Mammography and ^{99m}Tc-MIBI scintimammography in breast cancer diagnosis

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Abstract   The aim of this work has been to evaluate whether a diagnostic protocol based on the joint use of mammography and ^{99m}Tc-MIBI scintimammography can help to distinguish the lesions and to reduce the number of biopsies required in patients with suspected breast cancer. A total of 58 women were evaluated by palpation, mammography, scintimammography. Twenty-four patients were scintimammographed with ^{99m}Tc-MIBI at 10 min after injection. Thirty-four patients were taken double-phase scintimammography with ^{99m}Tc-MIBI 10 min and 60~90 min after injection. Based on mammography, the supicion degrees of malignancy were rated, and 30 results of malignancy were confirmed by histopathology. Based on mammography, 18 lesions were considered to be most probably benign (of which 3 were histopathologically breast cancer), 19 as indeterminate (of which 9 were histopathologically breast cancer), and 21 as malignant (of which 18 were histopathologically breast cancer). The results of early and delayed phases ^{99m}Tc-MIBI scintimammography were the same. The sensitivity, specificity and accuracy of scintimammography were 74.29%, 86.96% and 79.31%, respectively. Scintimammography gave 16 correct diagnosis in 19 mammogram indeterminate (84.2%) and demonstrated 5 out of 8 cases axillary lymph nodes metastasis (62.5%). These studies show that ^{99m}Tc-MIBI scintimammography used as a complementary testing technique to mammography is useful in the examination of patients with suspected breast cancer. The adoption of a joint mammography-scintimammography diagnostic protocol could considerably reduce the number of biopsies performed in patients with lesions of indeterminate mammographic suspicion of malignancy.

Keywords ^{99m}Tc-MIBI, Scintimammography, Mammography, Breast cancer

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1 INTRODUCTION

Breast cancer is one of the most common cancers in women. In north America and Europe, the annual incidence rate is high. There are nearly 180,000 new cases every year in US[1]. In China, as a whole country the incidence rate is lower than in US. But in Shanghai, the data is quite high. An epidemic investigation shows that the incidence rate increased from 28/100,000 to 42/100,000 during the period 1994-1998[2]. To reduce

the mortality associated with this disease, a primary diagnostic aim is to optimize the common screening methods or develop new modalities to detect carcinoma in an early stage.

Physical examinations performed by an experienced physician and radiological mammography are the first step to the woman suspected breast cancer. Many studies have demonstrated that mammography is the most effective method and is superior to physical examination alone for early breast cancer detection. But it still has diagnostic limitations, the major problems exist in the assessment of patients with dense breast tissue, unclear microcalcifications or opacities, and in differentiating between scar and recurrence. An important drawback of mammography is its relatively low specificity and low positive predictive value[3]. Mammography can not always accurately differentiate benign from malignant lesions. Consequently many mammography directed surgical breast biopsies are benign.

Recently on nuclear medicine ^{99m}Tc-MIBI scintimammography has been reported in many articles[4~8] to have a high sensitivity and specificity for the detection of breast cancer. The major goal of this study was to evaluate whether a diagnostic protocol based on the joint use of mammography and ^{99m}Tc-MIBI scintimammography would help to differentiate between the malignancy and benign lesions and reduce the number of biopsies required in patients with suspected breast cancer.

2 MATERIAL AND METHODS

2.1 Patients

We retrospectively studied 58 women (age range 28~78 years, average age 52.3 year) with a clinically palpable mass in the breast. All patients had mammography and scintimammography within 4 weeks before the surgery. Inclusion criteria were: older than 19 year, presence of a mammography abnormality with palpable mass and candidate for biopsy or surgery. Exclusion criteria were galactosemia patients, male patients, pregnancy and concomitant severe medical condition.

2.2 Mammography

The mammography was performed in all patients in craniocaudal and mediolateral oblique projections using a dedicated mammography unit, and by an experienced radiologist, who was informed about the patient's history, clinical presentation, physical examination. The results were rated as: I=most probable benign; II=indeterminate; III=high probability malignancy.

2.3 Scintimammography

We divided 58 patients into two groups. Group I (24 patients) was imaged only early phase in which imaging was carried out 10 min after the injection of ^{99m}Tc-MIBI.

Group II (34 patients) was imaged double-phase was also which another delayed phase imaging was also carried out 60~90 min after the injection of ^{99m}Tc-MIBI. The 740 MBq 1110 MBq radiopharmaceuticals was injected of intravenously in the arm on the opposite side of known breast lesion to avoid false-positive uptake in the axillary lymph nodes.

Scintimammography was performed using a gamma camera with a parallel-hole, high- resolution collimator. The energy peak was centered at 140 kev with a 20% window. Data were recorded on a 256×256 matrix. Every planar image was acquired for 10 min. An anterior view in the supine position and 30° anterior oblique of both breasts and lateral were taken. For the lateral view, the patients lay prone on a foam cushion (PBI-3 Scintimammography Pad Set produced by PINESTAR, USA sent by IAEA) in which the breast were freely dependent at the time of imaging. In all views , the arms were raised and axillary regions were included in the field of view.

All focal or multifocal uptake of radiopharmaceutical higher than the background uptake of the breast in at least one view was considered a positive result. Diffuse breast uptake was not considered to be suggestive of malignancy. In all patients, the final diagnosis was established by histopathology.

