

Evaluation of sentinel node detection in vulvar cancer

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Abstract

BACKGROUND: In vulvar cancer, in a large portion of patients with early stages of the disease, the inguinal lymphadenectomy not only does not influence the overall survival and recurrence rate but may increase the incidence of complications. Sentinel lymph node (SN) detection is a promising technique for detecting groin lymph nodes, which may in future lead to less extensive use of surgical treatment. The aim of the study was to evaluate the feasibility of the sentinel node detection technique in patients with vulvar cancer.

MATERIAL AND METHODS: Between the years 2003 and 2005, we performed intraoperative lymphatic mapping on 10 patients with planoepithelial vulvar cancer. In eight cases, vulvar lesion was localized centrally, around the clitoris. The extent of the surgery included radical vulvectomy with bilateral inguinal lymphadenectomy in nine cases and unilateral inguinal lymphadenectomy in one case. For the lymphatic mapping, we employed two detection methods: ^{99m}Tc-labelled radiocolloid (activity 35–70 MBq) and blue dye (3–5 ml). Both techniques were used in six cases (60%), blue dye only in three cases and radiocolloid only in one case.

RESULTS: In each patient, we detected at least one sentinel lymph node. Sentinel nodes were localized in 14 of 19 operated groins (73.7%); a total of 25 SNs in all. The mean number of SNs for one groin was 1.78. Nodal metastases were found in four cases. In three cases, metastases were detected only in the SN. In one patient, two SNs with metastases were found in one groin and in the contralateral groin (without any SN) there

was one unchanged node, which transpired to be metastatic. This can be explained by a complete overgrowth of neoplasm in the lymph node resulting in lymph flow stasis and disabling tracer uptake. In five cases, an SN was found only in one groin — the first case is described above, in the second case the vulvar tumor was localized laterally, opposite to the groin without any SN. In the remaining three cases, we have used only one method of SN detection.

CONCLUSIONS: Lymphatic mapping in vulvar cancer based on the combined detection technique is a highly accurate method after adequate training of the surgeons.

Key words: vulvar cancer, sentinel lymph node

Introduction

At present, the standard surgical approach in vulvar cancer is the radical vulvectomy or hemivulvectomy with inguino-femoral lymphadenectomy. In this disease, metastatic cells initially spread through the lymphatic system. Inguinal lymph node metastases are the most important prognostic factor in vulvar cancer [1]. Due to the lack of a satisfactory method of preoperative evaluation of the inguinal lymph nodes status, inguinal lymphadenectomy is still the standard method of treatment. The main disadvantage of the inguinal lymphadenectomy is that it significantly increases the morbidity and mortality of the surgical treatment. Metastatic disease in inguinal lymph nodes depends on the vulvar tumor diameter and the depth of neoplastic infiltration. In lesions smaller than one centimetre, lymph node metastases are present in approximately 18% of cases [1].

For this reason, in a large proportion of patients with early stage disease, the lymphadenectomy does not influence the overall survival and recurrence rate but increases the treatment complication rate.

Sentinel lymph node (SN) detection is a promising technique showing groin lymph nodes in patients with early vulvar cancer. In most published studies, the SN detection rate reaches 100% [2–4] with only six reported cases of false negative sentinel nodes [4–7]. After future validation of this technique, lymphatic mapping will lead to less extensive surgical treatment.

The aim of the study was to evaluate the feasibility of the sentinel node detection technique in patients with vulvar cancer.

Material and methods

Between years 2003 and 2005, we performed intraoperative lymphatic mapping on ten patients with planoepithelial vulvar can-

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Table 1. Characteristics of patients enrolled in the study

	Mean value	Range
Patient age [year]	66	37–76
Operation time [min]	189.5	150–240
Hospital stay duration [day]	29.5	13–69

cer. Characteristics of patients is shown on Table 1. The study was approved by the Local Ethical Committee and all patients signed an informed consent before enrolment.

Tumor size according to TNM staging was: T1 lesions — 4 cases, T2 lesions — 6 cases.

In eight cases, the vulvar lesion was localized centrally, around the clitoris. In the remaining two cases, the tumour was located laterally.

The extent of the surgery included radical vulvectomy with bilateral inguinal lymphadenectomy in nine cases, and unilateral inguinal lymphadenectomy in one case. Additionally, in four cases, pelvic lymphadenectomy was performed.

For the lymphatic mapping, we employed two detection methods: Tc^{99m} labelled radiocolloid (Amersham Sorin, Italy) and blue dye (Methylenblau Vitis, Neopharma, Chiengau, Germany). Both techniques were used in six cases, blue dye injection only in three cases and radiocolloid injection in one case.

Radiocolloid was injected intradermally around the tumor (total dose 35–70 MBq) under local anaesthesia 15 to 120 minutes before surgery. Blue dye (3–5 ml) was injected after general anaesthesia, approximately 15 minutes before the operation.

Sentinel lymph nodes were localized using a hand held gamma probe and direct visualization. All radioactive or coloured inguinal lymph nodes were regarded as the sentinel nodes. All removed inguinal nodes were evaluated during standard pathological examination.

Results

In each patient, we have detected at least one sentinel lymph node. A description of each case is presented in Table 2. Sentinel

nodes were localized in 14 of 19 operated groins (73.7%), in all a total 25 SN. The mean number of SN for one groin was 1.78.

