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Диагностика патологии и аномалии сосково-ареолярного комплекса: серия клинических случаев

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АННОТАЦИЯ

Сосково-ареолярный комплекс — особая анатомическая и гистологическая структура. Вариабельность нормального строения, широкий спектр патологических процессов и сложность диагностической визуализации вызывают трудности у врачей лучевой диагностики и клиницистов.

Наиболее часто в диагностике патологии сосково-ареолярного комплекса используют ультразвуковую диагностику и маммографию. При неоднозначных результатах предшествующих методов и для оценки распространённости процесса применяют магнитно-резонансную томографию с внутривенным контрастированием.

Магнитно-резонансная томография молочной железы — наиболее чувствительный метод выявления особенностей строения, диагностики доброкачественных и злокачественных заболеваний, затрагивающих сосково-ареолярный комплекс. Магнитно-резонансная томография полезна в качестве дополнительного диагностического инструмента при неоднозначных результатах маммографии и ультразвукового исследования. Магнитно-резонансная томография позволяет визуализировать ретроареолярную зону, подходит для диагностики папиллом, аденом, болезни Педжета, протоковой карциномы *in situ* и инвазивного рака.

В статье дано описание клинических случаев диагностики патологии и аномалий сосково-ареолярного комплекса, что может быть полезно для врачей лучевой диагностики, гинекологов, клинических ординаторов.

Ключевые слова: клинический случай; рак молочной железы; сосково-ареолярный комплекс; маммография.

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Diseases and abnormalities of the nipple-areolar complex: a case report series

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ABSTRACT

The nipple-areolar complex is a specific anatomical and histological structure. Normal structure and pathological process variabilities and the complexity of diagnostic imaging cause difficulties for radiologists and physicians. Breast magnetic resonance imaging is highly sensitive for structural features and nipple-areolar complex cancer detection. Magnetic resonance imaging is a useful diagnostic tool when mammography and ultrasound findings are inconclusive. It allows visualization of the retroareolar region, suitable for the diagnosis of papillomas, adenomas, Paget's disease, ductal carcinoma in situ, and invasive ductal carcinoma.

This is a case report on identifying the pathology and anomalies of the nipple-areolar complex, which may benefit radiologists, gynecologists, and residents.

Keywords: case report, breast disease, nipple-areolar complex, mammography.

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乳头乳晕复合体的病理和异常的诊断： 一系列临床病例

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简评

乳头乳晕复合体是一种特殊的解剖学和组织学结构。正常结构的变异性、病理过程的广泛性和诊断成像的复杂性给放射科医生和临床医生带来困难。乳房磁共振成像是检测结构特征、诊断涉及乳头乳晕复合体的良性和恶性疾病的最灵敏方法。在乳腺钼靶和超声检查结果不明确的情况下，磁共振成像作为一种额外的诊断工具非常有用。磁共振成像允许看到乳腺后区，适合诊断乳头瘤、腺瘤、佩吉特氏病、导管原位癌和浸润性癌。

我们在这篇文章中描述了乳头乳晕复合体的病理和异常的临床病例，这可能会对放射科医生、妇科医生和临床住院医师有用。

关键词：临床病例，乳腺癌，乳头乳晕复合体，乳腺钼靶。

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BACKGROUND

The nipple–areolar complex (NAC) is a unique breast area. NAC consists of various cells and specific tissues that are responsible for the outflow and secretion of breast milk during lactation. [1] NAC is susceptible to a wide range of conditions including developmental anomalies, benign processes (inflammation, infection, and benign tumors), and invasive and non-invasive cancers. [2]

The evaluation of the NAC is a challenging task for clinicians and radiologists. In this area, pathological processes often have nonspecific clinical and radiological signs, which make establishing a correct diagnosis difficult and time consuming.

The differential diagnosis of NAC conditions requires the review of a patient's medical history and visual assessment of the skin, abnormal nipple discharge, nipple retraction, inversion, palpable formations, etc.

