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ORIGINAL ARTICLE

Problems in diagnostics of breast diseases

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Summary

Background: The aim of the study was to determine the diagnostic problems encountered in breast diseases, their causes as well as the methods of the procedure in such cases.

Material/Methods: Clinical and mammographic examinations were conducted in 5445 women aged 35–70 years. The patients were divided into 3 groups: group I comprised 4200 patients after screening (aged 50–69 years), group II – 915 (aged 40–49) and group III – 330 high-risk patients. Additional sonomammography was performed in 336 women (8%) in group I, 192 (21%) in group II and on all the patients in group III.

Anamnesis, palpation, mammography (MMG) in 2 projections and magnified X-rays were performed. In cases of an unclear image the following procedures were undertaken: sonomammography (USG), fine needle aspiration (FNA), mammotomy and surgical biopsy

The MMG and USG images were evaluated in BI-RADS scale. The false positive and false negative results were established.

Results: In group I, 228 FNA biopsies (5.4%) were carried out, 55 cancers (1.3%), 32 false positive, 5 false negative radiological results were diagnosed. In II group 21 women underwent FNA, false positive radiological diagnoses occurred in 14 cases. In group III comprising 60 women who had undergone FNA, 18 cancers were observed. These proved false positive diagnosis in 8 cases and false negative in 4 cases.

It was found, that the most common reasons for error were due to dense cysts displaying with irregular outlines and microcalcifications accompanying hormonal dysfunction. The displacement of tumors near the pectoral muscle or the nipple also interfered with establishing the correct diagnosis.

Conclusions: The diagnostic problems can be due to the inherent limitations of the methods, the physical nature of the breast and localization of the changes. The diagnosis of the benign process should be established on the basis of radiological, cytological and histopathological methods. The radiologically unclear changes should be diagnosed with the use of FNA/ core biopsy, mammotomy or surgical biopsy. In cases of hormonal dysfunctions and during the conservative treatment, follow-up after 6 months is suggested.

Key words: diagnostics • problems • breast diseases

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Background

Standard diagnostics of breast diseases is based on clinical examination, mammography (MMG) and/or complementary ultrasonography (USG), depending on the patient's age. USG is performed in young patients, whereas MMG is recommended for patients over 40, and in high risk group over 35 years of age [1]. Focal changes are subjected to cytological evaluation on fine needle aspiration biopsy (FNA) or histopathology based on core needle biopsy, mammotome

Table 1. Number of women, sonomammographies, FNA biopsies and breast cancers depending on the examined group.

Group	Number of pts	Number of USG	Number of FNA	Number of cancers
I.	4200	336 (8%)	228 (5.4%)	55 (1.3%)
II.	915	192 (21%)	21 (11%)	0
III.	330	330 (100%)	60 (18%)	18 (5.45%)

(MMT), or surgical biopsy [2]. Centers equipped with magnetic resonance imaging (MRI) use this method in dubious cases, especially when the results of physical examination and other diagnostic methods are unclear [3].

All of these methods have specific advantages and limitations, which, in turn, makes the radiologist's decision very important for the further course of the patient.

The aim of the paper was to present the cases which may be difficult to diagnose by imaging techniques, to attempt the analysis of their causes and to recommend the further methods and procedures to be used.

Materials and methods

In 2005 and during the first 9 months of 2006, 5445 women aged 35–70 years, including 4200 entitled to screening for breast cancer (50–69 years), and 915 aged 40–49 years taking advantage of a preventive program sponsored by the Municipal Administration Office in Szczecin „Healthy breasts in 40-year-olds" underwent clinical examination and mammography; 330 women were patients treated in the Outpatient Department of Genetics of the Pomeranian Medical University in Szczecin. Complementary USG was performed in the screening group on 336 (8%) cases, in the group of 40-year-olds in 192 (21%) and in the risk group in all the patients – in half of the cases 6 months after MMG.

Each subject completed before the examination a questionnaire with personal information and anamnesis, according to the model form recommended by the National Health Fund (NFZ). Palpation examination was carried out by a physician, who instructed the patients how to perform self-examination of the breasts and axillary lymph nodes on that occasion Then the women underwent mammography in 2 projections, performed according to the commonly accepted standards. Targeted images and zoom images with pressure applied were obtained for better visualization of suspicious lesions.

USG was performed with a linear 7.5–12 MHz head according to commonly accepted procedure. USG of the thyroid was additionally performed in all women diagnosed with benign or malignant breast diseases.

