VIA MEDICA

Nuclear Medicine Review 2002
Vol. 5, No. 2, pp. 171–174

ISSN 1506–9680

The role of sentinel node detection techniques in vulvar and cervical cancer

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[Received 28 VII 2002; Accepted 31 X 2002]

Abstract

The sentinel node is the first lymph node that receives the lymph drainage from the primary tumour. The pathological status of the sentinel node should reflect the histopathology of the entire regional lymph drainage area — both vulvar and cervical cancer spread through the lymphatic system. In gynaecological oncology recent studies have confirmed the utility of the sentinel node concept in vulvar and cervical cancer.

Three techniques for sentinel node localisation are available. The preoperative lymphoscintigraphy and intraoperative hand-held gamma probe detection require the administration of the technetium-99m-labelled colloid around the tumour. The other method is based on the injection of the patent blue dye — during the surgery of the sentinel node because of the dye uptake becomes visible.

Following detection, the sentinel lymph node can be removed separately and assessed with ultrastaging and immunohistochemical staining. In the early stages of vulvar and cervical cancer the lymph nodes metastases rate is relatively low — in most cases lymphadenectomy is not necessary. The determination of the regional lymph nodes' pathological status may limit the extent of the surgical treatment.

The sentinel node detection rate is relatively high and depends on the applied technique. This technique may play an important role in the treatment of vulvar and cervical cancer.

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This paper describes the details of sentinel node identification and reviews the literature.

Key words: sentinel node, vulvar cancer, cervical cancer, lymphoscintigraphy

Introduction

The sentinel lymph node concept was introduced in the year 1977 by Cabanas in his work on penile carcinoma [1]. The sentinel node is the first lymph node that receives the lymph drainage from the primary tumour. The pathological status of the sentinel node should reflect the histopathology of the entire regional lymph drainage area [2–5] — both vulvar and cervical cancer spread through the lymphatic system. For instance a negative result of the histopathological examination of the sentinel node should predict the absence of the metastases in the remaining lymphatic basin.

This idea has already been widely applied in surgical treatment of breast cancer and malignant melanoma cases [2–6]. In recent years in gynaecological oncology the results of preliminary studies have confirmed the utility of the sentinel node concept in vulvar and cervical cancer [2].

Three techniques for the sentinel node localisation are available [9, 12–15]. The preoperative lymphoscintigraphy and intraoperative hand-held gamma probe detection require the administration of the radioisotope-labelled colloid around the tumour. The last method is based on the injection of the patent blue dye — during the surgery the sentinel node uptakes the dye and becomes visible.

The sentinel node detection rate is relatively high and depends on the applied technique. This technique may play an important role in the treatment of vulvar and cervical cancer.

Description of the method of radionuclide sentinel node detection techniques

Usually, one day before the planned operation, a sulphur colloid or albumin colloid labelled with ^{99m}Tc is administered (total dose approximately 10–20 MBq depending on the tumour size). In patients with vulvar cancer the tracer is injected intradermally

around the tumour. In the case of cervical cancer four injections are made, each within one quadrant of the cervix. After the tracer administration lymphoscintigraphy is performed and the places of increased radiocolloid absorption are marked on the patient's skin [9, 13, 14, 23].

During the surgery under general anaesthesia and after preparing the access to the regional lymphatic tissue (determined by the preoperative lymphoscintigraphy) approximately 2–4 ml of 1% patent blue dye is injected analogically to the radiocolloid tracer administration [9, 12, 15]. Finally the sentinel node localisation is carried out with the hand-held gamma probe and is assisted with the direct identification of the stained lymph nodes. The resected sentinel node is sent for pathological examination.

After removal of the first sentinel node a gamma hand probe is used to assess the remainder of the lymphatic basin. If there is an elevated number of gamma counts in the second node it will be sent for pathological evaluation as a second sentinel node. The remaining regional lymph nodes are also taken off during the following part of the operation [9, 13, 23].

