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SUT BEZINING NOLAKTASION YIRINGLI-YALLIG'LANISH KASALLIKLARI: ETIOLOGIYA, PATOGENEZ VA TASHXIS

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Annotatsiya

Mazkur maqolada nolaktasion sut bezining yiringli-yallig'lanish kasalliklarining (NSBYYK) etiologiyasi, patogenezi va diagnostikasi bo'yicha zamonaviy ma'lumotlar tizimlashtiriladi, differensial xirurgik yondashuv asoslanadi. NSBYYK kamida to'rtta mustaqil morfologik fenotipni o'z ichiga oladi: autoimmun (GLM, IgG4-assotsirlangan), yuqumli (C. kroppenstedtii, MRSA) va obstruktiv-yallig'lanish (periduktal mastit) shakllari. C. kroppenstedtii qaytalanish xavfini 2,64 marta oshirishi (95% DI 1,4–4,9), penisilinga chidamlilik esa 70% ni tashkil etishi aniqlangan. Yiringli membrananing morfologik pishib-etilish bosqichi — etilmagan (<2 mm), o'rtacha pishgan (2–4 mm), pishgan (>4 mm) — xirurgik amaliyot hajmini belgilovchi asosiy mezon sifatida asoslab berilgan. CD68, CD138, IgG4/IgG, Ki-67 kengaytirilgan IGX paneli yordamida morfologik verifikatsiya zaruriy shart ekanligi isbotlangan.

Kalit so'zlar

nolaktasion mastit, granulematoz lobulyar mastit, periduktal mastit, IgG4-assotsirlangan mastit, Corynebacterium kroppenstedtii, yiringli membrana, tashxis, immunogistokhimiya.

NON-LACTATIONAL MASTITIS: ETIOLOGY, PATHOGENESIS AND DIAGNOSIS

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Abstract

This article systematizes current data on the etiology, pathogenesis and diagnosis of non-lactational mastitis (NLM) as a basis for differentiated surgical management. NLM encompasses at least four independent morphological phenotypes with fundamentally different pathogenetic mechanisms: autoimmune (granulomatous lobular mastitis — GLM; IgG4-associated mastitis), infectious (C. kroppenstedtii, MRSA) and obstructive-inflammatory (periductal mastitis — PDM) forms. C. kroppenstedtii was shown to increase recurrence risk 2.64-fold (95% CI 1.4–4.9) with 70% penicillin resistance. The morphological maturity of the pyogenic membrane — immature (<2 mm), moderately mature (2–4 mm) and mature (>4 mm) — is substantiated as the key criterion for determining operative volume. Morphological verification with an extended IHC panel (CD68, CD138, IgG4/IgG, Ki-67) is justified as a mandatory prerequisite for evidence-based surgical decision-making in NLM.

Keywords

non-lactational mastitis, granulomatous lobular mastitis, periductal mastitis, IgG4-associated mastitis, Corynebacterium kroppenstedtii, pyogenic membrane, diagnosis, immunohistochemistry.

НЕЛАКТАЦИОННЫЕ ГНОЙНО-ВОСПАЛИТЕЛЬНЫЕ ЗАБОЛЕВАНИЯ МОЛОЧНОЙ ЖЕЛЕЗЫ: ЭТИОЛОГИЯ, ПАТОГЕНЕЗ И ДИАГНОСТИКА

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Аннотация

В статье систематизированы современные данные об этиологии, патогенезе и диагностике нелактационных гнойно-воспалительных заболеваний молочной железы (НГВЗМЖ) как основа для дифференцированного хирургического подхода. НГВЗМЖ объединяет не менее четырёх самостоятельных морфологических фенотипов: аутоиммунный (ГЛМ; IgG4-ассоциированный мастит), инфекционный (C. kroppenstedtii, MRSA) и обструктивно-воспалительный (ПДМ). Установлено, что C. kroppenstedtii повышает риск рецидива в 2,64 раза (95% ДИ 1,4–4,9) при 70% резистентности к пенициллину. Морфологическая зрелость пиогенной мембраны — незрелая (<2 мм), умеренно зрелая (2–4 мм) и зрелая (>4 мм) — обоснована как ключевой критерий выбора объёма операции. Аргументирована необходимость морфологической верификации с расширенной ИГХ-панелью (CD68, CD138, IgG4/IgG, Ki-67) как условия дифференцированного хирургического лечения НГВЗМЖ.

Ключевые слова

нелактационный мастит, гранулематозный лобулярный мастит, перидуктальный мастит, IgG4-ассоциированный мастит, Corynebacterium kroppenstedtii, пиогенная мембрана, диагностика, ИГХ.

