Management of Primary Necrotizing Fasciitis of the Breast: A Systematic Review

La prise en charge de la fasciite nécrosante primaire du sein :
une analyse systématique

Ryan D. Konik, MD¹ and Gregory S. Huang, MD¹

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Abstract

Purpose: Necrotizing fasciitis (NF) is a life-threatening infection that involves spreading necrosis of the subcutaneous tissue and fascia that affects the extremities, abdominal wall, and perineum. Primary infection of the breast is a rare occurrence. Shah et al described the first case of primary breast NF and recommended radical “pseudotumor” excision and delayed skin closure months after resolution. Numerous other cases reported were successfully managed with different strategies. We aimed to summarize management options for primary breast NF through a systematic review of the literature. **Methods:** A systematic review of English literature was performed using PubMed. A total of 58 abstracts were reviewed. Data were abstracted from 25 cases that met inclusion criteria. **Results:** A total of 25 cases of primary NF of the breast without an inciting event were found within the literature. Common initial operations included total mastectomy (36.0%), excisional debridement (32.0%), and partial mastectomy (12.0%). A total or radical mastectomy was completed for definitive source control in 13 (52.0%) cases. A total of 18 cases underwent reconstruction. Split-thickness skin grafts (44.4%) and delayed primary closures (33.3%) were the most common methods of reconstruction. **Conclusion:** Majority of cases with primary breast NF are managed with a total mastectomy to gain source control. Reconstruction using split-thickness skin grafts was most common. Other options included delayed primary closure, full thickness skin grafts, local tissue rearrangement, and pedicle flap reconstruction. Reconstruction should be patient dependent, but the whole arsenal of the reconstructive ladder may be used.

Résumé

Objectif : La fasciite nécrosante (FN) est une infection au potentiel fatal responsable d'une nécrose croissante des tissus sous-cutanés et du fascia et qui touche les membres, la paroi abdominale et le périnée. L'infection primaire du sein est rare. Shah et coll. ont décrit le premier cas de FN primaire du sein, ont recommandé une excision radicale de la « pseudotumeur » et ont reporté la fermeture cutanée pendant des mois après la résolution. La prise en charge de nombreux autres cas déclarés a été positive grâce à diverses stratégies. Les chercheurs souhaitent résumer les possibilités de prise en charge de la FN primaire du sein à l'aide d'une analyse systématique des publications scientifiques. **Méthodologie :** Les chercheurs ont procédé à une analyse systématique des publications anglophones dans PubMed. Ils ont examiné un total de 58 résumés et colligé les données de 25 cas qui respectaient les critères d'inclusion. **Résultats :** Au total, les chercheurs ont extrait 25 cas de FN primaire du sein non précédés d'un événement incitatif. Les opérations initiales courantes incluaient une mastectomie totale (36,0 %), un débridement excisionnel (32,0 %) et une mastectomie partielle (12,0 %). Dans 13 cas (52,0 %), les chercheurs ont constaté une mastectomie totale ou radicale pour assurer le contrôle définitif de la source. Au total, 18 cas ont subi une reconstruction. Les greffes dermo-épidermiques (44,4 %) et le report des fermetures primaires (33,3 %) constituaient les principales méthodes de reconstruction. **Conclusion :** La majorité des cas de FN primaire du sein étaient pris en charge par une mastectomie totale pour parvenir à contrôler la source. La

¹ Department of General Surgery, St. Elizabeth Health Center, Youngstown, OH, USA

Corresponding Author:

Ryan D. Konik, Department of General Surgery, St. Elizabeth Health Center, 1044 Belmont Ave, Youngstown, OH 44504, USA.
Email: rdkonik@mercy.com

reconstruction par greffe dermo-épidermique était la plus courante. Parmi les autres options, soulignons le report de la fermeture primaire, la greffe dermo-épidermique pleine épaisseur, la réorganisation tissulaire locale et la reconstruction du lambeau pédiculaire. La reconstruction doit être adaptée à chaque patiente, mais peut faire appel à tout l'arsenal de l'échelle de reconstruction.

Keywords

necrotizing fasciitis, breast, necrotizing soft tissue infection, management

Introduction

Necrotizing fasciitis (NF) is a life-threatening infection involving rapidly spreading necrosis of the subcutaneous tissue and fascia. Patients often present in septic shock with multi-organ failure. Clinical examination findings may demonstrate erythema, swelling, pain disproportionate to examination, necrosis, blisters, bullae, and crepitus. Common locations for NF include the extremities, abdominal wall, and perineum.¹ Comorbidities associated with NF include diabetes mellitus, peripheral vascular disease, alcoholic liver disease, immunosuppression, and obesity.^{2,3} An inciting event, such as a traumatic injury, insect bite, injection site, or procedural site, is identified as the cause of the infection in the majority of cases.⁴ The breasts are a rare location for such an infection, with most cases presenting after trauma or surgical intervention. Primary NF of the breast is often misdiagnosed as an abscess or cellulitis leading to treatment delays.⁵ Prompt assessment and treatment are pivotal for successful patient outcomes.

