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A N I N T E R N A T I O N A L J O U R N A L

Problems and Pitfalls in Vulvar and Cervical Cancer Sentinel Node Scintigraphy

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ABSTRACT

After the introduction for penile cancer, the sentinel lymph node imaging is increasingly applied in various types of cancer. After the initial learning phase, 105 patients with vulvar and 24 with cervical cancer have been investigated. In vulvar cancer all the imaged sentinel nodes were discovered by the portable probe intraoperatively. No false negative sentinel node was observed. The most critical issue is the tracer application. Performed strictly intradermally, the sentinel node shows up immediately. Concomitant use of isosulfan blue dye did not improve the results and was stopped therefore. Similarly, more superficial (intra/subendothelial) application brings up better results as compared to deeper injection in cervical cancer patients. No false negative results were seen. Apparently, an almost 100% detection is possible. Our findings clearly show that tracer application is the key for successful imaging. If not done properly, sentinel node may appear later or may even more likely be missed.

Key words: sentinel lymph node - vulvar cancer - cervical cancer -scintigraphy

INTRODUCTION

Cabanas in 1977 originally was defining sentinel lymph node in penile cancer patients. Already at this time lymph drainage imaging in melanoma has been done in many centers including ours to define the drainage of lymph flow without recognizing its unique clinical relevance. The unique concept says that a histologically negative sentinel lymph node predicts that the remaining lymph nodes will be tumor free. The reliability of this concept has been assessed in melanoma (Morton et al., 1992) and breast cancer patients (Cox et al., 1988) so far and is currently applied for a variety of other tumors such as in the maxillofacial region (Hyde et al., 2002), colorectal (Basilio et al., 2006), breast (Frisell et al., 2001), esophageal and gastric (Kitagawa et al., 2005), cervical (Hubalewska et al., 2003), vulvar (De Hullu et al., 2000) and penile (Valdés Olmos et al., 2001) cancer. We are reporting our experience with vulvar and cervical cancer. We performed the first vulvar cancer sentinel node scintigraphy in 1999 (Granegger et al., 1999) and cervical in 2001 (Sinzinger and Meghdadi, 2001), preliminary data were published in 2002.

PATIENTS AND METHODS

Patients (T1, T2) received a total of 12 MBq ^{99m}Tc-nanocolloid (GE Healthcare Buchlar GmbH and Co.KG, Braunschweig, Germany) in 1 ml saline intradermally divided in 4 parts in each

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quadrant around the tumor using an insulin syringe (BD 1 ml syringe, Luer-Lok™ Tip; BD, New Jersey, USA). In cervical cancer 0.5 – 1.5 ml were used. Lymphoscintigraphy was performed with a double-headed gamma camera using a low energy high resolution collimator. Static images were performed at 5, 30, 60 and 90 minutes after tracer application. If possible, the sentinel was marked on the skin and the gamma camera images were available to the surgeon before starting the operation.

Table 1 - Patients characteristics.

Cancer	N	Age (range)	Age (mean)
Vulvar	105	32 – 89	66.09
Cervix	24	31 – 56	44.40

Histopathological examination of the sentinel node and the other nodes was done after hematoxylin/eosine staining and serial sectioning. Nodes initially were cut into 2 to 3 mm slices and then each block again at 400 µ distance. The count rate in-vivo and in-vitro was measured, localization and count rate of all suspected sentinel nodes was documented. Radioactive nodes were separated and lymph node dissection performed.
In negative sentinel nodes additional immunohistochemical examination was done.

RESULTS

Sentinel nodes appear mainly on the ipsi-lateral (tumor) side. From the ones showing up immediately presenting 1 sentinel only (n = 24, 22.86%), the overwhelming majority (n = 22, 22.95%) appeared on the ipsilateral side (Table 2). Only in 4 cases there were more than 2 sentinels showing up immediately on the ipsilateral side, no one at the contralateral side. In 5 patients (4.76%) a sentinel node was found up to 30 minutes, in 1 (0.95%) at 60 minutes. A total of 22 sentinel nodes (20.95%) were showing up as late as after 30 minutes, 7 others (6.67%) even later at 60 minutes. 22 patients (20.95%) showed 1 sentinel node immediately on both sides. In the other patients a variety of combinations was seen concerning site, number and time of appearance. In 6 patients a clear transport along the lymph vessel was discovered. The maximal number of sentinels seen in one patient was 5; 3 patients also presenting the primary tumor more than 1 cm from the midline, exhibited a sentinel node on the contralateral side, one of them showing even 2 nodes.