INTRODUCTION

Non-lactational mastitis (NLM) is a heterogeneous group of inflammatory conditions characterised by fundamentally different pathogenetic mechanisms: autoimmune (granulomatous lobular mastitis — GLM; IgG4-associated mastitis), infectious (Corynebacterium kroppenstedtii, MRSA) and obstructive-inflammatory (periductal mastitis — PDM). NLM accounts for up to 33% of all inflammatory breast diseases [4, 7]. Recurrence rates under existing approaches reach 15–65%, depending on the form and treatment modality [1,4].

This paper is Part I of a two-part series; Part II addresses surgical treatment. Particular attention is given to pyogenic membrane morphology — an

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underappreciated yet decisive factor in surgical decision-making and recurrence risk stratification.

LITERATURE SEARCH METHODS

Narrative review. Databases: Scopus, WoS, PubMed (2015–2025). Search queries: "non-puerperal mastitis", "granulomatous lobular mastitis etiology", "periductal mastitis pathogenesis", "IgG4-related mastitis", "Corynebacterium mastitis breast", "pyogenic membrane breast abscess". Inclusion criteria: studies n≥30, systematic reviews, international consensus documents. Initial screening yielded 187 sources; 13 were included after applying inclusion/exclusion criteria.

CLASSIFICATION AND EPIDEMIOLOGY

NLM is not a single nosological entity. At least four clinico-morphological phenotypes are recognised (Table 1). The systematic review by Fattahi A.S. et al. [2] (71 studies, n=4,735) reported a mean patient age of 34.98 years and a mean inflammatory mass diameter of 4.64 cm. The number of NLM publications increased more than six-fold between 2000 and 2023 [12], reflecting growing clinical interest.

Data for the Central Asian region are absent from indexed literature, which constitutes a significant evidence gap and directly justifies the present dissertation research.

Table 1. Clinico-morphological characteristics of main NLM forms

Form	Age	Pathogen / mechanism	Morphology	Recurrence	Ref.
GLM	17–42 yr	Autoimmune / Ck	Epithelioid granulomas, no caseation	4–65%	[1,3,5]
PDM	30–55 yr	Ck, staphylococci, anaerobes	CD138+ plasma cells, ductus ectasia	20–40%	[6]
IgG4 form	35–65 yr	Autoimmune (IgG4-RD)	Storiform fibrosis, IgG4/IgG >40%	<10% *	[9]
Inf. abscess	Any age	C. kroppenstedtii, MRSA	Neutrophilic infiltration, pyogenic membrane	15–50%	[7,8]

* With adequate steroid therapy. Ck — C. kroppenstedtii; GLM — granulomatous lobular mastitis; PDM — periductal mastitis.

ETIOLOGY AND PATHOGENESIS

Autoimmune mechanisms in GLM

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The pathogenesis of GLM is based on an aberrant immune response to lobular epithelial antigens, resulting in lobulocentric epithelioid granulomas without caseating necrosis [5]. Predisposing factors include hyperprolactinaemia (including antipsychotic-induced), α1-antitrypsin deficiency, and prior breast surgery. Differentiation from tuberculous mastitis requires negative PCR for M. tuberculosis and absent caseation.

Role of Corynebacterium kroppenstedtii

Zeng W. et al. [7] (n=133) demonstrated that C. kroppenstedtii (Ck) increases recurrence risk 2.64-fold (95% CI 1.4–4.9; p=0.003), with 70% penicillin resistance. Ck is a lipophilic bacterium with a strong capacity for biofilm formation within the pyogenic membrane wall, ensuring persistence of infection despite adequate drainage. Identification requires MALDI-TOF mass spectrometry. Zhou F. et al. [8] reported 89% remission with rifampicin-based triple therapy; β-lactams are ineffective.

IgG4-associated mastitis

Morphological criteria [9]: >10 IgG4-positive plasma cells per high-power field; IgG4/IgG ratio >40%; storiform fibrosis and/or obliterative phlebitis. This phenotype responds selectively to steroid immunosuppression. Kiyak G. et al. [9] documented that a substantial proportion of IgG4-mastitis cases are initially misidentified as malignancy, leading to unnecessary surgery.

PDM pathogenesis and pyogenic membrane morphology

PDM originates from duct obstruction and ectasia (ductus ectasia), followed by extravasation of ductal contents into the stroma and CD138+ plasma cell infiltration. Ck and Staphylococcus spp. are detected in 74% of PDM patients vs 31% in GLM (p<0.001) [6].