Imaging is an important component of diagnosing NAC conditions. Standard mammography and ultrasonography have some limitations. Images are especially difficult to interpret because of mobility, superficial location, and varying density of breast structures. The retroareolar region is difficult to assess on mammograms; thus, in this area, abnormalities often remain unnoticed. This is why magnetic resonance imaging (MRI) is increasingly important for the diagnosis of NAC conditions.

While planning the surgical treatment, it is important to detect whether the NAC is involved in the tumor process. When breast cancer involves the NAC, the tumor is classified as T4, which determines the disease stage (prognosis) and makes it impossible to save the nipple during mastectomy. On the contrary, precise determination of tumor borders with uninvolved NAC provides new opportunities for organ-preserving breast surgeries. [3]

Contrast-enhanced MRI is the most sensitive method of diagnosing breast cancer. [4] Breast MRI is performed for confirming the results of mammography and ultrasonography, breast cancer staging, evaluating the effectiveness of neoadjuvant chemotherapy, and determining the more precise localization of the lesion during biopsy. [5] MRI may be used in patients with abnormal nipple discharge as an additional diagnostic tool when standard mammography and ultrasonography are inconclusive. [6]

CASE REPORTS

Case Report 1

A 59-year-old patient complained of erosive changes in the nipple (Fig. 1). Physical examination revealed erythema, erosion, and nipple retraction. Doppler ultrasonography with color flow mapping revealed increased blood flow in the nipple projection (Fig. 2). Mammography findings were normal. To assess the extent of disease spread, breast MRI with contrast enhancement was performed. The



Figure 1. Erosive nipple changes in Paget's disease.

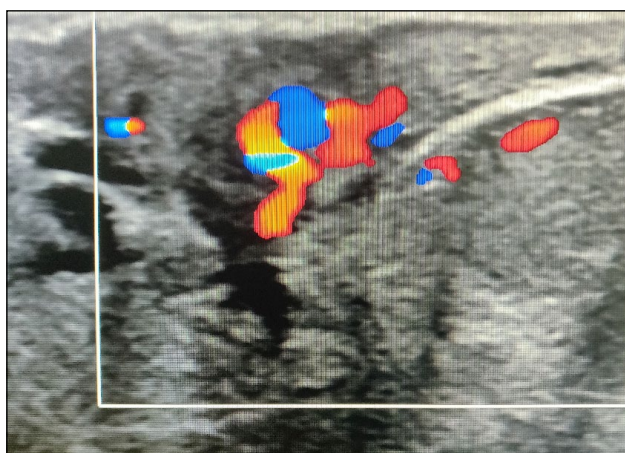


Figure 2. Paget's disease: increased blood flow on color Doppler imaging.

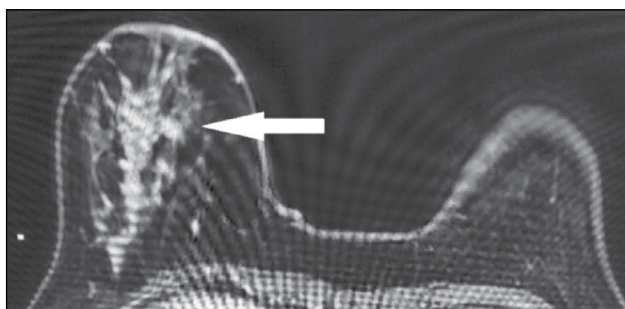


Figure 3. Magnetic resonance imaging of Paget's disease (early enhancement phase): the retroareolar area of segmental enhancement from the nipple level to the posterior breast (arrow).