3 RESULTS

Thirty of the 58 patients had a histopathologically proven malignancy: 10 invasive ductal carcinoma, 1 intraductal carcinoma, 16 invasive lobular carcinoma, 2 lobular carcinoma *in situ*, 1 squama carcinoma. Eight patients of those had axillary lymph nodes metastasis. The size of carcinomas ranged from 6 mm to 6.2 cm in diameter, with a mean diameter of 22 mm. The remaining 28 patients had different benign lesions, including 12 fibroadenomas, 12 adenosis, 1 chronic mastitis, 2 lipoma, 1 ductal epithelial hyperplasia.

In goup I, the final histopathology diagnosis showed 12 were malignancies and 12 were benign lesions. There were 11 true-positive, 5 false-positive, 7 true-negative and 1 false-negative. The size of false-negative lesion was 0.8 cm in diameter. Scintimammography found 3 positive in axillary region. In group II, the result of two phases was the same, and the tracer washout of delayed phase was more than early phase. 34 patients scintimammography with double-phase showed 15 true-positive(2 patients were positive in axillary region) and 4 false-positive and 13 true-negative, 2 false-negative. Two false-negative cases the lesions were 0.8 and 0.6 cm. The average diameter of lesions in 35 positive cases were 2.3 cm. As whole 58 patients, the sensitivity and specificity of ^{99m}Tc-MIBI scintimammography were 74.29% and 86.96%, respectively (Table 1). ^{99m}Tc-MIBI scintimammography detected 5 patients (62.5%) had axillary lymph nodes metastasis.

In all 58 patients, mammograms were interpreted as revealing a high probability benign in 18 examinations, an indeterminate in 19 and a high probability malignancy in 21. In the 18 lesions with a high probability of benign, the pathology results indicated only 3 cases (17.3%) of malignancy. In the 19 lesions evaluated by mammography with an indeterminate, the pathology demonstrate 9 cases (47.4%) of malignancy. Eighteen of

21 lesions (85.7%) with a high mammographic probability of malignancy were diagnosed as malignancy. Scintimammography gave 16 correct diagnosis in 19 mammogram indeterminate (84.2%)). Sensitivity and specificity of mammography was calculated from 39 patients (19 indeterminate mammographies were not included, Table 1). Mammogram showed the smallest lesion was 0.6 cm and the largest lesion was 6.5 cm.

Table 1 Scintimammography with ^{99m}Tc-MIBI versus mammography

	Scintimammography	Mammography
Total	58	39
True-positive(TP)	26	18
False-positive(FP)	9	3
True-negative (TN)	20	15
False-negative (FN)	3	3
Sensitivity/%	74.29	85.71
Specificity/%	86.96	83.33
Accuracy/%	79.31	84.6

4 DISCUSSION

In the last few years, several studies have investigated the usefulness of ^{99m}Tc-MIBI scintimammography in the evaluation of patients with suspected breast cancer. This radiopharmaceutical, with its cationic charge and lipophilicity, is passively transferred across the cell membrane and concentrated in the mitochondria, making it a good marker of viable tumor tissue[4]. The overall results of these studies are , in general, good,with a sensitivity between 72%, 94% and a specificity between 84% and 94%[4,5,8−10]. In our study the sensitivity is 74.29%, specificity is 86.96%, which is similar to the above reports. On the other hand, ^{99m}Tc-MIBI scintimammography can find some axillary lymph nodes metastasis.

In our study, the FP cases were nine. Considered as possible causes of the FP results are hyperproliferative breast disorders, especially hyperplasia associated with atypia, and adenomas with high mitotic activity or local inflammation. How could we decrease the FP? We used early-phase and delayed-phase imaging in scintimammography. We presumed that the tracer uptake of malignant tumors would be persistent on delayed phase in contrast to the uptake of benign lesions, which would wash out on delayed images. Unfortunately in this study we could not see that. Lu et al[11] found that delayed-phase imaging was not beneficial for detecting breast cancer, but Abrus et al[12] using a breast prone position, found that late-phase images were optimal in detecting breast tumors. Whether double phase scintimammography is beneficial for diagnosis of breast cancer needs further investigation.

As with ^{99m}Tc-MIBI scintimammography, the major shortage for breast cancer detection is the size of the primary tumor. In this study lesions having a diameter of more than 2 cm were easily detected, but in the 3 FN cases the lesions were all smaller than

1 cm. If we excluded these 3 lesions, the specificity of scintimammography was 100%. This might be relative with equipment's resolution. To improve it, SPECT should be used. Tiling *et al*[13] found no increase in sensitivity between planar and SPECT detections performed in the same patients.

Mammography is a diagnostic technique of unquestionable usefulness in screening for breast cancer. But there is a large interobserver variability in its interpretation. The sensitivity of mammography for demonstrating breast cancer ranges between 85% and 90%, with dense breast tissue being the main cause of FN or indeterminate results. The conventional options to those patients are between biopsy and mammography again in. Confirmed the usefulness of ^{99m}Tc-MIBI scintimammography in the study of breast cancer, we believe scintimammography jointed evaluation of the results obtained by mammography in a diagnostic protocol of breast cancer do help in differentiating the lesions.

We propose that the lesions with a high mammographic suspicion of malignancy a breast biopsy must be performed. In lesions with indeterminate mammographic probability of malignancy and with a diameter >1 cm, the inclusion of ^{99m}Tc-MIBI scintimammography may have important consequences in reducing the number of biopsies. If the lesion < 1 cm in mammography, it would be biopsied or a short-term follow up.

5 CONCLUSION

^{99m}Tc-MIBI scintimammography used as a complementary technique to mammography is a useful test in the examination of patients with suspected breast cancer. The adoption of a joint mammography-scintimammography diagnostic protocol could considerably reduce the number of biopsies performed in patients with lesions of indeterminate mammographic suspicion of malignancy.

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