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Short communication

The usefulness of sentinel lymph node detection in vulvar cancer — a short communication

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Abstract

BACKGROUND: The sentinel lymph node (SLN) biopsy is a solution for decreasing the extent of surgery with a significant reduction of the incidence of complications without influencing treatment results.

MATERIAL AND METHODS: We performed the sentinel lymph node procedure in 24 women with vulvar cancer. In 14 cases, only the blue dye technique was applied, and in 10 cases ^{99m}Tc-labelled nanocolloid with blue dye was administered simultaneously. The extent of the surgery included radical vulvectomy in 23 patients and a wide local excision in 1 patient. In 15 patients unilateral inguinofemoral lymphadenectomy was performed and in 9 cases bilateral lymphadenectomy. The total number of operated groins was 39.

RESULTS: SLNs were detected in 34/39 of operated groins (87.2%). In 4 cases (16.6%) tumour metastases to the lymph nodes were found. In total, 10 metastatic lymph nodes were detected in 9 sentinel-nodes and in 1 non-sentinel node. In three patients the nodal metastases were found only in the sentinel nodes. In one patient the metastases were found in the contralateral groin in two SLNs. There were no false nega-tive sentinel lymph nodes. With the sole use of blue dye, SLNs were found in 79.5% of groins. The additional administration of the radiocolloid improved SLN detection to 88.9% of groins.

CONCLUSIONS: The parallel use of the ^{99m}Tc labelled radiocolloid and blue dye enables high sentinel node detection rates by adequately trained surgeons.

Key words: sentinel lymph node, vulvar cancer, lymphoscintigraphy

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Introduction

Vulvar cancer is quite a rare disease. It accounts for approximately 4% of gynaecological malignancies. Each year around 27,000 women worldwide are diagnosed with vulvar cancer. Rates range from 0.3/100,000 in Asia to about 1.6–2.0/100,000 in North America and Europe [1].

The primary treatment of vulvar cancer is surgical — depending on its type and size. The tumour can be excised with the adequate margins or radical vulvectomy can be performed. Additionally, inguinofemoral lymphadenectomy is performed in all cases except microinvasive vulvar cancer (invasion less than 1.0 mm). The incidence of lymph node metastases in early vulvar cancer is approximately 25–35% — therefore, in most patients, inguinofemoral lymphadenectomy does not influence the treatment results and only increases the complication rate [2]. Because vulvar cancer occurs mostly in elderly patients, a crucial aspect of the treatment is maintaining perioperative complications at the lowest possible level. Complications of inguinofemoral lymphadenectomy include: wound infections (20–40%), lymphatic leg oedema (30–70%), and increased risk of recurrent erysipelas [2].

In order to decrease the extent of surgical intervention, a reliable method is needed for evaluating the status of the inguinofemoral lymph nodes. So far, few preoperative assessment methods have proved useful (3). A potential solution for "tailored" treatment of the vulvar cancer is sentinel lymph node biopsy (SLNB). The sentinel lymph node (SLN) is the first lymph node that

receives the drainage from the primary tumour site and the first one which presents with the metastases — therefore, the negative sentinel lymph node predicts the absence of the metastases in the respective group of the lymph nodes [2]. Vulvar cancer has special features which advocate applying sentinel lymph node detection:

— the disease can be diagnosed at an early stage with a low rate of lymph node metastases;
— there exists the anatomical proximity of the regional lymph nodes, so there is a possibility of decreasing the extent of the lymphadenectomy, if negative SLN is found — with subsequent reduction of the complication rate without the negative influence of the treatment results.

The first report on sentinel node detection in vulvar cancer was presented in 1994 by Levenback et al. With blue dye administration the SLN was detected in 86% of patients [4]. Newer studies show a high SLN detection rate (up to 100%) when utilising radiolabelled nanocolloid [5]. Regarding prognosis, in 2008 Van der Zee et al. published the results of a large, multicentre prospective study analysing the safety of SLNB in vulvar cancer of tumour diameter < 4 cm — ones with a low risk of nodal metastases [2]. In this study, the surgery in patients with negative SLN included radical vulvectomy only. In cases of positive SLN, an additional radical inguinofemoral lymphadenectomy was performed. The mean observation time was 35 months (2–87 months). In a group of 259 patients with unifocal vulvar lesions and negative SLN, groin recurrence was found only in 2.3% (6 cases) and the 3-year survival was 97%. There was no significant statistic difference in the rates of groin recurrence and the overall survival when compared to a group of patients with radical inguinofemoral lymphadenectomy. In the group with the SLNB procedure there was a statistically lower incidence of perioperative complications and improved quality of life compared to the group with standard treatment [2].

Aim of the study

The aim of the study was to evaluate the usefulness of blue-dye-guided and radio-guided sentinel lymph node biopsies (SLNB) in early vulvar cancer. We aimed to assess the sentinel lymph node detection rate, the negative predictive value of the method, and the optimal sentinel node detection technique.

