

CLINICAL EVENT: DUCTAL CARCINOMA IN SITU OF THE BREAST WITH MULTIFOCAL GROWTH

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L.N. Korostyleva, A.D. Makarov, Z.D. Gurieva, N.M. Sleptsova, A.S. Innokentieva

The carcinoma in situ is a noninvasive form of the mammary gland cancer presented by malignant cells localized in the epithelium and not penetrating the basement membrane, but potentially, capable of invasion. The latest developments in the molecular genetics, discovery of oncogenes and tumor growth suppressing genes confirm the opinion that the carcinoma in situ is an early phase of the genuine breast cancer. These neoplasms possess various biological properties and differ in the risk of progressing into invasive cancer and treatment practices.

Key words: ductal carcinoma in situ (DCIS), mammography, ultrasonography, tumor biopsy, lumpectomy, mastectomy.

Recently, the world has been witnessing a growing trend of detecting clinically latent forms of the breast cancer: minimal forms and carcinoma in situ (CIS). It has become possible thanks to improved mammography and ultrasonography equipment along with new techniques of target biopsy of pathological focus. (1,2). In countries conducting the population mammography screening, carcinoma in situ accounts for 20-40% of all newly detected breast cancers. In some centers in the USA and Western Europe, one CIS occurs per every two cases of invasive breast cancer detected during mammography (5,6). The term 'carcinoma in situ', in fact, stands for two diseases: ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS). In the TNM international breast cancer classification, carcinoma in situ is considered stage 0, with a primary tumor being coded as Tis. In the international classification, CIS is a minimum tumor with limited spread, requiring a thorough microscopic examination to be detected. Ductal carcinoma in situ often spreads in segments, sometimes involving two or more breast quadrants, so DCIS may be initially a diffused (multi-center) disease. It is proved by the fact that a morphological study of DCIS patients often reveals multiple foci of non-invasive and invasive cancer, sometimes. The more histological sections are studied, the more cancer foci are discovered. As stated in the medical literature, multiple foci occurs in 30% of DCIS patients (3,4). Clinical diagnostics of DCIS is difficult in cases when a tumor is not palpable and there are no nipple discharge. DCIS are divided into two groups: clinical - a tumor is palpable - and subclinical, when a tumor is detected by mammography, only. Treatment prognosis and tactics differ for these two forms. In most cases, DCIS is detected during mammography or ultrasound examination and often is characterized by micro calcification and rarely by the nodular pattern deformation. Radiological diagnostics of ductal carcinoma in situ is complicated since it declares itself by micro calcification foci, only. Palpable CIS forms are treated with US-controlled biopsy or stereotaxic biopsy. With non-palpable CIS, sectoral breast resection is conducted as a diagnostics final stage. The operation is performed after a thorough study of the pathological focus on mammography images. The morphological shape of carcinoma in situ is one of the important factors determining the disease treatment tactics. Surgical intervention remains the most efficient treatment of CIS, as an organ protection operation or mastectomy. First, the wide use of organ protection operations (sectoral resection with chemo or not) resulted in increased occurrence of local recurrence. After the organ protection operation, the recurrence reaches 30-50% (6,7). However, the currently common mastectomy in all DCIS patients is disputable. There is a continuous discussion on the extent of operations with DCIS as it is difficult to predict which treatment would be the best in this or that case, not leading to recurrence of the disease. In case of recurrence, about 50% of patients develop not CIS but invasive cancer, as the morphological study of the specimen shows.



Clinicians face an important task - to decide on the optimum DCIS patients treatment tactics. To do so, it is necessary to classify patients into groups: with favorable and unfavorable course of the disease. Different extent of the operation is caused by the biological properties of carcinoma in situ.

