

## Case Report

### Primary necrotizing fasciitis of the breast. Case series with 5 patients

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#### Abstract

Necrotizing fasciitis (NF) is an aggressive, necrotic, life-threatening infection of the soft tissues. The delay on treatment is generally accompanied by almost 90 % lethality according to the development of septic shock and its associated complications. Primary Necrotizing Fasciitis of the Breast (PNFB) is seen extremely rare. To date, breast necrotizing fasciitis have been reported only as a limited number of case reports in the literature. PNFB is commonly misdiagnosed as cellulitis, mastitis, abscess or inflammatory breast cancer. Although PNFB is a very rapid and aggressive disease, which can be fatal. Delayed cases were unfortunately resulted in mortality due to several consequential reasons. Therefore, careful and detailed evaluation of all cases irrespective of age, especially those with risk factors and comorbidities, could be life saving in respect of early diagnosis and timely treatment. Our aim is to present the analysis and treatment modalities of five primarily seen PNFB, in this case series.

**Key words:** Breast infections; mortality; necrotizing fasciitis; septic shock; treatment.

*J Infect Dev Ctries* 2022; 16(5):902-908. doi:10.3855/jidc.14914

(Received 15 February 2021 – Accepted 05 December 2021)

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#### Introduction

Necrotizing fasciitis (NF) is an aggressive, necrotic, life-threatening infection of the soft tissues. NF has also a progressive nature with accompanied by thrombosis of arteries, leading to gangrene of the skin and subcutaneous tissue, as well as manifestations of severe intoxication and multiple organ failure [1]. The delay on treatment is generally accompanied by almost 90% lethality according to the development of septic shock and its associated complications [2]. NF is seen more often in extremities, perineum and abdominal wall, and Primary Necrotizing Fasciitis of the Breast (PNFB) is seen extremely rare. To date, breast necrotizing fasciitis have been reported only as a limited number of case reports in the literature. Our aim is to present the analysis and treatment modalities of five primarily seen PNFB, in this case series.

#### Case Series

Age, comorbidity, demographics, microbiological culture results, treatment modalities and surgical interventions performed are summarized in Table 1 and

detailed blood results are summarized in Table 2. Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC) scores of patients are summarized in Table 2 [3]. An example of the pathological specimens of the patients; severe inflammation and destructive ductus rich from neutrophils that have broken down the breast lobules are presented in Figure 1.

#### Case 1

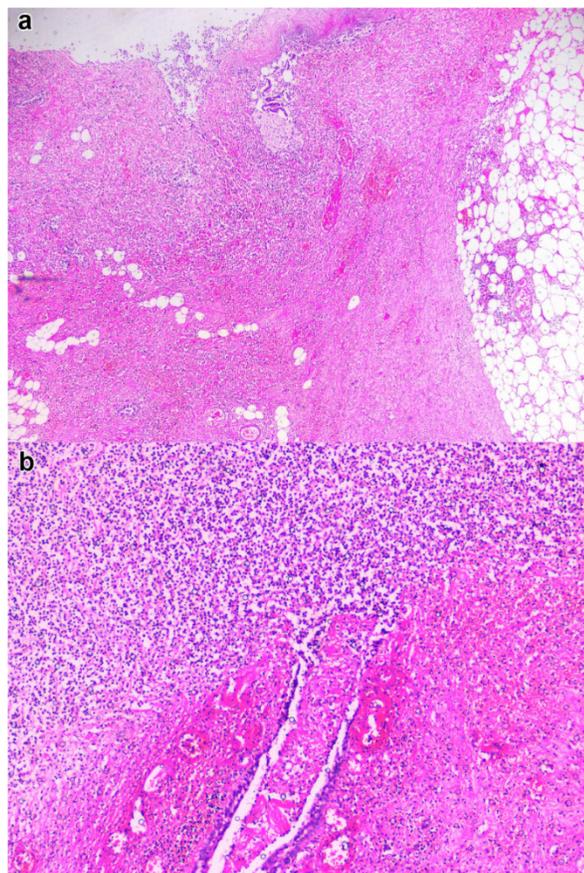
A 35-year old female presented complaints of deteriorated general condition, loss of consciousness, fever and respiratory distress. She had a diagnosis of mastitis and she was discharged with a prescription for oral amoxicillin clavulonate 2×1 g and recommendations for care a weeks ago in a different health care unit. There was widespread erythema, dark color changes, edema, and necrotic areas consistent with wet gangrene together with crepitation in the left breast. The necrotic areas and crepitation were extended from the left axilla and left arm anteromedial surface as far as the left elbow (Figure 2).