In the pathology laboratory the sentinel nodes are examined with routine staining (eosin and haematoxylin). If the nodes turn out negative on the procedure the ultrastaging (step sectioning with 400 mm interval) and cytokeratin staining can be used. The remaining regional lymph nodes are evaluated using routine staining methods [9, 12].

Review of literature

Vulvar cancer

Vulvar cancer spreads predominantly through the lymphatic system. Lymphadenectomy is an indispensable part of the surgical treatment. The resection of the lymph nodes has two aspects — a therapeutic and a diagnostic one. Surgical treatment of vulvar cancer is associated with a significant mortality rate (up to 2% of cases) and a high percentage of postoperative complications, such as delayed wound healing and lymphatic leg oedema [2, 7].

The incidence of lymph node metastases in vulvar cancer depends on the clinical stage of the disease — in the early cases it amounts to 20% [2, 8, 9]. In most patients with vulvar cancer, surgical treatment is too radical. The possibility of the precise determination of the pathological status of the inguinal lymph nodes, including detection of micrometastases, could result in limiting the extent of surgery.

The first results of intraoperative lymphatic mapping in patients with vulvar cancer were published in the year 1994 and 1995 by Levenback et al. [10, 11]. The sentinel node was found in 86% of patients using the patent blue dye. Recent data of Levenback et al. based on the material of 52 patients confirm the high rate of sentinel node localisation with the blue dye (88% of patients, 75% of dissected groins). The authors also defined the factors associated with the failure to identify the sentinel nodes — the type of previous biopsy, the location of the tumour and the clinical experience of the surgeon [12].

Terada et al. applied lymphoscintigraphy together with patent blue dye — the sentinel node was detected in all 9 patients with vulvar cancer [13]. On pathological examination the use of the ultrastaging and cytokeratine staining revealed micrometastases in 2 of 14 lymph nodes negative on standard histopathological staining.

De Cicco et al. employed the intraoperative lymphoscintigraphy and managed to localise the sentinel node in all 37 patients [14]. There was complete agreement between the results of the pathological examination of the sentinel node and the regional lymph nodes — in all 29 patients with negative sentinel nodes there were no metastases in the remaining nodes.

In another study based on 59 patients (11 unilateral and 48 bilateral lymphadenectomies) de Hullu et al. report the sentinel node detection in 95 of 107 operated groins [15]. Identification mainly relied on intraoperative lymphoscintigraphy because patent blue dye technique enabled the identification of only 60% of the sentinel nodes. On pathological evaluation there were no false-negative cases. With the use of step sectioning and the immunochemical staining four metastatic sentinel nodes were found in the group of 102 nodes negative on pathological examination.

In the recent data based on 26 cases of vulvar cancer reported by Sliutz et al. preoperative lymphoscintigraphy showed focal uptake in sentinel nodes in all 26 patients [9]. Intraoperatively in 20 cases one sentinel node was found unilaterally and in the other 6 patients two or more nodes were detected bilaterally. Histologically positive sentinel nodes were found in 9 cases with no false negative findings.

Cervical cancer

In the case of patients with cervical cancer in the FIGO I and II clinical stage (neoplasmatic process limited to uterus or expanding to the parametrium and vagina – suitable for surgical treatment) the incidence of metastatic disease in the lymph nodes amounted respectively to 0–16% and 24–31% [17]. Like with vulvar cancer, a prevalent group of patients has no benefit from radical lymphoadenectomy. The absence of metastases in a sentinel node enables the avoidance of radical surgery and consequently a potential reduction in morbidity.

The usefulness of this method is still being evaluated. The lymphatic mapping procedure in cervical cancer encounters some technical difficulties. The lymphatic drainage in cervical cancer is much more complex than in vulvar cancer and it is unclear whether a cervical cancer may drain to several lymphatic nodes simultaneously. Additionally — except for small lesions located on the exocervix — a precise injection of tracer around the tumour is generally not possible [2, 18].