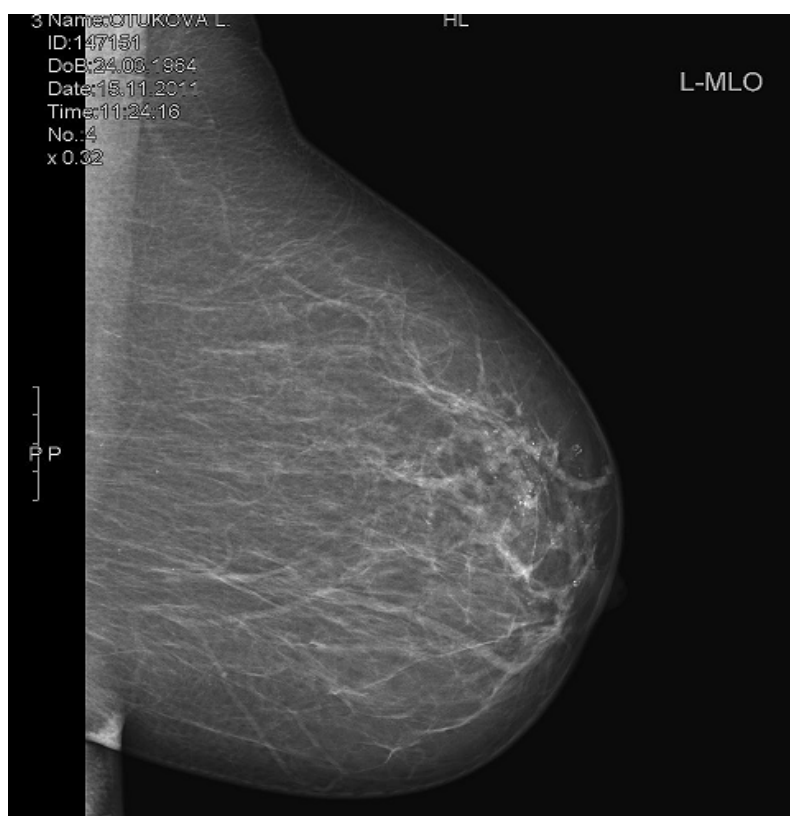
We are carrying out our own clinical study. Patient O., 48, entered the surgery ward № 1, Clinical Center, Republic's Hospital № 1-Center of Medicien, with a preliminary diagnosis – *Suspicio cancer mammae sinistrae*. Accompanying diseases: grade 2 hypertensive disease, arterial hypertension 2, risk of cardie-vascular complications, *Зриск* CCO 3, type 2 insular diabetes, medium severity, chronic viral hepatitis C, minimally active, fatty liver hepatosis, chronic pyelonephritis. The general condition is relatively satisfactory. Height - 165 cm, weight - 97 kg, overweight – 36. Anamnesis: first discharges of serohemorrhagic nature from the left mammal gland (LMG) ducts appeared in autumn 2010. Gynecological anamnesis: menstruation started at the age of 15, set in at once, every 28-30 days. Pregnancies - 4, childbirths - 4, lactation after all childbirths to 11-12 months, a plugged duct in LMG. Menstrual and ovary irregularities started in 2009, the last menstruation in 2010. Status localis: macromastia, the mammal glands are symmetrical, the nipples and areolas are unchanged, no discharge at the moment of study. Palpation of the mammal glands reveals involutive changes, diffusive nodular stroma, mainly in the external quadrants projection, with no obvious nodular formations. The LMG upper external quadrant (UEQ) projection shows a dotted trace of biopsy, with no nodular formations below. Palpation detects enlarged lymph nodes in the both axillary zones, mobile, not knitted together, painless. The study conducted: color mammography (Picture 1,2), LMG tomosynthesis (Picture 3,4). Skin strips are thin, even along the entire length. The nipples are not deformed. With the fatty involution in the background, there are areas of unpronounced fibrosis in stromal structures and remains of granular tissues. At the edges of the LMG upper quadrants, there are multiple pleomorphic micro- and macro calcification forms, located in segments with 39-41 mm range, some of them are visible in the retromammillary area in the form of clusters. Ultrasonography shows clear differentiation in the mammal gland tissues. The skin is a hyperechoic even strip. The nipples are unchanged. A fatty component dominates the stroma. With the subcutaneous fat in the background, there are visible Cooper's ligaments in the form of hyperechoic linear shadows covering the fat lobules. The granular layer shows increased echogenicity, with hyperechoic linear nodules. The LMG shows widened to 4 mm retroareolar ducts, in the UEQ they are widened to 3 mm, their walls are compacted, there are numerous minor hyperechoic signals visible. The regional lymph nodes are invisible. Conclusion: Multiple pleomorphic segmental micro-macro calcification areas in the UEQ of the LMG. Is that ductal cancer? The histological stereotactical biopsy conclusion - a fibrosis tissue with cells suspicious of ductal cancer, cytological conclusion - the cytogram is typical of the ductal cancer. On 06 March 2012 the operation was performed under general anesthesia - sectoral resection of the LMG with the skin being dissected in the biopsy place in the UEQ projection and removal of the subareolar zone. The result of the subareolar zone express biopsy - fibrocystic mastopathy with the duct epithelium cells proliferation, no malignant growth detected. Macroscopically, the removed breast section was represented by fatty tissue and wasn't subjected to express freezing. The final morphological study of the post-operation specimen diagnosed ductal cancer in situ in a large number of histological sections without any indications of the invasive growth (Fig. 1,2). Given the morphological conclusion received and impossibility to exclude other foci of ductal carcinoma in situ (multifocal growth) in the remaining breast tissue, the patient was taken to hospital again for eradication. On 11 April 2012 the patient was operated - mastectomy on the left with axillary lymph-dissection. The planned histological study - a mammal gland with granulomatosis, with intraductal cancer structures detected in the same area. There are atypical ductal dysplasia in other areas of the breast. All studies of the lymph nodes in the axillary area (14 pieces) failed to show metastases. The further morphological study of all post-operation specimen revealed the high grade of malignancy of the ductal cancer in situ (high grade DCIS). There was conducted the immune-histological-chemical study of the tumor - estrogen receptors

