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WHOLE ORGAN SUBSERIAL SECTION EXAMINATION OF OCCULT BREAST CARCINOMA

Niu Yun 牛昀 Fu Xilin 傅西林 Fan Yu 范宇 Fang Zhiyi 方志沂

Tianjin Cancer Hospital and Institute, Tianjin 300060

In mastectomy specimens, the primary foci of occult breast carcinoma were usually examinated by routine histopathological method, but the result was not satisfactory. The detecting rates of primary foci were 50%-56% in China and 45%-75% in some other countries. In this study, whole organ subserial section was performed in 20 cases of occult breast cancer from April, 1988 to February, 1994. Primary foci were found in 16 cases (80%) by microscopic examination. Diameters of 10 foci were less than 1.0 cm with the smallest as 0.3 × 0.1× 0.1 cm. In addition, occult multiple foci were detected in 5 cases (31.25%), which would be very difficult to be found by routine histopathological examination. ER, PgR and monoclone M_4G_3 assays were performed for positive lymph nodes to confirm the primary foci to be breast cancer. The possible causes for the failure of detection of the primary foci by whole organ section are discussed.

Key words: Breast cancer, Diagnosis, Pathology

The diagnosis of occult breast cancer and searching for its primary foci was difficult in clinical and pathological practice.[1-3] Twenty cases of occult breast cancer who were diagnosed with positive axillary lymph nodes were examined using whole organ subserial section examination for searching the intermammary primary foci.

MATERIALS AND METHODS

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General Data

Twenty cases of occult breast cancer had underwent radical or modified radical mastectomy in Tianjin Cancer Hospital from April, 1988 to February, 1994, and its primary foci were examined by means of whole organ subserial section. All patients were female. Their ages ranged from 33 to 66 years with the mean age as 49 years. Axillary nodes enlargement was the initial symptom in 16 cases, ipsilateral superclavicle lump, 3 cases, and abdominal soft tissues metastases followed by ipsilateral axillary nodes enlargement, 1 case. The diameter of the lymph nodes were 1.0 — 6.0 cm. Poorly differentiated metastatic adenocarcinoma was identified in 16 cases lymph nodes after biopsy. Adenocarcinoma cells were found in other 4 cases by fine needle aspiration. ER and PgR were assayed in 13 cases metastatic lymph nodes by enzyme linked histochemistry, with 12 and 9 cases positive, respectively. Immunohistochemistry was used for the detection of M_4G_3 MoAb of breast cancer, and metastatic lymph nodes were positive in 8 out of the 9 cases. The results suggested that metastatic carcinoma originated or came from the ipsilateral breast. On clinical examination, all patients had no palpable breast mass. Five cases were diagnosed suspicious breast carcinoma and 4 cases, abnormal structure, by means of mammographic examination. Three of the four cases using infrared light scanning were considered as malignant tumor. No possible primary carcinoma was detected on the preoperative chest roentgenograms, upper digestive tract contrast examination, ultrasonic abdomen

examination and gynecology examination.

Procedure of Performing Whole Organ Section

It referred to Fu's report[4]: Fresh mastectomy specimen were observed and local lymph nodes were dissected. Having wiped out muscles and periphery fat tissues, complete breast specimen was frozen in -20 ℃ freezer and then cut up in slices of 0.5 cm thickness serially. Each specimen was cut into 11-28 slices and fixed with 10% formalin (48 hr), dehydrated by stepped alcohol (144 hr), saturated by paraffin (96 hr), and then embedded with paraffin. Breast tissue sections of 5-8 μm thickness were cut with lietz 1400 type large piece microtome. The sections were stained (HE method) and were observed microscopically(Figure 1).

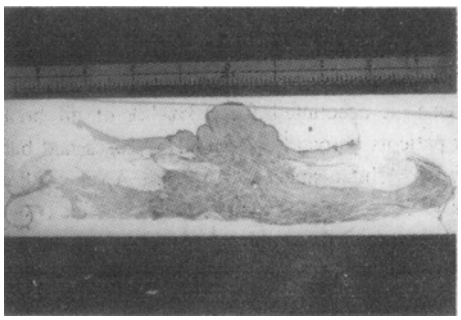

Fig 1. Whole organ section (H & E).

