

It's Not Yeast: Retrospective Cohort Study of Lactating Women with Persistent Nipple and Breast Pain

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Abstract

Introduction: Health care providers treating lactating women for nipple and breast pain often attribute symptoms to *Candida albicans* infection. However, multiple other conditions may present with pain, erythema, and pruritis. We explored the experience of a breastfeeding medicine practice that received referrals for patients failing antifungal therapy and who desired further evaluation for alternative diagnoses.

Materials and Methods: We conducted a retrospective chart review of breastfeeding women referred for evaluation of “yeast” to a breast surgery/breastfeeding medicine practice from July 2016 to August 2019.

Results: Twenty-five women met inclusion criteria. Median age was 33 (range 24–43) and median months postpartum was 4 (range 0.5–18). All 25 women reported minimal to no improvement on oral and/or topical antifungal therapy. In addition to history and examination, milk culture was obtained in four women, punch biopsy in one, and core needle biopsy in one. No woman was confirmed to have a diagnosis of *Candida*. Diagnoses were changed to the following: subacute mastitis/mammary dysbiosis ($n=8$), nipple bleb ($n=6$), dermatitis ($n=6$), vasospasm ($n=2$), milk crust ($n=1$), hyperlactation ($n=1$), and postpartum depression ($n=1$). Treatment included discontinuation of antifungal medication, as well as the following per individual diagnoses: antibiotics and probiotics; 0.1% triamcinolone cream; heat therapy; discontinuation of exclusive pumping; and antidepressant medication and counseling referral. All women experienced resolution of symptoms following revision of diagnosis and change in management (range 2–42 days).

Conclusion: While persistent nipple and breast pain in breastfeeding is often attributed to *Candida*, this cohort demonstrates that providers should consider multiple other conditions in their differential diagnosis. Accurate, timely diagnosis is crucial, as pain is a risk factor for premature cessation of breastfeeding. Symptomatic resolution occurs on appropriate therapy.

Keywords: yeast, thrush, *Candida*, breast pain, nipple pain

Introduction

NIPPLE AREOLAR COMPLEX and deep breast pain causes significant morbidity among breastfeeding dyads and has been associated with early cessation of breastfeeding.¹ A complex variety of issues may contribute to the development of this pain, and require careful evaluation by health care providers. The most common etiology involves improper

latch and positioning,² most often related to engorgement and inadequate education and support.¹ Other conditions include subacute mastitis/mammary dysbiosis, nipple blebs, dermatitis, vasospasm, and functional pain.^{3,4}

In addition, providers caring for breastfeeding dyads have attributed symptomatology of redness, itching, and breast and nipple areolar complex pain to a diagnosis of *Candida albicans*.⁵ This has been termed “mammary candidiasis,”

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“thrush,” or “intraductal yeast.” Other symptoms in which *Candida* has been implicated include cracking of the nipple, fullness of the breast, erythematous skin, and shooting pain into the axilla.⁵ Mothers may receive the diagnosis of cutaneous or intraductal yeast infection after their infant has been treated for thrush.⁵

Despite the frequency of this diagnosis, little evidence exists to support yeast as an etiologic agent in this patient population. Most patients undergo treatment without confirmation of a pathological fungal organism present in milk nor the skin.^{5,6} Women may undergo antifungal therapy with oral medication, topical application of liquids or creams, and utilize caustic agents such as Gentian violet.⁷ Although there is some evidence that antifungal treatment is effective,⁸ this is likely related to the anti-inflammatory effects of the intervention rather than a true diagnosis of yeast. Therefore, they may experience temporary relief of symptoms, but frequently return with lack of resolution.

Antifungal treatment by mouth should be used judiciously, and topical antifungal agents can macerate and ulcerate skin, potentiating pain and vasospasm.⁹ To prevent harm from unnecessary antifungal treatment as well as definitively resolve symptoms to prevent early cessation of breastfeeding, providers should avoid presumptive diagnoses of *Candida* infection. This study explores the experience of a breastfeeding medicine practice that received referrals for patients failing antifungal therapy and who desired further evaluation for alternative diagnoses.