The management of NF involves fluid resuscitation, broad-spectrum antibiotics, and prompt surgical intervention. Shah et al described the first case of primary NF of the breast in a 50-year-old diabetic female. A 6-point management plan was recommended from his observations and included radical “pseudotumor” excision, reexploration of the wound within 24 hours, and delayed skin closure several months after complete recovery.⁶ Since that report, there have been numerous reported cases of primary NF of the breast with management strategies deviating from the initially proposed recommendations. Several questions arise from these new observed strategies such as whether a total mastectomy is required for definitive source control, if the timing to reconstruction must be several months after source control, and if there are other successful reconstruction methods other than delayed primary closure. Primary NF of the breast presents a unique clinical scenario. There is no review in the literature summarizing these management strategies. The objective of this study was to summarize potential management strategies, including source control operations and reconstruction methods through a systematic review of the literature.

Methods

A systematic review of English literature was performed using PubMed without temporal limitations. A search strategy using the phrases “primary necrotizing fasciitis” or “breast necrotizing fasciitis” or “breast necrotizing soft tissue infection” or

“breast gangrene” was used to obtain relevant abstracts. This search strategy obtained a total of 409 articles, which was narrowed down to 52 relevant articles after reviewing the titles. An additional 6 articles were obtained from cross examination of references from selected titles. A total of 58 articles were selected for potential abstract review by the authors. From that cohort, a total of 19 articles were excluded from this selection secondary to no available abstract ($n = 12$), non-English language ($n = 5$), and description of a non-necrotizing infection ($n = 2$). The remaining 39 articles were assessed for qualitative analysis eligibility. Inclusion criteria for qualitative analysis included NF localized to the breast and primary infection without an inciting event, such as an underlying cancer or prior procedure. A total of 13 articles were excluded based on inclusion criteria.⁷⁻¹⁹ A single case series was excluded because of inadequate data.²⁰ Therefore, a total of 25 articles were included in the qualitative analysis. The majority of these articles were single case reports of primary necrotizing infections. Data abstracted included age, comorbidities, mortality, time to presentation, initial source control operation, time to second-look operation, definitive source control operation, microbiology cultures, reconstruction, and time to reconstruction. Statistical analysis was accomplished using Microsoft Excel 2011. A PRISMA flowchart of the literature search is provided in Figure 1.

Results

A total of 25 cases of primary NF of the breast without an inciting event were found in the literature. Information on articles included in the qualitative analysis is provided in Table 1. There were 2 cases of mortality (2/25) with a mortality rate of 8.0%. The average age among the study population was 46.2 ± 16.0 years. Demographics and significant comorbidities are included in Table 2. Average time to initial presentation was 6.6 ± 4.3 days. Initial source control operations included total mastectomy (36.0%, 9/25), excisional debridement (32.0%, 8/25), partial mastectomy (12.0%, 3/25), debridement with sparing of the nipple areolar complex (8.0%, 2/25), incision and drainage (4.0%, 1/25), radical mastectomy (4.0%, 1/25), and bilateral radical mastectomy (4.0%, 1/25), as shown in Table 3. Average time to a second look operation was 3.3 ± 3.4 days. Several cases reported multiple operations to obtain source control. These data were summarized into a definitive source control subcategory shown in Table 3. Three definitive source control categories were established identified as all mastectomies (modified and radial

Figure 1. PRISMA flow chart of literature search.

mastectomies), all debridements (nipple areolar complex sparing and nonsparing), and partial mastectomy. The majority of patients required a mastectomy for definitive source control 52.0% (13/25), whereas 32.0% (8/25) of patients were managed with serial debridements and 16.0% (4/25) underwent partial mastectomies. The analysis of microbiology cultures revealed that 40.0% (10/25) of infections were caused by polymicrobial flora and 20.0% (5/25) of infections secondary to *Streptococcus pyogenes*. Other infectious agents included *Streptococcus milleri*, *Serratia marcescens*, *Streptococcus sanguis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Corynebacterium striatum*, and *Clostridium septicum*.

Only 18 cases of the 25 analyzed provided adequate information on reconstruction methods. The average time from definitive source control to reconstruction was 15.6 ± 11.7 days. The various reconstruction methods used are included in Table 4. The majority of patients underwent either split-thickness skin grafting 44.0% (8/18) or delayed primary closure 33.3% (6/18). A subcategory analysis examined reconstruction methods for those groups of patients who underwent a total mastectomy, serial debridements, or partial mastectomy

for definitive source control (Table 5). From the mastectomy group, most patients underwent split-thickness skin grafting 30.8% (4/13) or delayed primary closures 23.1% (3/13). The remaining mastectomy cases did not include reconstruction management information. Majority of patients who underwent serial debridements for infection control underwent split-thickness skin grafting (50.0%, 4/8) for reconstruction. In the partial mastectomy group, 50.0% (2/4) underwent delayed primary closure.

