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Tanis, P.J.

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CHAPTER THIRTEEN

Feasibility of Sentinel Node Lymphoscintigraphy in Stage I Testicular Cancer

Departments of Surgery, Urology and Nuclear Medicine, The Netherlands Cancer Institute / Antoni van Leeuwenhoek Hospital, Amsterdam, the Netherlands

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The management of the regional lymph nodes in stage I testicular cancer is still surrounded by controversy. As a result of the low incidence of occult lymph node metastases, primary treatment for non-seminomatous germ cell tumours (NSGCT) in the form of retroperitoneal lymphadenectomy or chemotherapy results in overtreatment with associated morbidity in 70% to 75% of the patients. Overtreatment in seminomatous germ cell tumours (SGCT) with routine adjuvant radiotherapy is even higher, because occult metastases are present in less than 20% of the patients. On the other hand, a surveillance policy results in detection of lymph node metastases at a later stage and requires an intensive, frequent follow up with costly examinations. Until now, methods for selection of patients who need adjuvant therapy are not satisfactory.

There is a need for techniques to predict which patients are most likely to have occult retroperitoneal disease. Positron emission tomography (PET) has been used in testicular cancer for the evaluation of postoperative beds to find residual tumour, but was found to be unreliable for staging.¹ The technique of lymphatic mapping with sentinel node biopsy can potentially be the solution for the selection problem. Before the sentinel node era, lymphoscintigraphy using intratesticular injection of colloidal gold (¹⁹⁸Au) has been described in literature.²³ The purpose of the present study was to determine the feasibility of lymphoscintigraphy using technetium-⁹⁹m (⁹⁹mTc) nanocolloid for identification of the sentinel node in testicular cancer.

**Patients and methods**

Five patients with clinically stage I testicular cancer underwent lymphoscintigraphy. The mean age of the patients was 36 years (range 21 to 52 years). The primary tumour was situated on the right side in one patient and on the left side in four patients. Except for the first patient, local anaesthesia was obtained with a funicular block using lidocain 2%, performed by the urologist in the outpatient clinic. In the nuclear medicine department, a single dose of ⁹⁹mTc-nanocolloid (Amersham Cygne, Eindhoven, the Netherlands) in a mean volume of 0.22 ml (range 0.15 to 0.30) was injected with a fine type of needle into the funicus in the first patient and into the testicular parenchyma in the following four patients. The mean dose was 99 MBq with a range from 52 to 135 MBq.

Shortly after injection, anterior and lateral dynamic twenty-second images were obtained with a dual-head gamma camera (ADAC Vertex, Milpitas, CA, USA) during ten minutes to visualise the lymphatic flow and to determine the sequence of hot spots that appear. Static images with a cobalt-57 source behind the patient were obtained during five minutes immediately following the dynamic study. Late static images were obtained two to 24 hours after injection.

In the last two patients, lymphoscintigraphy was followed by intraoperative lymphatic mapping via a transperitoneal laparoscopic approach on the same day. The sentinel node was identified with the aid of intratesticular injected patent blue dye in a volume of 1.0 ml and an endoscopic gamma ray detection probe (Europrobe, Euromedical Instruments, Le Chesnay, France). This study protocol was approved by the Medical Ethical Committee and informed consent was obtained.
Results

The funicular administration route in the first patient resulted in five hot spots in the ipsilateral inguinal region after two hours, representing lymphatic drainage from the scrotum (figure 1). Intratesticular administration resulted in visualisation of one sentinel node in the ipsilateral para-aortic region in two patients (figure 2), two sentinel nodes in the ipsilateral para-aortic region in one patient and lymph node uptake was absent in the remaining patient. All retroperitoneal sentinel nodes together with afferent lymphatic vessels were visualised during the dynamic study. Static images revealed multiple second- and higher-echelon lymph nodes in the three patients with visualisation. In one of these patients, a hot spot in the superficial inguinal region was observed after two hours in addition to the hot spots in the retroperitoneal area (figure 3).

Figure 1. Lymphoscintigraphy after injection of 99mTc-nanocolloid in the right funiculus (F) showing five hot spots in the ipsilateral inguinal region after two hours, representing lymphatic drainage from the scrotum.

Figure 2. Lymphatic drainage of a testicular carcinoma (T) via an afferent lymphatic vessel to a sentinel node (arrow) and multiple higher-echelon lymph nodes in the para-aortic region.
Laparoscopic exploration revealed two radioactive sentinel nodes without blue discoloration adjacent to the aorta near the origin of the renal vessels in one patient. Exploration in the patient without visualisation on lymphoscintigraphy did not result in identification of a radioactive or blue-stained sentinel node, but two lymph nodes without tracer-uptake were harvested. All excised lymph nodes were free of tumour.