For those reasons the rate of sentinel node detection in cervical cancer is lower than in vulvar cancer.

One of the first reports regarding sentinel node identification in cervical cancer was made by Verheijen et al. [4]. The authors used three methods of detection (preoperative and intraoperative lymphoscintigraphy, patent blue dye injection). The highest sentinel node detection rate (8 out of 10 patients) was obtained with intraoperative lymphoscintigraphy.

O'Boyle et al., applying the patent blue dye method, concluded that the primary cervical tumour size is an important factor positively influencing the detection rate [18]. In this study the sentinel node was found in 60% of cases.

Another paper by Levenback et al. reports a high detection rate (100%) in patients with cervical cancer, utilising a hand-held intraoperative gamma probe [20]. In the same group of patients preoperative lymphoscintigraphy detected at least one sentinel node in 26 of 30 patients (87%)

Some studies dealt with the evaluation of the sentinel node techniques with the use of laparoscopy. D'Argent et al. managed to find the sentinel node in 59 of 69 patients (85%) with patent blue dye technique [21]. The failures were explained by an insufficient amount of the administered dye. Similar data presented by Malur et al. found the sentinel node during laparoscopy in 78% of cases, utilising intraoperative lymphoscintigraphy and patent blue dye [22].

Discussion

The sentinel node concept is widely discussed in oncological gynaecology. A number of studies on that issue have been published, but still there are no standards of sentinel node detection [15, 21–24]. There is a need to confirm the presumptions about the sentinel node concept — verifying the relation between the presence of the metastases in the sentinel node and the remaining regional lymph nodes. All authors stress the necessity of opening multi-centre, randomised studies concerning the use of the sentinel node detection technique.

Before introducing the procedure into routine treatment, several other problems must be solved first, such as unifying the techniques, verifying the sensitivity of the method, identifying probable modifying factors and precise determination of the lymphatic flow in both cervical and vulvar cancer.

The results of the studies published so far indicate that the most effective technique for the sentinel node localisation is intraoperative gamma probe node detection assisted by blue dye administration. The preoperative lymphoscintigraphy did not improve the sentinel node detection rate and had significantly complicated the whole procedure [19, 20]. On the other hand in the cases of vulvar cancer, the preoperative lymphoscintigraphy allowed a determination of the lateralisation of the lymph flow.

There is a decreased probability of sentinel node detection in patients who were treated with chemotherapy or radiotherapy prior to surgical treatment, who underwent an operation involving the lymphatic basin prior to the oncological treatment or in patients with macroscopic changes in the regional lymph nodes. There was an impaired radiotracer and dye penetration including the cancer-related occlusion of the cervical stromal lymphatic system [2, 12, 18]. Other possible reasons were: excessive vaginal or peritoneal spillage or disruption of the lymphatic channels during initial dissection.

An important problem affecting the validation of the lymphatic mapping concept in vulvar cancer is the low morbidity of this disease. Therefore, obtaining data from prospective randomised trials will be difficult.

The authors are not familiar with any reports concerning adverse events due to radiocolloid administration. The applied amount of the Tc^{99m} — labelled colloid does not exceed the radiation safety standards — including the patient, surgical team and hospital staff [2, 14]. A severe anaphylactic reaction after the patent blue dye administration is possible but very rare [2].

Another complication of the procedure is a pulse oximetry desaturation observed shortly after the dye injection. This event is attributed to the dye properties to absorb the wavelengths used to measure the oxygen saturation. The arterial blood gas determination confirms the patient's condition.

Conclusions

1. Sentinel node detection, frequently applied in the surgical treatment of breast cancer and malignant melanoma, seems to have a potential value in gynaecological oncology for lymphatic mapping in vulvar cancer and cervical cancer.
2. Lymphoscintigraphy has a higher sentinel node detection rate than blue dye injection, but the best results have been achieved using these two methods together.

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