Detection of Axillary Lymph nodes

The mean number of axillary lymph nodes each surgical specimen was 28 (ranging from 9 to 66). The number of positive lymph nodes was: 1-3 in 7 cases, 4-7 in 2 cases, more than 8 in 11 cases.

Chemotherapy And Radiotherapy

Preoperative chemotherapy had been performed on 18 cases. Postoperative chemotherapy and radiotherapy were given to 17 and 18 patients, respectively. All cases were followed-up for 20 months to seven years.

RESULTS

Gross Observation

Two specimens contained suspicious mass, which were located at the inner lower quadrant and subareola, with 1.5 cm and 0.4 cm largest diameter, respectively. A firm region was felt in another two specimens. Nipple sunken and skin edema were noticed in 3 cases, respectively.

Microscopic Observation

Primary foci were detected in 16 cases (80%). Among them, single focus were found in 11 cases and double foci were found in 5 cases (31.25%). Pathological types of the primary foci are shown in Table 1 and Figure 2-4. The sizes of microscopic lesion were from 0.3 × 0.1 × 0.1 cm to 5.5× 1.2×1.0 cm in 13 cases. Diffuse tumor component involving entire breast was seen in the other 3 breast carcinoma. Ten foci were less than 1.0 cm in their largest diameters. No characteristics were shown in quadrant distribution of the cancer foci. Lymph-vessel involvement were observed in 7 cases. Slight to seriousobserved in 7 cases. Slight to serious

Table 1. Pathological type of primary foci and lymph-vessel involvement

Primary Foci	Pathological Type	No. of Cases	Cases of Lymph-vessel Involvement
Single	Ca. simplex	5	3
	Infiltrating ductal Ca	5	2
	Medullary Ca	1	0
Double	Ca. simplex and Ca. simplex	2	1
	Ca. simplex and infiltrating ductal Ca.	1	1
	Ca. simplex and intraductal Ca.	1	0
	Intraductal Ca. and intraductal Ca.	1	0
Total		16	7

Fig 2. Occult infiltrating ductal carcinoma focus on microscope, 0.6 cm in its largest diameter (H & E × 40)

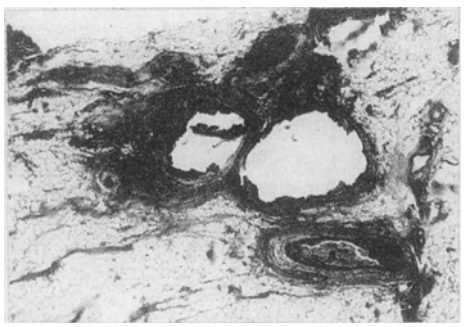

Fig 3. Occult intraductal carcinoma focus on microscope, 0.3 cm in its largest diameter (H & E × 40)

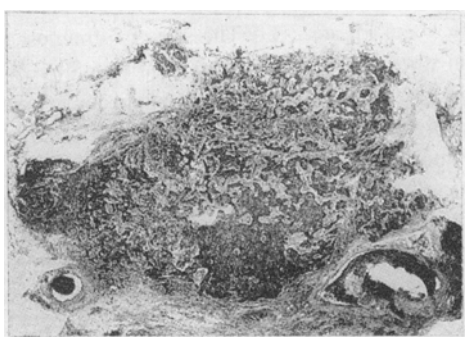

Fig 4. Occult carcinoma simplex focus on microscope, 0.4 cm in its largest diameter (H & E × 20)

papillariosis and ductalepithelium hyperplasia had been found in the 4 specimens with no primary cancer foci detected.

Follow-up Results

Of the 16 cases who had evidence of primary foci, 1 died from distance metastases 15 months later, 2 were alive with chest cavity metastases 4 years and 6 months after surgery respectively, at last follow-up and the remaining 13 patients survived disease-free at a follow-up of 20 months to 7 years after operation. Of the 4 patients who hadn't demonstrated primary foci, 2 cases died of bone and lung metastasis with 2 years. Until then, no extramammary primary focus had been discovered. Another 2 cases survived disease-free for 6 years and 2 and a half years, respectively.