expression – positive (+) 4 (Fig. 3); progesterone receptors expression – positive (+)7 (Fig. 4); expression of mutant gene-suppressor p53 - 3%; the proliferative tumor pool for expression Ki-67 - 0%. The post-operation period course was smooth, with immediate agglutination. Taking into consideration the positive expression of steroid hormones receptors in the tumor cells, the patient has been proscribed hormone therapy (tamoxifen 20 mg a day, for a long period).

In our clinical case, the decision on the operation extent was based on the following factors: 1) radiological indicators of the multifocal tumor growth - the segmental position of micro calcification in projections of several ducts and their branches with over 4 cm range; 2) the result of the morphological study - multiple foci of ductal carcinoma in situ in a large number of histological sections. The age of the patient, multifocal growth of ductal cancer in situ, the grade of tumor's malignancy present a high risk of recurrence. Therefore, mastectomy is the only radical surgical treatment for a similar group of DCIS patients with multifocal growth.

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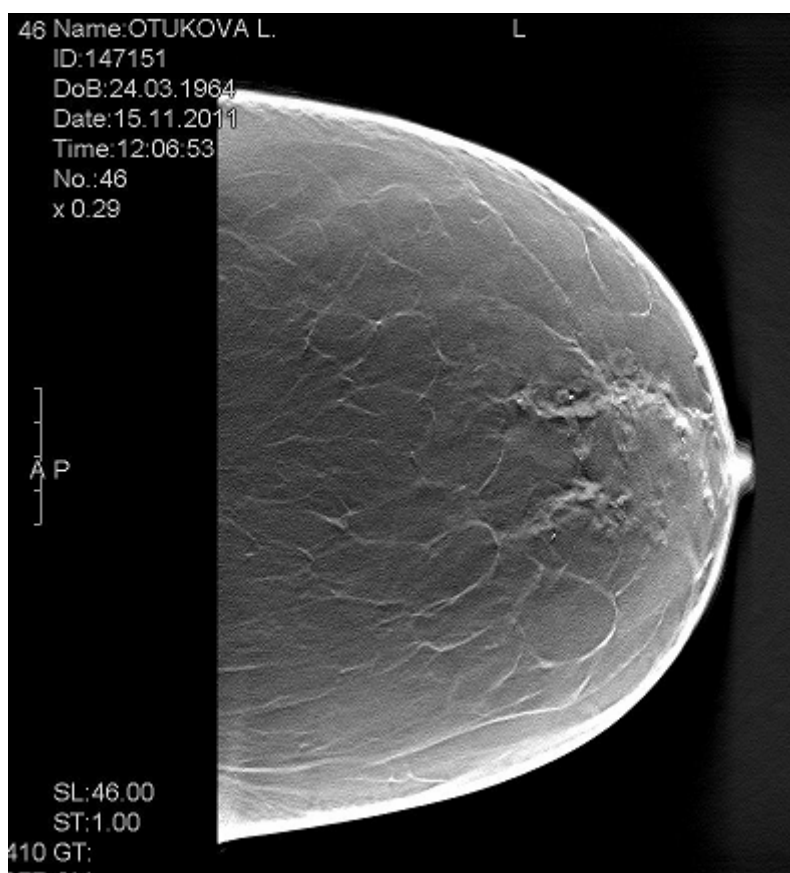
Picture 1. Digital mammography of the left mammal gland in oblique projection.