Table 2 - Sentinel node in vulvar cancer.

Site	N	%
Ipsi- (total)[*)]	29	27.62
1	22	20.95
2	3	2.86
> 2	4	3.81
Contra- (total)[*)]	5	4.76
1	2	1.90
2	3	2.86
> 2	0	0.00
Ipsi- + contra- (total)	71	67.62
1 (each)[*)]	22	20.95
3 (total)	33	31.43
> 3 (total)	16	15.24

[(*)] showing up immediately

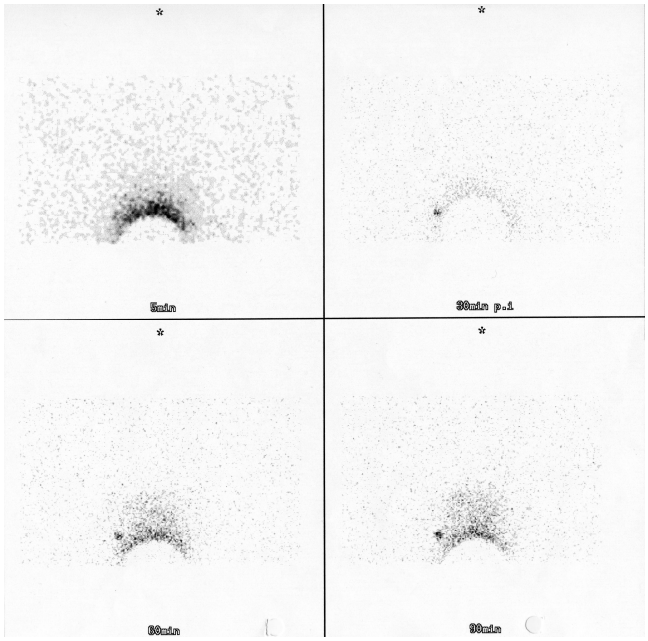

Figure 1 - Typical example of a suboptimal, sentinel node showing up above the shielding on the contralateral right hand side only faintly after 30 minutes.

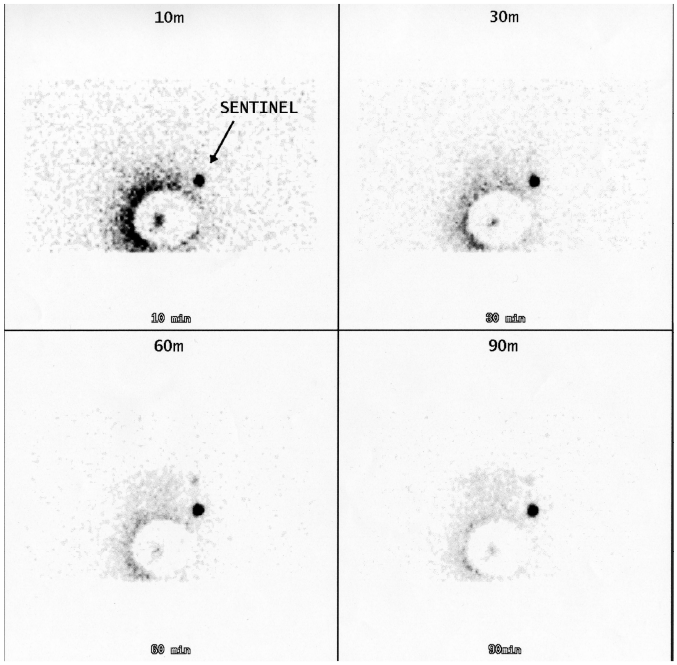

Figure 2 - Ipsi-lateral sentinel showing up immediately, while after 30 minutes an additional proximal node seems to appear, showing up significantly at 60 minutes and later

Figure 3 - Left side vulvar cancer with one sentinel node on each side showing up immediately. On the left hand side a second one appears around 30 minutes after tracer administration