**Table 1.** Patient Characteristics.

Patient	Age	Comorbidities	Results of microbial culture	Blood culture	Surgical intervention
1	35	DM*, RA** (Use of Prednisolone, Methotrexate)	Polymicrobial and “Mixed anaerobic microorganism and gram positive cocci”	Polimicrobial and “Mixed anaerobic microorganism and gram positive cocci”	Radical mastectomy, Partial latissimus dorsi resection, wide debridement from left shoulder to elbow
2	53	DM*	Gram (-) enteric bacteria “ <i>Escherichia coli</i> ”	No growth.	Radical mastectomy, debridement, pectoralis major resection
3	82	DM*	Mucormycosis/ <i>Enterobacter cloacae</i> in follow up”	None	Debridement, mastectomy, wide chest wall resection
4	61	DM*, KAH*** Intracranial Mass (use of dexamethasone)	Polymicrobial/“ <i>Pseudomonas aeruginosa</i> in follow up”	1st: Coagulase negative <i>Staphylococcus</i> ; 2nd: No growth	After breast conserving surgery + recurrent debridements
5	43	HT****	Polymicrobial “ <i>Staphylococcus epidermidis</i> /Polymicrobial positive cocci, contamination?”	None	After breast conserving surgery + recurrent debridements

\* Diabetes mellitus; \*\* Rheumatoid arthritis; \*\*\* Coronary artery disease; \*\*\*\* Hypertension and culture could not be taken again due to the death of the patient in the early period.

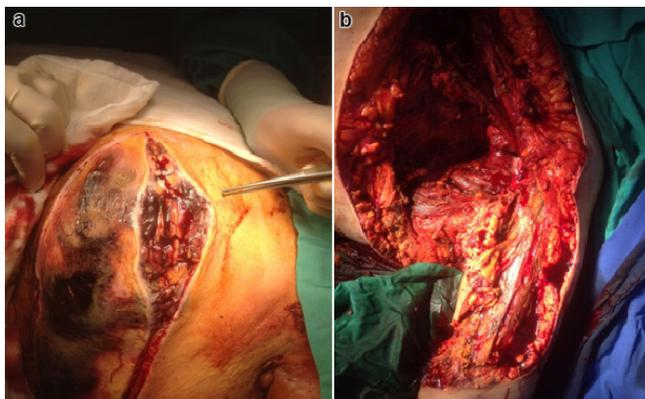
**Figure 1. a:** Severe inflammation, which has advanced into adipose tissue, disrupted the breast lobules (Hematoxylin Eosin; X4 obj). **b:** Severe inflammation rich in neutrophils. Destructive ductus is seen in the middle. (Hematoxylin Eosin; x10 obj).



**Figure 2. a:** Necrotizing fasciitis including edema, cellulitis and necrotic areas in the left breast. **b:** Axilla and left arm anteromedial surface.



**Figure 3. a:** Extensive resection of infected tissues with an elliptical incision from the sternum extending to the left axilla. **b:** Appearance of healthy tissue after radical mastectomy, partial latissimus dorsi resection, and extensive debridement of left arm anteromedial surface.



**Table 2.** Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC) scores.

Patient	Hb (g/dL)	White cells (10 <sup>9</sup> /L)	Sodium (mmol/L)	Creatinine (mg/dL)	Glucose (mg/dL)	C-reactive protein (mg/L)	LRINEC* Risk score [3]
1	12.3	18.2	125	1.94	495	314	11
2	14.6	16.7	131	0.95	616	47.4	8
3	12.1	18.5	128	1.51	424	510	9
4	10.7	18.6	130	0.88	446	358	10
5	11.9	12.9	134	0.65	124	72.9	7