Picture 2. Digital mammography of the left mammal gland in frontal projection.



Picture 3. Tomosynthesis of the left mammal gland in oblique projection.



Picture 4. Tomosynthesis of the left mammal gland in frontal projection.

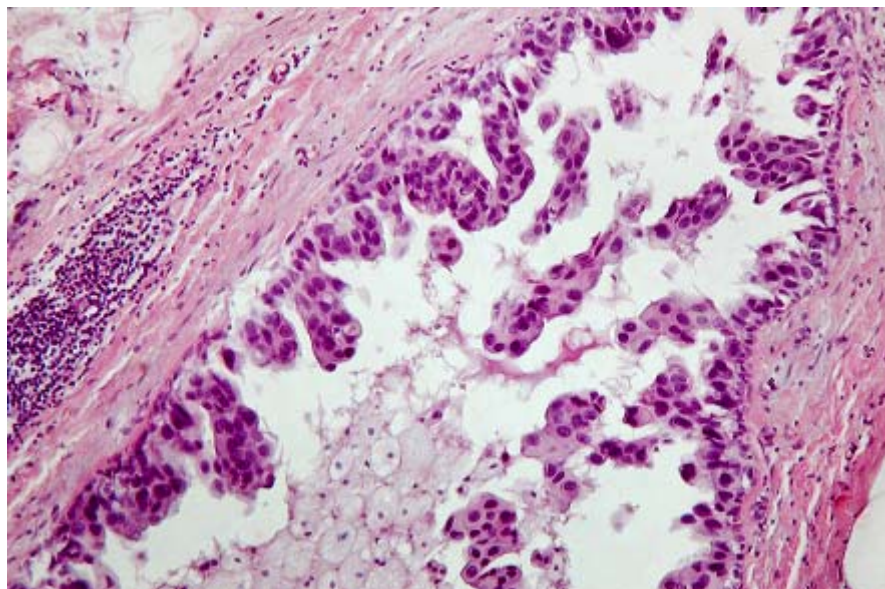


Figure 1. Histopathologic feature of ductal carcinoma in situ.
(Hematoxylin-eosin, magnification – x200)

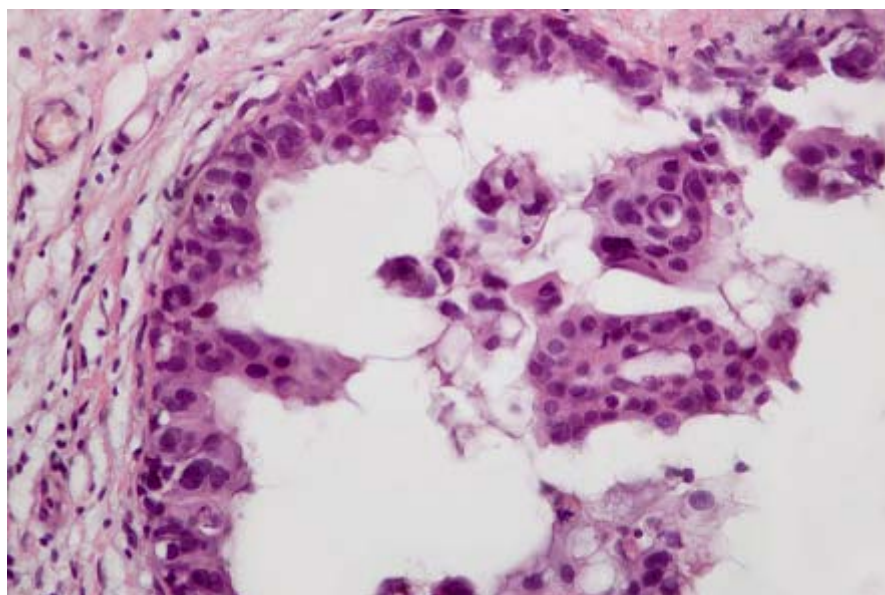


Figure 2. Histopathologic feature of ductal carcinoma in situ.
(Hematoxylin-eosin, magnification – x200)

