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Robert Chrzan[1], Lucyna Rudnicka[2], Tadeusz Popiela Jr[1], Wojciech Nowak[1], Beata Podsiadło-Kleinrok[1]

The problems with histopathological verification of breast microcalcification clusters in the stereotactic mammotome biopsy specimens

[1]1-st Chair and Department of General and Gastrointestinal Surgery, Collegium Medicum, Jagiellonian University, Kraków,
[2]Chair and Department of Pathology, Collegium Medicum, Jagiellonian University, Kraków

The aim of the study was analysis of the cases, where histopathological examination failed to confirm the presence of breast microcalcifications in the SMB (stereotactic mammotome biopsy) specimens.

Between 2000 – 2004, 242 patients underwent SMB under the guidance of digital mammography to verify breast microcalcification clusters of BI-RADS (Breast Imaging Reporting and Data System) 3–5 categories. In 39 of these patients histopathological examination did not confirm microcalcifications despite visualization on the radiograms. All such cases were additionally evaluated under polarized light microscope to detect microcalcifications containing birefringent calcium oxalate deposits.

In all 39 patients only benign breast abnormalities were detected. In none of these cases breast microcalcifications were revealed in the additional evaluation under polarized light microscope.

In some cases histopathological examination of the SMB specimens of breast microcalcifications may not confirm their presence despite visualization on the radiograms. The bioptates sent for the examination should be placed in the order of sampling at the same level and in such form embedded in the paraffin blocks. Radiograms confirming the location of microcalcifications should accompany the specimens. If standard assessment does not demonstrate microcalcifications, serial cutting and additional evaluation under polarized light microscope are recommended.

Introduction

Breast microcalcifications are among the main symptoms of breast cancer found on mammography. The detection of microcalcifications is important especially in the early stages of breast cancer, where they occur with higher frequency than in advanced stages, and in the majority of the patients are the only mammographic symptom of breast cancer. Pathological microcalcifications occur in over 80% of all ductal carcinomas in situ, being the only mammographic symptom of cancer in over 70% of these cases [12].

Their chemical composition is diverse and includes:

1. Microcalcifications containing calcium phosphate deposits – readily identified using staining with hematoxylin and eosin and showing no birefringence under a polarized light microscope. They make up about 90% of all microcalcifications and are associated with benign as well as malignant breast lesions.
2. Microcalcifications containing calcium oxalate deposits – usually unrecognized using conventional hematoxylin and eosin staining, however detectable under a polarized light microscope due to their birefringence. They make up about 10% of all microcalcifications and are predominantly associated with benign lesions [13].
3. Microcalcifications containing heavy metals deposits. In some cases spectroscope analysis detected the presence of microcalcifications containing heavy metals deposits [7] that may not be visualized in the histopathological specimens.

Molecular studies of the pathogenesis of microcalcification clusters showed that in cases of multiple microcalcifications breast cancer cells present strong expression of several bone matrix proteins including osteonectin (OSN), osteopontin (OPN) and bone sialoprotein (BSP). Under physiological conditions these proteins are involved in the crystallization of calcium phosphate into hydroxyapatite within bone matrix. Therefore, it is probable that microcalcifications develop as a result of the ectopic formation of calcium compounds mediated by the above agents [1, 2].

Detection of DNA in the central parts of microcalcifications in the breast cancer with high expression of BSP is the evidence for the development of microcalcifications around cells undergoing necrosis [3].

Moreover, in vitro studies showed that hydroxyapatite crystals may not only be a symptom of breast cancer but they also may actively stimulate its development by promotion of mitogenesis and matrix metalloproteinase expression [8].

It is presumed that strong expression of OSN, OPN and BSP besides locally stimulating the development of microcalcifications may also be associated with the high incidence of breast cancer metastases in bone tissue [1, 2].

In cases of breast microcalcification clusters requiring microscopic verification, stereotactic mammotome biopsy (SMB) – vacuum assisted core needle biopsy guided by digital mammography is more and more commonly used [4].

Mammotome needle allows removing large samples of tissue for the histopathological verification and therefore the results correlate better with the postoperative findings, compared to the conventional core needle biopsy.

Using digital mammography guidance for stereotactic location, biopsy needle control and evaluation of suspicious foci removal ensures high effectiveness of the procedure, without the need to wait for traditional film development.

The presence of microcalcifications on specimen radiograms is the evidence of their removal in SMB, whereas their presence in histopathological examination is the proof of removal and microscopic assessment of the proper part of a specimen (the region of pathology, not adjacent normal tissue).