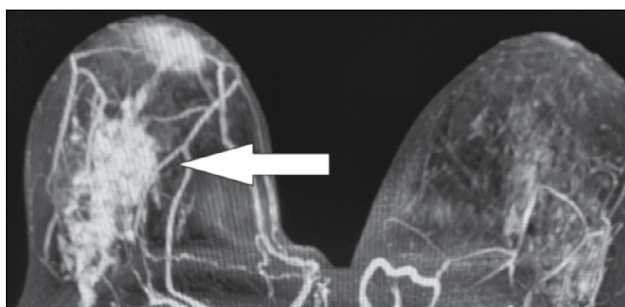


Figure 4. Magnetic resonance imaging of Paget's disease (maximum intensity projection): the retroareolar area of segmental enhancement from the nipple level to the posterior breast (arrow).

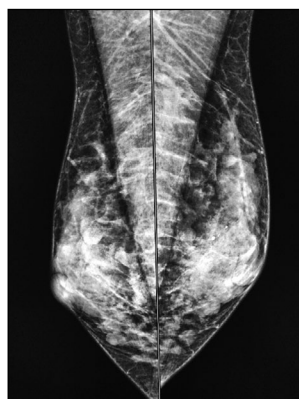


Figure 5. A nipple adenoma: mammography (mediolateral oblique projection).

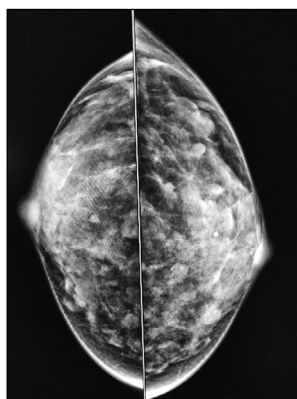


Figure 6. A nipple adenoma: mammography (craniocaudal projection).

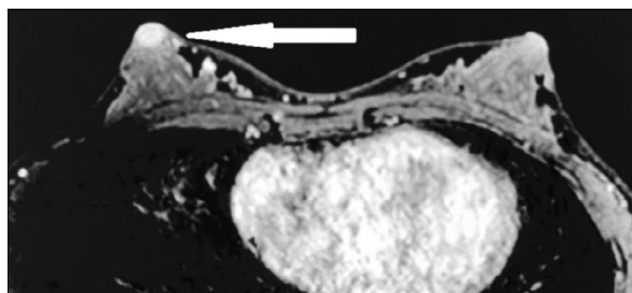


Figure 7. Magnetic resonance imaging of a nipple adenoma (early postcontrast series): a right nipple mass homogeneously accumulating a contrast agent (arrow).

early postcontrast series (Fig. 3) and maximum intensity projection (MIP) images (Fig. 4) showed a segmental contrast retroareolar area from the nipple level to posterior breast sections. Ultrasound-guided core biopsy followed by immunohistochemical analysis revealed Paget's disease of the nipple with high-grade intraductal carcinoma in situ. Receptors for estrogen (G3 ER) and progesterone (PR) were negative. Oncogenic protein Ki-67 was 45%.

Case Report 2

A 38-year-old patient complained of 1-month itching of the right nipple and skin discoloration. Breast ultrasonography and mammography findings (Figs. 5 and 6) were normal. The

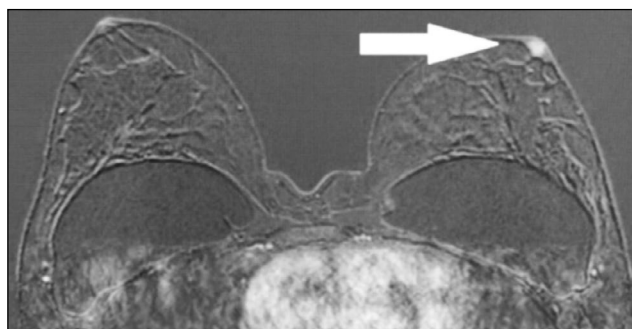


Figure 9. Magnetic resonance imaging (early postcontrast series): asymmetric contrast accumulation in the left nipple; normal finding (arrow).

