Original Article

Sentinel node detection failure due to defective labeling and large particle size of Tc-99m antimony sulfide colloid

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ABSTRACT

Introduction: Many radiotracers have been used for sentinel node mapping with acceptable results. The main difference between these radiotracers is the particle size. In the current study, we reported defective labeling of Tc-99m antimony sulfide colloid which resulted in large particle size.
Methods: Tc-99m-Antimony sulfide colloid was used for axillary sentinel node mapping of 45 breast cancer patients. The prepared kits were turbid and were used for the first 15 patients. For the remaining 30 patients, we used a filter (GyroDisc CA-PC Cellulose Acetate Membrane; 30 mm; Pore size: 0.2 µm) after labeling to remove the possible large particles of the prepared kits.
Results: On the lymphoscintigraphy images, at least one sentinel node could be identified in 5 and 29 patients of the unfiltered and filtered groups respectively (p=0.00001). Sentinel node detection by gamma probe was successful in 5 and 30 patients in the unfiltered and filtered groups respectively (p=0.000001).
Conclusion: Tc-99-Antimopny sulfide colloid is a suitable radiotracer for sentinel node mapping of the breast cancer patients. In case of any unusual turbidity of the labeled kit, it should not be used or at least be filtered before injection.

Keywords: Breast cancer, Sentinel node, Tc-99m-Antimony sulfide colloid, Lymphoscintigraphy.

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INTRODUCTION

Sentinel node biopsy is the standard method for regional lymph node staging in many solid tumors such as breast cancer (1), and melanoma (2). Since its introduction, this method has revolutionized the field of surgical oncology with significant reduction of morbidity due to regional lymph node dissections (3).

Usually two methods are used alone or in combination to identify the sentinel nodes during surgery, namely: radiotracers and blue dyes (4). Many radiotracers have been used for sentinel node mapping with acceptable results including: Tc-99m sulfur colloid (5), Tc-99m phytate (1), Tc-99m antimony sulfide colloid (6), etc. The main difference between these radiotracers is the particle size which can vary from very small for Tc-99m antimony sulfide colloid (3-30 nm) to very large in Tc-99m unfiltered sulfur colloid (100-600 nm) (7). Although the particle size cannot influence the accuracy of sentinel node biopsy, the time profile of sentinel node visualization and sentinel node uptake are extremely sensitive to this variable (8-10). The particle size itself has been reported to be affected by the labeling technique of the tracer (11-14).

In the current study, we reported defective labeling of Tc-99m antimony sulfide colloid which resulted in large particle size and low detection rate.

METHODS

During the time period of February to May 2011, 45 patients with the history of early stage breast cancer were referred to our department for sentinel node mapping. We used Tc-99m antimony sulfide colloid for sentinel node mapping of these patients. The labeling process was according to the manufacturer recommendations (15) in brief: 0.5 mL HCl (which is necessary for labeling process of the kit) was added to the kit with gentle shaking for couple of second, then 10-40 mCi Tc-99m pertechnetate (1 cc volume) was added to the kit and heated in the boiling 100º C water for 30 minutes. After cooling down, 1 mL phosphate buffer was added. The prepared kits which were turbid (unable to see through the vial) and were used for 45 patients among which 30 patients were injected with pre filtered kits (GyroDisc CA-PC Cellulose Acetate Membrane; 30 mm; Pore size: 0.2 µm). Figure 1 show the pre-filtered kit.

Fig 1. Labeled Tc-99m-Antimony Sulfide Colloid. Note the unusual turbidity of the prepared kit.

The technique of the sentinel node mapping was explained elsewhere (16). In brief: 0.5mCi or 1mCi/0.2mL (for 1-day and 2-day protocols respectively) of the tracer was injected into the peri-areolar area of the index quadrant in an intradermal fashion.

