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ORIGINAL ARTICLE

Fine-needle cytology in the follow-up of breast carcinoma

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Abstract The postoperative follow-up strategies for breast carcinoma (BC) utilize different procedures; the aim of this study was to investigate the role of fine-needle cytology (FNC) in the follow-up of BC patients. Two hundred sixty-six FNC samples from 190 BC patients have been reviewed. The target anatomical sites were 190 breast including 155 ipsilateral and 145 contralateral breast lesions and 76 extra-mammary nodules. Extra-mammary lesions included lymph nodes, thyroidal nodules, soft tissue lesions, (subcutaneous and sub-scars), salivary glands and deep located masses. Diagnostic distribution of the breast lesions was as follows: 51 positive, 15 indeterminate/suspicious, 119 negative and 5 inadequate. Positive cases included 43 ipsilateral and 8 contralateral BC, 9 BC in different quadrants from those of onset of the first BC. Sensitivity, specificity and accuracy have been 90, 91 and 90&, respectively. FNC, in a correct setting, is a reliable and effective method for the follow-up management of BC patients.

Keyword Fine-needle cytology · Follow-up · Breast carcinoma

Introduction

According to the National Comprehensive Cancer Network (NCCN) 2010 [1], the postoperative follow-up strategies for breast carcinoma (BC) utilize breast self-examination, clinical examination by specialists every 4–6 months for 5-years and mammographic imaging (RX) every 12 months; breast ultrasound (US) [2] is also conveniently associated with this follow-up procedure. The target of this follow-up is the omolateral breast as possible site of relapse and the contralateral one because of a higher risk of BC in these patients. As for the diagnostic value of any clinical and or instrumental finding on the corresponding patients, the level of attention is generally higher than those deserved to patients with a negative history for BC. Moreover, despite the quite standardized procedures for much of the imaging breast entities, in clinical practice, a direct evaluation is often requested also for mammary and extra-mammary reasonably benign images that should have not been further investigated in patients with a negative history, other than for clearly suspect lesions. In the last years, core needle biopsy (CN) has replaced fine-needle cytology (FNC) in the diagnosis of breast tumors in many institutions. Nonetheless, FNC is still used in many others with comparable levels of sensitivity and specificity [3–11]. Moreover, FNC is less expensive and invasive than CN and is associated with lower complication rate [3–11]. The diagnostic value of FNC is also enhanced by the immediate on-site evaluation (ROSE) of specimens that allows to give immediate reassurance to patients with no recurrence or contralateral BC avoiding unnecessary open biopsy and a timely management of those with suspicious or malignant lesions [2–4]. In addition, FNC allows the direct evaluation of extra-mammary nodules or masses, as lymph node, lung or thyroid nodules that may appear in the course of follow-up [3, 4]. The aim of this study was to assess the role of FNC in the follow-up of BC and to highlight its value when it is closely integrated to the clinical and radiological data.

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Materials and methods

The study was retrospectively performed; from the files of the Pathology Service, "San Giovanni di Dio e Ruggi d'Aragona," University of Salerno, 266 cytological samples from 190 patients, previously treated for BC, in the 6-year period 2010–2015 were retrieved. In all patients, the primary diagnosis of BC had been histologically proven. The series accounts for 188 women and 2 men with a median age of 58.3 years (raging from 26 to 88). The site of the primary tumor was the left (104 cases) and the right (86 patients) breast, including 3 metachronous and 4 synchronous bilateral BC. The new location appeared after a median time of 59.4 months (range 264–246) from the initial histological diagnosis of BC (Table 1). The target anatomical sites were 190 breast and 76 extra-mammary nodules, including 155 ipsilateral and 145 contralateral breast lesions. Extra-mammary lesions included 38 lymph nodes (23 axillary, 8 supraclavicular, 4 cervical, 3 inguinal), 13 thyroidal nodules, 11 soft tissue lesions, represented especially by subcutaneous and sub-scar chest wall nodules, 2 salivary gland nodule and 13 deep located masses (9 lung, 2 liver, 1 adrenal gland, 1 kidney). FNC of mammary and extra-mammary nodules was performed US- or CT-guide in the outpatient office of the Pathology Department or in the Radiology Department by cytopathologists or in the Surgery Departments by clinicians. In all cases (except FNC performed by clinicians), the first smear was immediately stained by Diff-Quik and on-site evaluated for adequacy (ROSE); the second smears were fixed in alcohol at 95° and stained with Papanicolaou stain. ROSE of positive cases oriented the application of ancillary techniques on additional smears and cell blocks. Cytological diagnostic categories were as follows: positive for malignant cells consistent with BC (C5) or with another neoplasm, indeterminate/suspicious (C3–C4), negative with or without specification (C2) and inadequate (C1) [4]. Histological or follow-up controls were available in 120 cases. Sensitivity and specificity were calculated.