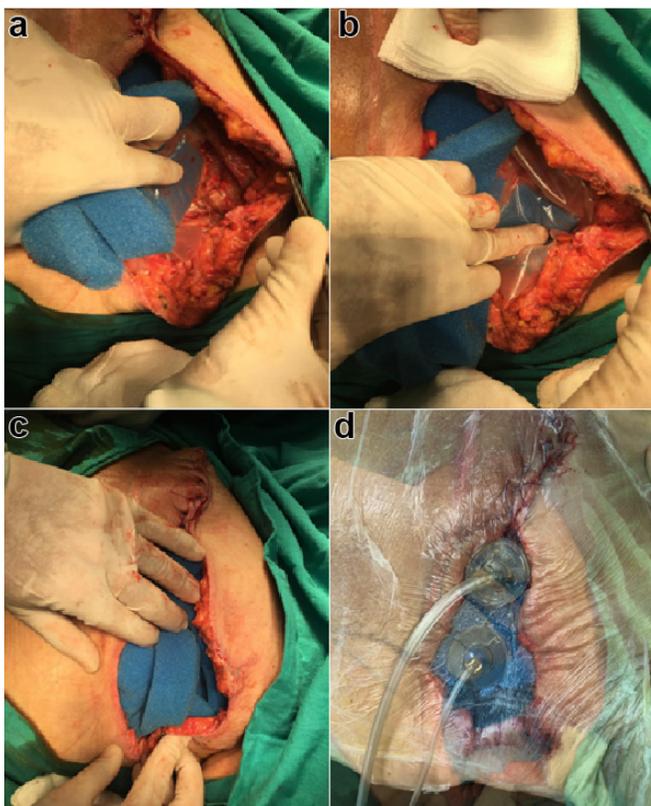
\* Laboratory risk indicator for necrotising fasciitis (LRINEC).

The excision of the necrotic areas on the skin of the left breast was performed via an elliptical incision extending from the sternum to the left axilla (Figure 3a). During the operation, the major and minor pectoral muscles of the left breast were seen to be completely involved and the lesions partially involved the left arm muscles and the latissimus dorsi muscle. Consequently, a radical mastectomy and partial latissimus dorsi resection were performed and the necrotic tissues in the arm were debrided via an anteromedial incision extending from the left shoulder to the elbow (Figure 3b). She had also diabetic ketoacidosis, and she was in the high-risk group with a LRINEC score of 11. Cardiovascular, respiratory and renal failure were seen on postoperative hour 8, then cardiac arrest developed due to septic shock and multiple organ dysfunction under routine follow-up in ICU.

**Case 2**

A 53-year-old woman, who had rubor and pain in her left breast for five days, applied to our hospital upon the development of a catarrhal wound extending to the left axilla. She had diabetic ketoacidosis, and she was in the high-risk group with a LRINEC score of 8. She underwent radical mastectomy with partial pectoralis major resection in emergency conditions. Because her

**Figure 4. a, b, c, d:** A protective layer is laid on the axillary artery, axillary vein and brachial plexus in the left axilla and application of NPWT.



skin flaps could not be closed, after modification ABThera™ (KCI, San Antonio, TX) was placed on the vascular pedicle, which were axillary artery and vein, and neural pedicle, which was brachial plexus as a protective layer (Figure 4). The patient underwent repeated debridement and 30 sessions of underwater hyperbaric oxygen therapy. The patient's skin flap and defect were closed with granulation and partial grafting, and the patient was discharged.

**Case 3**

A 82-year-old female patient, who was admitted to a different medical center with a complaint of rubor, swelling and increasing pain in her left breast for 1 week, received oral antibiotic treatment with a preliminary diagnosis of cellulite. She had diabetes with incompatible to drug intake and she also had a LRINEC score of 9. The patient was taken to the operating room under emergency conditions. The patient who underwent debridement and wide resection was taken to intensive care unit with NPWT treatment. As the necrotic area and infection findings continued during the follow-up and there was no decrease in the infection parameters, mastectomy was performed and it was followed up with NPWT. Wide chest wall resection was performed in the patient whose infection findings could not regress and the necrotizing picture was progressive. The patient, who was followed up as intubated in ICU, became exitus with the general condition deterioration

**Figure 5.** Patient who died due to multiorgan failure, circulatory disorder, and septic table with wide chest wall resection.



and progression of the septic shock table on the 8th day (Figure 5).

#### Case 4

A 61-year-old known diabetes patient and intensive smoker woman with coronary artery disease had a necrotizing fasciitis table that started with pain and rubor in the left breast. The patient, whose HbA1c value was measured as 16.4, was presented with a table of diabetic ketoacidosis. The patient with a history of oral dexamethasone use due to intracranial mass also had a LRINEC score of 10 and was in the high-risk group. After breast-conserving surgery, initially repeated debridement were made, then the antibiotherapy was given in order to glucose control, and she was followed up with instillation NPWT (NPWTi - d (VAC VERAFLU Therapy, KCI, an Acclity Company, San Antonio, Texas). When the granulation was achieved, the patient was covered with an intraglandular flap (Figure 6).