Materials and Methods

We performed a retrospective chart review of women referred to an outpatient breastfeeding medicine clinic in the United States between July 2016 and August 2019. Referral sources included lactation consultant, obstetrician-gynecologist, and patient self-referral. The study population was restricted to women who were referred for persistent symptoms despite previous diagnosis and treatment with antifungals for a “yeast infection.” This study was approved by the Presbyterian Healthcare Services Institutional Review Board 1477797-1.

Variables extracted included age, race/ethnicity, months postpartum, parity, breast pump use, presenting symptoms/signs, type of antifungal therapy, final diagnosis, treatments, and time to resolution of symptoms.

Final diagnosis was established by thorough history and physical examination, as well as selective use of adjunct diagnostic tests, including milk culture and breast biopsy. Subacute mastitis was diagnosed on the symptoms of deep, shooting, or aching breast pain. A white, yellow, or hemorrhagic blister-like lesion covering the surface of one or multiple nipple orifices confirmed the diagnosis of nipple bleb. Dermatitis was confirmed by the presence of erythematous and flaking skin involving the areola or breast, and included symptom of pruritis. Vasospasm diagnosis involved the presence of a white contracted nipple that was associated with shooting pain from the nipple into the breast exacerbated by change in temperature, such as exiting a shower to a cold room or after pumping or breastfeeding. Milk crust was diagnosed in a patient who was pumping exclusively and developed a tenacious white crust over the entire surface of her nipple. Postpartum depression was diagnosed in the setting of

nonspecific breast and nipple pain with no associated physical examination findings and a concurrent history of sadness, loss of interest in activities, insomnia, and frequent crying.

Results

Of 214 women referred during the study time period, 25 women met inclusion criteria. The median age was 33 years (range 24–43) and median months postpartum at presentation was 4 (range 0.5–18). The study population comprised 15 white patients (60%), 7 Hispanic patients (28%), 2 Asian patients (8%), and 1 Middle Eastern patient (4%). Nine patients were primiparous (36%). Eight were using a breast pump (32%), one exclusively (4%).

Patients had been previously diagnosed with *Candida* for multiple different complaints: nipple and/or breast pain ($n=17$), white nipple lesion ($n=8$), and persistent skin redness ($n=6$). Thirteen patients presented with more than one symptom, and seven had infants who were diagnosed with oral thrush.

All reported minimal to no improvement on any antifungal therapy, including topical nystatin ($n=11$), topical miconazole ($n=4$), topical clotrimazole ($n=1$), gentian violet ($n=3$), coconut oil ($n=3$), all-purpose nipple ointment (which includes a steroid, antifungal, and antibacterial)¹⁰ ($n=7$), and/or oral fluconazole ($n=13$). More than 1 agent was used with 10 patients, and 6 antifungals had been used in 1 patient before referral. Due to lack of resolution and one patient's concern for Paget's disease, a rare form of breast cancer that presents with nipple scaling and erosion,¹¹ patients were referred for further evaluation.

To establish a diagnosis, in addition to history and physical examination, milk culture was obtained in four women, punch biopsy in one, and core needle biopsy in one. A breast milk culture positive for *Streptococcus mitis* corroborated the diagnosis of subacute mastitis in a patient who also reported nipple and breast pain. A patient with symptoms of subacute mastitis that included pain and nipple flaking underwent punch biopsy that showed changes associated with chronic rubbing. This biopsy was performed due to older patient age and strong family history of cancer, and the intent was to rule out Paget's disease. This was a different patient than the one who presented concerned for Paget's disease herself and had a clear diagnosis of dermatitis. A patient diagnosed with blebs also underwent a core needle biopsy of an area of underlying plugging that demonstrated a suspicious appearance on imaging but showed dense lactational tissue on final pathology.

No woman was confirmed to have a diagnosis of superficial nor intraductal *Candida*. Diagnosis was changed to the following: subacute mastitis ($n=8$), multifocal bleb ($n=3$), focal nipple bleb ($n=3$), dermatitis ($n=6$), vasospasm ($n=2$), milk crust ($n=1$), hyperlactation ($n=1$), and postpartum depression ($n=1$).

Treatment included discontinuation of antifungal treatment as well as the following:

- Subacute mastitis: 4–6-week course of macrolide antibiotics (azithromycin 500 mg daily for all patients with the exception of one course of erythromycin 500 mg BID) or probiotics (*Lactobacillus salivarius* and *Lactobacillus fermentum*) due to patient preference to avoid treatment with antibiotics.