MMG and USG images were assessed according to BI-RADS scale (Breast Imaging Reporting and Data System) [1, 4]. The MMG apparatus and image evaluation procedures were subject to quality control tests.

USG-guided mammotome biopsies were performed in 22 patients with BI-RADS 3 and 4 using 11 and 8 G needles.

MRI was not performed because of lack of the appropriate equipment in West Pomerania region.

In case of USG abnormalities suspicious of pathologic process (cysts, solid tumors), FNA was performed, and in those of over 5-month duration, mammotome biopsy, and in case of lesions invisible under USG – sterotaxic MMG-guided wire placement. Additionally, patients with BI-RADS 3 and 4 microcalcifications invisible under USG were referred for MMG-guided mammotome biopsy performed in the Regional Oncology Center in Szczecin – the number of such procedure was limited for economic reasons.

The breast structure was assessed on imaging as lipomatous, lipo-adenomatous, adeno-lipomatous, and "dense" adenomatous. Image interpretation was described according to the model presented in NFZ forma, and in the comments section recommendations concerning accessory investigations, further management and active treatment were given.

Results

Problems encountered during imaging diagnostics procedures were due to:

1) difficulties in carrying out the procedure – small or very large breasts, condition after implant surgery

2) dubious interpretation of the image

3) difficulties in decision-making concerning further diagnostic and therapeutic management

Table 1 lists the number of USG examinations and biopsies in all three patient groups compared with the number of cancer diagnoses. It shows that most USG examinations, in proportion to the number of patients, were performed in the risk group and in „40-year-olds", the lowest number in the screening group. It was associated with more „dense" breast tissue structure in younger women as well as with the special „vigilance" in case of Genetics Department patients.

Table 2 presents the number of patients as well as the false positive and false negative diagnoses in the examined groups. MMG and USG findings suspicious of cancer (BI-RADS 4), which proved to be benign lesions in FNA, MMT and surgical biopsy were regarded as false positive, and lesions diagnosed as BI-RADS 2 and 3, found on FNA, MMT and surgical biopsy to be cancers – as false negative results. In "difficult to interpret" MMG and USG images, adenomatous or lipo-adenomatous breasts with signs of mastopathy, distorted architecture and "dense" cysts

Table 2. Histopathological results of malignant tumors in the examined groups of patients.

Histopathologic diagnosis	Number of pts	
	Group I	Group III
1. DCIS	14	2
2. CDI	20	4
3. Ca medullare atypicum	5	2
4. Ca lobulare invasivum	12	2
5. Ca in fibroadenoma	2	1
6. Ca tubulo-lobulare		1
7. Tumor cells in FNA	2	6
Total	55	18

Table 3. Number of false positive and false negative diagnoses in the examined groups.

	Number of diagnoses	
	False positive	False negativee
Group I	32 (0.76%)	5 (0.12%)
Group II	14 (1.53%)	0
Group III	8 (2.42%)	4 (1.21%)

Note: The percentage was calculated in relation to the number of examinations in the particular group.

with irregular contours and heterogenous echostructure were predominant. Microcalcifications among mastopathic lesions aroused diagnostic doubts, especially if found in control MMG images with no previous diagnosis of hormonal dysfunction.

Discussion

The essential task of prophylactic control examinations, including screening, is detection of cancer at an early stage. The group which benefits most from such examinations are premenopausal women, in whom hormonal dyfunctions of thyroid and ovaries are the underlying conditions associated with breast diseases [5]. They may coexist with breast cancer and sometimes they can cause it as well.

Mammography is associated with technical problems in men, women with very small breasts or very large ones which do not fit the 24 x 30 cm tray, or in patients with chest deformation [6, 7]. Changes in the ribs and sternum may project on mammography film mimicking tumor foci located deep close to the thoracic wall (fig.1a, 1b, 1c) or some projections may "fail to cover" the whole mammary gland area. In such cases, the findings may be verified by palpation and USG. Tumors located peripherally (fig. 2), directly on at the borderline with the skin, deep in the vicinity of the thoracic wall, may also be difficult to visualize [8]. Patients with mastalgia demonstrate guarding against compression applied during mammography, which leads to „dense" images causing diagnostic problems especialaly in adenomatous breasts. Sclerosing adenosis accompanying diseases of the thyroid gland is one of such examples (fig. 3a, b, c). Appropriate treatment of the thyroid and hyperprolactinemia leads to alleviation of painful symptoms and change in breast „density" as well as improves the conditions for compression on mammography [9,10].

