Recurrent Paget's disease of the vulva in a myocutaneous flap: Case report and review of the literature

W. A. Tjalma[1,2], *M.D., Ph.D.*; **I. D. Cooremans**[1], *M.D.*; **W. Jeuris**[3], *M.D.*;
E. A. Van Marck[3], *M.D., Ph.D.*; **J. M. Monaghan**[2], *M.B., F.R.C.S. (Ed), F.R.C.O.G.*

[1]*Division of Gynecologic Oncology, Antwerp University Hospital, Antwerp (Belgium)*
[2]*Northern Gynecological Oncology Centre, Queen Elizabeth Hospital, Gateshead (U.K.)*
[3]*Department of Pathology, Antwerp University Hospital, Antwerp (Belgium)*

Summary

A 74-year-old patient with recurrent Paget's disease of the vulva in the gluteus maximus island myocutaneous flap 11 years after a hemivulvectomy with reconstruction is presented. This report is only the second case of recurrent noninvasive Paget's disease in a reconstructive flap. The English literature on this subject is reviewed with special attention to the biological behavior of these tumors.

Key words: Paget; Vulva; Recurrence; Myocutaneous flap.

Introduction

Paget's disease of the vulva is a rare condition, accounting for approximately 1% of all vulvar neoplasias [1]. In 12% of the cases it is an invasive Paget, in about 30% there is a concomitant underlying invasive adenocarcinoma and in 20-30% there is an associated malignancy (synchronously or asynchronously) in other organs, most frequently the breast and genitourinary tract [1-5]. Anal involvement of Paget's disease carries about a 70% risk of a subjacent anal or rectal adenocarcinoma [6].

Surgery is the recommended treatment for primary and recurrent extramammary Paget's disease [2, 7]. Preferable is a wide local excision. However sometimes a more extensive procedure is indicated and in rare cases reconstructive surgery with a graft is performed [8, 9].

Despite complete resection, recurrence rates have been reported as high as 38% [2, 10]. Surprisingly there are only eight reports in the English literature which describe a recurrence of Paget in a skin graft [8, 11, 12-14]. The present report is only the second case of recurrent noninvasive Paget's disease of the vulva in a myocutaneous flap. Recurrences after adequate resections are a controversial feature of this entity. In an attempt to elucidate this feature the current literature on the subject is reviewed with particular attention to the biological behavior of this tumor.

Case Report

A 74-year-old woman consulted her gynecologist for the follow-up of her extrammammary Paget's disease of the vulva. The Paget's disease was diagnosed in August 1988 and treated by a right hemivulvectomy. All margins were free and the vulva defect was closed using a right myocutaneous gluteus maximus island flap. The patient was complaining of pruritus for the last few months. Inspection of the vulva raised the suspicion of Paget disease on both sides of the vulva. No other abnormalities were found by physical examination. A biopsy was taken and the histology report confirmed the diagnosis. A vulvectomy was performed in January 1999. Intraoperative frozen sections were used to define tumor-free surgical margins. The vulval defect was closed by performing a skin-plasty. The postoperative period was disturbed by a pneumonia, urinary and vulvar skin infection. There was no breakdown of the wound and the patient was discharged from the hospital 22 days after her operation.

Histopatological examination of the resected specimen showed that the left hemivulva was largely involved by intraepithelial Paget's disease. On the right side not only the tissue surrounding the gluteus maximus island flap but also the flap itself was completely involved by intraepithelial Paget's disease.

Discussion

Paget's disease of the vulva affects predominantly postmenopausal women with a mean age of 72 years [3]. The most frequent clinical symptom is pruritus (77%). There is often a delay of more than three years between the onset of symptoms and the histopathologic diagnosis. This delay may reflect a delay in seeking medical attention or a lack of knowledge of the disease in the general medical community [1, 3, 5, 7, 9, 12]. Almost three-quarters of patients have been treated previously (74%) with steroid cream and/or antifungal agents [3].

Macroscopically a moist vulva is seen in which there are patches of hyperkeratotic tissue interspersed with rivulets of raw, reddened tissue [15]. Microscopically the Paget cells are characterized to be large, round or oval cells with abundant, pale cytoplasm, which is occasionally vacuolated. The cells have irregular nuclei and are singly or in cluster under the epidermis. The Paget's cells stain positive for periodic acid Schiff (PAS) reagent, mucicarmine, fuchsin, aldehyde and carcinoembryonic antigen (CEA). CEA is a valuable marker for excluding Paget disease from other epithelial lesions and for the confirmation of invasive Paget's disease.

