed less than 30% of tumor tissue. Solid areas were not found. Mitotic rate was low (2 mitoses per 10 high-power fields). A few normal acini of the Bartholin's gland were present. The perineural infiltration was prominent. Intravascular invasion was not seen. The recurrent tumor exhibited the same morphology as the primary lesion. Lymph node involvement was not documented. Immunohistochemistry was carried out for smooth muscle actin (SMA), S-100 protein, carcino-embryonal antigen (CEA), vimentin, epithelial membrane antigen (EMA), neuron specific enolase (NSE), cytokeratin, estrogen receptors and progesterone receptors (Dako, Glostrup, Denmark for all antibodies) by an avidin biotin complex method. Basaloid cells at the periphery of cribriform and tubular structures were positive for SMA and S-100 protein. A few luminal cells were EMA and cytokeratin positive. Estrogen and progesterone receptors were negative.

DNA content was determined by flow cytometry paraffin technique. Histogram revealed a DNA diploid tumor with low S-phase fraction of 3.43%.

Discussion

ACC accounts for approximately 10% of Bartholin's gland carcinomas. Similar tumors are found in various locations, including the salivary glands, breast, skin and lung. In the female reproductive tract, ACC occurs more frequently in the cervix. Few cases of ovarian ACC have been described [3]. The tumor is slow growing, with a tendency for perineural infiltration, which is probably responsible for the pain, burning sensation of pruritus. Frequently the lesion is misdiagnosed as a cyst or inflammatory process [4, 5]. In our case, the tumor was misinterpreted as a foreign body granuloma, being located in the episiotomy scar at the vaginal introitus.

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Szanto and co-workers [6] proposed a grading system for ACC of the salivary glands based on the proportion of solid areas in tumor tissue, which correlates well with prognosis. Perzin *et al.* [7] separated predominantly the tubular pattern as the best differentiated and prognostically the most favorable type of ACC. A solid histologic appearance has a significantly lower survival rate [8, 9]. It seems that the growth pattern of ACC in the Bartholin's gland area does not have the same prognostic implications. The most common histologic type of ACC of the Bartholin's gland is a cribriform or mixed (with minor foci of tubular or solid areas) pattern. Milchgrub *et al.* [5] have described two cases with pure and predominantly (less than 10% of cribriform formations) tubular growth pattern. However, one patient died six years after the diagnosis was established. A solid type of ACC of the Bartholin's gland has bot been described.

Cell cycle analysis of ACC was carried out only in a small number of cases. In order to evaluate the prognostic significance of DNA content and SPF, Greiner and coworkers [9] have analyzed 37 cases of ACC of salivary gland origin by a flow-cytometry paraffin technique. DNA-aneuploid tumors were not identified.

Decreased survival rate for two tetraploid cases was insufficient to make a definitive conclusion. High SPF (>4.45%) was associated with death from disease. Our data are in agreement with those reported by Ronsenberg *et al.* [10]. In a series of five cases of ACC, they revealed a normal DNA diploid pattern and a very low SPF in each case. However, the patients were followed-up from two to 13 years without evidence of recurrent disease.

Immunohistochemistry, as evidenced by SMA, S-100 and cytokeratin positivity supported dual myoepithelial and ductal differentiation. Similar type of reactivity was detected in tubular form of ACC [5].

There are some speculations about the hormonal sensitivity of ACC. Copeland [11] found that in 50% of patients under the age of 42, ACC coexisted with pregnancy. In our case the first symptom appeared three months after delivery. Progesterone receptors were identified in one case of ACC by immunoperoxidase technique [1], while in our case the receptors were negative.

The consensus about the optimal treatment has not been achieved. The initial surgical therapy most often includes wide local excision or vulvectomy. Out of 34 cases of ACC reviewed, ipsilateral or bilateral lymph node dissection as a part of initial therapy was performed in 16 patients [2, 4, 5, 10, 11-14]. Ipsilateral lymph node metastasis was found in one case [14], while metastatic disease in contralateral lymph nodes has not been reported in the available literature. Local recurrence can be expected even in the case of negative surgical margins. In one study, of five patients who developed recurrence, in only one case were the surgical margins positive [2]. Copeland [11] and Rosenberg [10] have demonstrated a benefit of irradiation in patients having positive resection margins. Hematogenous spread occurs in the lungs, bones and liver. Complete remission of metastatic ACC of the parotid gland following combination chemotherapy has been achieved [15, 16]. The use of chemotherapy in ACC of the Bartholin's gland has been limited to a small number of cases, which prevents definitive conclusions.

According to Copeland [11] and Lelle [2] the 10-year progression-free interval was 38% and 33%, respectively, compared to a survival rate of 59% and 100%, respectively, confirming a protracted although malignant clinical course of the disease.

In conclusion, the Bartholin's gland is a rare primary site of ACC. The correct diagnosis is often delayed. The optimal management for individual patients is not defined, mostly due to the lack well established prognostic factors. Local recurrence can be expected even if the resection margins are free of tumor. Histology, DNA content and SPF were not found to be related to disease recurrence. Hormonal sensitivity has not been confirmed.

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Address reprint requests to:
MAJA KRASEVIC, M.D.
Department of Pathology
Medical Faculty-Rijeka
Br. Branchetta, 20
51000 (Croatia)