Condition after implant mammoplasty also makes it necessary to reduce compression to prevent damage of the prosthesis. Thus, the mammary gland is either obscured by the implant or the compression of the visualized part is too weak. USG is much more useful and easier to perform in women after mammoplasty, because the head can be applied at various angles (fig. 4) [11].
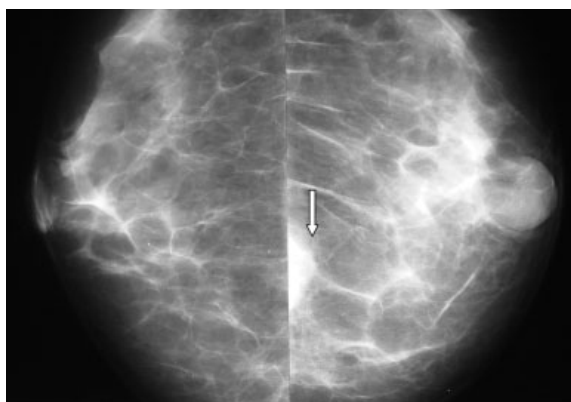

Figure 1 A. Mammogramms of both breasts in c-c projection. The shadow visible as a tumor at the wall of the thorax on the left side.
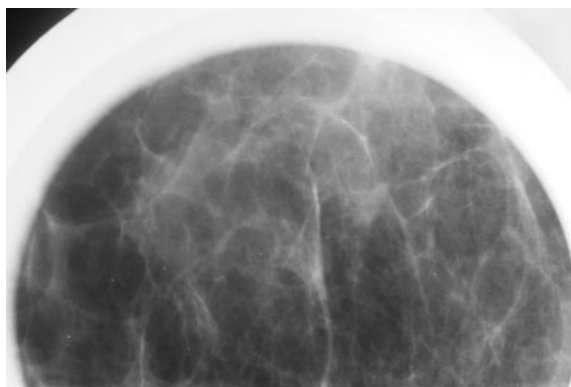

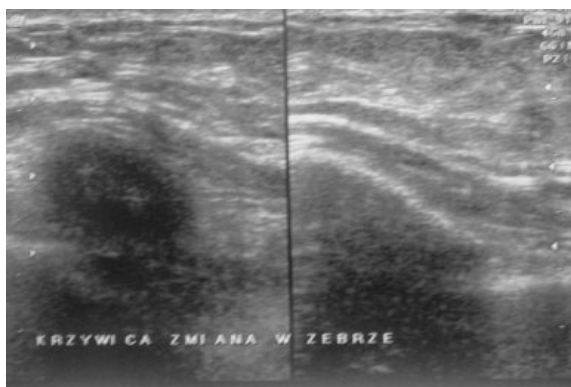**Figure 1 B.** Magnified X-ray targeting the suspicious region revealing no changes.

Figure 1 C. Sonomammography image of the left breast – post-rachitic changes in the vertebra, breast image normal.
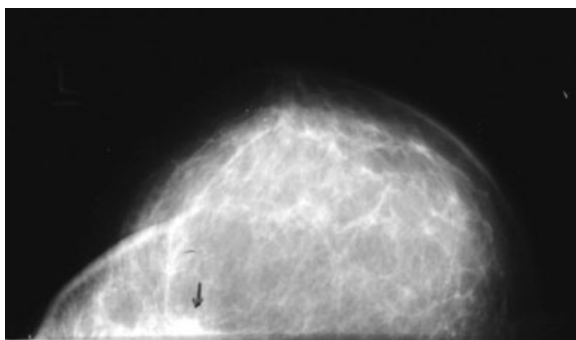
Figure 2. Mammography image in c-c projection, malignant mass located at the thoracic wall, where only part of the tumor and thickened skin are visible.

