

Misleading Presentations of Malignant Breast Diseases – Role of Clinical Cytology

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ABSTRACT

We described two examples with misleading presentations to draw attention to the role of clinical cytology as a part of multidisciplinary approach to breast lesions. In the first case – Paget's disease of the nipple, there was no obvious clinical and radiological evidence of breast cancer, while the second case – primary non-Hodgkin lymphoma of the breast imitated advanced breast carcinoma. The question is whether accurate and fast diagnoses can be made without cytological examinations. It must be kept in mind that first-hand clinical information and contact with the patient is necessary in rendering accurate cytological diagnoses.

Key words: breast diseases, breast neoplasms, clinical cytology, diagnosis

Introduction

Neoplastic breast lesions are complex diseases requiring the collaboration of a number of health disciplines for their diagnosis, treatment and follow up. In diagnostics, the combination of clinical examination, breast imaging and cytological or other tissue diagnosis (triple test) achieves a high level of accuracy. Full and careful clinical examination has been permanently emphasized as well as the exchange of information between the physicians involved. However, this is not always sufficient. Cytology has become a well-established diagnostic tool¹ consisting of two aspects – exfoliative and aspiration cytology. In case of breast cytodiagnosics, the exfoliative component served for the assessment of nipple discharge and scarification of suspected skin lesions. Fine needle aspiration is used for every palpable or non-palpable lesion which can be visualised by radiological techniques (ultrasound and mammography). Examination of enlarged regional lymph nodes is also an essential part of this diagnostic procedure. Cytodiagnosis is accurate, simple, fast, non-invasive, and cost-effective. But, the quality of cytological diagnoses is highly operator dependent and relies on correct clinical information^{2–5}. This implies adequate education and the cytologist's experience on cytomorphology of a number of organs and tissues to recognise and diagnose both common and rare diseases. Furthermore,

cytology is not only a laboratory discipline and the term »clinical cytology« includes implicit contact with in-patients and outpatients. First hand information about the patient's history and physical examination, self-handling of the material for analysis, rendering the decision for repeated sampling and close cooperation with the radiologist and other members of the team enables taking into consideration clinical and radiological, not only microscopic findings. The following two examples demonstrate the importance of such an approach.

Case 1

A forty-six-year-old female with no palpable breast mass, with normal mammography and ultrasound findings came for a regular control. A few months ago, she had left-sided breast nipple discharge. It was from one duct, very scanty, and dark coloured. At that time cytological examination of the discharge found no cells at all. At the follow-up examination there was no discharge. But careful physical examination revealed hardly noticeable shallow erosion of the left nipple (Figure 1). In scarification smears of the erosion we found single cells with large hyperchromatic nuclei and moderate amount of



Fig. 1. Case 1 – Shallow erosion of the nipple.



Fig. 3. Case 2 – Enlarged and deformed right breast.

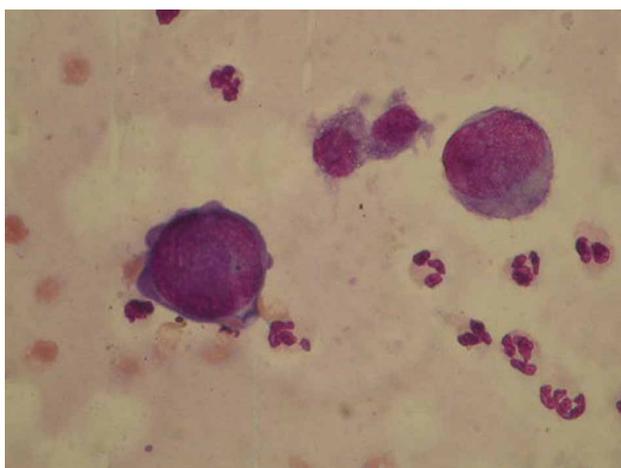


Fig. 2. Case 1 – Malignant epithelial cells in scarification smear (MGG, x 1000).

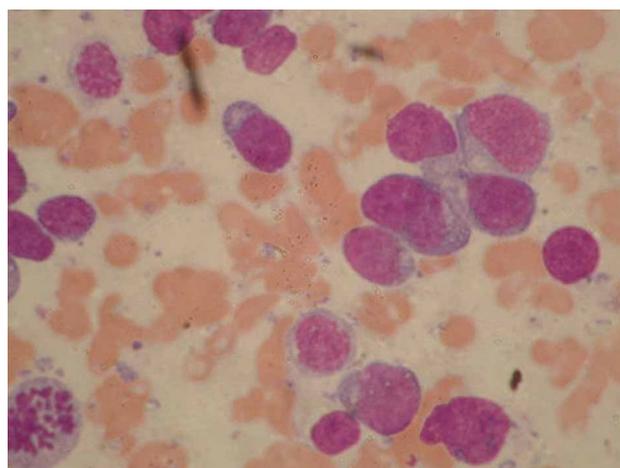


Fig. 4. Case 2 – Numerous atypical lymphoid cells (MGG, x 1000).

the cytoplasm. Neutrophils, histiocytes and peripheral blood were found in the background (Figure 2). Given the typical clinical and cytological features, the diagnosis of Paget's disease was rendered. Histologic examination of the excised nipple with areola and subareolar breast tissue found intraductal carcinoma in situ with one cluster of malignant cells close to the basal layer of the skin. Surgical management was followed by irradiation of the entire left breast.