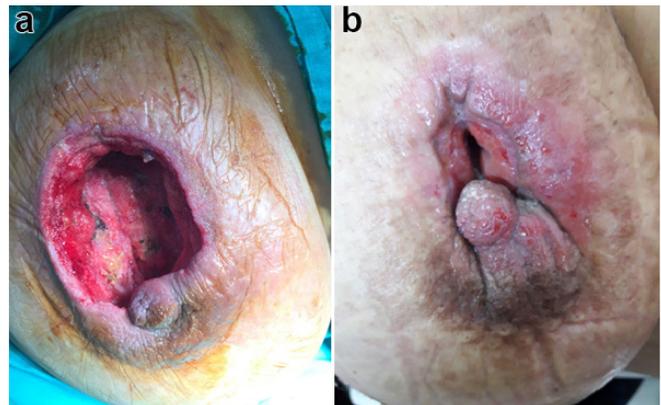
#### Case 5

A 43-year-old female patient was admitted to our clinic due to rubor, temperature increase and have severe pain in her right breast for about 3 weeks with the history of using irregular and short-term amoxicilline and clavulanic acid, in advance. The right breast was compatible with necrotizing fasciitis and the patient without comorbid disease had intense smoking

**Figure 6.** Breast conserving surgery, recurrent debridements, and patient whose infection findings regressed after NPWT and granulation was achieved.



**Figure 7. a, b:** The findings of the infection regressed and granulation was achieved before the patient was discharged with intraglandular flaps.



and a history of chronic alcoholism. The patient with insufficient self-care was provided with appropriate antibiotherapy, granulation with NPWT. The patient underwent repeated debridement and breast-conserving surgery, was followed up with NPWT. When repeated debridement were applied, the patient's infection findings regressed (Figure 7a) and when granulation was achieved, the patient was closed with an intraglandular flap (Figure 7b).

## Discussion

NF is a rarely seen but extremely aggressive disease. In addition, being even more rare breast involvement can lead to have extra difficulties in differential diagnosis the disease in question. PNFB is commonly misdiagnosed as cellulitis, mastitis, abscess or inflammatory breast cancer [4-6]. The two cases that resulted with mortality, who were treated in primary care centers with different pre-diagnoses of breast infection in advance, indicate the fact that the diagnostic difficulties related to the disease. However, the fact that breast infections or abscesses of these patients were not surgically drained or had no glucose regulation under appropriate conditions and were not treated with appropriate antibiotherapy may also lead to their disease being progressed to PNFB. In cases with basic skin changes, the NF diagnosis is made from detailed physical examination. However, in some cases with suspicious skin findings, there may be a need for laboratory tests and imaging examinations. Wong *et al.* developed the Laboratory Risk Indicator for Necrotizing fasciitis (LRINEC) [3]. According to the LRINEC score based on the serum CRP, WBC, Hb, Na, Creatinin, and Glucose values, the first case was in the high-risk group with a score of 11 points. There is a 75 % risk of NF development at values > 8, so the patient

in question was already in high-risk category. In addition, in the grading made according to the clinical findings, the patient was evaluated as grade 3 (late stage) as there was crepitation, a darkening of the skin and tissue necrosis reaching gangrene [7]. As the patient was at an advanced clinical grade and had a high LRINEC score, diagnostic imaging was not considered necessary. When our patients are evaluated in terms of LRINEC scores, it will be seen that all but one of our patients are in high risk group.

Several risk factors have been identified in the development of NF such as advanced age, diabetes mellitus, chronic alcoholism, obesity, immune suppression, vascular disease, malignancy, skin biopsies and a history of trauma [5,6,8-10]. The first patient was a young age at the diagnosis, and PNF developed without any history of trauma or intervention. However, it could have been related to uncontrolled DM and long-term treatment of methotrexate (MTX) and corticosteroids for rheumatoid arthritis. As DM causes suppression of the immune system, it has several endocrine and cellular effects. Furthermore, as reported by Nizami *et al.* in a similar case, the intake of corticosteroids and MTX further increased the risk [11]. Uncontrolled diabetes in all four patients seems to be the crucial risk factors as well. The BMI of the all the patients were also high and so that the obesity must also be accepted as another risk factor. The fifth patient was not diabetic, on the other hand, she had a serious smoke addiction, and she was referred to our hospital according to breast infection, lately.