- Nipple blebs and dermatitis: Topical 0.1% triamcinolone cream three times daily for 2 weeks.
- Vasospasm: Heat therapy.
- Hyperlactation and milk crust: Discontinuation of pumping.
- Postpartum depression: Antidepressant and counseling referral.

All women experienced resolution of symptoms on definitive therapy (range 2–42 days) (Table 1). Patients were followed in clinic at standard 2-week intervals to allow for evaluation of progress and resolution of subacute mastitis, blebs, and dermatitis. Some patients in the other diagnostic categories were reevaluated at more variable intervals based on provider concern.

Discussion

Breast and nipple pain while breastfeeding represents a challenging diagnostic dilemma and requires careful evaluation of the breastfeeding dyad. While mammary candidiasis has been implicated as an etiologic agent of symptoms involving shooting pain, redness, and cracking of the nipple,¹ rarely, if ever, have providers confirmed this diagnosis with culture. Instead, without clear evidence to document its presence as a pathologic agent, “mammary candidiasis” has been called “difficult to treat” and labeled as a cause of early cessation of breastfeeding.⁵

Because antifungals exhibit significant strong anti-inflammatory activity as well as antibacterial effects,¹² patients may experience some temporary relief of symptoms in the absence of a true fungal infection. For example, *Staphylococcus aureus*, one of the bacterial causes of mammary dysbiosis, has been shown to be susceptible to oral antifungals.¹³ However, many patients who present with a presumptive diagnosis of “mammary candidiasis” complain of persistent symptoms and present for repeated evaluation and/or treatment. Providers should first assess latch and positioning and persistent engorgement, and then consider other etiologies aside from *Candida* if symptomatology fails to resolve.

In the discussion below, we first review the evaluation and appropriate treatment for confirmed infant or maternal *Candida*, and then describe alternative diagnoses that providers should consider when evaluating a patient for persistent and/or recurrent pain during lactation.

Infant diagnosis of thrush

Incidence rates of thrush in infants range from 5% to 7% in healthy infants, whereas immunocompromised neonates in the neonatal intensive care unit (NICU) experience fungal infections at a higher rate.¹⁴ Symptoms include white patches on the infant’s buccal mucosa as well as oral aversion in some cases.¹ If an infant is diagnosed with thrush, sterilization of maternal pump parts is not necessary as thrush is related to a disruption of host microbiome rather than a contagious pathogen such as *Herpes simplex*.¹⁵

If patients and providers do question a concurrent diagnosis of maternal *Candida* based on history and physical examination, a breast milk culture should be obtained for diagnosis. A skin scraping for gram stain and culture can rule out a *C. albicans* infection. Mothers of NICU infants often are exclusively pumping and are at higher risk for allergic

contact dermatitis, irritant dermatitis, and hyperlactation. These etiologies of pain should be evaluated.

Cutaneous *Candida* of the breast

On the breast, cutaneous fungal infection with *Candida* most often occurs in the inframammary fold or axilla.¹⁶ Treatment includes topical antifungals such as nystatin cream or powder; oral fluconazole should be used judiciously and is most often not necessary to clear these cutaneous presentations. Breast pathology literature does not support yeast occurring on the nipple areolar complex, nor in an intraductal manner.

Dermatitis of breast

Dermatitis occurs with allergic and irritant etiologies, and may present with erythema, edema, and scaling of the skin (Fig. 1).¹⁷ Women with a history of eczema or psoriasis are at risk for having these conditions appear on the nipple areolar complex. Allergic contact dermatitis presents more commonly with pruritus, whereas patients experiencing irritant contact dermatitis usually complain of stinging and pain.¹⁷ Because of the latent period associated with allergic contact dermatitis, symptoms may take weeks to even years to appear after the patient repeatedly contacts the allergen.¹⁷ Common agents contributing to dermatitis in the breastfeeding population include the following: nipple balms/creams, breast pads, nursing bras, new detergents, topical medications such as antifungals, pump parts, and substances the baby is touching or ingesting and then transferring to the mother via mouth to nipple contact.¹⁸

Most often, the specific allergen can be difficult to identify. Therefore, women should be counseled about eliminating any new potential allergens that they had introduced before onset of symptoms. For confirmation of diagnosis, physicians can perform a punch biopsy of the affected breast or nipple areolar complex skin. Patients presenting with characteristic signs can be treated with a strong topical daily steroid based on clinical presentation alone.

