

Clinical practice guidelines for diagnosis and treatment of patients with non-puerperal mastitis: Chinese Society of Breast Surgery (CSBrS) practice guideline 2021

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The term non-puerperal mastitis (NPM) refers to a group of benign breast diseases of unknown cause that occur in non-puerperal women. The main pathological types are periductal mastitis (PDM) and granulomatous lobular mastitis (GLM). The main clinical manifestations of NPM are breast masses and breast abscesses. Associated fistulas, sinuses, or ulcers can form in the later stages; these tend to be persistent and to fail to heal. The natural course of these conditions is about 9 to 12 months and they frequently recur. There is currently no standard treatment. To help clinicians to make the correct diagnosis and formulate an appropriate treatment plan, the Chinese Society of Breast Surgery has reviewed published reports and conducted discussions between experts to determine the key issues to be included in clinical practice guidelines for NPM. This group has also studied the grading of recommendations assessment, development, and evaluation system, evaluated the relevant evidence, and formulated the following clinical practice guidelines (2021 version) for the diagnosis and treatment of NPM, the aim being to provide a reference standard for breast clinicians.

Level of Evidence and Recommendation Strength

Level of evidence standard^[1]

Recommendation strength standard^[1]

Recommendation strength review committee

A total of 79 members of the voting committee of this guideline, including 66 breast surgeons (83.5%), four

oncologists (5.1%), four radiologists (5.1%), two pathologist (2.5%), one radiation therapist (1.3%), and two epidemiologists (2.5%).

Target Audience

Chinese breast disease specialists.

Recommendations

Recommendation 1: Diagnosis.

	Method	Level of evidence	Strength of recommendation
1.1	Diagnostic method		
1.1.1	Ultrasound ^[2]	I	A
1.1.2	Detection of pathogenic microorganisms ^[3]	II	A
1.1.3	Pathological diagnosis ^{[2],*}	I	A
1.2	Type of biopsy		
1.2.1	Core needle biopsy ^[4,5]	I	A
1.2.2	Vacuum-assisted breast biopsy ^[6]	II	B

* On microscopic examination of hematoxylin and eosin-stained sections, periductal mastitis is characterized by greatly dilated ducts filled with pink material, abundant fatty acid crystals, and infiltration of lymphocytes, plasma cells, and neutrophils around the dilated ducts. Granulomatous lobular mastitis manifests as multifocal non-caseating granulomas centered on lobular units of the breast and composed mainly of epithelioid cells, Langhans giant cells, neutrophils, and lymphocytes. They vary in size and may be accompanied by microabscesses.

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Recommendation 2: Pharmacotherapy.

	Therapeutic schedule	Level of evidence	Strength of recommendation
2.1	Granulomatous lobular mastitis		
2.1.1	Corticosteroids ^{[7],*}	III	B
2.2	Periductal mastitis		
2.2.1	Anti-infective treatment during acute inflammation ^{[3],†}	II	A
2.2.2	Anti-mycobacterial drugs for periductal mastitis with fistula formation or ulceration ^{[8,9],‡}	III	B

*Prednisone or methylprednisolone can be used. The usual dosage is prednisone 0.75 mg·kg⁻¹·day⁻¹, a 2-week course being recommended. The dose should be reduced gradually once the symptoms have resolved. The time to complete resolution is highly variable (1.5–20 months).
 †Broad-spectrum antibiotics are used to control the inflammatory response in the acute phase; however, antibiotic treatment alone cannot cure this condition. ‡Isoniazid (300 mg/day), rifampicin (450 mg/day) combined with ethambutol (750 mg/day) or pyrazinamide (750 mg/day). Published reports recommend treatment for 9 to 12 months.

Recommendation 3: Surgery.

	Surgery	Level of evidence	Strength of recommendation
3.1	Abscess		
3.1.1	Incision and drainage ^[10]	I	A
3.1.2	Needle aspiration with ultrasound guidance may be considered for unilocular abscesses (<3 cm) ^[11,12]	II	A
3.2	Sinus and fistula		
3.2.1	Fistulectomy ^[13]	III	B

Discussion

The causes of NPM are unclear and there is a lack of evidence-based data on diagnosis and treatment. In this guideline, the recommendations for means of diagnosing NPM and obtaining biopsies, pathological classification, and drug and surgical treatment are based on a combination of findings of retrospective studies and the panel members' experience in diagnosis and treatment.