The microbial culture results were determined as polymicrobial in cases 1, 4, and 5, while culture results were determined gram (-) enteric bacteria, and mucormycosis in cases 2, and 3, respectively. The culture results of the patient reported production of mucormycosis is a different result and Type IV has been described as a fungal infection [12,13]. Mucormycosis is an invasive infection caused by opportunistic fungi, and primary cutaneous mucormycosis is usually related with traumatic injuries, but immunocompromised cases are associated with underlying conditions such as diabetes mellitus and malignancies [14].

The differences of our patients from the cases reported in literature were the histories without previous breast surgery, biopsy or trauma. Two of our PNF patient died because of septic shock which caused to multiple organ failure. In the treatment of PNF, standard approaches must be applied just as for NF in other regions. These approaches are appropriate fluid and electrolyte treatment under ICU conditions, broad spectrum antibiotic therapy until the culture

results are received, and the timely application of aggressive surgical debridement. Very high mortality rates have been reported in delayed cases especially with comorbidities. The extent of the surgery to be applied is determined on the principle of not leaving any necrotic tissue. To date, various operations have been applied to the cases, ranging from selective debridement to radical mastectomy in literature. Without doubt, this range is determined by the extent of the necrotic tissue. When it is considered that the current case was delayed and of an advanced stage, it was necessary to apply extensive surgical debridement and radical mastectomy. Although mastectomy has been applied to most of the cases according to the literature, the two of our patients was undergone radical mastectomy. Complete or partial resection of the Musculus pectoralis major was performed in three of our patients. Open abdomen negative pressure therapy system was modified and applied on the axillary vein, brachial plexus and axillary artery with using a special protective layer. This sheath and low pressure use are beneficial in the protection of vascular and neural structures. NPWT was routinely used in dressing, especially after surgical debridement of infected tissues in all our patients. NPWT products with instillation were generally preferred with various antiseptics after the first debridement and when the infection was brought under control, and defect closure became the primary priority, standard products were used after. NPWT the negative pressure creates tension that stimulates granulation tissue formation as well as reduces wound size with contraction and bacterial load [15]. The negative pressure in NPWT leads to an increased improving microcirculatory blood supply thus encourages migration of inflammatory cells into the wound region and eliminating extravascular edema [16]. Also, this promotes and accelerates the formation of granulation tissue by removing bacterial contamination, end products, exudates and debris compared with traditional dressing and a additional mechanisms that facilitate wound healing include secure wound coverage and stimulation of angiogenesis [17,18].

Two of our patients who died were unable to receive Hyperbaric Oxygen Therapy (HBOT) due to their early instability during intensive care follow-ups. In addition the other 2 patients were unable to receive HBOT due to low cardiac ejection fraction and previous lung pathology. HBOT was able to be used in only one patient. Although the effectiveness of HBOT is controversial, its use has been proposed to improve wound healing and survival in patients with NF by

possibly increasing oxygen tension at the ischemic wound bed, facilitating the action of cytotoxic leukocytes, and improving antibiotic delivery via hyperoxygenation [15,18]. It has been determined that our patients who lost their lives were referred from the outer center and there was a delay in diagnosis and appropriate surgical treatment. Mortality resulted in both patients having uncontrolled DM and one patient's immunocompromised due to the steroid used. All patients had to be followed up in the intensive care unit in the postoperative period. Recurrent surgical debridements were applied to the patients except for a patient who died after diagnosis and surgical emergency operation. Until the infection findings of the patient who underwent NPWT regressed, the skin or tissue flaps of the patients were not closed and planned closure applications were started when clinical and biochemical improvement in the infection findings began.

Anatomically superficial fascia system of the breast anchorage to the deep fascia of the chest at the breast's perimeter is the circum mammary ligament. The Cooper ligaments, which are specialized vertical cutaneous ligaments, travel from the posterior lamina fascia, through the breast gland and anterior lamina, to anchor in the skin. It should be known that these anatomical structures and facial connections have an impact on the progression and spread of the NF and should be taken into consideration in treatment planning [19].

## Conclusions

Although PNFB has been very rarely reported in literature, it is a very rapid and aggressive disease, which can be fatal. Delayed cases were unfortunately resulted in mortality due to several consequential reasons. Therefore careful and detailed evaluation of all cases irrespective of age, especially those with risk factors and comorbidities, could be life-saving in respect of early diagnosis and timely treatment. Nevertheless, it must not be forgotten that this disease could result in death because of the rapid and aggressive course.

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**Conflict of interests:** No conflict of interests is declared.