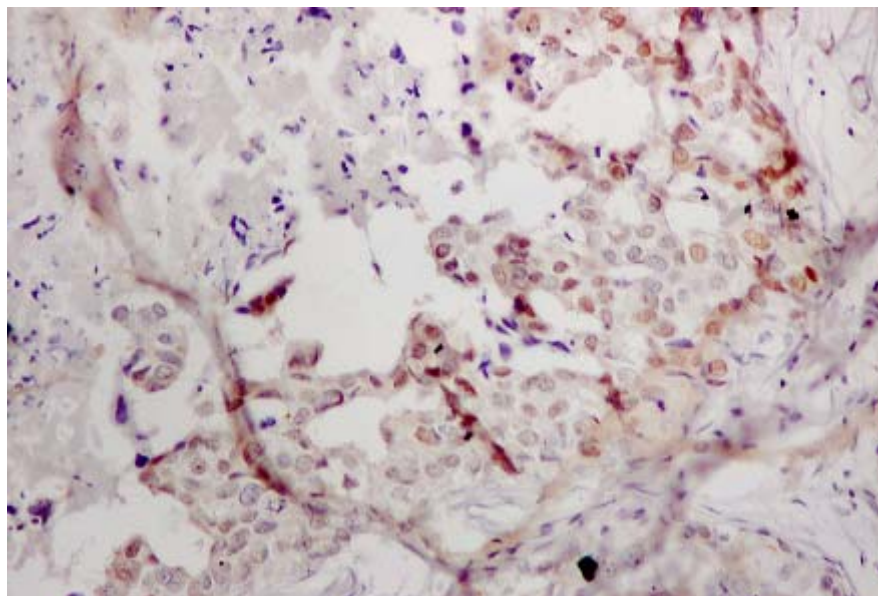


Figure 3. Immune-histological-chemical study of expression to estrogen receptors in a tumor. For most cells, the reaction is positive (brown coloration).

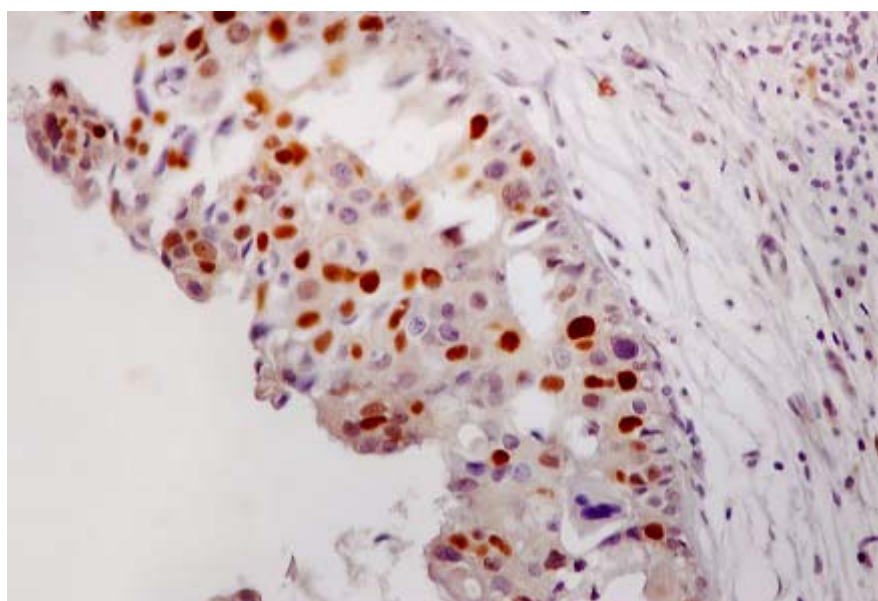


Figure 4. Immune-histological-chemical study of expression to progesterone receptors in a tumor. For most cells, the reaction is positive (brown coloration).

About the authors: Lyubov Nikiforovna Korostyleva, Candidate of Medical Sciences, Associate Professor, Department of Surgical Pathology and Dentistry, Institute for Post-graduate Medical Studies, North-Eastern Federal University, korln@mail.ru; Albert Dmitrievich Makarov, Candidate of Medical Sciences, Associate Professor, Department of Hospital Surgery, Medical Institute, North-Eastern Federal University; the Republic's Hospital № 1 – Center of Medicine: Zinaida Dmitrievna Gurieva, oncologist-mammologist, Candidate of Medical Sciences; Natalia Mikhailovna Sleptsova, radiologist; Alexandra Stepanovna Innokentieva, pathomorphologist.