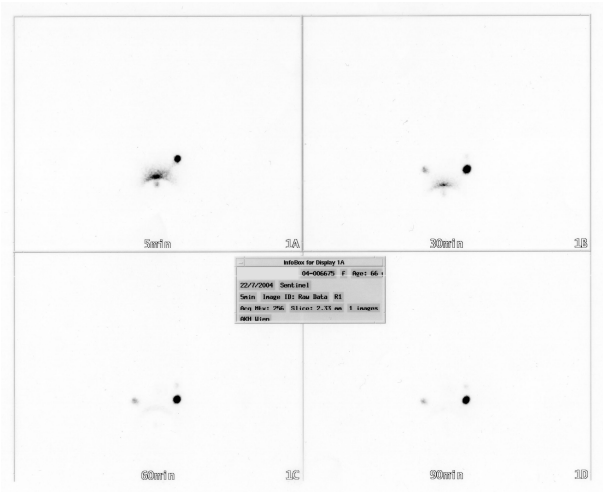

Figure 4 - Immediate appearance of an ipsi-lateral sentinel on the left hand side. Later on (at 30 minutes) a faint sentinel on the right hand side is appearing too. After 60 minutes also a very faint one proximal to the left.

Cervical cancer sentinel nodes present mainly bilateral along the pelvic wall and next to the cervix (table 3), while in those cases with unilateral appearance sentinel localization next to the cervix is predominant.

Table 3 - Sentinel node in cervical cancer.

Site	Number	%
bilateral	17	70.83
pelvic wall	2	8.33
next to cervix	5	20.83
both	10	41.67
unilateral	7	29.17
pelvic wall	1	4.17
next to cervix	4	16.67
both	2	8.33

DISCUSSION

Sentinel lymph node scintigraphy is now widely performed for both, vulvar cancer (De Hullu et al., 2000) and cervical cancer (Van de Lande et al., 2007).

Wydra et al. (2003) found that the superficial administration of the radiocolloid into the cervix provides a higher sentinel node detection rate compared to deeper administration, a fact we can strongly support. All the negative images in the learning phase apparently were due to inappropriate administration. In order to avoid false negative imaging, strictly intradermal injection combined with an at least 60 minutes follow-up and a trained, experienced team are key requirements. From the point of the application technique, both vulvar and cervical cancer are probably the most difficult ones. Hauspy et al. (2008) found that in vulvar cancer being at least 1 cm from the midline no contralateral sentinel node appeared, a finding we were unable to confirm. In contrast to Hauspy we found a higher rate of bilateral nodes (67.62% vs. 46%).

Overall, vulva sentinel shows excellent findings. Various authors with significant number of cases (Louis-Sylvestre et al., 2005, Moore et al., 2003, Hauspy et al., 2008, De Hullu et al., 2000) reported no false negative node. Vulva sentinel is probably one of the most relevant ones combining reduction of postoperative morbidity of these mainly older aged patients with excellent results.

RESUMO

Após a introdução para câncer do pênis, a imagem do linfonodo sentinela é cada vez mais aplicada nos diversos tipos de câncer. Após a fase inicial de aprendizagem,105 pacientes com câncer vulvar e 24 com câncer cervical foram investigados. No câncer vulvar todas as imagens de nodos sentinela foram descobertas por sonda portátil durante o exame. Nenhum nodo sentinela falso negativo foi observado. A questão mais crítica é a aplicação do traçador. Realizada pela via intradérmica, o nodo sentinela surge imediatamente. O corante *isosulfan blue* não melhora os resultados e seu uso concomitante foi abandonado. Do mesmo modo, a aplicação mais superficial (intra/subendotelial) apresenta melhores resultados quando comparada com a administração mais profunda em pacientes com câncer cervical. Não foram observados resultados falsos negativos. Aparentemente, uma detecção de aproximadamente 100% é possível. Nossos achados mostram claramente que a administração do traçador é um ponto chave para uma imagem com qualidade. Se não for feita corretamente, o nodo sentinela pode aparecer tardiamente ou pode até ser perdido.

Palavras-chave: linfonodo sentinela, câncer vulvar, câncer cervical, cintilografia.

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