The pyogenic membrane is the key morphological structure of a non-lactational abscess, determining the operative plan. Three maturity stages are identified (Table 2):

Table 2. Morphological stages of the pyogenic membrane and their surgical implications

Maturity stage	Histological features	Thickness	Surgical implication
Immature (acute)	Neutrophilic infiltrate, early granulation tissue, loose stroma	<2 mm	Aspiration / limited incision; biofilm minimal
Moderately mature	Granulation + early fibrosis, CD68+ macrophages, lymphoplasmacytic	2–4 mm	I&D ± membrane excision recommended

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Maturity stage	Histological features	Thickness	Surgical implication
	infiltrate		
Mature (chronic)	Dense fibrous capsule, Ck biofilm in matrix, abundant CD68+	>4 mm	Mandatory membrane excision; preservation = infection persistence
Unformed (phlegmon)	Diffuse necrosis, no distinct membrane	—	Necrectomy + VAC therapy

Authors' classification based on morphometric data from references [7, 8]; prospective validation is required.

In Ck-associated abscesses, biofilm within the pyogenic membrane matrix survives drainage of cavity contents. Excision of the mature membrane is a morphologically justified operative step [7, 8,13].

DIAGNOSIS

Clinical presentation

NLM presents as a painful breast mass with fluctuation, local erythema and skin hyperthermia occurring outside the lactation period. Clinical presentation frequently mimics inflammatory breast cancer [9, 11]. Mandatory initial assessment includes: exclusion of lactation, history of smoking, antipsychotic and immunosuppressive medication use. Smoking is an independent predictor of central (subareolar) abscess and recurrent PDM [6].

Ultrasound — the primary tactical tool

Ultrasound (US) with colour Doppler is the mandatory first-line modality and directly guides therapeutic decision-making. Parameters to assess: (1) maximum cavity diameter; (2) unilocular vs multilocular morphology; (3) location (subareolar / intramammary / retromammary); (4) pyogenic membrane thickness — an indirect marker of morphological maturity. MRI with DWI is indicated to exclude malignancy in atypical cases [3].

Morphological verification

US-guided core biopsy is a mandatory pre-operative step. IHC panel: CD68, CD138, IgG4 and IgG, Ki-67, Ziehl–Neelsen stain. IgG4/IgG >40% screening should be incorporated into the standard NLM diagnostic protocol [9]. Intraoperative frozen section biopsy of the pyogenic membrane is indicated in cases of recurrent abscess, sterile culture and atypical clinical course.

Laboratory and microbiological diagnostics

Minimum standard: FBC, CRP, procalcitonin. In patients with autoimmune history: ANA, ANCA, serum IgG4 (normal <135 mg/dL), prolactin. Biomedical

markers (lipid profile, hormonal status) [10] facilitate identification of predisposing factors. Culture with MALDI-TOF identification and antibiogram is mandatory in all NLM forms.

RECURRENCE PREDICTORS

Three predictor groups are identified. Microbiological: Ck (OR 2.64 [7]), MRSA, β-lactam antibiotherapy for Ck. Clinical: central (subareolar) localisation associated with PDM [6], smoking, multilocularity on US, diameter >3 cm during aspiration. Morphological (surgically modifiable): mature pyogenic membrane >4 mm with incomplete excision; Ck biofilm within the abscess wall. Morphological predictors represent the only group directly amenable to surgical correction — this forms the scientific basis of the algorithm described in Part II.

LIMITATIONS

The narrative design permits subjective source selection. Data for the Central Asian population are absent from indexed literature, limiting direct extrapolation of recommendations without regional adjustment. RCTs on NLM diagnostics are practically non-existent; all recommendations are based on retrospective cohort data (GRADE: low). The pyogenic membrane thickness thresholds (<2, 2–4, >4 mm) represent an authors' classification requiring prospective validation within the dissertation study.

CONCLUSIONS

1. C. kroppenstedtii is the leading pathogen in infectious NLM forms (OR of recurrence 2.64; 70% penicillin resistance); MALDI-TOF identification and rifampicin-based antibiotherapy are mandatory.

2. IgG4/IgG >40% is the pathognomonic morphological criterion for IgG4-associated mastitis; IgG4/IgG screening should be incorporated into the standard NLM diagnostic protocol.

3. Pyogenic membrane maturity (immature <2 mm / moderately mature 2–4 mm / mature >4 mm) is the key surgically actionable criterion determining the necessity and extent of membrane excision.

4. Evidence on NLM for the Central Asian population is absent; development of regional clinical data is a priority objective of the present dissertation.

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