DISCUSSION

Occult breast carcinoma was first reported by Halsted .[1] He drew attention to this phenomenon in 1907 under the heading of "cancerous axillary glands with nondemostrable cancer of the mamma." In his report, breast tumors developed in all three patients with enlarged axillary nodes without palpable breast masses 1-2 years before a carcinoma was detected in the breast. It accounted for 0.3%-1% of all breast cancer patients abroad.[1,2,5,6] About 60 cases had been reported in China since 1982. From April 1988 to February 1994, approximately 2500 patients with breast carcinoma have been admitted and treated surgically in Tianjin Cancer Hospital. The 20 cases occult breast cancer in this study accounted for 0.80%.

It is usually considered that axillary lymphatic metastases most frequently come from the ipsiteral breast carcinoma in female.[1,3,7] Primary site of metastatic ipsilateral superclavicle lump is much more difficult to identify. The diagnosis could be made through general examination excluding extramammary primary cancer, observation of histopathological structures of the lymph nodes matastases, ER, PgR[8] and M_4G_3 MoAb assay[2] of the lymphatic metastases.

In mastectomy specimen, the primary focus were usually difficult to be found by means of routine histopathological examination. Zhang Wenjie, et al.[3] reported 4 cases of occult breast cancer. Though breast specimens were cut in slices every 0.5 — 1.0 cm and suspicious parts were carefully chosen to make section, no primary foci was detected in total 4 specimens. Shi songkui reported[9] that only 10 out of the 20 specimens had primary foci found. The detecting rate ranged from 50%-56% and 45%-75%,[2]
in China and abroad, respectively. Such low detecting rate was not sufficient enough to prove preoperation diagnosis and conduct adjuvant therapy.

As early as in the twenties, whole organ section technique had been put into pathological examination of breast cancer. Gallager (1969) and westbrook (1971) had used this method to the diagnosis of occult and early stage breast cancer. In china, Fu Xilin, et al.(1988)[4] applied it to the research of multifocal lesion of breast cancer. In our study, 20 cases of occult breast cancer were examined by means of whole organ subserial section. Primary focus had been showed in 16 cases (80%). The detecting rate of the primary focus had been improved to the highest level ever reported in literature.

Our results indicated that whole organ section was of great value for pathologist in the detection of occult breast cancer. Its prominent merit was the high detecting rate of primary focus. As for foci less than 1.0 cm in diameter, tumor located in the depths of the breast, tumor tissues randomly infiltrating that didn't form solid mass, this method was a great help in establishing diagnosis.

While the detecting rate was very low with routine histopathological method, with the whole organ subserial section, multifocal occult breast cancer could be detected with ease. In our study, 5 cases (31.25%) were demonstrated as double primary foci, similar to the incidence of 40%-45% reported by Schwartz (1978), Deziel (1984), Baron (1990).[1] Most of the multifocal cancer were subclinical microscopic lesions which would be missed easily and frequently with routine section. However, whole organ section is better to solve this problem.

In addition, whole organ subserial section had the advantage of accurate location of original foci, correct diagnosis of its histopathological type and easy observation of lesions in the pericancer focus as well as histopathological changes in other quadrants.

Of cause, this method still have some limitations: 1) The detective rate could not come up to 100%. 2) It's cost was higher than that of routine section's. 3) Skillful technique was needed to make section. In our study, 4 primary foci had not found by means of this method. The possible causes for the failure to confirm the presence of primary breast cancer might be: 1) Specimens were cut up slices of 0.5 cm thickness, and tumor less than 0.5 cm in diameter might have been left out. 2) Owing to the large histological blocks made (some reaching 10.5× 4.5 cm), the small focus may be cut off in the preparation of the largest section. 3) As a result of preoperative chemotherapy for 2-3 courses, cancerous cells might obviously degenerate in some sensitive cases and were beyond recognition.

we agreed with the viewpoint of most scholars that treatment should continue as breast cancer, in case of no primary foci found in breast.[7,10] Positive result of ER, PgR, and anti-human breast cancer monoclonal antibody on the metastatic lymph nodes could help in further confirming the diagnosis of breast primary cancer.[1,2] The 4 such cases in our study have been treated as breast cancer and followed-up for 2-6 years. Primary foci from other parts of the body had not been discover and further observation were needed.

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