Comprehensive assessment of patients with NPM should include identifying clinical manifestations, performing auxiliary investigations, and determining the histopathology. To make this diagnosis, breast tuberculosis and specific granulomatous lesions must be excluded. The panel recommends breast ultrasound as the optimal imaging modality for patients with suspected NPM; this can be used to evaluate the lesion's characteristics and the number and extent of any abscesses.^[14] There is limited

evidence for the value of mammography in diagnosing NPM. Breast magnetic resonance imaging has greater specificity. Diffusion-weighted imaging may assist in differentiating between PDM and GLM^[15]; however, because there is little evidence for this, the panel does not recommend magnetic resonance imaging as a routine imaging modality.

The clinical manifestations of PDM and GLM are similar; however, the treatment and prognosis differ. The panel recommends that NPM be diagnosed by pathological examination of a specimen and considers that core needle biopsy is the optimal means of obtaining the required tissue. In patients undergoing incision and drainage, a specimen can also be taken from the wall of the abscess cavity. Because fine-needle aspiration yields such a small amount of tissue, the panel does not recommend it as a routine means for pathological examination in patients with NPM.

The role of corticosteroids in the treatment of GLM has recently attracted increasing attention. Retrospective studies have shown that oral steroid treatment is effective in 72% to 86% of cases, the ipsilateral recurrence rate being 4% and the contralateral recurrence rate 0.97%.^[16,17] A meta-analysis has shown similar rates of recurrence of GLM after medical versus surgical treatment.^[18] However, medical treatment is less traumatic; the panel therefore considers that oral steroid therapy can be given priority to GLM patients. Surgical treatment enables accurate pathological diagnosis and removal of affected tissue. Studies have shown that surgery is effective in 79% to 91.7% of cases, the recurrence rate being 1% to 50%.^[19,20] Surgical complications include delayed incision healing, poor cosmetic outcomes, breast fistula formation, nipple retraction, skin flap necrosis, hematoma, persistent infection, and pain. The panel has made no recommendations regarding immunosuppressive treatment because of the lack of high-level evidence for this treatment modality.

Patients with pathologically confirmed PDM and sinus formation may have non-tuberculous mycobacterial infection. In such cases, 9 to 12 months of anti-mycobacterial treatment is reportedly effective.^[9] In view of the lack of definitive evidence concerning the causes of PDM, the panel recommends collecting specimens for microscopic examination and bacterial culture from patients with suspected NPM. If possible, DNA sequencing should be used to identify pathogenic bacteria. The panel believes that, in patients with PDM, surgical treatment in general, and the specific procedure in particular, should be selected on the basis of the clinical stage of the disease and type of patient. Appropriate timing of surgery is important. The decision to perform a mastectomy should be made with care.

Drainage is the mainstay of treatment when breast abscess formation. Pus can be drained by ultrasound-guided puncture or an incision into the abscess. In the absence of high-level evidence, the panel considers that <3 cm unilocular abscesses should be drained by ultrasound-guided aspiration, whereas consideration should be given

to surgical incision and drainage as first-line therapy for larger (clinically >3 cm), multiloculated, or longstanding abscesses.

Appendix: Pathological features of periductal mastitis and granulomatous lobular mastitis Periductal mastitis, <http://links.lww.com/CM9/A563>.

Conflicts of interest

The expert committee for these guidelines declares no conflicts of interest. These guidelines are intended to serve as a reference for breast disease specialists in clinical practice. They are not to be used as a basis for medical evaluation, nor to play an arbitrating role in the handling of any medical disputes. Additionally, these guidelines are not intended as a reference for patients or non-breast specialists. The Chinese Society of Breast Surgery assumes no responsibility for consequences arising from the inappropriate application of these guidelines and reserves the right to interpret and revise them as necessary.

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