In young women, cancers are usually due to gene mutations and the prognosis is much worse than in older patients [12]. They also present many diagnostic problems, because lesions seemingly „benign" turn out to be malignant in 40% of cases [12]. In our material, we noted such a situation in 4 patients from the risk group, whose lesions were assessed as benign, whereas on FNA malignant tumor cell sere found. On the other hand, lesions suspected to be malignant in 8 women were not diagnosed as such on FNA and surgical biopsy; apocrine metaplasia, adenosis sclerosans and fibrocystic mastopathy were diagnosed. The lesions were dense cystes and mastopathic changes with clusters of microcalcifications. As it follows from the studies carried out in cooperation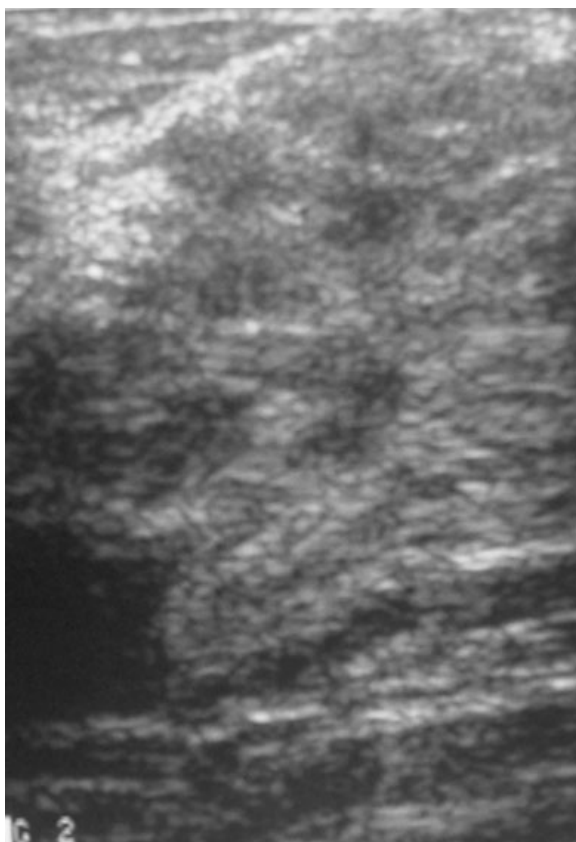 with the department of Genetics and Pathomorphology, in women with BRCA1 and 2 gene mutations lesions appearing as benign in radiological images demonstrate sometimes signs of malignancy in cytologic smears and histopathologic investigations; correlation between the results of radiodiagnostics and histopathology is found in ca. 60% of cases (fig. 5). Also the literature describes atypical USG and MMG findings in women with genetic predispositions for breast and/or ovarian cancer, recommending MRI as the most reliable method [13]. For this reason, the treatment of all focal lesions in the high risk group involves radical surgery.

Similar problems with breast tissue assessment were encountered in the group of women aged 40–49, whose dense, adenomatous breasts are often due to hormonal dysfunctions, hormonal treatment, and, as a result, present "atypical" MMG and USG images [9, 14]. Diagnosis of lesions based on MMG only is unreliable; USG, used as a complementary diagnostic technique also does not always give unequivocal results, especially in women examined for the first time.

Diagnostic "hypersensitivity" may also be associated with more and more demanding attitudes of the patients. Unfortunately, there are only a few centers in Poland which can offer free prophylactic programs for women aged 40–49. Transferring the responsibility for financing these procedures to oncologists or gynecologists has considerably
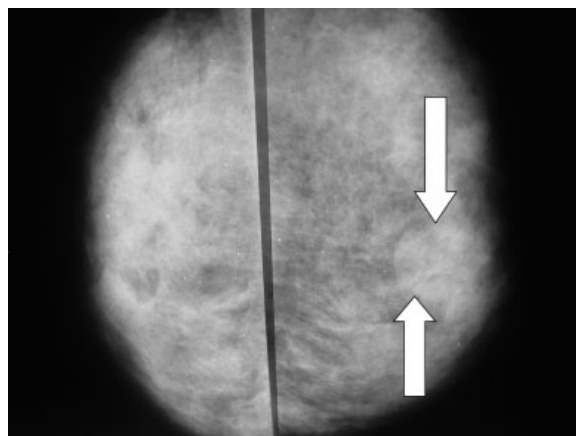

Figure 3 A. Bilateral mammography in c-c projection. „Dense" breasts with a benign tumor on the left side (sclerosing adenosis).
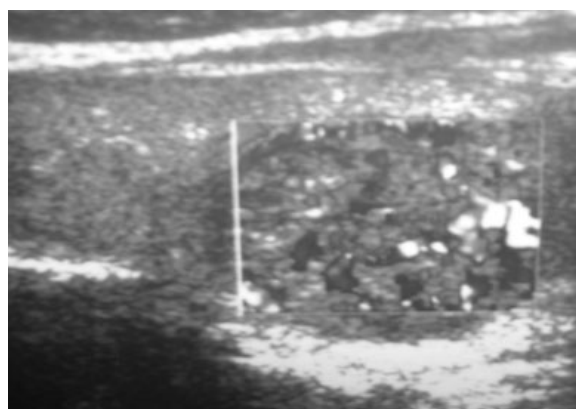

Figure 3 B. Sonomammography revealing a pattern of sclerosing adenosis.