Nodal metastases were found in four patients (cases no. 1, 3, 4, 5). In three cases, metastases were located only in the sentinel nodes. In the one remaining patient (case no. 1) there were two SNs with metastases in the right groin, and in the left groin there was one metastatic lymph node which was not visualised as an SN. This case will be discussed later on.

In case number four, in one groin two SNs were found using both detection techniques. Unexpectedly, nodal metastasis was diagnosed at less radioactive and less intensive blue dye uptake.

We analysed five cases where we could not detect any SN in either of the operated groins. In the first case (no. 1), only one metastatic non-sentinel node was found as previously described. In the second case (no. 2), vulvar lesion was located unilaterally. Following the principles of lymph flow from the vulva [8], we did not expect to find the SN in the contralateral groin. In the remaining three cases (no. 3, 7, 8), we employed only one detection method.

We also compared results obtained with each detection method. With the blue dye, we were able to find SNs in 12 of 17 groins (70.5%), with a total of 18 SNs detected (1.5 SNs per groin). Using radiocolloid tracer, we achieved a detection rate of 83.3% (SNs found in 10 of 12 groins), with a mean of 1.7 SN per groin.

Discussion

The present study confirms the accuracy of lymphatic mapping in the vulvar cancer. Although we were able to detect an SN in each patient with no false negative cases, we have encountered some difficulties, which show important limitations to this technique.

In 80% of cases, vulvar lesion was localised in the midline. In such cases, lymph drainage from the tumor can reach both groins, which implies the need for bilateral SN detection [8]. In our study, we were unable to find SNs in both groins in four cases with centrally located lesion. The most interesting of these is case no. 1, in which we found two SNs on the right side, both containing neoplastic cells and on the left side only one metastatic node without any tracer uptake. As the two SNs in the right groin contained the only metastasis for this group of inguinal

Table 2. Characteristics of ten cases of sentinel node detection in vulvar cancer

Case no.	Tumour localization	Lymphadenectomy	Blue dye	Tc ^{99m}	SN	Right side				Left side			
						SN no.	SN +	Inguinal nodes +	SN	SN no.	SN +	Inguinal nodes +	
1	Midline	Bilateral	1	1	1	2	1	0	0	0	0	1	
2	Lateral	Bilateral	1	1	0	0	0	0	1	2	0	0	
3	Midline	Bilateral	1	0	0	0	0	0	1	2	1	0	
4	Midline	Bilateral	1	1	1	2	0	0	1	2	1	0	
5	Midline	Bilateral	1	1	1	1	0	0	1	2	1	0	
6	Midline	Bilateral	1	1	1	3	0	0	1	2	0	0	
7	Midline	Bilateral	1	0	0	0	0	0	1	1	0	0	
8	Midline	Bilateral	0	1	1	1	0	0	0	0	0	0	
9	Lateral	Unilateral	1	1	N/A	N/A	N/A	N/A	1	1	0	0	
10	Midline	Bilateral	1	0	1	2	0	0	1	2	0	0	

N/A — not attending

lymph nodes, this case does not deny efficacy of this technique. The single metastatic node found on the left side can be regarded as a "missing" sentinel node. Failure of the tracer to pass through the lymphatics to the lymph node can be explained by a complete overgrowth of the neoplastic process in this node. In the literature there are cases available presenting identical clinical findings in vulvar cancer [3, 4, 9, 10] and in large breast cancer trials [11, 12]. Thus in the case of centrally located vulvar cancer without bilateral SN detection it should be treated as a failure in lymphatic mapping.

As mentioned before, there were another three cases of medial vulvar lesion where we failed to find SN in one groin. Although there were no metastases in the groins without SNs, those results are unsatisfactory. We suggest that there are two explanations for those results. Firstly, in all three cases we used only one detection technique (blue dye in two, radionuclide in one). Secondly, this study reports our initial experience with lymphatic mapping in vulvar cancer and there certainly exists a 'learning-curve' which influences detection rates when beginning to use this procedure. According to de Hullu [13] the minimal number of cases necessary to achieve reliable results in vulvar cancer is at least ten cases (15–20 groins).

Due to the small number of cases in the present study, it is not possible to compare the effectiveness of each detection method. Although it seems that the radiocolloid tracer offers a better SN detection technique, in order to obtain the highest diagnostic accuracy use of the combined technique seems to be most suitable.

In case no. 4, two separate SNs were detected in one groin, both blue and radioactive. Unexpectedly, neoplastic cells were found in the node with lower radioactivity and less intensive blue dye uptake (so-called 'echelon-node'). This finding shows that after removal of the first SN it is imperative to look carefully for any potential echelon-nodes remaining in the groin. For this purpose, the most suitable technique is the intraoperative hand-held gamma-probe, which allows us to avoid extensive dissection of the groins. Moreover, it is necessary to perform an intraoperative pathologic examination of all removed nodes in order to get reliable information about the inguinal lymph nodes' status.

Conclusions

1. Lymphatic mapping in vulvar cancer based on the combined detection technique is a highly accurate method after adequate training of surgeons.
2. After removal of the SN it is necessary to exclude the presence of additional 'echelon-nodes' in the dissected groin.
3. In the case of centrally located vulvar tumours, it is imperative to detect an SN in both groins.
4. Due to the satisfactory results of preliminary studies on sentinel node detection in vulvar cancer, a multi-centre, randomized study should be performed in future.

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