Material and methods

We performed the sentinel lymph node detecting procedure in 24 women with early vulvar cancer. The inclusion criteria were: confirmed squamous cell carcinoma with preoperative biopsy, no suspicion of inguinofemoral lymph node metastases and confirmed consent for participation in the study. The Local Ethics Committee approved the study protocol. Clinical data are given in Table 1.

Two detection techniques were used: in 14 cases (58.4%), only the blue dye technique was used (Methylen-Blau Vitis 1%, Neopharma, Aschau, Germany). In 10 cases (41.6%) the blue dye technique along with lymph node detection was performed utilising a hand-held-gamma probe with the ^{99m}Tc-labelled nanocolloid (Nanocoll, Nycomed Amersham Sorin, Saluggia, Italy). Both tracers were injected intradermally around the tumour. The nanocolloid radiopharmaceutical of activity of 1–2 mCi was administered 15–120 minutes before surgery in a volume of 1–2 ml. Blue dye in a volume of 2–4 ml was given after general anaesthesia approximately 15–20 minutes before starting the surgery. The SLNs were detected with a hand-held gamma probe (Neo2000, Neoprobe Corporation, Dublin, Ohio, USA) and/or by direct visualization of the blue-dyed nodes. The SLN was identified, if the node capsule was blue-stained and/or the node was radioactive (at least 5 times more than the background activity). Sentinel nodes were sent for pathological evaluation.

Table 1. Clinical data

FIGO stages (patients)	IB — 16 II — 1 IIIA — 5 IIIB — 2
Tumour localization	central — 15 patients (62.5%) unilateral — 9 patients (37.5%)
Patients' age	66.2 years (range: 37–86 years)
Hospital stay after surgery	16.2 days (range: 7–55 days)
Duration of surgery	180 minutes (range: 105–240 minutes)

The extent of surgery included radical vulvectomy in 23 patients and wide local excision in 1 patient. In 15 patients with lateral vulvar tumour (more than 2 cm from the midline), unilateral inguinofemoral lymphadenectomy was carried out, and in the remaining 9 cases bilateral lymphadenectomy was performed. The efficacy of the procedure was evaluated according to the SLN detection "per groin". The total number of operated groins was 39.

Results

At least one sentinel lymph node was detected in every patient, altogether in 34/39 (87.2%) of the operated groins. In total 63 sentinel lymph nodes were found, and the mean number of the SLN found in one groin was 1.85. In four cases (16.6%) metastases to the lymph nodes were found and 10 metastatic nodes were detected (9 SLN, 1 "non-sentinel"). In three patients the nodal metastases were shown only in the sentinel node. In one patient two SLNs with metastases in the contralateral groin were detected with no SLN found in the ipsilateral side. In the analysed group there were no false negative sentinel lymph nodes (negative SLN with positive "non-SLN" nodes).

SLN detection failure was shown in 5 cases in which the SLNs were found only in one of the operated groins. In the first case, described above, in one groin only a "non-SLN" metastatic node and two metastatic SLNs in the contralateral groin were found. In the second case both tracers were administered 15 minutes before the start of the surgery, which could cause limited tracer penetration. In the remaining 3 cases, only blue dye was used. Additionally, all the cases with SLN detection failure occurred in the first half of the study (2003–2006) (when the surgeons were less trained in SLN technique) than in the second half of the project (see discussion).

As a comparison with the results obtained with the different SLN detection techniques, when the sole use of the blue dye method was applied, the sentinel lymph nodes were found in 31 of 39 operated groins (79.5% detection rate).

The additional administration of the radiocolloid allowed the SLN detection to increase to 88.9% of the operated groins (16 of 18 groins).

Discussion

Those results confirm the usefulness of the sentinel lymph node detection in vulvar cancer patients. We detected the SLN in every patient. The overall detection rate of 87.2% is acceptable from the surgeon's point of view. This detection rate is slightly lower than that recently reported in the literature [2, 5], but it also included 5 cases with unilateral SLN detection only, which influenced the final result.

Firstly, it should be pointed out that the SLN detection failure in the initial period after implementation of the technique might be strongly influenced by the "learning curve". De Hullu et al. estimated that in order to achieve adequate skills in performing the SLN detection procedure, it is necessary to perform it on approximately 10 patients [15–20 operated groins) [6]. This study confirms our observations — all the failures to detect the SLN were found in the in the first half of our study. In the second part (11 patients) the SLN detection rate was 100%.

We have found no false negative SLNs, although the number of patients in the study was too small to evaluate the negative predictive value. Because of the low incidence of nodal metastases in early vulvar cancer, most of the studies analysing the SLN detection technique in vulvar cancer consisted of too few patients to adequately evaluate the incidence of the false negative SLN [5]. In two studies with more than 50 cases analysed, the negative predictive value was lower than 1%. Ansink et al. reported false negativity in 2 cases in a 51-case series, and Levenback et al. reported 2 false-negative cases in a 52-patient series, respectively [7, 8].

