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Case Report

Necrotizing Fasciitis caused by Streptococcus pyogenes: A case report and literature review of disease diagnosis and management

Abstract

Background: A 55-year-old male presented to the emergency room at a local hospital complaining of chest discomfort and severe left elbow pain.

Case Presentation: Erythema and symptoms of peripheral neuropathy were evident in the left hand. The patient reported recent trauma to his left elbow; however a radiograph of the left arm was unremarkable for fracture. After being admitted to the intensive care unit for observation, he developed worsening pain out of proportion and progressive decreased sensation in his left hand.

Diagnosis: Initially, left arm compartment syndrome was suspected and treated accordingly. After surgical intervention, the patient's subsequent symptoms and preliminary blood culture results revealed Gram positive cocci in chains, indicating necrotizing fasciitis. The isolate was identified as group A beta-hemolytic *Streptococcus* (GABS).

Treatment and Follow-up: Broad-spectrum antibiotics given at outset were extended with additional antibiotics. Treatment consisted of five separate surgeries involving extensive debridement of necrotic tissue amounting to approximately 55 to 65 percent of the patient's body surface area. The patient was eventually released to a burn center for skin grafting and wound closure and in less than three months, he expired.

Case Presentation

A 55-year-old morbidly obese male presented to the emergency room with a recent history of trauma to his left elbow. He came in due to gradually increasing pain. His past medical history included paroxysmal atrial fibrillation, very minor cardiomyopathy with an ejection fraction of 50%, right bundle branch block with left anterior fascicular block, kidney stones, hypertension, and chronic use of blood anticoagulant. His family history was positive for coronary disease. He also had a history of alcohol consumption of 3 to 12 times per week although he denied it at the time of admission.

Upon arrival, the patient was febrile (38.8°C) and complained of nausea, vomiting, and diarrhea. Along with an atrial flutter, he had mildly worsening renal insufficiency. Computed Tomography (CT) scan results of his chest, abdomen, and pelvis were normal. The patient's progressive elbow swelling and erythema were comparable to left arm

compartment syndrome. He was then taken to surgery where fasciotomies of his forearm and left carpal tunnel release were performed. Post operatively, the patient experienced severe shock with hypotension and required increased amounts of pressor medications. Symptoms of erythema progressed from his left arm to his left chest and his preliminary blood culture results demonstrated Gram positive cocci (GPC). Additionally, his complete blood count (CBC) was significant for toxic granulation, vacuolization, and Dohle bodies.

The patient was immediately returned to surgery where a diagnosis of necrotizing fasciitis (NF) was reached. Brownish fluid collected during surgery was sent to the laboratory for Gram stain and culture. The Gram stain revealed GPC in chains. The isolate was properly identified as penicillin sensitive group A beta-hemolytic *Streptococcus* (GABS). Hematology results from the second day of admission are presented in table 1 and all final microbiology results are available in table 2.

Despite prompt administration of antibiotics and surgical

debridement, the disease progressed to include parts of his left chest, back, left thigh, and buttock. Within less than four days the patient underwent a total of five surgical procedures involving extensive excision of necrotic tissue in order to contain the disease process. He was eventually transferred to a burn center for further care where less than three months later he expired.

Background

Group A beta-hemolytic streptococcus (GABS), also known as *Streptococcus pyogenes*, is a non-motile, Gram-positive coccus shaped bacteria. This adaptive human pathogen is well-known for infecting the oropharynx resulting in pharyngitis. It can also contribute to more serious invasive diseases such as toxic-shock syndrome and necrotizing soft-tissue infections [1-4]. Several serotype strains, M1 and M3 being the most prevalent within the United States, are known to cause NF [1-4]. This infection is generally community acquired and primarily occurs in the extremities [2]. The first account of NF dates back to 1783, when Claude Pouteau first described the disease [1,3]. Similar cases have been documented throughout the nineteenth and twentieth centuries, specifically in military

Table 1: Hematology and Coagulation Laboratory Results.

Tests Patient's	Results	Reference Ranges
RBC count	3.75 x 10 ⁶ /μL (3.75 x 10 ¹² /L)	3.8-5.4
Hemoglobin	11.5 g/dL (115 g/L)	12.9-16.1 (129-161)
Hematocrit	33.7% (0.337)	38.0-47.0 (0.38-0.47)
Platelet count	107 x 10 ³ /μL (107 x 10 ⁹ /L)	150-450
WBC count	3.27 x 10 ³ /μL (3.27 x 10 ⁹ /L)	3.4-10.6
Manual differential		
Neutrophils	20% (0.20)	36-66 (0.36-0.66)
Lymphocytes	1% (0.01)	23-43 (0.23-0.43)
Monocytes	3% (0.03)	1-7 (0.01-0.07)
Basophils	1% (0.01)	0-2.0 (0.00-0.02)
Band Neutrophils	34% (0.34)	5-11 (0.05-0.11)
Metamyelocytes	35% (0.35)	0-1 (0.00-0.01)
Myelocytes	5% (0.05)	0-1 (0.00-0.01)
Atypical Lymphocytes	1% (0.01)	0 (0.00)
RBC Morphology	Abnormal	
Platelet Estimate	Low	Normal
Polychromasia	1+	
Toxic Granulation	Present	Absent
Vacuoles	Present	
Dohle Bodies	Present	Absent
Prothrombin Time	22.2 seconds	12.1-15.3
International Normalized Ratio	1.9 seconds	0.8-1.2*
Partial Thromboplastin Time	54.8 seconds	22.0-36.5*
Fibrinogen	464 mg/dL	195-450
D-Dimer	1.12 μg/dL	0.00-0.50