**Discussion**

This study shows the feasibility of lymphoscintigraphy to identify sentinel lymph nodes in testicular cancer patients. The method is easy to perform and is well-tolerated. No side effects were observed. Lymphoscintigraphy can potentially be of clinical value in combination with an intraoperative technique of lymphatic mapping to identify occult lymph node metastases in clinically node-negative testicular cancer. This approach enables better selection of patients who may benefit from adjuvant therapy after orchectomy and avoids unnecessary morbidity. In our institution, the current adjuvant treatment for stage I testicular cancer consists of radiotherapy to the para-aortic and ipsilateral pelvic nodes in SGCT and chemotherapy in the form of BEP (bleomycin, etoposide and cisplatin) with or without salvage surgery in case of relapse during surveillance in NSGCT. The main disadvantage of radiotherapy to this region is the two- to three-fold increased risk of secondary solid tumours. Chemotherapy regimens for NSGCT are associated with long-term toxicity such as decrease in glomerular filtration, Raynaud’s phenomenon, impaired spermatogenesis, ototoxicity and neurotoxicity, besides the acute toxicity.4
In other institutions, routine retroperitoneal lymphadenectomy is still applied in NSGCT patients. The use of nerve-sparing and unilateral lymphadenectomy has reduced morbidity, but ejaculatory dysfunction, for example, occurs in about 10%. Some studies have tried to solve the problem of patient selection by identifying factors associated with occult lymph node metastases, such as tumour size, tumour invasion of testicular lymphatics and veins, and tumour marker half-life. However, patient selection based on these factors will result in high false-negative and false-positive rates.

Detection of occult lymph node metastases in a direct way has been shown to be more promising. Following the work of Cabañas and Morton who were the pioneers in exploring the sentinel node concept, the technique of lymphatic mapping has gained widespread popularity in the treatment of several malignancies. The hypothesis of sequential dissemination was also explored in testicular cancer. In 1987, Weissbach and Boedefeld stated that "a more limited approach strictly for the purpose of pathological staging, which aims at the prevention of long-term damage without compromising diagnostic accuracy, must be based on the knowledge of the pathways of lymphatic dissemination and, particularly, on the first site of nodal involvement". The primary sites of lymphatic drainage have been defined by looking for the sites of a solitary metastasis in retroperitoneal dissections. The variability in anatomical patterns as shown in these studies requires the use of the technique of lymphatic mapping to identify the lymph nodes on a direct drainage pathway from the primary tumour.

In analogy to funicular lymphangiography, we started with funicular injection of the radiocolloid for lymphoscintigraphy, because this was assumed to be the least painful administration route. But at the level of the funiculus, only a few collecting lymphatic vessels are present and it is hard to inject the radiocolloid exactly into these vessels unless these are surgically canulated. Consequently, the radiocolloid will be absorbed by lymphatic capillaries of the scrotum with subsequent drainage to superficial inguinal nodes (figure 1). Therefore, we changed the administration route after the first patient. Even when intratesticular injection is performed, inguinal drainage may occur because of spill in the needle tract through the scrotum as we observed in one patient (figure 3). The rapid lymphatic drainage form the testicle necessitates dynamic gamma camera acquisition to enable differentiation between first- and second-echelon lymph nodes in the retroperitoneum. Late images seem to be indicated to exclude unexpected drainage patterns.

Following the lymphoscintigraphy, we performed a laparoscopic retroperitoneal sentinel node biopsy in the same session as orchietomy in two patients. The laparoscopic approach requires longer operative time than an open procedure, but it is a minimal invasive procedure with low rates of intraoperative and postoperative complications and short convalescence to normal life. In none of the two explored patients blue lymphatics or blue nodes were encountered, probably due to inadequate timing of injection. Further experience is needed to determine the proper use and value of blue dye, especially in patients without scintigraphic visualisation. What might be the consequences for adjuvant treatment in the future if the described sentinel node procedure turns out to be a technically successful and reliable
technique? Sentinel node positive patients can be treated with an adjuvant short-course chemotherapy or radiotherapy in case of NSGCT or SGCT respectively. Investigators who used two courses of BEP to treat clinical stage I NSGCT show that more than 95% of the patients with occult lymph node metastases can be cured with short course chemotherapy.\textsuperscript{10} This results in reduction of chemotherapy and dose related morbidity, because otherwise NSGCT patients with lymph node metastases during surveillance would have been treated with four courses of chemotherapy in a later phase. The approximate 80% reduction in the routine application of adjuvant radiotherapy for SGCT obviously leads to a substantial reduction of morbidity as well.

\textbf{Conclusion}

Preliminary data shows that lymphoscintigraphy for sentinel node identification is feasible in stage I testicular cancer using intratesticular radiocolloid administration. In combination with laparoscopic sentinel node biopsy, identification of occult lymph node metastases may prevent under- or overtreatment in the future.

\textbf{References}