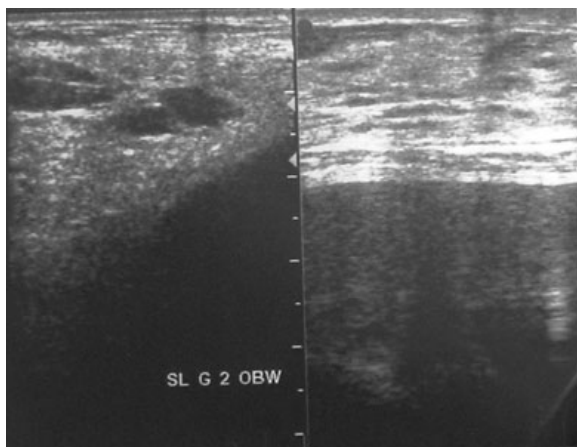**Figure 3 C.** The same patent , USG of the thyroid – a benign tumor.

Figure 4. Sonomammography after breast implant surgery – small cysts and enlarged milk ducts.

Figure 6. Mammography image in c-c projection. Two cancer foci – spicular (arrow) and oval with indistinct outlines (arrow head).

Figure 5. Sonomammography carried out in a woman from high risk group – three small cysts with suspicious microcalcifications – DCIS.
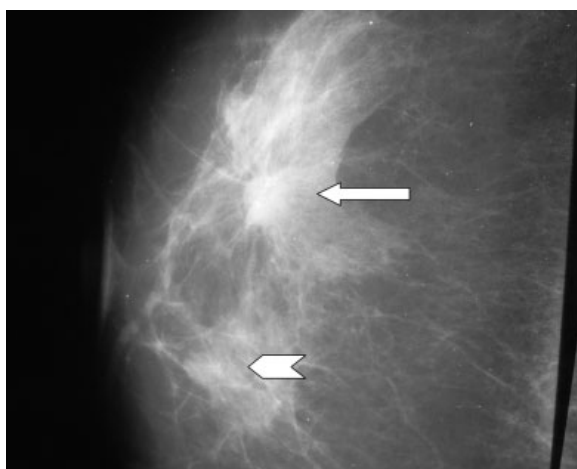

Figure 7. Mammography image of the right breast in oblique projection – a tumor with microcalcifications (fibroadenoma) and centrally a tumor with visible outlines – ductal carcinoma.

limited the availability of these examinations. Even numerous educational programs highlighting this issue will not be very helpful, if the attitude to the problem of prevention remains unchanged. We are not surprised that each of the examined women wanted to know the nature of her disease and not only to be told that her lesion was a benign one. If it was a benign lesion, what type was it? Why did it develop? Was it a transient disturbance, or a result of other, long-term hormonal dysfunction? Eventually, each patient diagnosed with one or more focal lesions asked a question where she should go next with the problem and which specialist should provide her with further treatment or observation – an oncologist-surgeon? gynecologist-endocrinologist? or a specialist in thyroid diseases? The patients expect to get such recommendations, obviously in addition to scheduling the date and type of a control radiological examination.