* INR Therapeutic Ranges: 2.0-3.5seconds, PTT Therapeutic Ranges: 70.0-100.0secs. (0.3-0.7 u/mL heparin) and 51.0-67.0secs. (0.1-0.3 u/mL heparin)

Table 2: Microbiology Laboratory Results

Tests	Results	Reference Ranges
Blood Cultures (2 sets)		
Aerobic bottles	GPC in chains	No growth at 5 days
Anaerobic vottles	GPC in chains	No growth at 5 days
Organism	Group A Beta Hemolytic Streptococcus	
Penicillin MIC	0.016 (Sensitive)	
Wound Culture (Left arm tissue)		
Gram stain	Rare WBC's, Few GPC in pairs	
Organism 1	Group A Beta Hemolytic Streptococcus (4+)	
Anaerobic culture	No anaerobes isolated	
Tissue Culture (Left arm tissue)		
Gram Stain	No WBC's, No organisms, Rare squamous epithelial cells	
Organism 1	Group A Beta Hemolytic Streptococcus (3+)	
Anaerobic culture	No anaerobes isolated	

Additional Tests:

No *Staphylococcus aureus* isolated from groin or nares
 No growth from urine culture
 No *Salmonella*, *Shigella*, *Campylobacter*, *Aeromonas*, or *Plesiomonas* isolated from stool culture
Clostridium difficile toxin was negative
 No Acid Fast Bacteria isolated in blood at 6 weeks
 No fungus isolated in blood at 4 weeks.

hospitals during war times [3,4]. The actual term necrotizing fasciitis didn't come about until 1952 [3,4].

Studies show that NF can occur despite health status and current research has created speculations about the role of host immunological factors in relation to disease protection or predisposition [5]. Still, risk factors exist such as peripheral vascular disease, diabetes, malignancy, obesity, trauma, surgery, intravenous drug use, or insect bites [5]. Conversely, reports of pediatric cases are rare with the exception of countries where the disease is widespread [1,5]. Within the United States, an estimated 10,000 cases of NF caused by GABS occur annually, 1500 of them resulting in death [5].

In addition to GABS and *Staphylococcus aureus*, other aerobic and anaerobic pathogens may be present in NF cases, including *Bacteroides* and *Clostridium*. Facultative aerobic organisms grow because polymorphonuclear neutrophils (PMNs) exhibit decreased function under hypoxic wound conditions, thus, lowering the oxidation/reduction potential and enabling more anaerobic proliferation resulting in acceleration of the disease process [6]. Spread of the infection from the subcutaneous tissue to the deep fascial planes is facilitated by bacterial enzymes and toxins. This causes vascular occlusion, ischemia, and tissue necrosis [4,6]. Superficial nerves are damaged, producing the characteristic localized anesthesia. Septicemia ensues with systemic toxicity. NF soft-tissue infections involve rapid and extensive necrosis of the superficial fascia that results in high morbidity and mortality despite prompt treatment [3].

Pathogenesis

Most necrotizing infections, approximately 80%, occur secondary to trauma or a surgical process in which the external defense system is breached [7,8]. Cases arising from minor injuries, such as scratches and insect bites are often due to GABS [4,5,8] Pathogenesis can be attributed to several molecular functions that allow the organism to quickly adapt to the host environment [6,9]. First, they can alter their transcriptome in response to changes in the environment, the growth conditions, and their stage of growth [6,9]. Second, their expression of virulence factors facilitates tissue invasion and vascular dissemination [6,9]. For example, the virulence factors Secreted Streptococcal Carboxylic Esterase (SSE), Streptolysin O (SLO), and Streptococcal Phospholipase A2 (SlaA) directly damage host tissue while SLO, Immunoglobulin G Degrading Cysteine Protease (Mac1/IdeS) and *Streptococcus pyogenes* Cell Envelope Protease (SpyCEP) indirectly damage host tissue by inducing coagulopathy, inactivating PMNs and cleaving immune molecules [6,9]. Third, these organisms produce proteins designed to subvert the body's immune system [6,9]. For instance, the protein Mac1 accomplishes this by both mimicking a host cell receptor and cleaving IgG, ultimately enhancing survival [6,9].

Additionally, pathogenesis may be contingent on the molecular genetics of the host.

Evidence shows that the same strain of GABS can produce exceedingly different clinical manifestations in separate individuals [4,5,10]. Aside from the previous risk factors mentioned, it is speculated that both host immunological and genetic factors influence the development and outcome of invasive GABS infections [10]. In relation, certain HLA class II haplotypes may confer protection from severe systemic disease, whereas other haplotypes increase risk [10].

