Methods and Technology

Significance of methylene blue dye for localization biopsy of nonpalpable breast lesions

Jun Tang,1,2 Xi Wang,1,2 Yao-Pan Wu,1,3 Xin Wang,1,4 Zhen-Qiang Lian,1,2 Jian-Hua Fu1,4 and Ming-Tian Yang1,2,*

1State Key Laboratory of Oncology in South China; 2Department of Mammary Gland Disease; 3Medical Imaging and Interventional Center; 4Department of Thoracic Surge; Cancer Center, Sun Yat-sen University; Guangzhou, Guangdong P.R. China

Key words: breast neoplasm, excisional biopsy, methylene blue dye, nonpalpable breast lesion, mammography, diagnosis

Background and Objective: With advances in mammographic equipment and techniques, more and more nonpalpable breast lesions have been detected. This study was to investigate the application of methylene blue dye for localized biopsy to diagnose nonpalpable breast lesions. Methods: In total 138 patients with suspicious malignant, nonpalpable breast lesions between August 2002 and October 2006 were enrolled. A small dose of methylene blue was injected into the lesion under mammographic guidance. The dyed tissues were excised completely via an optimal incision, and radiographys was obtained to confirm the removal of the nonpalpable lesion. The specimen weight and incision length were measured. Results: Suspicious lesions in all 138 patients were accurately excised. Eighty-four (60.9%) patients were confirmed as breast cancer, and 54 (39.1) were diagnosed with benign lesions. The mean length of the incision was 4.6 cm (range 3.2–5.3 cm), and the mean weight of the resected specimen was 42 g (range18–86 g). All patients achieved stage I healing. Conclusions: Excisional biopsy is recommended for nonpalpable breast lesions which are highly suggestive of malignancy by imaging examination. Methylene blue guided localization and excisional biopsy is a safe, relatively simply procedure with high diagnostic accuracy.

With progress in mammographic equipment and techniques, the amount of clinically nonpalpable breast lesions is increasingly detected by imaging examinations. Assessment and proper management of this category of lesions is important, and needs to be settled urgently. We summarized our experience in the application of methylene blue dye in mammography-guided stereotactic biopsy.

Materials and Methods

Patient selection. A total of 138 patients who had no clinically palpable breast lesions, but were highly suggestive of malignancies by mammography were selected in the Sun Yat-sen University Cancer Center from August 2002 to October 2006. Seventy-two patients (52.2%) had calcified spots, 19 (13.7%) had star-shaped nodules, 16 (11.6%) had local structural distortion, and 31 (22.5%) had coexistence of the multiple signs. Patients were aged between 34–72 years, with a median age of 45 years. The main reasons for hospital referral of these patients were as follows: routine health check-up in 60 asymptomatic cases; routine screening for the contralateral breast in 42 cases who were previously diagnosed with unilateral breast; nipple discharge (22 cases); and cyclical breast pain (14 cases).

Stereostatic localization mammography guided excisional biopsy. Before surgery, localization of lesions was performed through stereotactic mammography followed by puncturing a 21G needle into the center of the lesion, and then 0.1–2 ml of 1% methylene blue was injected after confirmation by the imaging examination. Subsequently, patients were sent to the operating room. The lesion location was initially confirmed according to preoperative mammogram findings, then the horizontal distance from the lesion to the nipple (a) was measured in the cranio-caudal view (Fig. 1 A), and the vertical distance from the lesion to the nipple (b) was measured in the lateral view (Fig. 2 B). The patient was then laid flat on an operating table. Taken the nipple as the reference point, a perpendicular line was drawn according to the horizontal distance where the quadrant of a lesion is in; a horizontal line according to the perpendicular distance was also drawn. The crossover point of the two lines represented the surface projection of the lesion. After local or general anesthesia, a small incision was made on the crossover point, generally 3–4 cm in length, or extended if necessary. From the incision site, glandular tissues stained blue were explored and excised completely. After a lesion was excised, the upper, lower, inner and outer excision margins were marked by sutures. The specimens were weighed, the incision lengths were measured, and the specimens were photographed and compared with the corresponding preoperative images to ensure the precision of excision. Subsequently, frozen sections of specimens were sent for pathological examination. Patients were correspondingly managed based on the pathological results.
Results

Suspicious lesions in all 138 patients were successful excised, with an accuracy rate of 100%. Eighty-four cases (60.9%) were pathologically diagnosed as breast cancer, among which 23 (27.4%) were intraductal carcinoma in situ, 35 (41.6%) were microinvasive carcinoma, and 26 (31%) were invasive carcinoma. The largest diameter of a tumor ranged from 0.2 to 2.1 cm, with a mean diameter of 1.2 cm. Axillary lymph node metastasis was reported in five (6.0%) cases. Fifty-four (39.1%) cases were diagnosed with benign lesions. The average weight of resected tissues was 42g (range 18–86 g). The average incision length was 4.3 cm (range 3.2–5.3 cm). Among the 84 patients with breast cancers, 41 received modified radical mastectomy, 43 received partial mastectomy plus axillary lymph node clearance or sentinel lymph node biopsy. Among the 97 patients who received partial mastectomy, including benign cases and malignant ones who underwent breast conservation therapy, a collapse of the breast at the biopsy site was reported in only five (5.1%) cases.