False negative results obtained in screening concerned lesions with rather regular outlines and saturated „dense" cysts (BI-RADS 3). These foci were associated with long-term hormonal therapy, but their „atypical appearance" was the basis for additional FNA. Finding tumor cells led to
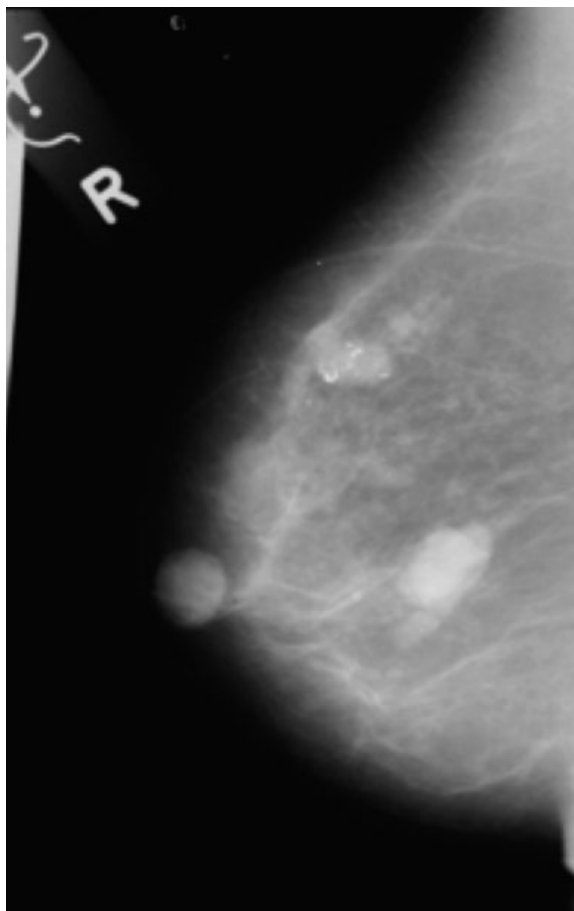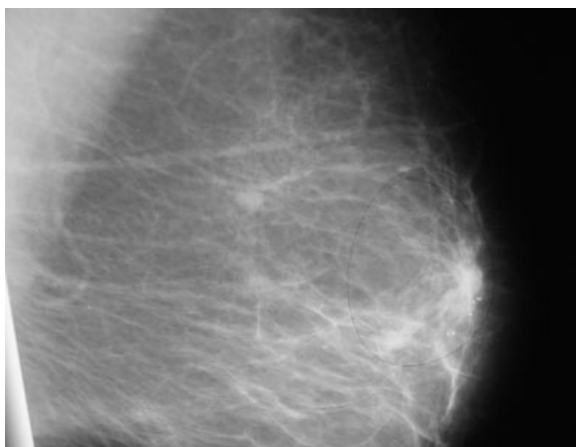
Figure 8 A. Left breast mammography in oblique projection – a retromamillary tumor with outlines difficult to evaluate.
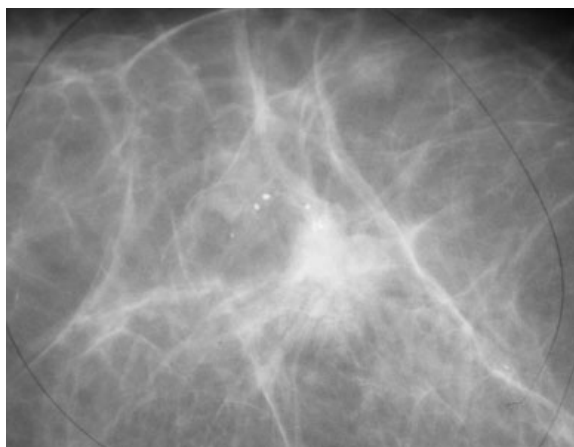

Figure 8 B. The same patient, zoom mammography, targeted on the retromamillary region. A spicular tumor with microcalcifications – invasive ductal carcinoma.
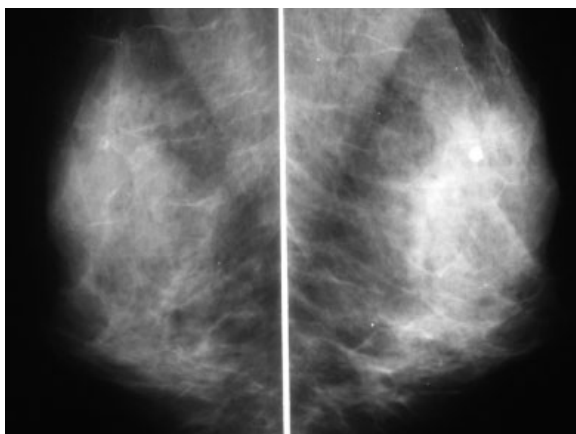

Figure 9. Bilateral mammography in oblique projection. Asymmetric mastopathy of the left breast after mastitis.
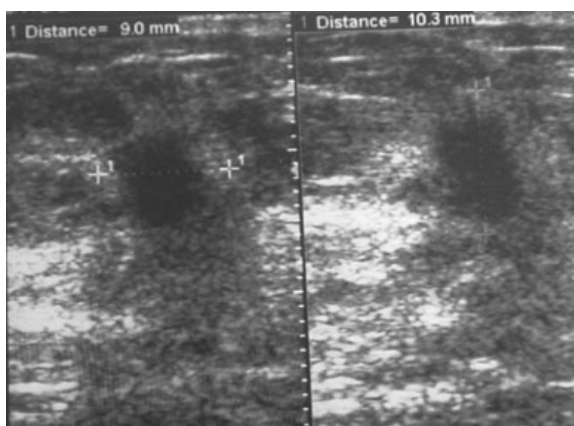

Figure 10. Sonomammography showing a dense hypoechoic focus with irregular pattern – a cyst in chronic hormonal dysfunction.

quick institution of treatment. However, if the patient had been scheduled for control examination, the therapy would have been considerably delayed [9,10].