Nipple bleb

Nipple blebs are inflammatory lesions on the surface of the nipple that vary in appearance from a light “milk blister” to a more tenacious fibrinous deposition that can obstruct milk, leading to plugging and mastitis (Fig. 1). Nipple blebs can cause significant pain with latching, and this pain may radiate deep into the breast during and after feeds. Patients often describe the pain as sharp and shooting. Blebs are treated most effectively with topical steroid treatment to reduce the inflammatory infiltrate,¹⁹ and may improve with measures to reduce underlying plugging in the deeper breast. When biopsied, blebs show no evidence of association with fungal elements.^{19,20}

Nipple vasospasm

Vasospasm of the nipple results from constriction of peripheral blood vessels in response to cold temperatures (Fig. 2). It results in discoloration of the nipple areolar complex, hardening of the nipple, and pain. Due to the complex innervation patterns of the breast and nipple areolar complex, this pain may radiate deep into the breast.

TABLE 1. SUPPLEMENTAL DATA OF STUDY PATIENTS

Diagnosis	Mother age (years)	Race/ethnicity	Infant age (months)	Primiparous	Pumping in addition to breastfeeding	Symptoms	Baby thrush before presentation	Previous antifungal treatment	Investigations	Definitive treatment	Time to resolution (days)
Subacute mastitis	34	White	10	Yes	Yes	Bilateral nipple pain	Yes	Topical nystatin	BM culture + Strep mitis	Probiotics × 28 days (oral)	28
Subacute mastitis	31	White	2	Yes	Yes	Bilateral burning/pain	No	Fluconazole	BM culture no growth	Azithromycin × 28 days (oral)	28
Subacute mastitis	35	Hispanic	10	No	No	Bilateral nipple pain/cracking	Yes	Topical nystatin, topical miconazole		Azithromycin × 28 days (oral)	28
Subacute mastitis	39	White	0.5	No	No	Left breast and nipple pain	No	Fluconazole		Azithromycin × 28 days (oral)	28
Subacute mastitis	32	White	1	Yes	Yes	Bilateral breast/nipple pain	Yes	Topical nystatin		Erythromycin × 28 days (oral)	28
Subacute mastitis	33	Hispanic	4	No	No	Bilateral deep, stabbing pain; right nipple bleb	No	Multiple courses fluconazole, gentian violet		Azithromycin × 42 days (oral)	42
Subacute mastitis	28	Hispanic	3	Yes	Yes	Deep breast and nipple pain	No	APNO	Punch biopsy—chronic rubbing	Azithromycin × 28 days (oral)	28
Subacute mastitis	34	White	15	No	No	Painful/red/swollen left nipple	No	Fluconazole		Azithromycin × 42 days (oral)	42
Multifocal bleb	34	White	6	No	No	Bilateral pain, blebs	No	Topical nystatin	BM culture no growth	Probiotics, (oral); lecithin (oral)	28
Multifocal bleb	35	Hispanic	4	No	No	Pain, white spot	no	Fluconazole		Lecithin (oral); triamcinolone (topical)	14
Multifocal bleb	33	White	5	No	Yes	“Milk blisters” following mastitis	No	Fluconazole		Lecithin (oral)	28
Focal bleb	43	Asian	5	No	No	Left nipple pain, swelling, bleb	No	Fluconazole, APNO	Core needle biopsy—lactating adenoma	Lecithin (oral); triamcinolone (topical)	28
Focal bleb	34	Hispanic	4	No	Yes	Bleb	yes	Fluconazole, gentian violet		Lecithin (oral); triamcinolone (topical)	28
Focal bleb	29	Asian	2.5	Yes	Yes	Left nipple bleb	No	Topical nystatin, APNO		Lecithin (oral) Triamcinolone (topical)	28
Dermatitis	29	White	2	Yes	Yes	Painful nipples, flaking	Yes	Topical nystatin, APNO		Triamcinolone (topical)	14
Dermatitis	37	White	6	No	No	Bilateral nipple pain and redness	Yes	Fluconazole, topical nystatin, APNO, coconut oil		Triamcinolone d/c Coconut oil (topical)	14
Dermatitis	35	White	14	No	No	Red/flaking/itchy areola	No	Fluconazole, clotrimazole		Triamcinolone (topical)	20
Dermatitis	25	Hispanic	14	No	No	Red/itchy/painful areola and breast	Yes	Topical miconazole		Triamcinolone (topical)	14
Dermatitis	32	White	18	Yes	Yes	Bilateral red breasts	No	Topical miconazole, coconut oil		Triamcinolone (topical)	5
Dermatitis	35	White	3	No	No	Red/flaking/itchy nipple	No	Topical nystatin		Triamcinolone (topical)	14
Vasospasm	28	Hispanic	1	No	Yes	Pain	No	Topical nystatin		Warmth	7
Vasospasm	30	White	3	Yes	Yes	Pain, fissures	No	Topical nystatin, fluconazole, APNO		Warmth, d/c pump, wound care	11
Milk crust	29	White	2	No	Yes, exclusively	Right nipple pain, crust	No	fluconazole, gentian violet, APNO, topical Miconazole, topical nystatin, coconut oil		Warmth, d/c exclusive pumping, sertraline (oral)	10
Hyperlactation	24	White	1	Yes	Yes	Bilateral pain, engorge-ment	No	Fluconazole		d/c Triple feeds/pump, regulate production	4
Depression	28	Middle Eastern	1	No	No	Bilateral breast/nipple pain	No	Fluconazole		Sertraline (oral) recommended but pt declined; discontinued breastfeeding per pt desire	30

