Paget's disease of the vulva. A ten-year experience

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Summary

Background: Paget's disease of the vulva is a rare neoplasmatic lesion which mainly affects postmenopausal women. *Method: Results*: We conducted a retrospective study during the period January 1996 till December 2005 in which 11 cases of Paget's disease were detected. The clinical manifestations, management, specific pathological features, treatment and prognosis of each patient are presented. *Conclusion*: Surgical treatment is the current standard and long-term follow-up is required.

Key words: Paget's disease of the vulva; Diagnosis; Management; Prognosis.

Introduction

In 1874 Sir James Paget described mammary Paget's disease. Extramammary Paget's disease of the vulva was first described by Dubrenilh in 1901 [1]. In 2007, just over 250 cases of vulvar Paget's disease were reported in the literature. It is a rare (1-2%) neoplastic vulvar lesion [2-4] usually described as a very slowly developing invasive adenocarcinoma or adenocarcinoma in situ. It usually affects postmenopausal women and appears as a macular, solitary, reddish circular lesion. The clinician should always remember that invasive vulvar adenocarcinoma coexists in 15-25% of the cases. Furthermore, it should be pointed out that it also coexists with other malignancies, especially breast cancer [5-8]. It is usually found in one of the labia but it can also be found in the clitoris, cervix, perineum or anus [9]. The histological characteristics include pathognomic cells of Paget which are large cells with pale clear cytoplasm and large round hyperchromatic nuclei in clusters or solid nests within the epidermis [10] which show specific immunohistochemical characteristics. Four forms of Paget's disease are described in the literature: i) intraepidermal vulvar Paget's disease, ii) minimally invasive vulvar Paget's disease, iii) invasive vulvar Paget's disease, iv) vulvar Paget's disease with an underlying apocrine gland carcinoma [4,10]. The treatment of such a lesion varies and could include wide local excision, partial vulvectomy and radical resection for invasive adenocarcinoma ± inquinofemoral lymphadenectomy [11-13]. Margin-controlled surgical excision of all the involved epidermis is the most effective treatment [14, 15]. Recurrence of the disease is often seen (12-58%) which emphasizes the need for careful postoperative follow-up [15, 16]. The high recurrence rates after local excision could be explained due to horizontal or vertical migration of the disease within the epidermis [17, 18].

Method

This is a retrospective study including cases of Paget's disease of the vulva in the period January 1996 up to December 2005. The epidemiology, clinical manifestations, management, and outcome of each case are presented. Although, our hospital is a tertiary center, the rarity of such a disease explains the small number of our cases. All the patients were examined on an external basis having a suspicious lesion in the labia with itching, burning or pain. We searched the hospital data base including patient records, surgery reports and histology specimens in order to note the patient's age, clinical manifestations, cytology, chosen surgical treatment, recurrences, coexistence or not of vulvar carcinoma or malignancies in other sites such as the breast or urothelium and finally follow-up. Recurrence of the disease was defined as a new lesion in a period > 6 months after the surgery.

Results

The median age of the patients was 64 years ranging from 53 up to 75 years; one, three and seven patients were nulli-, prima-, secundi-gravida, respectively. The most usual clinical symptom was pruritus of the vulva (9/11 patients) followed by pain (8/11), while five patients found the suspicious lesion themselves. Dysuria and vaginal discharge were noted in two and two patients, respectively. No patient received hormone replacement treatment. Three of 11 patients received treatment for diabetes mellitus type 2 and four of 11 thyroid hormone for hypothyroidism. One patient had a previous history of breast cancer operated on three and a half years before. Papanicolaou smears revealed no serious pathology except for two of 11 patients with cervicitis (the same patients who presented with vaginal discharge). The topography of the lesion was four in the right labium, five in the left labium and two were bilateral. In only one patient was there an underlying invasive vulvar carcinoma, but the pruritus was heavier. It should be mentioned that all the patients had delayed diagnoses due to the use of topical steroids. One, seven and three patients underwent Ultracision, simple vulvectomy and radical vulvectomy with inguinofemoral lymphadenectomy, respective-

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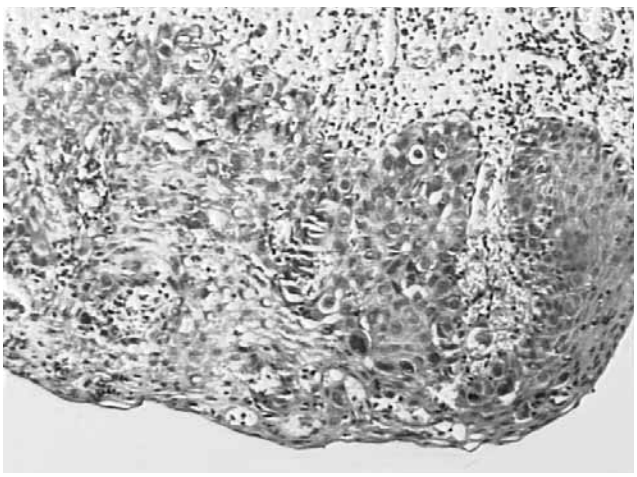
Fig. 1