Discussion

Necrotizing fasciitis is a life-threatening infection involving the fascia and subcutaneous tissues. Typical clinical examination findings include erythema, swelling, pain disproportionate to examination, necrosis, blisters or bullae formation, and crepitus. Patients may present in septic shock with multi-organ failure. The extremities, trunk, and perineum are commonly affected locations.² The cause of necrotizing infections are often attributed to a trivial event, such as a traumatic injury, insect bite, or injection.⁴ Primary NF of the breast without an

Table 1. Case Studies Included in the Systematic Review.

References	Year	Initial operation	Additional operation	Reconstruction	Outcome
Shah et al ⁶	2001	Right mastectomy		Delayed primary closure	Survived
Nizami et al ²¹	2006	Right debridement	Right mastectomy	Split-thickness skin graft	Survived
Rajakannu et al ²²	2006	Right mastectomy		Split-thickness skin graft	Survived
Wong et al ²³	2008	Right partial mastectomy		Delayed primary closure	Survived
Hanif et al ²⁴	2008	Left mastectomy	Left debridement		Survived
Delotte et al ²⁵	2008	Right mastectomy			Survived
Keune et al ²⁶	2009	Left debridement	Left mastectomy		Survived
Venkatramani et al ²⁷	2009	Left mastectomy			Survived
Vishwanath et al ²⁸	2011	Right mastectomy	Right debridement	Split-thickness skin graft	Survived
Soliman et al ²⁹	2011	Right I&D	Right NAC-sparing debridement	Split-thickness skin graft	Survived
Parker et al ³⁰	2011	Right partial mastectomy	Right debridement		Survived
Kaczynski et al ¹	2012	Right debridement	Right partial mastectomy	Delayed primary closure	Survived
Adachi et al ³¹	2012	Right debridement	Radical mastectomy	Split-thickness skin graft	Survived
Ablett et al ³²	2012	Left mastectomy	Left debridement	Delayed primary closure	Survived
Rehman et al ³³	2012	Bilateral radical mastectomy			Deceased
Pote et al ³⁴	2013	Right debridement		Split-thickness skin graft	Survived
Yaji et al ³⁵	2014	Left mastectomy			Deceased
Muftu et al ³⁶	2014	Left debridement	Left debridement	Delayed primary closure	Survived
Yang et al ³⁷	2015	Left NAC-sparing debridement	Left debridement	Split-thickness skin graft	Survived
Lee et al ³⁸	2015	Left NAC-sparing debridement	Left debridement	Negative-pressure vac	Survived
Lee et al ⁵	2016	Right debridement	Right debridement	Latissimus dorsi flap	Survived
Marongiu et al ³⁹	2016	Right debridement	Right debridement	Full-thickness skin graft	Survived
Ward et al ⁴⁰	2016	Left radical mastectomy	Left debridement	Delayed primary closure	Survived
Fayman et al ⁴¹	2017	Right mastectomy	Right debridement	Split-thickness skin graft	Survived
Konik et al ⁴²	2017	Left partial mastectomy		Local tissue rearrangement	Survived

Table 2. Demographics of Study Population.

Comorbidities	Totals (n = 25)	%
Hypertension	7	28
Diabetes mellitus	6	24
Obesity	4	16
Immunocompromised	3	16
COPD	1	4
Asthma	1	4
Smoker	1	12

Table 4. Common Reconstruction Methods after Final Source Control Operation.

Reconstruction	Totals (N = 18)	%
Split-thickness skin graft	8	44.4
Delayed primary closure	6	33.3
Full-thickness skin graft	1	5.6
Local tissue rearrangement	1	5.6
Negative-pressure wound vac	1	5.6
Latissimus dorsi flap	1	5.6

Table 3. Initial Source Control Operation and Definitive Source Control Operation.

	Totals (N = 25)	%
Initial source control operation		
Total mastectomy	9	36.0
Debridement	8	32.0
Partial mastectomy	3	12.0
Debridement with sparing NAC	2	8.0
Incision and drainage	1	4.0
Radical mastectomy	1	4.0
Bilateral radical mastectomy	1	4.0
Definitive source control operation		
Mastectomy	13	52.0
Serial debridement	8	32.0
Partial mastectomy	4	16.0

Abbreviation: NAC, nipple-areolar complex.

Table 5. Reconstruction Methods after Mastectomy, Serial Debridement, and Partial Mastectomy.