APNO, all-purpose nipple ointment.

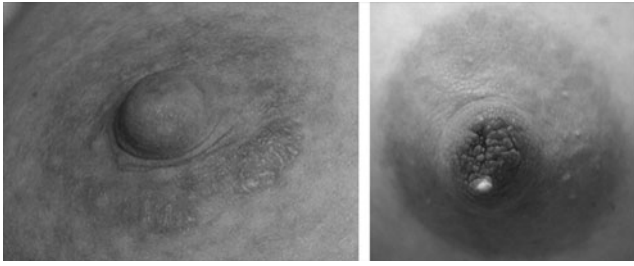


FIG. 1. Clinical presentation of dermatitis of the nipple areolar complex (**left**) and nipple bleb (**right**).

Hyperlactation, suboptimal infant latch, and temperature fluctuations exacerbate vasospasm. Nipple vasospasm responds well to constant heat, which can be achieved with insulating breast warmers. Patients can use warm rice packs or commercial products that can be warmed and positioned in bras. Calcium channel blocking agents can be prescribed in severe cases, although warmth and wound care should be recommended as first-line interventions.²¹

Subacute mastitis/mammary dysbiosis

Subacute mastitis, or mammary dysbiosis, is theorized to represent an imbalance of the breast flora that results in biofilm formation and colony overgrowth, leading to ductal obstruction, chronic inflammation, and pain during lactation (Fig. 3).²² This diagnosis should be considered in patients who experience deep, aching breast pain that may emanate to the nipple areolar complex, often in association with recurrent plugging, breast tenderness, intermittent acute mastitis, recurrent nipple blisters, and biofilm formation within the ducts.²² Breast milk samples in these patients demonstrate a higher concentration of *Staphylococcus epidermidis*, *S. aureus*, *S. mitis/oritis*, and *Streptococcus salivarius* relative to control.²² They do not show a higher concentration of *C. albicans* compared to samples from controls.

Mothers may complain of nipple burning and itching after the infant is diagnosed with oral thrush. There is evidence of interspecies communication via small secreted metabolites



FIG. 2. Clinical presentation of vasospasm of the nipple.