Clinical Presentation

The rarity of this disease combined with its initial clinical similarity to cellulitis makes prompt diagnosis difficult [2-4,10]. History of trauma, severe localized pain, heat and swelling, flu-like symptoms, and redness are all common early indications of NF [1]. Additionally, signs of sepsis, such as increased heart or respiratory rates, along with local symptoms or signs, such as severe spontaneous pain, skin pallor, or muscle weakness may indicate NF when skin necrosis is not yet apparent [1]. Cellulitis, edema, and skin discoloration or gangrene are observed at the site of infection in 90, 80, and 70% of cases, respectively [10].

Unlike cellulitis, in which the subcutaneous tissues are easily palpitated, NF wound infections have a wooden-hard feel [8]. Direct inspection during surgery will reveal swollen, dull gray fascia, a brownish exudate and despite deep dissection, no pus will be present [8]. Ultimately, clinical judgment and observance of the subcutaneous tissue or facial planes during operation are essential in the diagnosis of NF [8].

Laboratory role in diagnosis

Acidosis, anemia, electrolyte abnormalities, coagulopathy, and an elevated white blood cell count are commonly present in patients with NF [3,4]. Early on, laboratory results for C-reactive protein (CRP) and creatine kinase (CPK) are helpful in differentiating GABS NF from cellulitis. Both test values are typically elevated in patients with GABS NF [3]. Gram stain of the exudate collected during surgery can provide physicians with information about the pathogen and therefore treatment options [4,8] However, tissue cultures or positive blood cultures are typically used for definitive bacteriologic diagnosis. Still, some find that tissue biopsies for frozen section analysis are necessary to definitively diagnose NF [2,8]. If tissue biopsies are collected for diagnosis they should not be collected from areas of necrosis, but from the deep tissues in order to avoid bacterial misrepresentation due to the presence of superficial contaminants [2,8]. Along with chemistry and microbiology results, complete blood count and manual differential also indicate when a bacterial infection is present. Neutrophilia or a left shift, toxic granulation, vacuolization, and Dohle bodies can all be present in cases of bacterial infection [4].

Treatment

Patients with symptoms of NF should immediately be placed on intravenous antibiotics, which can be adjusted later based on the microbiological identification and sensitivities [4,5]. Clindamycin and penicillin are the drugs of choice in patients with GABS NF [4,5,8]. The basis for selecting these two antibiotics is as follows: clindamycin has been shown (by in vitro studies) to suppress toxins and control cytokine production more efficiently than penicillin and β -lactam antibiotics; however, increasing resistance of GABS to macrolides necessitates administration of penicillin [4,5,8].

Prompt fasciotomy and surgical debridement are the primary means of treatment following the diagnosis of NF [7,8]. Failure to respond to antibiotics or progressive toxicity, fever, or hypotension while receiving antibiotics therapy signify the need for surgical intervention [7,8]. During surgery, the extent of debridement is determined based on the amount of necrotic tissue. Easy dissection along the fascia by a blunt instrument and/or gas in the affected tissue suggests necrotic tissue and both require additional incision and drainage [8]. Multiple surgical procedures and even amputation may be necessary to contain the disease [3,7,8]. Medications can be administered to raise blood pressure and in some cases, a hyperbaric oxygen chamber may be helpful [2,4,5].

Lastly, aside from isolating patients with NF, individuals exposed to the patient should undergo preventative treatment with clindamycin [5]. After the disease process is controlled, patients should be transferred to a burn center for split-thickness skin grafting for wound closure [7,8]. The outcome of NF following surgical intervention closely resembles full thickness burn injuries and therefore, burn centers are best equipped to care for NF patients [7,8].

Case Conclusion

The patient initially demonstrated clinical signs of left arm compartment syndrome. Following surgical treatment, he developed severe shock requiring administration of phenylephrine and norepinephrine to constrict blood vessels and to raise blood pressure. Additionally, progressive symptoms of erythema became evident in his left arm and left chest. Subsequently, he was returned to surgery where the actual diagnosis of NF was determined. Concurrently, his first preliminary blood culture bottles were positive for GPC. Along with a combination of piperacillin and tazobactam and vancomycin covered from outset, the patient was given ciprofloxacin hydrochloride and clindamycin. His differential results correlated to his diagnosis with a left shift, toxic granulation, vacuolization, and Dohle bodies. Final identification and sensitivity determined that the organism present in the blood cultures, aerobic wound culture, tissue cultures and brownish exudate collected during surgery, was penicillin sensitive GABS.

Throughout surgical treatment, the patient received large amounts of fluids and at one point required platelet transfusion and fresh frozen plasma due to thrombocytopenia thought to be secondary to sepsis. After the disease process was contained and the patient was considered hemodynamically stable he was transferred to a burn center. Unfortunately, during recovery he expired.

Conclusion

This case study confirmed that NF is difficult to diagnose due to its general initial clinical presentation and rare incidence. It further established that the invasive nature of GABS soft-tissue infections directly correlates to the importance of prompt diagnosis and antimicrobial and surgical treatments. Future research is still needed to solidify the significance of risk factors and microbial and host factors in the molecular pathogenesis of the disease.

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