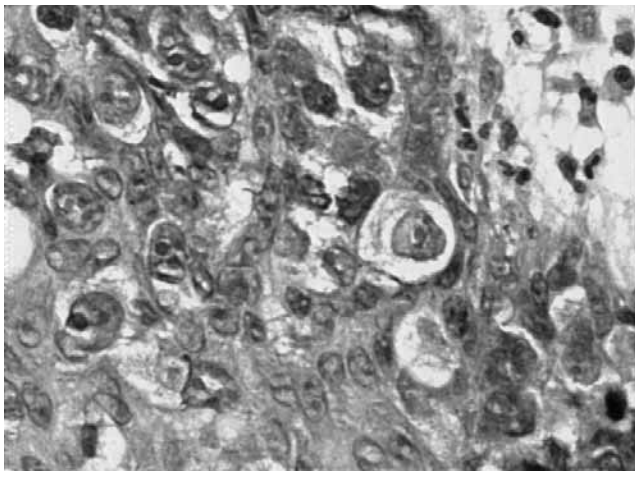


Fig. 2

Figure 1. — Histological section of Paget's disease of the vulva showing infiltration of the squamous epithelium by large neoplastic cells (hematoxylin–eosin x 100).
Figure 2. — Histological section of vulvar Paget's disease showing large Paget cells with clear cytoplasm and atypical nuclei with prominent nucleoli (hematoxylin–eosin x 250).

ly. In all the patients a frozen section was obtained which revealed free surgical margins in ten of 11 patients but the final histology showed nine of 11 women had free surgical margins. The two patients without free margins underwent further surgical excision. In all our cases, the typical characteristics of Paget's disease were evident (Figures 1, 2). Neoplastic cells showed a negative reaction to melanoma and squamous cell markers and were positive for glandular differentiation. In the case of the patient with a history of breast cancer, an additional marker (GCDF-) was performed, specific for breast epithelia. The negative reaction of the vulvar lesion proved that this case was a primary vulvar lesion rather than metastatic spread from the breast. Three of the 11 patients had a recurrence. The first one 14 months after the first operation (Ultracision), the second (with coexistence of vulvar carcinoma) 23 months after radical vulvectomy and the third 36 months after a simple vulvectomy. A correlation with the absence of free surgical margins was found in the two of these three patients. All of them underwent further surgical excision. The follow-up of the patients ranged from 27 up to 64 months and included a visit in our office every three months for two years, and then anually.

Discussion

Paget's disease is a disease of postmenopausal women [1]. Although, we did find a case of a 35-year-old patient with the lesion during our Pubmed search [19], in our study all the women were postmenopausal with a median age of 64 years and a minimum of 12 years duration of menopause. It should be mentioned that our patients had delayed diagnosis of disease due to the use of topical corticosteroids for the treatment of pruritus as a misdiagnosis of an eczematous lesion. The median diagnosis period was six months. Late diagnosis was also because many patients preferred not to visit the gynecologist due to personal taboos or even due to fear of a malignancy.

When such a lesion is found by a gynecologist the differential diagnosis should include contact dermatitis, fungal infections, lichen sclerosis and VIN [20]. A biopsy of the suspicious lesion could provide the diagnosis but it should always be remembered that an invasive cancer may coexist nearby. One study showed that diagnoses could be made in 15.8% of patients through suspicious cells in the Papanicolaou smears [21], however we did not find such a correlation.

Our diagnoses were based on clinical manifestations (pruritus, burning, pain, lesion) and biopsy of the lesions. The differential pathological diagnosis includes malignant melanoma and early epidermal cancer. Immunohistochemistry investigation of melanoma markers (Melan A, S100) and cytokeratins of high and low molecular weight specific for adeno- and squamous cell carcinoma is valuable in the final diagnosis.

Treatment of the disease is usually surgical. The nearby clitoris might make the operation technically more difficult but the prognosis is the same. Some authors believe that the recurrence rates could range from 0-31% up to 25-75% in patients with free or positive surgical margins [4, 15, 22-24]. None of our patients with free surgical margins had a recurrence whereas two of 11 (18.2%) with positive surgical margins did. It should be mentioned that this was different from the findings of other studies [22, 25].

Vulvar Paget's disease may coexist with other malignancies such as breast or urothelium cancers [16, 26]. Only one of our patients had a previous history of breast carcinoma. Although, we did not perform breast scanning or cystoscopy, no woman during our follow-up period revealed such a malignancy.

The limitation of our study is the small number of patients due to the rarity of the disease, however we believe that our study represents an example of the clinical manifestation, management, and prognosis of Paget's disease.

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