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Table 1. — *Survey from the literature of recurrent Paget's disease in skin-grafted areas.*

Author	Age	Treatment	Margin	Recur (months)	Treatment	Invasive Paget
Beecham, 1976	57	SVE + SG	Free	24	WLE+SG	No*
		second recurrence in SG		60	WLE	No*
de Jonge *et al.*, 1988	66	SVE + SG	Unknown	132	RVE + SG	No
Misas *et al.*, 1990	70	SVE + SG	Free	108	RVE	No
DiSaia *et al.*, 1995	69	SVE + SG	Free	31	RHVE + PE	No
	64	SVE + SG	Free	48?	E + SG	No
		second recurrence in SG		84	PVE + SG	No
Geisler *et al.*, 1995	64	SVE + SG	Free	12	SVE + SG	Yes, MSI
Yoshitatsu *et al.*, 1997	68	E + GMCF**	Free	62	WLE + STSG	No
Tjalma *et al.*, present	63	HVE + GMMCF	Free	125	VE	No

SVE = skinning vulvectomy; RHVE = radical hemivulvectomy; PVE = partial vulvectomy; PE = proctectomy; E = excision;
SK = skin graft; GMCF = gracilis myocutaneous flap; GMMCF = gluteus maximus myocutaneous flap; MSI = minimal stromal invasion;
? = time not clearly mentioned in article; * the only case with associated adenocarcinoma of glandular skin (twice);
** patient who also received adjuvant chemotherapy (mitomycin C and tegafur).

The natural history of Paget's disease is not clearly defined in the literature. It is tempting to suggest that Paget's disease is a combination of three different types. The first form is totally confined to the epidermis with an intact basement membrane (intraepithelial). The second type can be described as where the Paget cells break through the basement membrane and invade the underlying dermis (minimal invasive Paget's if < 1 mm and invasive Paget's > 1 mm). Thirdly, the Paget's disease associated with a subjacent adenocarcinoma or associated malignancy in other organs [10].

Surgery is the recommended treatment. A problem with surgery is the fact that the histologic involvement is often greater than the visible lesions. It is difficult to obtain a free margin, despite the use of frozen sections or intraoperative intravenous fluorescein with ultraviolet lighting [1, 7, 10]. Occasionally the resections can be so extensive in order to achieve tumor-free margins, that myocutaneous flaps or skin grafts have to be used to cover the resulting large denuded areas [8, 9].

Until now only eight patients have been reported to develop recurrent Paget lesions in a skin graft (Table 1) [8, 10-14]. From the eight patients, only one was associated with an underlying dermal adnexal adenocarcinoma [11] and one with minimal stromal invasion [13]. In one case the patient was treated 68 months earlier for vulvar Paget's before having surgery with a skin graft [13]. In three cases there were also "recurrences" outside the skin graft on other occasions after the operations [8, 10]. Twice a recurrence occurred in the same grafted area [8, 11]. The mean age at the initial diagnosis was 66 years (range 63-70) and the mean recurrence time was 60 months (range 12-132).

When observing the behavior of skin grafts into areas where Paget disease was previously removed it is interesting to note that half of the recurrences were within the previous skin graft [8, 10-12] and the other half were recurrences both within and outside the previous skin grafts [8, 10, 12-14, present]. From this latter group, three patients had discontinuous areas outside the graft tissue.

There are several possible explanations for a recurrence. The first explanation is the possibility of residual tumor due to incomplete resection at the primary site. The second explanation is based on the multifocality of the disease. Histogenetically the Paget cells represent a spectrum from totally undifferentiated basal-type cells to the clear cells of the apocrine epithelium [8]. The transformation of these pluripotent germinative cells in the epidermis is an elucidation for the multifocality of the disease. Based on these findings it is likely to assume that there are skip lesions. It is our opinion that "recurrences" at a distant site from the primary one are due to unresected skip lesions rather than new lesions. Another possible explanation is the direct implantation from the contralateral side ("kissing disease"). A more general cause for local recurrences is the ability of the local milieu (carcinogenic stimulus) to cause epithelial differentiation in the basal cell layer of the original or grafted skin [10, 12]. However if this is the case they would better be called "new" lesions than recurrences. More recently it was proposed that recurrences were due to retrodissemination [8]. This hypothesis is based on the fact that the intraepithelial process disseminated within the skin via lymphatics or other vessels creating normal tissue bridges between sites of involvement. In the situation of recurrences with an adenocarcinoma beneath the epidermis [11] or with a minimal stromal invasion of Paget [13] there is evidence to suggest that Paget's disease of the vulva is caused purely by intraepithelial spread [11]. A dermal carcinogenic stimulus together with the intraepidermal spread seems to be the most logical explanation for the recurrence in a skin graft.

In conclusion: Paget's disease can recur in different ways and after several years. A recurrence of Paget's disease in a musculocutaneous graft is possible, although rare when compared to the high recurrence rate in patients where the vulvar defect is primarily closed. All patients with Paget's disease of the vulva need thorough long-term follow-up.

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Address reprint requests to:
WIEBREN A. TJALMA, M.D., Ph.D.
Division of Gynecologic Oncology
University Hospital Antwerp
Wilrijkstraat 10, 2650 Antwerp
(Belgium)
e-mail: wiebren.tjalma@uza.uia.ac.be