Results

Diagnostic distribution of the breast lesions was as follows: 51 positive, 15 indeterminate/suspicious, 119 negative and 5 inadequate (Table 1). The positive cases included 43 ipsilateral and 8 contralateral BC, 9 BC in different quadrants from those of onset of the first BC (Table 1). As far as the diagnostic distribution of extra-mammary FNC, 38 lymph node, 9 lung, 2 liver, 1 thyroidal metastases and 1 peritoneal and 6 soft tissue infiltration by BC were detected. In 2 lymph nodal and 1 lung FNC, metastases from ER-negative poorly differentiated carcinoma were diagnosed (Fig. 1). Second malignancies were diagnosed in 2 cases concerning inguinal lymph nodes involved by B cell, non-Hodgkin lymphoma and by ovarian carcinoma. Data concerning extra-mammary FNC in BC patients are summarized in Table 2. The positive cytological diagnoses were confirmed by histological examination in all the cases. In 15 breast FNC, diagnosed as C3 (8 FNC contralateral BC) and C4 (7 ipsilateral BC and 1 contralateral BC), only for 10 cases histological controls were available. Subsequent histological examination of indeterminate/suspicious revealed BC in 4 cases, and benign proliferation in 6 cases. Fifty-nine out of the 119 negative FNC were histologically controlled and revealed 9 fibroadenoma, 15 nonproliferative and proliferative fibrocystic changes without atypia, 29 post-biopsy changes, 6 steatonecrosis, 1 ductal ectasia and 31 unspecific. Two false negative were also detected represented by sub-scar BC relapse (Table 2). As far as the extra-mammary FNC in BC patients, 45 negative FNC were represented by 20 reactive lymph nodes (Fig. 2) , 13 goiter and 1 chronic thyroiditis, 4 granuloma, 1 lipoma, 5 inflammatory and 1 amartoma of the lung, 2 nodular steatosis of the liver, 2 pleomorphic adenoma of the parotid. Positive cases were 27 BC metastases, 2 non-Hodgkin lymphoma (NHL) and 1 lymph node metastatic ovarian carcinoma. Eight negative cases were histologically controlled and confirmed negative in 6 cases and diagnosed as false negative in 2 cases of lobular BC recurrence. The remaining negative cases were confirmed

Table 1 Fine-needle cytology of mammary nodules in the follow-up of 190 breast cancer patients

FNC	Ipsilateral	Contralateral	Histological controls	Total
Positive (C5)	43	8	51 BC	51
Negative (C2)	100	19	52 negative, 3 false negative	119
Suspicious (C3–C4)	12	3	4 BC, 11 negative	15
Inadequate (C1)	3	2	5 negative	5
	158	32		190

BC breast carcinoma

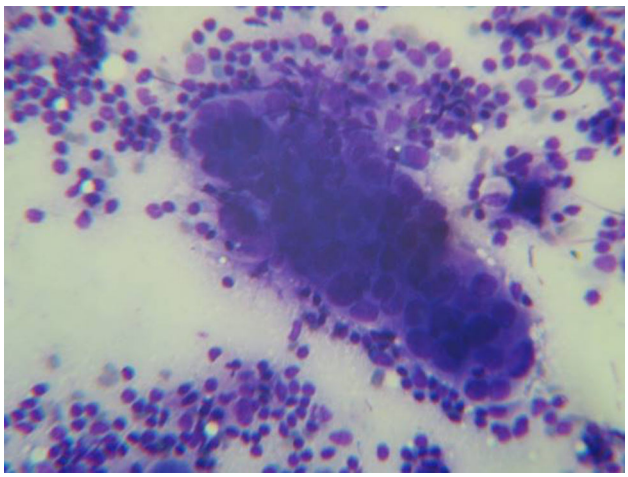

Fig. 1 Lymph node breast carcinoma metastasis FNC showing a group of malignant ductal cells with lymphocytes in the background (Diff-Quik stain 430×)