In our study, in patients with a midline tumour, we had 5 failures in bilateral SLN detection. In such cases, due to bilateral lymph drainage [9], it is necessary to find the SLNs in both groins. Failure to detect the sentinel lymph node in one groin causes the need for radical unilateral inguinofemoral lymphadenectomy. Analysis of the possible factors causing SLN detection failure can help to improve the procedure.

A case in which the metastatic node was found in the groin with no SLN found in the ipsilateral side, whilst two SLN with metastases were detected in the contralateral groin, is quite illustrative. This case does not deny the assumption of the sentinel node concept in vulvar cancer. Detection of two metastatic sentinel lymph nodes in one groin is sufficient to correctly assess the "nodal status", whereas the single metastatic lymph node in the contralateral groin is the one which should be detected as the SLN, but there was no tracer uptake. Identical cases in vulvar cancer patients have been reported by Fons et al. and Merisio et al. [10–11], also in breast cancer patients [12–13]. The authors suggest that the potential cause of the tracer uptake failure is the overgrowth of the tumour within the node. Such a condition may induce the potential pitfalls of the sentinel node detection procedure. In order to minimize the risk, radical inguinofemoral lymphadenectomy should be performed, if no SLNs are detected.

In the remaining four cases with SLN detection failure, the factors related with tracer administration should be pointed out. In one case the interval between the injection of the tracer and the start of the surgery was too short, and in three cases only blue dye was used.

Due to the small number of patients, in our study an appropriate comparison of SLN detection techniques was difficult to perform. Our observations suggest that the use of the "combined method" (radiocolloid and blue dye) enables a higher SLN detection rate (by about 10%) to be achieved. Although the blue dye administration is simpler, it is associated with a higher number of SLN detection failures. Our experience with the sentinel lymph node biopsy also confirms the utility of the combined technique. The administration of both tracers gives the possibility to use their unique features in subsequent steps of the SLN procedure. The radiocolloid study enables determination of the initial localization of the SLN before any skin incision is performed. The presence of the blue dye in the lymphatic vessels and the lymphatic nodes additionally facilitates the detection of the sentinel lymph node during groin preparation.

Conclusions

The sentinel lymph node detection procedure enables high detection rates, if performed by an adequately trained surgeon.

The optimal sentinel lymph node detection technique is the simultaneous use of ^{99m}Tc labelled radiocolloid and blue dye.

References

1. Sankaranarayanan R, Ferlay J. Worldwide burden of gynaecological cancer: the size of the problem. Best Pract Res Clin Obstet Gynaecol 2006; 20: 207–225.
2. Van der Zee AG, Oonk MH, De Hullu JA et al. Sentinel node dissection is safe in the treatment of early-stage vulvar cancer. J Clin Oncol 2008; 26: 884–889.
3. Oonk MH, de Hullu JA, van der Zee AG. Current controversies in the manage-ment of patients with early-stage vulvar cancer. Curr Opin Oncol 2010; 22: 481–486.
4. Levenback C, Burke TW, Gershenson DM. Intraoperative lymphatic mapping for vulvar cancer. Obstet Gynecol 1994; 84: 163–167.
5. Hakim AA, Terada KY: Sentinel node dissection in vulvar cancer. Curr Treat Options Oncol 2006; 7: 85–91.
6. de Hullu JA, Oonk MH, Ansink AC et al. Pitfalls in the sentinel lymph node procedure in vulvar cancer. Gynecol Oncol 2004; 94: 10–15.
7. Ansink AC, Sie-Go DM, Velden J van der et al. Identification of sentinel lymph nodes in vulvar carcinoma patients with the aid of a patent blue V injection: a multicenter study. Cancer 1999, 86: 652–656.
8. Levenback Ch, Coleman RC, Burke TW. Intraoperative lymphatic mapping and sentinel node identification with blue dye in patients with vulvar cancer. Gynecol Oncol 2001; 83: 276–81.
9. Iversen T, Aas M. Lymph drainage from the vulva. Gynecol Oncol 1983; 16: 179–189.
10. Fons G, ter Rahe B, Sloof G, de Hullu J, van der Velden J. Failure in the detec-tion of the sentinel lymph node with a combined technique of radioactive tracer and blue dye in a patient with cancer of the vulva and a single positive lymph node. Gynecologic Oncology 2004; 92: 981–984
11. Merisio C, Berretta R, Gualdi M et al. Radioguided sentinel lymph node detec-tion in vulvar cancer. Int J Gynecol Cancer 2005; 15: 493–497.
12. Rink T, Heuser T, Fitz H et al. Results of a standardized protocol for sentinel node imaging in breast cancer with Tc-99m labeled nanocolloidal albumin. Nuk-learmedizin 2001; 40: 80–85.
13. Borgstein PJ, Pijpers R, Comans EF et al. Sentinel lymph node biopsy in breast cancer: guidelines and pitfalls of lymphoscintigraphy and gamma probe detec-tion. J Am Coll Surg 1998; 186: 275–283.