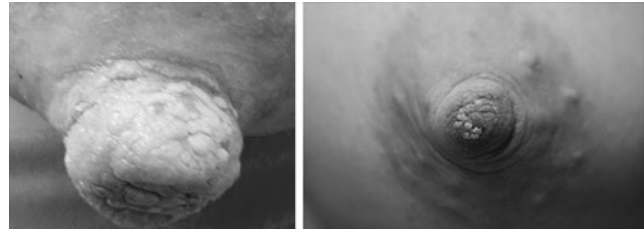


FIG. 3. Clinical presentation of subacute mastitis (**left**) and milk crusting (**right**).

between *C. albicans* and *Staphylococcus* species, which may promote bacterial biofilm formation, a hallmark of mammary dysbiosis.^{22,23} Evaluation and treatment of subacute mastitis include resolving hyperlactation, performing breast milk culture, and using targeted antibiotics, often for a longer duration than that used in acute mastitis.²⁰ A previous chart review demonstrated resolution of mammary dysbiosis symptoms with a several week course of antibiotics.²⁴ Several week treatment of mammary dysbiosis is similar to that of chronic bacterial prostatitis.²⁵

While evidence is still emerging regarding the efficacy of probiotics in treating breastfeeding complications such as acute and subacute mastitis, they may offer promise as an alternative to traditional antibiotic therapy.²⁶

Milk crust and hyperlactation

Patients who exclusively pump breast milk and lack the mechanical debridement of an infant's mouth on the surface of their nipples may develop chronic milk crusting. Some argue this crusting is related to alterations in the milk microbiome and may represent a biofilm (Fig. 3).²⁷ In addition, hyperlactation, or production of breast milk in excess of what is needed for infant growth, may predispose patients to acute and subacute mastitis due to milk stasis, and also cause nipple surface changes associated with mammary dysbiosis and biofilms.²⁷ Unless patients are experiencing symptoms of hyperlactation or subacute mastitis, they can be reassured that this milk crust is not pathologic and repeated attempts to "clean" the nipple will potentiate tissue trauma.

Functional pain and depression and anxiety

Patients suffering from depression and anxiety will experience pain differently than nondepressed individuals because of higher sensitization of second order neurons.²⁸ The selective serotonin reuptake inhibitor class of drugs has been demonstrated to decrease pain.²⁹ Patients experiencing heightened sensitivity to pain, which may reflect an overactive histamine response, may benefit from beta blockers, antihistamines, and neurotropic drugs.³⁰ However, these medications may affect milk production and cause maternal and infant sedation.³⁰ Musculoskeletal pain should also be evaluated.³¹ Any patient presenting with persistent nipple areolar complex and/or deep breast pain in whom other medical conditions have been ruled out should be further evaluated for functional pain syndromes and peripartum mood and anxiety disorders. Health care providers can further offer support by addressing psychosocial issues and referring to additional trained professionals as indicated.³²

Conclusion

Although exact incidence is unknown due to lack of data, there is poor evidence to implicate *C. albicans* as a diagnosis in the lactating population. Pain, erythema, and pruritis may be related to a multitude of other etiologies and these should be explored.

This study is limited by its retrospective and descriptive nature, including the fact that patients were followed at standard 2-week intervals for chronic conditions and their actual time to resolution may have been earlier than when they returned to clinic. It is possible that patients with a true fungal infection resolved before presentation, although they all reported they had persistent and unchanged symptoms. Some women may have had multiple or different diagnoses before presentation.

In addition, most patients were treated based on clinical presentation alone without confirmation of diagnosis with more objective or quantitative measures such as punch biopsy or milk culture. However, milk culture may not always grow an organism even in the setting of clinical subacute mastitis and isolation of bacteria does not always imply causation. Furthermore, performing a punch biopsy of every suspected classically presenting dermatitis case would cause undue patient morbidity. While no necessary intervention should be avoided in the setting of suspicious masses or other concerning breast findings in lactation, an unnecessary punch biopsy near the nipple or areola could disrupt breastfeeding due to challenges with wound healing and infant latch or milk expression.

When mothers present with erythema, itching, and nipple and/or deep breast pain during lactation, we advocate for increased awareness of several common diagnoses as described above. While topical yeast infections can occur in the inframammary fold or axilla in immunocompromised and obese patients, no definitive evidence exists to support fungal infections of the nipple areolar complex or breast parenchyma in immunocompetent lactating women. Health care providers and patients should be aware of the risks of extended antifungal therapy by mouth and local irritation and excoriation caused by topical antifungal agents to the nipple and infant mouth.

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