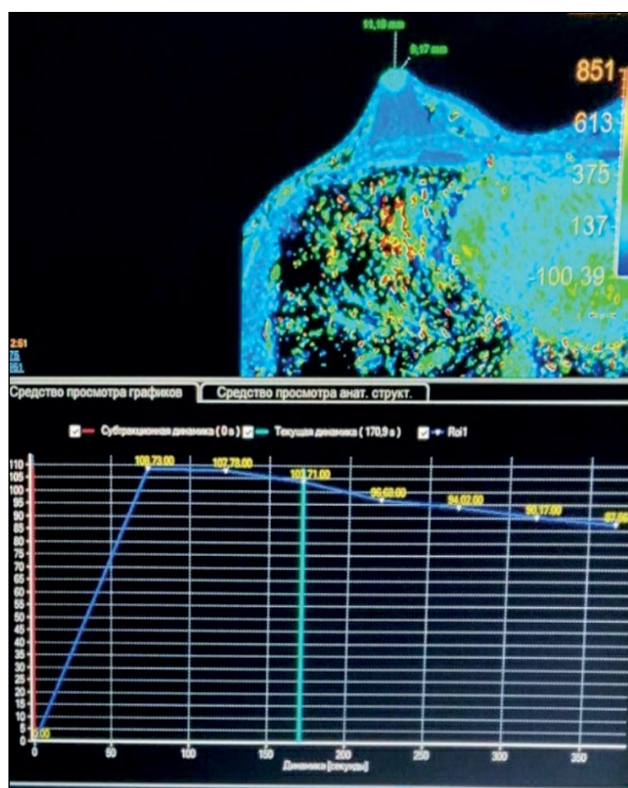


Figure 8. Magnetic resonance imaging of a nipple adenoma (parametric map): a right nipple mass with rapid contrast enhancement and subsequent elimination, type III graphic curve.

breast was examined by contrast-enhanced MRI. The early postcontrast series revealed a right nipple mass homogeneously accumulating a contrast agent (Fig. 7). A parametric map showed a nipple mass with rapid contrast enhancement and subsequent elimination, a type III graphic curve (Fig. 8). Morphological verification revealed nipple adenoma.

Case Report 3

In a 43-year-old patient who had no complaints, the breast was examined by MRI to assess the integrity of implants. The asymmetric enhancement of the left nipple was accidentally found (Figs. 9 and 10). Three-year dynamic observation did not reveal any unfavorable changes.

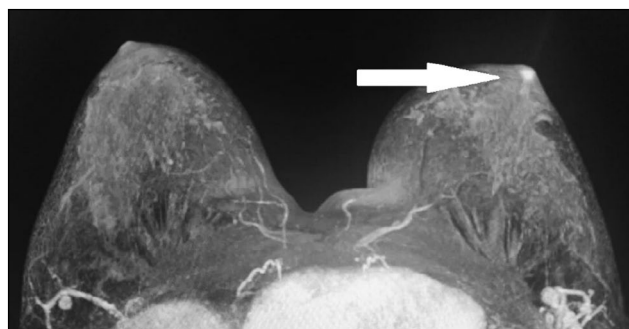


Figure 10. Magnetic resonance imaging (MIP): asymmetric contrast accumulation in the left nipple; normal finding (arrow).

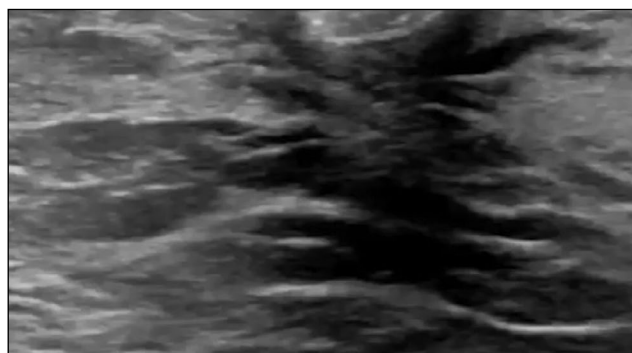


Figure 11. Ultrasound image of the left breast with the inverted nipple.