Interval cancers known in screening practice may represent the „calculated risk margin" but such explanation given to a patient will be justified neither by the court, nor, which is even more obvious, by the woman affected by the disease. For this reason, the radiologist must establish as reliable diagnosis as possible, based, if necessary, on many different diagnostic and therapeutic procedures.

Unequivocal evaluation was also difficult in case of postoperative scars with suspicion of relapse, as well as radiotherapy-induced and postinflammatory changes – in such cases anamnesis was very helpful [7]. In case of unpalpable and additionally multifocal changes, meta-stases from the primary tumors are sometimes impossible to diagnose by MMG and USG; coincidence of benign and malignant lesions additionally complicates the diagnosis [10, 15, 16]. Diagnostic problems are also encountered in cases of fatty degeneration, postoperative scars, scars left by abscesses and in lactating breasts [7, 17]. Multifocal changes present in one breast can be malignant (fig. 6),

or both benign and malignant (fig. 7), which is not always reflected in MMG and USG images.

Caution is required in perimamillar lesions causing retraction of the nipple or located close to it. Zoom images and additional projections, as well as USG, are very helpful in such cases (fig. 8 a, b).

Asymmetrical mastopathic lumps require particular caution so as not to overlook a malignant process; during the first examination their character should be classified and recorded in the interpretation to avoid additional projections or USG during subsequent control examinations (fig. 9).

Microcalcifications present as one of the most problematic diagnostic signs, especially if they occur in clusters. Microcalcifications disseminated in „dense" adenomatous breasts are typical signs of hyperestrogenism, hyperprolactinemia and in 80% of cases – hypothyroidism. Not only the diagnosis, but also the decision concerning further control examinations can be a problem. Untreated lesions (in 50% of cases) demonstrate progression of radiological signs. On the basis of our own experience we believe that
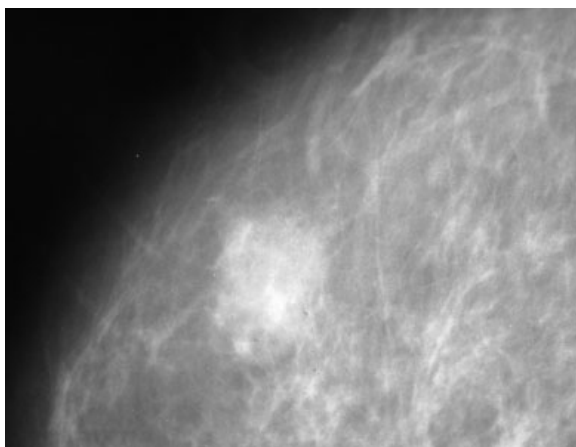
Figure 11 A. Mammography targeted on the tumor with regular outlines but with micro-calcifications – invasive ductal carcinoma.
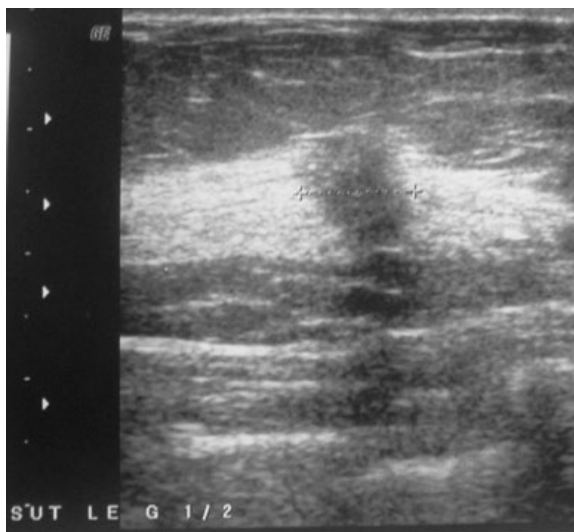

Figure 11 B. Sonomammography of the same patient – hypoechoic change with micro-calcifications and central echo.
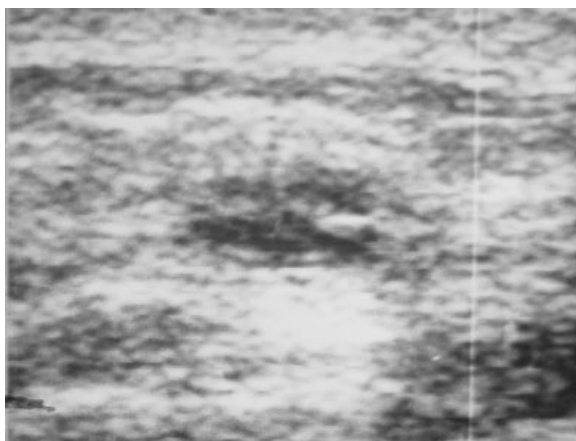