Case 2

A sixty-seven-year-old female was referred from her general practitioner to the surgeon because of a very large, palpable right breast mass (Figure 3). Although the surgeon had no doubt about the malignant nature of the lesion based on its clinical appearance, he wanted a cytological consultation. On palpation, the breast was elastic and smooth with swollen skin and large haemorrhagic blisters in the lateral parts. Axillary lymph nodes were not palpable, and no abnormality in the left breast

was found, a fact subsequently confirmed radiologically. During the procedure, the needle penetrated the lesion without resistance and haemorrhagic yield was obtained by aspiration. In the smears of the aspirated material, necrotic debris with numerous picnotic and a few preserved cells were present. Fine needle aspiration was repeated several times at different locations of the affected breast until adequate material was observed. In those highly cellular aspirate smears we found well preserved atypical lymphoid cells. The cells were intermediate and large sized with rounded, sometimes eccentrically situated nuclei and with a moderate amount of basophilic cytoplasm. The nuclei had a fine dense chromatin structure and multiple irregular nucleoli. (Figure 4) Immunocytochemically, the cells were positive for LCA (leukocyte common antigen) and CD 20 (marker of B-cell differentiation). Immunostaining for cytokeratin and CD 3 (marker of T-cell differentiation) was negative. The cytological diagnosis was large cell B-cell non-Hodgkin lymphoma. Subsequent histologic examination of an open biopsy specimen confirmed this diagnosis. The further staging ascertained breast as a primary localisation of lymphoma,

and therapy was initiated according to the haematologic protocol.

Discussion

Paget's disease is a particular form of ductal carcinoma accompanied by involvement of the nipple epidermis and accounts for less than 5 percent of all breast cancers. Microscopically, the nipple epidermis is infiltrated by large ovoid or round cells with occasionally hyperchromatic and irregular nuclei. Cytoplasm are abundant and clear. The cells are isolated or constitute small clumps usually located in the deeper layers of the epithelium⁶. The early detection of the disease carries a more favourable prognosis and makes breast conserving surgery possible⁷. In most cases, at this stage the carcinoma is not noticeable by palpation or by radiological methods, so patients with any nipple complaints deserve a detailed evaluation⁸.

Primary lymphomas of the breast are rare and represent less than 1 percent of primary malignant breast neoplasms. Breast lymphomas may be divided into two distinct clinicopathologic groups. One group, that affects younger patients and is associated with pregnancy or lactation, presents with bilateral breast involvement and has a rapidly fatal clinical course. The second group affects older women with unilateral breast disease and has a variable clinical course. Virtually all breast lymphomas are of B-cell origin. The morphology of cells depends on the type of the particular lymphoma. The appropriate treatment is chemotherapy and/or radiotherapy^{8–10}.

There is a striking difference between these two cases in their clinical presentation, but there is similarity because both of them can be misleading. In the case of Paget's disease, no certain sign of malignancy was found. Unilateral, dark coloured discharge from the nipple is very important, but was not present at the moment of examination. Other clinical and radiological findings were also normal. The small, shallow erosion of the nipple skin made an impression of a harmless tiny wound. Nevertheless, scarification of the lesion was done and malignant cells were found by cytological analysis of the smear. If the lesion had been overlooked or if the material for analysis had been inadequate and sampled in an inadequate way, the beginning of treatment would have been delayed.

In the case of primary non-Hodgkin lymphoma all clinical and radiological findings led to the conclusion of advanced breast carcinoma. Adequate material for cytological analysis was obtained after several attempts. This also helped to determine the proper location for open biopsy. Atypical lymphoid cells, which were found in the adequate aspiration smears, pose no diagnostic problem because at our department we perform cytodiagnostics of all organs and tissues. The patient was spared from unnecessary mastectomy and exploration of axillary lymph nodes with accompanying complications.

The accuracy of cytological diagnosis considerably depends on the cytologist's competence and on the quality of clinical data. In the diagnostic settings, cytodagnosis gives more information, but in certain cases, this is the only proper information about the patient.

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ZAVARAVAJUĆE PREZENTACIJE MALIGNIH BOLESTI DOJKE – ULOGA KLINIČKE CITOLOGIJE

SAŽETAK

Opisali smo dva primjera zavaravajućih prezentacija bolesti dojke da privučemo pažnju na ulogu kliničke citologije kao dijela multidisciplinarnog pristupa bolestima dojke. U prvom slučaju Pagetove bolesti bradavice dojke, klinički i radiološki se ne uočavaju znakovi karcinoma, dok drugi slučaj primarnog non-Hodgkin limfoma, imitira uznapredovali karcinom dojke. Upitno je bi li se brzo došlo do točnih dijagnoza bez citološke pretrage. Uz to, treba imati na umu da su neposredne kliničke informacije i kontakt s bolesnikom preduvjet za ispravnu citološku dijagnozu.