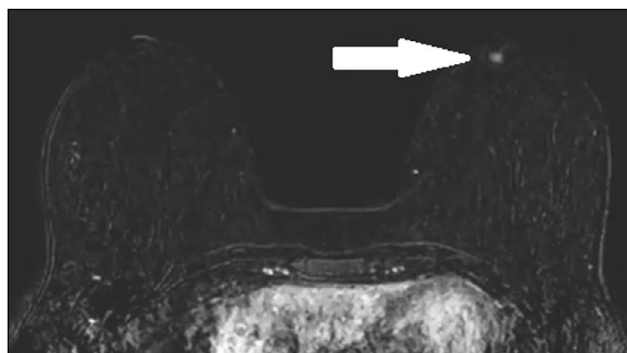


Figure 12. Magnetic resonance imaging (subtraction): a retroareolar mass with accumulation of contrast agent (inverted nipple, arrow).

Case Report 4

In a 38-year-old patient who had no complaints, a routine medical examination showed a left nipple inversion. Ultrasonography of the left breast revealed no abnormalities (Fig. 11). MRI with intravenous contrast (Fig. 12) showed asymmetric contrast accumulation with a retroareolar mass accumulating the contrast agent (inverted nipple). No focal breast pathology was detected.

DISCUSSION

The NAC is a pigmented area in the most protruding part of the breast, the site where milk ducts converge, draining 15–20 breast lobes. [7] Given its complex anatomy, [8] superficial location, and mobility, this area requires special attention during clinical examination and imaging.

In clinical practice, ultrasonography and mammography are the most used methods for NAC pathology detection. If imaging modalities revealed conflicting findings, MRI with intravenous contrast enhancement is used to assess the extent of disease spread.

Ultrasonography has some advantages as a method of NAC examination. In addition to being widely available and not requiring ionizing radiation, ultrasonography provides a good spatial resolution of this superficial region, making it possible to characterize small lesions in the retroareolar region. [9]

Mammography is the most sensitive technique for detecting calcifications. In the NAC, calcifications are uncommon and usually benign, such as cutaneous, calcified intraductal detritus, and calcifications due to fat necrosis. Microcalcifications can be seen in relation to intraductal carcinoma, sometimes associated with Paget's disease. [10] Mammography is less sensitive than ultrasonography because of the greater density and mobility of this part of the breast. [11]

For mammography, the breast must be positioned correctly. [10] The nipple must be located tangentially at least in one projection, ideally in both craniocaudal and mediolateral projections. In patients with inverted nipples (normal variation), nipples should be tangential and symmetrical.

Dynamic contrast-enhanced MRI is the most sensitive method for diagnosing breast diseases. In breast cancer, MRI provides valuable information on the extent of disease spread and can be used to plan the treatment and establish a prognosis. [12] When evaluating a NAC tumor, MRI has high sensitivity (90%–100%), moderate specificity (80%–90%), and high negative predictive value (98%) [3]; thus, it can be used for establishing a diagnosis if mammography and ultrasonography results are conflicting and the clinical presentation is nonspecific. [13] The advantages of MRI include providing high-resolution images and possibility for dynamic contrast enhancement. If contrast accumulation is early, intense, asymmetric, and heterogeneous with subsequent contrast elimination, it may be indicative of a malignant neoplasm. [14] MRI is required for preoperative planning to determine the extent of nipple-sparing mastectomy in breast cancer treatment. [15–17] Finally, MRI can be used as a supplementary method to mammography and ultrasonography in the diagnosis of abnormal nipple discharge and percutaneous biopsy. [18]

We describe a clinical case of diagnosis of Paget's disease with a false-negative mammography result. MRI with intravenous contrast enhancement allowed us to determine the real extent of the disease spread. Paget's disease accounts for 1%–3% of all breast carcinomas. It is characterized by the presence of neoplastic cells in the nipple epidermis [19] and clinically manifested as erythema, erosion, and ulceration of the nipple, sometimes combined with a palpable retroareolar mass and/or nipple retraction or discharge. Differential diagnosis includes atopic or contact dermatitis, malignant melanoma, Merkel cell carcinoma, mycosis fungoides, nipple adenoma, and ductal exocrine carcinoma. As in our case, to establish the final diagnosis, skin biopsy and immunohistochemistry are required.