Figure 12. Sonomammography – zoom image of the cyst with irregular outline with protein molecules resembling microcalcifications in appearance.
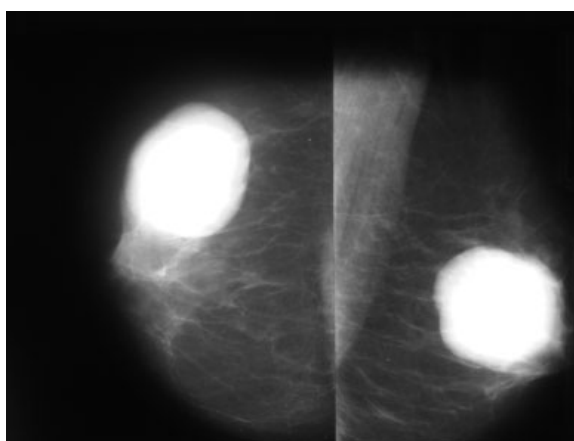

Figure 13 A. Mammogram of the left breast – a tumor with regular outlines, cyst.

Figure 13 B. Sonomammography of the same patient, non-homogeneous cyst with the foci suspicious of papilloma. FNA – thickening of the cyst wall without symptoms of hyperplasia.

control MMG should be performed after a year in order to assess microcalcifications, and in case of cyst-like lesions or small cysts – control USG 6 months after the commencement of treatment. Also tumors with regular outlines located amongst mastopathic lesions seen in MMG, and those presenting on USG as hypoechoic, densely saturated foci with uneven contours arouse suspicion. Such appearance is characteristic e.g. of "old" cysts with irregularly thickened walls, resembling malignant lesions (fig. 10, 11 a, b). Typical, dark-green fluid withdrawn from them on FNA demonstrated the presence of histiocytes. Histopathological investigations revealed in most cases apocrine metaplasia, benign dysplasia and fibrocystic mastopathy. In USG images, protein particles present in the cyst lumen resemble microcalcifications in appearance (fig. 12), and in case of irregular cyst outline require decision concerning further management – FNA or observation. A similar decision should be made in case of numerous microcalcifications visible on MMG performed in women belonging to the high risk group and with hormonal dysfunction.

Diagnostic problems can also be caused by atypical cysts. Women (in very rare cases also men) present in oncology,

gynecology and radiology departments, with sudden-onset nodules, apin, abscess or mamillary discharge. Atypical cysts suspicious of hyperplasia should be investigated by biopsy (fig. 13 a, b). After the diagnosis of fibrocystic degeneration is established, the radiologist should propose further diagnostic management – observation and time of control examination, biopsy or cyst resection, collection of material for cytology, examination of other organs in case of hormonal dysfunction. Further treatment by an oncologist, gynecologist and/or endocrinologist should also be suggested; control USG or MMG 6 months after the commencement of conservative treatment is recommended in such cases.

Such management algorithm has proven to work very well in our Department of Radiology and in West Pomerania region since the start of prevention programs for women 40–70-years old, sponsored by the Regional Health Fund in Szczecin. Since the establishment of the National Health Fund (NFZ), the examination have been available only for a limited number of women from the screening age group, and family doctors, gynecologists and a few oncologists were unable to cope with the demand for radiological diagnostics. We hope that introduction of a nationwide screening program will not only improve early diagnostics of breast tumors,

but will also facilitate the diagnostics by subsidies for modern equipment and quality assurance systems in radiology.

Conclusions

1. Diagnostic problems in breast diseases can be due to inherent limitations of the diagnostic methods used, the mammary gland structure and localization of the lesions,

2. The diagnostic criteria for benign and malignant lesions are not always clear, especially in high risk patients,

3. Hormonal dysfunctions and concurrent malignant lesions developing on their background present most diagnostic problems,

4. Diagnosis of a benign breast tumor should be based on the results of imaging, cytology, and histopathology, especially in the risk group,

5. Suspicious radiological lesions require verification by a biopsy – fine/core needle, mammotome or surgical, and in the course of conservative treatment of diagnosed hormonal dysfunctions – control imaging examinations at 6-month intervals.

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