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SCIENCE DIRECT

Gynecologic Oncology 97 (2005) 151–154

Gynecologic Oncology

www.elsevier.com/locate/ygyno

Sentinel node localization should be interpreted with caution in midline vulvar cancer

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Received 28 September 2004
Available online 19 January 2005

Abstract

Objective. Carcinomas of the vulva situated on the midline or close to it, are supposed to have a bilateral lymphatic drainage. The aim of this study was to evaluate sentinel node identification in these tumors.

Methods. Between April 2002 and February 2004, 17 patients with operable vulvar cancer situated on, or close to the midline were entered in a prospective study. All patients underwent sentinel node identification with ^{99m}Tc-labelled nanocolloid (preoperative lymphoscintigraphy and intraoperative use of a handheld probe). Depending on the surgeon, intraoperative blue dye was associated. Radical excision of the tumor and routine bilateral lymphadenectomy were then performed. Sentinel nodes were sent separately for histologic examination. Negative sentinel nodes on hematoxylin/eosine were further examined with immunohistochemistry.

Results. One or more sentinel nodes were identified in the 17 patients and in 21 of the 34 groins. In 5 patients, the sentinel nodes were metastatic. There was no false negative (negative sentinel node and metastatic non-sentinel node). In 13 patients, lymphoscintigraphy and then intraoperative identification suggested a unilateral drainage of the tumor with sentinel nodes localized in only one groin. Among these 13 patients, 3 groins with no sentinel node identified contained in fact massively metastatic nodes.

Conclusion. Unilateral finding of a sentinel node in tumors of the midline does not preclude a metastatic node in the other groin. Lymph node assessment should remain bilateral in these lesions.

Keywords: Vulvar carcinoma; Sentinel node

Introduction

Vulvar carcinoma is a rare disease and accounts for less than 5% of gynecologic malignancies. Surgery is the main treatment. When invasion by the tumor is more than 1 mm depth, surgery includes inguinofemoral lymph nodes dissection for both therapeutic and prognostic purposes. Lymphadenectomy has deleterious side effects. On the short term, many patients suffer from wound breakdown or infection. On the long term, the most impairing sequela is leg lymphoedema, which was reported in about 20% of the cases in a Gynecologic Oncology Group (GOG) study [1].

Sentinel node (SN) biopsy is an appealing solution to this problem. The first description of this technique in the vulva, using blue dye, was by Levenback et al. in 1994 [2]. Since then, several studies have demonstrated that a combined technique using blue dye and a ^{99m}Tc-labelled nanocolloid could lead to better detection rates with a false negative rate (negative SN and metastatic nodes in the remaining of the lymphadenectomy) close to zero [3–9].

Our department is a referral center for vulvar disease. We treat about 25 vulvar cancers per year. In 2002, we began to assess the entire teamwork from scintigraphy to histology,

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doi:10.1016/j.ygyno.2004.12.013

via the surgical procedure. At this occasion, we studied prospectively the specificities of SN identification in tumors located on the midline or close to it, i.e., tumors with bilateral drainage.

Patients and methods

Patients

All patients presenting in our department with an operable primary vulvar carcinoma were eligible for the study if: (1) they had an indication for lymph nodes assessment (i.e., tumor with at least 1 mm depth of invasion), and if (2) the inguinofemoral lymphadenectomy had to be bilateral (i.e., tumors located on the midline or with a medial extension less than 1 cm from the midline). Patients with a prior excisional biopsy were excluded from the study. Clinically palpable groin nodes were not a criterion for exclusion. This prospective research protocol was approved by the Institutional Review Board. All patients gave written informed consent.

SN identification

On the day before surgery, each patient underwent three intradermal peritumoral injections for a total of 30 MBq of ^{99m}Tc-labelled nanocolloid (Nanocis® , Schering SA, Gif sur Yvette, France). This was immediately followed by a lymphoscintigraphy to locate the SN, using a dual-headed gamma camera. It is known that vulvar tumors can have more than one SN in each groin [2–9]. The site of the SNs was located with an handheld gamma detection probe (Europrobe®, EuroMedical Instruments, Le Chesnay, France) and marked on the skin with a pencil.

Optionally, depending on the surgeon, blue dye was used intraoperatively. In this case, just after general anesthesia and 10 min before inguinal incision, patent blue dye (total: 2 ml) was injected at the same locations as the radioisotope. After inguinal incision, the blue lymphatic channel was seek for, and followed up to the blue SN. This node was checked for radio activity with the handheld gamma detection probe. When no blue node was seen, or when blue dye was not used, the SN was identified only by its radioactivity. After removal of the SNs, the groin was reexamined with the probe to detect residual radioactivity and make sure that all SNs had been identified and removed. Afterwards, a complete inguino femoral dissection was performed and sent apart to the pathologist. Ablation of the tumor was then carried out through a separate incision.

Histopathology

Two sections were taken every 3 mm of the greatest dimension of the SN. One section was examined with hematoxylin and eosin staining (H/E). When no metastases were seen on standard coloration with H/E, the other section was immunostained for cytokeratin AE1–AE3 (Biogenex, San Ramon, CA).

Results

Patients

Between April 2002 and February 2004, 17 patients with midline or close to the midline tumors were entered in the protocol and 34 inguino femoral dissections were performed. Median age was 62.4 years (range 34 to 80 years). Eight patients had T1 tumors and 9 had T2. Two patients had clinically suspicious lymph nodes (N1).

SN identification

SNs were identified in all 17 patients, and in 21 of the 34 groins operated on. Mean number of SN per groin was 2.1 (range 1 to 3). In every patient, lymphoscintigraphy localized one or more SNs. When a node was seen at lymphoscintigraphy, it could always be identified per operatively with the detection probe. Blue dye injection, which was optional, was performed in only 14 cases, corresponding to 28 lymph node dissections. The blue dye could identify SN in only 13 of these dissections. Only twice did the blue dye identify a SN that was not radioactive. In these two cases, it was a second or third SN, additional to the SN already identified with the detection probe. In 13 of the 17 patients, preoperative lymphoscintigraphy and then intraoperative blue dye showed only unilateral SNs.

Histopathologic examination

Seven patients had metastatic nodes, one on them bilaterally. In Table 1 are the details of groin analysis in these patients.

On a groin basis, the SNs were negative in 16 out of the 21 groins where they were identified. In no case was a non-sentinel node positive if the SN was negative. Therefore, there was no false negative (i.e., negative sentinel node and positive non-sentinel node) and the negative predictive value of a negative SN was 100% (95% CI, 81–100%). In only one groin, immuno-staining revealed a micrometastatic SN. In this case, the remaining nodes of the groin were negative for disease. Five groins (corresponding to 4 patients, including the 2 with clinically suspicious nodes) contained metastatic SN on routine examination. In 2 of them, there were also metastatic non-sentinel nodes.

Three groins out of the 13 (cases 1, 2, and 3, Table 1) with no SN identified on lymphoscintigraphy had massively metastatic nodes. All of them had been clinically