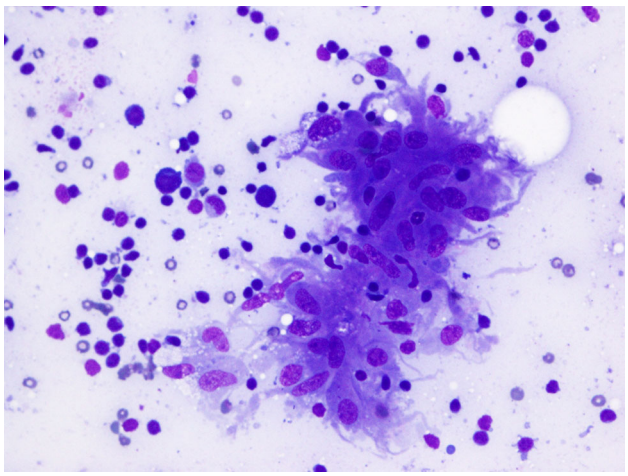

Fig. 2 FNC of a breast nodule suspected to be a carcinoma relapse showing epithelioid cell in granulomatous arrangement (Diff-Quik stain 430×)

by subsequent clinical and instrumental follow-up, which assessed not changes of the original lesion. Inadequate cases concerned the breast (1 BC and 1 contralateral BC), 2 axillary lymph nodal and 1 wall chest nodule metastases. All inadequate cases [5] were breast FNC performed by clinicians. Sensitivity, specificity and accuracy were then calculated with the following results: 90, 91 and 90&, respectively.

Discussion

Fine-needle cytology is a robust and effective diagnostic procedure that is used in different organs and pathologies including breast pathology [3–11]. Nonetheless, in the last decade the using of FNC in BC screening has gradual declined and the CN is used as alternative method for the evaluation of breast lesions [6]. The major limitations of FNC are represented by the operator dependence, a lightly lower sensitivity and the impossibility, respect to CN, to distinguish in situ from invasive BC. This distinction is important at the time of the first diagnosis, as it allows a single-step operative procedure that includes a sentinel lymph node biopsy for invasive BC; but in the BC follow-up, other information may be necessary. FNC is a noninvasive and cheap technique with fast turnaround time, well tolerated by the patients [7]; these advantages may be exploited for the early detection and treatment of locoregional relapse, contralateral BC and lymph nodal or distance metastasis in BC follow-up. Moreover, these advantages are enhanced in case of patients suffering from additional pathologies that absorb much of the attention and cares [11–35]. As reported above, the accuracy of FNC is related to the operator's experience and the presence of specialized cytologists [2, 3]. In fact all the inadequate cases of the present series were performed by clinicians.

Table 2 Extra-mammary fine-needle cytology in the follow-up of 76 breast cancer patients

Target	Negative	Positive	Suspect	Total
Lymph node	20 (reactive)	18 (15 BC metastases, 2 NHL, 1 ovary carcinoma metastasis)	0	38
Thyroid	13 (goiter)	1 (BC metastasis)	0	14
Soft tissue*	4 (3 granuloma, 1 lipoma)	5 (BC relapses)	2	11
Lung	6 (1 amartoma, 5 inflammatory cells)	3 (BC metastases)	0	9
Liver	2 (nodular steatosis)	1 (BC metastases)	0	3
Adrenal gland	0	1 (BC metastasis)	0	1
Salivary glands	2 (pleomorphic adenoma)	0	0	2
	45	30	2	77

* Under scar tissue

Conversely, inadequate FNC performed by cytopathologists was immediately repeated, re-evaluated and distributed in the corresponding diagnostic categories. However, the inadequate rate of this series was 1.9%, so far less than QC (breast cancer quality performance indicators) indicators for FNC results (inadequate rate: <20%) according to the QC indicators [1] for FNC results of NHS breast screening programme. FNC has also been used, by the use of cell block preparation, for the assessment of prognostic factors and predictive biomarkers such as estrogen and progesterone receptors and HER-2/neu oncogene [8]. Small sample size and sampling issues limit the ability of FNC to reliably diagnose specific breast pathology entities; these entities include atypical ductal hyperplasia, low-grade ductal BC, lobular BC, papillary lesions and atypical sclerotic lesions [9]. In particular, lobular BC shows predominantly dispersed, isolated, small- to mid-sized tumor cells and stromal fibrosis. This characteristic expression pattern may also be observed in metastases and in sub-scar recurrences creating problems of sampling and differential diagnosis. In fact both our two false negatives (sub-scar right wall chest nodules) were lobular BC. In the first case, the sample was composed almost exclusively of hyaline stroma; in the second case, diagnosed as proliferative fibrocystic changes (C3), the review of the slides showed only a few clusters of cells with mildly enlarged nucleus and occasionally showed atypical isolated, epithelial cells that were underestimated. The revision of suspected case, not confirmed by histology, showed cohesive groups composed of cells with enlarged nuclei with small, distinct nucleolus, which were over-estimated. In conclusion, data from the current study indicate that FNC, in a correct setting (expert operator in breast cytology and sampling techniques associated with the on-site evaluation of FNC specimens), is a reliable cost-effective method for the follow-up management of breast cancer patients.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Statement of human and animal rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this type of study formal consent is not required.

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