The aim of the study was analysis of the cases, where histopathological examination failed to confirm the presence of breast microcalcifications in the SMB specimens.

Material and Method

Between 2000–2004, in the 1-st Department of General and Gastrointestinal Surgery, Collegium Medicum, Jagiellonian University, 242 patients underwent SMB under the guidance of digital mammography to verify breast microcalcification clusters of BI-RADS (Breast Imaging Reporting and Data System) 3–5 categories.

Cylindrical tissue samples were stored in plastic cassettes allowing for the x-ray evaluation of the presence of microcalcifications.

Obtained specimens were fixed in 10% buffer formalin and sent for histopathological evaluation in the Department of Pathology, Collegium Medicum, Jagiellonian University.

Material embedded into paraffin blocks, cut and stained with hematoxylin and eosin was analyzed under a microscope. Histopathological examination verified the type of lesion and the presence of microcalcifications.

In the study we analyzed 39 patients, where histopathological examination of SMB specimens did not confirm the presence of microcalcifications despite their visualization on the radiograms.

This group made up 16.1% of all women subjected to SMB to verify breast microcalcification clusters. All such cases were additionally evaluated under a polarized light microscope to detect microcalcifications containing birefringent calcium oxalate deposits.

Results

In the analyzed group of 39 patients, histopathological examination of the SMB specimens revealed only benign lesions (laesio fibrosa et cystica, hyperplasia intraductalis, metaplasia apocrinalis, adenosis sclerosans, fibroadenoma, papilloma intraductalis).

In none of these cases breast microcalcifications were revealed in the additional evaluation under a polarized light microscope.

Discussion

The lack of breast microcalcifications in the histopathological evaluation of SMB specimens from 39 women (16.1%), despite their presence confirmed on the radiograms, required explanation. As it turned out after analysis of bibliography, some researchers encountered this problem and tried to explain it.

Stein and Karlan [11] did not confirmed the presence of microcalcifications in 7% of histopathological results. They attributed it to inadequate sampling in 25% of cases, lack of explicit description by the pathologist in 33%, presence of oxalate crystals that required examination with polarizing lenses in 17% and unexplained loss of tissue probably related to processing in 25%.

In the study of D'Orsi [5] breast microcalcifications were not confirmed by histopathological examinations in about 26% of cases. He attributed it to the loss of calcium compounds during the preparation of paraffin blocks in about 50% of cases and to the method of paraffin blocks sectioning in which tissue was discarded or calcific particles were fractured and ejected by the microtome blade in about 50%. Only in 0.5% of cases microcalcifications were not visualized due to the fact that calcium oxalate is not detectable in the conventionally stained specimens, and requires evaluation under a polarized light microscope [6].

To reduce the number of cases, where breast microcalcifications are not verified histopathologically, some authors recommend not only using radiograms confirming the location of microcalcifications in specimens and additional evaluation using a polarized light microscope [9, 15], but also performing paraffin tissue block radiography for proper blocks sectioning [10].

Thurfjell [14] demonstrated that in 2.4% of cases a primary benign histopathological diagnosis was changed to malignant due to the use of tissue block radiography.

In none of our cases breast microcalcifications were revealed in the additional evaluation under a polarized light microscope, so it is presumed that the failure may be attributed to the method of material preparation. At the beginning the first series of SMB specimens were not located on the plate in the order of sampling but mixed altogether and as such provided for histopathological examination and embedded in paraffin blocks. It was observed that providing biopsy specimens placed in the order of sampling at the same level and paraffin embedding in such a form significantly decreased the number of undetected microcalcifications (as example 17 cases in 2001 and 6 cases in 2004).

Conclusions

1. In some cases histopathological examination of the SMB specimens from breast microcalcifications clusters may not visualize calcifications despite previous detection on the radiograms.
2. SMB specimens for histopathological verification should be placed in the order of sampling at the same level and as such embedded in the paraffin blocks.
3. In every case a radiogram of a specimen documenting the presence and location of microcalcifications should be provided for histopathological examination.
4. If standard histopathological examination does not demonstrate microcalcifications, serial cutting and optionally additional evaluation under a polarized light microscope are recommended.

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Address for correspondence and reprint requests to:
Robert Chrzan
1-st Department of General and Gastrointestinal Surgery
Collegium Medicum, Jagiellonian University
Kopernika 40, 31–501 Kraków