Imaging techniques are of critical importance because in 90% of cases, Paget's disease is associated with ductal carcinoma in situ or invasive cancer. [13, 20] In primary mammography, images with enlarged NAC and anterior breast third are important. Skin thickening, retroareolar masses, or pleomorphic microcalcifications may be detected. Ultrasonography showed no characteristic signs. It may help

identify dilated subareolar ducts, calcifications, and nipple changes.

In 22%–71% of cases, mammography provides a false-negative result [21], and in this case, breast MRI is indicated to identify abnormalities and deter the extent of disease spread. [20] Characteristic MRI findings include asymmetry, thickening, flattening, retraction of the NAC, and uneven contrast accumulation in this area. MRI allows evaluating adjacent structures and axillary lymph nodes.

Case 2 demonstrates the complexity of the diagnostic search in a nipple adenoma. Ultrasonography and mammography revealed no abnormalities, and the correct diagnosis was established only by MRI followed by biopsy. A nipple adenoma (erosive adenomatosis or subareolar papillomatosis) is a rare variant of intraductal papilloma. Clinical manifestations include a small palpable nodule under the skin of the nipple, which is usually associated with inflammatory nipple changes (pain, redness, and swelling). Skin involvement results from the growth of glandular epithelium toward the skin surface. Skin manifestations are similar to Paget's disease, squamous cell carcinoma, eczema, psoriasis, or infection. Histological verification is the gold standard for definitive diagnosis. Mammography and ultrasonography usually do not provide valuable information. Ultrasonography may show a hypoechoic nodule in the nipple or subareolar region. [22]

Cases 3 and 4 prove that asymmetric contrast accumulation in MRI is not necessarily a sign of pathology. Normally, in MRI, both nipples accumulate the contrast agent at the same rate and intensity. However, nipple asymmetry may be the normal variation. Possible reasons include special NAC anatomy, breast size, breast compression and friction with clothing, blood flow variations, and local inflammation. [12] Some physiological features and differences are involved in contrast accumulation in NAC structures. Both breasts usually show symmetrical thin rings of enhancement. In some cases, enhancement is asymmetrical in the early phase and becomes symmetrical in later phases. In a study of 530 normal nipples in 265 asymptomatic women, Gao et al. used T1-weighted NAC images to describe three areas of enhancement. [12]

Nipple inversion is a benign condition associated with the insufficient ability of the mesenchymal tissue to fix the nipple in the right position. [12] It occurs in 4% of women and men. Nipples are convex in 75% of women, flat in 23%,

and inverted in 2%. MIP images are well suited for assessing the morphology and symmetry of the NAC. On postcontrast images, the nipple should be hypo- or isointense compared with the enhanced parenchymal tissue in the background. [12]

Nipple inversion, retraction, and asymmetry are normal but may also be indicative of pathology. In differential diagnosis, obtaining a detailed medical history, comparing with results of previous examinations, and providing ongoing monitoring are recommended.

CONCLUSION

The complex anatomy of the NAC requires a special multimodal approach to diagnosing pathologies in this area. In many cases, such conditions have nonspecific clinical and radiological manifestations, which can complicate the diagnostic process. Imaging techniques play an important role in this process. Clinicians and radiologists must be aware of the advantages and disadvantages of each technique and interpret the results of various modalities. To make a precise diagnosis, clinical, radiological, and histological data must be comprehensively evaluated. Our case reports show examples of asymmetric NAC changes in normal and pathological conditions.

ADDITIONAL INFORMATION

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Consent for publication. Written consent was obtained from the patients for publication of relevant medical information and all of accompanying images within the manuscript in Digital Diagnostics journal.

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