After injection of the tracer gentle massage was applied to the injection site for 1 min. Anterior and lateral spot views were obtained 2 min after the injection (3min/image, 128×128matrix) using a dual head gamma camera (E.CAM Siemens), equipped with a parallel hole low energy high resolution (LEHR) collimator. In case of sentinel lymph node non-visualization

delayed imaging up to 60 min was obtained. Patients were operated on 2-4 h and 24 h after injection of the radiotracer for 1-day and 2-day protocols, respectively. In the operating room, 2ml patent blue V or methylene blue dye was injected in a periareolar fashion to all patients. A sentinel node was defined as any hot node (using RMD navigator GPS system or EUROPROBE) or a blue tract leading to a blue node or combination of the above.

The decision to perform axillary lymph node dissection was based on the frozen section results of harvested sentinel lymph nodes. For patients with sentinel node detection failure during surgery, axillary lymph node dissection was also performed .

SPSS version 11.5 was used for statistical analyses. For comparison of quantitative variables between filtered and unfiltered groups independent sample t-test and for the categorical variables Fisher's exact test or Monte Carlo technique was used. P-values less than 0.05 were considered statistically significant.

RESULTS

The characteristics of the patients are shown in Table 1. At least one sentinel node could be identified in 5 and 29 patients of the unfiltered and filtered groups respectively (p=0.00001) on the lymphoscintigraphy images. Sentinel node detection by gamma probe was successful in 5 and 30 patients in the unfiltered and filtered groups respectively (p=0.000001). Blue dye detection rate was not statistically different between groups (10/15 and 22/30 in the unfiltered and filtered groups respectively).

Table 1. Characteristics of the patients

	Unfiltered kit	Filtered kit	P value
Age	45±12	47±10	0.56
Tumor size	2.5±1.2	2.6±1.1	0.78
Tumor location			
Upper lateral	7	14	0.915
Lower lateral	3	5	
Upper medial	2	4	
Lower medial	2	5	
Central	1	2	
Sentinel node detection			
Lymphoscintigraphy	5	29	0.00001
Blue dye	10	22	0.732
Gamma probe	5	30	0.000001
Overall	5	30	0.000001

DISCUSSION

Sentinel node biopsy for the early breast cancer patients can be performed with two methods, namely blue dye, radiotracer or both in combination (17). Various radiotracers have been used for sentinel lymph node biopsy with comparable results (18). The main difference between these radiotracers is the particle size (7) which can affect time of sentinel node visualization dramatically (8, 19). This can also affect the tracer uptake in the sentinel nodes as small particle size leads to rapid movement in the lymphatic system and higher uptake (5).

Fig 2. Syringe filter after use for filtering. Note significant amount of the tracer trapped in the filter (dark orange color of the filter).

Fig 3. Filtered kit. Note reduction of the turbidity which is due to removal of the large particles.

It has been shown that the production and labeling process of the radiotracers can affect the purity or particle sizes of the final product (11-14). This is especially true for Tc-99m-Antimony sulfide colloid since the labeling process of this tracer has several steps namely heating in boiling water (20, 21).

We have used this kit since the introduction of sentinel node biopsy in to the clinical practice in our department with excellent results (22). Usually the prepared kit in final step shows some turbidity which is normal since this tracer is colloidal in nature (15). Patients injected with no pre-filtered kit show lower detection rate (33%) in either lymphoscintigraphy or gamma probe was lower than usual. Quality control of the preparation demonstrated so the radiotracer was filtered to remove large particles.

For the next 30 patients the results were strikingly different from the unfiltered kits. Detection rates with lymphoscintigraphy and gamma probe during surgery were 96.6% and 100% respectively. This shows that low detection rate can be related to the size of the particles (9).

Filtering of the prepared kits however, has its own drawbacks. Most of the labeled particles would be separated from the original kit lowering the specific activity of the filtered tracer (Figures 2 and 3). As a result, volume of tracer will be increased for each patient. This can increase the pain of the intradermal injection dramatically.

CONCLUSION

Tc-99m-Antimopny sulfide colloid is a suitable radiotracer for sentinel node mapping in patients with breast cancer. The preparation and labeling of this kit is very laborious and needs strict. In case of any unusual turbidity of the labeled kit, it should

not be used or at least be filtered before injection.

Conflict of interest

One of the authors (Gholamali Shabani) works for kit production division of AEOI.

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