	Totals	%
Reconstruction for mastectomy		
Split-thickness skin graft	4	30.8
Delayed primary closure	3	23.1
Undetermined	6	46.2
Reconstruction for debridement		
Split-thickness skin graft	4	50
Delayed primary closure	1	12.5
Latissimus dorsi flap	1	12.5
Negative-pressure wound vac	1	12.5
Full-thickness skin graft	1	12.5
Reconstruction for partial mastectomy		
Delayed primary closure	2	50
Local tissue rearrangement	1	25
Undetermined	1	25

inciting event, such as a prior operation, is a rare event. The standard of treatment is fluid resuscitation, broad-spectrum antibiotics, and urgent surgical debridement of non-viable tissue. Shah et al described a case of primary NF of the breast and advocated for a 6-point management strategy that included a radical “pseudotumor” excision, reexploration within 24 hours of initial operation, and delayed primary closure several months after the infection had been cleared.

Several comorbidities associated with NF include diabetes mellitus, peripheral vascular disease, alcoholic liver disease, obesity, and immunosuppression.^{2,3} The comorbidities of the patients within this systematic review are similar to the majority having diabetes mellitus or hypertension. Obesity and immunosuppression were other common comorbidities identified.

Prompt diagnosis is critical for survival and breast salvage. Delays in diagnosis are common, as cutaneous findings may not be readily apparent secondary to the thicker tissue between the deep fascia and skin. When cutaneous signs are evident, the damage is extensive and most likely necessitates a mastectomy. Based on the results of this systematic review, a total mastectomy was required to obtain source control in many of the cases. However, serial debridements and, occasionally, a partial mastectomy were all that was needed for surgical treatment of the infection. This may have been possible secondary to a large amount of subcutaneous tissue and the breast’s robust blood supply. It is pivotal to remove all necrotic tissue during excisional debridement in order to obtain complete infection control. Therefore, we recommend complete resection of necrotic tissue while being cognizant of preserving as much healthy breast tissue as possible. Still, it is imperative that a second look of the operative area be performed within 24 to 48 hours after the initial debridement in order to obtain adequate source control.

There are 2 types of NF infections according to microbiology cultures. Type I infections are the result of polymicrobial infections by both aerobic and anaerobic organisms. Type II infections are caused by monomicrobial organism such as *S pyogenes*. Polymicrobial organism were found to be the most common cause of infections in this review. *Streptococcus pyogenes* was found to be the second most common.

In terms of reconstruction, split-thickness skin grafts were the primary reconstruction method used in the majority of cases. Reconstruction options are largely dependent upon the final amount of breast tissue available and the area of resection. Other options include delayed primary closure, full-thickness skin grafts, local tissue rearrangement, and pedicle flap reconstruction. The whole arsenal of the reconstructive ladder may be employed. Reconstruction can occur once the infection has cleared, and the patient is stable enough for another operation. There is no benefit to waiting several weeks until proceeding with reconstruction, evidenced by the average time to reconstruction of about 2 weeks.

Shah et al described the first case of primary NF of the breast in a 50-year-old diabetic female. A 6-point management plan was established for the treatment of such an infection from

his observations. The plan advocated for a radical “pseudotumor” excision, reexploration of the site within 24 to 48 hours, and delayed primary skin closure several months after recovery.⁶ It is apparent that many cases of breast NF result in a total mastectomy from this systemic review. However, this type of infection may be managed by serial debridements or a partial mastectomy. Regardless, the removal of all necrotic tissue is imperative in order to eradicate the infection. The wound should be re-explored within 24 to 48 hours either in the operating room or at bedside, depending upon the patient’s clinical status. Reconstruction of the defect may be completed once the infection has been controlled, and the patient’s clinical status permits. This usually occurred within 2 weeks of the final source control operation. Split-thickness skin grafting was the main method of reconstruction, instead of delayed primary closure.

A limitation of this study is that it contains a limited number of case reports, therefore making inferences from these data difficult. Despite the lack of cases, this systematic review does provide an adequate reference for treatment and reconstructive options when dealing with NF of the breast.

Based on this systematic review, we propose several management strategies for the treatment of primary NF of the breast. First, a prompt diagnosis is critical to patient’s overall outcome. The patient should be resuscitated with crystalloid fluids and broad-spectrum antibiotics administered. Operative source control intervention should be completed as soon as a diagnosis is established. Debridement of necrotic tissue should be completed until healthy, viable tissue is encountered, which may necessitate a complete mastectomy. Reexploration of the wound should be completed in 24 to 48 hours to ensure the removal of all necrotic tissue. There are a wide variety of reconstruction options with split-thickness skin grafts being a common choice. Reconstruction of the defect can be completed within 2 weeks or once the patient is stable and free of infection.

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ORCID iD

Ryan D. Konik, MD <https://orcid.org/0000-0002-6433-8524>

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