Discussion

Substantial progress has been made in the diagnosis for early breast cancer, even for some clinically nonpalpable malignant lesions with the development of mammographic diagnostic techniques and an increased awareness of cancer prevention. Thus, these patients are offered early treatments with satisfactory outcomes. The 10-year overall survival rate of patients with early breast cancer reaches up to 92.5%. The American Society of Therapeutic Radiology and Oncology has established breast imaging reporting and data system (BI-RADS), which classifies clinically nonpalpable lesions into seven categories, among which BI-RADS 5 is the category highly suggestive of malignancy. It is reported that the malignancy rate of category BI-RADS 5 is about 77–97%. Excisional biopsy is a diagnostic as well as a therapeutic approach for those patients, which is recommended for these patients. In our study, mammogram images of all patients were studied by both radiologists and experienced surgeons. After excisional biopsy, only five (6%) out of 84 (60.9%) patients diagnosed as breast cancer were found axillary lymph node metastases. The malignancy ratio was slightly lower than that of BI-RADS 5 category previously reported, which is possibly because of discrepancy in the preoperative diagnosis standard. The high malignancy ratio (60.9%) acquired in our study suggests that excisional biopsy should be recommended for cases who are highly suggestive of malignancy by imaging examinations.

There are a number of methods available for excisional biopsy for clinically nonpalpable breast lesions. Wire-guided excisional biopsy is safe, accurate and causes rare complications, therefore it has been generally and widely adopted. However, the localization wires may be easily bent. If the procedure is not initiated from an incision made on a puncture site of the skin, the position of the wire tip may be difficult to localize within the breast. If an incision is made on the puncture site, the procedure is more invasive and traumatic. Moreover, the cost of a localization wire is relatively expensive, and this technique is not well developed in China. Tissue dye-guided excisional biopsy for nonpalpable breast lesions was developed in the 1980’s. The advantage of this method is that it is intuitive, a lesion can removed upon tissues which are stained blue. In the past, after the injection of the dye, the puncture pathway was dyed as well with a small amount dye injected during needle withdrawal, and an incision was made along the blue-dyed puncture pathway. However, if the puncture site was rather far away from a lesion, enlarged incision wounds and trauma were inevitable, which were unbeficial for cosmetic purposes. We have applied the technique of stereotactic mammography for localization of highly suspected malignant lesions followed by methylene blue dye-guided biopsy since 2002. The vertical compression force occurs during a shot of the cranial-caudal view, and the relative vertical distance is altered while the horizontal distance is not, and vice versa, when a shot of the lateral view is taken. Therefore, we should measure the shortest distance from a lesion to the nipple according to the preoperative cranial-caudal and lateral mammographic images, and make a skin incision closest to the lesion, thus to avoid unnecessary enlarged

Figure 1. Craniocaudal (A) and lateral (B) screen-film mammograms of the breast of a breast cancer patient. (a). the horizontal distance from the lesion to the nipple; (b). the vertical distance from the lesion to the nipple.
incision wounds or removal of excessive tissues. All 138 patients in this study with nonpalpable breast lesions were diagnosed accurately. Although a few patients had diffused calcifications, their diagnosis was not affected. The mean incision length of the patients was 4.3 cm, and the shortest one was 3.2 cm. The biopsy incision sites of patients who were confirmed with breast cancer were all close to the tumor, and were resected in the following surgery. Thus possible local recurrences due to incomplete resection of the biopsy incision site could be avoided.

Blue dye diffuses fast in tissues, causing excessive resection of blue-dyed tissues, and finally results in postoperative deformation of the breast. This limits the clinical application of blue dye. Riedl et al. adopted a carbon-dye, which diffuses slower than blue-dye, to guide biopsy and reveal that the carbon-dye and wire localization show similar accuracy, but the carbon-dye method is cheaper in terms of cost-effectiveness. We suggest that the volume of injected dye is the main factor that would result in excessive blue-dyed tissues. In our preliminary studies, we injected about 1–2 ml of blue dye, which caused the excessive removal of normal tissues and breast deformation. Therefore, we modified the procedures and reduced the injection volume of the dye to 0.1–0.2 ml. The tissue boundaries dyed blue were significantly minimized. As long as preoperative localizations are precise, biopsy would be successful and would not cause breast deformation. The mean weight of resected tissues in this study was 42 g. Among the 97 patients who underwent partial mastectomy, only five patients had a collapse of the breast at the incision site due to a large volume of injected dye. Application of a reduced amount of blue dye minimizes the area of dispersion, prevents excessive resection of normal tissues, but does not compromise the precision of biopsy.

Clinically nonpalpable breast lesions, which are highly suggestive of malignancy by radiological findings, account for a high proportion in pathologically confirmed breast cancer. Excisional biopsy is recommended for these lesions. In the absence of the localization wire, stereostatic mammography with methylene blue dye-guided excision is also a desirable biopsy technique. It is a safe, cheap and relatively simple procedure with high diagnostic accuracy, which should be recommended.

References