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Case Report

Disseminated Intravascular Coagulation with Extensive Skin Lesions.

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Abstract: - Disseminated intravascular Coagulation (DIC) is a systemic syndrome characterized by widespread thrombosis, end-organ dysfunction, and, paradoxically, hemorrhage. DIC can manifest as an acute, life-threatening emergency or a chronic, subclinical process. This variation depends on the process's intensity, speed, and morbidities from its root cause, including trauma, sepsis, and malignancy. In DIC, cutaneous manifestations can be pronounced, with the severity of skin lesions often reflecting the seriousness of the underlying systemic disease. Stevens - Johnson syndrome (SJS) is an immune-mediated mucocutaneous reaction that results in painful skin lesions leading to necrosis and sloughing. The cause is predominantly drug-induced. Necrotizing fasciitis is a bacterial infection resulting in extensive soft tissue necrosis, primarily superficial and deep fascia and overlying subcutaneous fat. In advanced stages, there is the development of large necrotic patches that appear black or gangrene. In this report, we describe a case of a patient who presented to the emergency department in septic shock due to bacteremia. The patient developed cutaneous lesions during their hospitalization, which broadened the differential as to what the cause may be. This case highlights the importance of recognizing DIC-induced skin necrosis in the setting of streptococcus pneumonia bacteremia.

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Introduction:

Manifestations of infection by Streptococcus pneumonia range from asymptomatic nasopharyngeal carriage to disease associated with the respiratory tract or systemic disease, often resulting in sepsis. Microbial membrane

structures, like lipoteichoic acid of the cell wall contribute strongly to the immunological response and release of inflammatory mediators associated with acute inflammation [**2**]. In particular, this infection can generate some degree of coagulation activation. Propagation of these inflammatory mediators with physiological impairment of the anticoagulation pathway due to systemic inflammatory activation results in fibrin deposition and platelet activation [**3**]. When the coagulation activation is more robust, clotting factors are consumed to an even stronger degree and it may manifest as disseminated intravascular coagulation (DIC) [**1**]. DIC may complicate the clinical course of about one-third of patients with severe sepsis. One of those complications can present as skin necrosis.

Case Presentation:

This is a case of a 53-year-old female with a past medical history of hypertension, pulmonary embolism, and asthma who was brought to the hospital by her family due to severe lethargy and altered mental status. According to the family, she had complained of feeling unwell with nasal congestion the day before her presentation. On the morning of her admission, she appeared to be in her usual state of consciousness but suddenly became altered, lethargic, and barely responsive. This prompted her family to seek immediate medical attention.

Upon arrival at the Emergency Department (ED), the patient was found to be unresponsive but still maintaining her airway. Her vital signs were notable for a heart rate of 128 beats per minute, a respiratory rate of 24 breaths per minute, oxygen saturation of 100% on 6 liters of oxygen via nasal cannula, a rectal temperature of 105.4°F, and a finger stick glucose level of 16 mg/dL. During the initial physical examination, she was awake and oriented only to herself. Nuchal rigidity was not detected. Coarse breath sounds were audible on the respiratory exam, while the cardiovascular exam yielded negative findings. The integumentary exam revealed a flushed face and cold extremities with paleness in her bilateral distal phalanges, although the rest of her body was warm. Due to her fever, she was wrapped in cooling blankets. Relevant laboratory results can be found in Table 1, but let's summarize the key findings. Her white blood cell count was elevated to 22.3, and she exhibited severe thrombocytopenia with a platelet count of 27. Her blood urea nitrogen (BUN) and creatinine (Cr) levels were 26 and 3.750, respectively. Blood, urine, and sputum cultures were obtained, and she was promptly initiated on a sepsis protocol. This involved administering broad-spectrum antibiotics, including vancomycin and cefepime, intravenous fluids at a rate of 30 ml/kg, multiple doses of 10% dextrose to address persistent hypoglycemia and a dose of hydrocortisone. Despite her presentation, her blood pressure remained normotensive, eliminating the need for additional blood pressure support. Imaging studies, including head, chest, and abdominal CT scans, did not reveal any acute pathology.

In less than 24 hours, both urine and blood cultures returned positive results for Streptococcus pneumonia. Due to Streptococcus bacteremia leading to septic shock and altered mental status, the medical team decided to expand the antibiotic coverage to address the possibility of meningitis. The treatment regimen was adjusted to include vancomycin, ceftriaxone, and ampicillin. Additionally, a stress dose of steroids was introduced.

By the third day of her hospitalization, the patient's mental status had improved (she was alert and oriented to person, place, event, and time), and her hypoglycemia had resolved. However, her elevated white blood cell count persisted, and her thrombocytopenia worsened, dropping into the 20s. Laboratory results also indicated elevated D-dimer, fibrinogen, and haptoglobin levels (**refer to Table 1**). During subsequent physical examinations, the patient displayed a petechial rash across her body that gradually worsened, forming coalescing lesions accompanied by large fluid-filled blisters on her lower extremities (**see Fig 1**). Some sloughing of the oral mucosa was noted. The bullous formation covered less than 10% of her body surface area.

Initially, we considered several potential diagnoses, including Stevens-Johnson syndrome vs. toxic epidermal necrolysis (TEN) linked to Ceftriaxone use, DIC, autoimmune manifestations, Idiopathic thrombocytopenia purpura (ITP), thrombotic thrombocytopenic purpura, and a variant of pneumococcal sepsis. Given this array of possibilities, Ceftriaxone was discontinued after its second day and the patient was switched to Levaquin, aligning with the blood culture sensitivities. Lab results highlighted abnormal coagulation markers, elevated d-dimer, increased haptoglobin, reduced fibrinogen, few schistocytes on the peripheral smear, and no presence of anemia (**refer to Table 1**). Extensive autoimmune testing yielded no significant findings. Following the laboratory trends, we refined our diagnosis to DIC, likely stemming from pneumococcal sepsis.

Wound care and plastic surgery were consulted due to the worsening blistering lesions on her lower extremities. Plans for further imaging, specifically MRI of the lower extremities and surgical debridement, were set in motion. An ear, nose, and throat (ENT) consultation was also sought for the involvement of the oral mucosa in the rash. The oral examination did not indicate mucosal sloughing, and the oral rash was not indicative of SJS or TEN. The patient's oral lesions improved with symptomatic treatment. The MRI revealed nonspecific findings suggestive of a hyperimmune reaction, with the differential now focusing on SJS and toxic epidermal necrolysis (**as shown in Fig 2**). Following the

debridement, tissue samples were sent for both aerobic and anaerobic culture, while pathological samples were forwarded to the Johns Hopkins Lab for further analysis. The aerobic and anaerobic cultures did not yield any growth. Dermatopathological staining of the bilateral lower extremity samples did not show immune deposits using IgG, IgM, IgA, C3, or fibrin-specific conjugate antibodies. However, the staining revealed dermal-epidermal necrosis, scattered intravascular thrombi, and sub-epidermal blisters. These findings lent support to the idea that DIC could be the cause of the patient's skin lesions in the context of streptococcal septicemia.

Discussion:

DIC is commonly observed in patients with bacterial sepsis, and the likelihood of its occurrence increases with the severity of the systemic inflammatory response. Its manifestations span a spectrum of clinical patterns, from petechial to acro-ischemic presentations. This includes symptoms such as cyanosis in fingers and toes, the emergence of skin bullae, and dry gangrene episodes [**4**]. Within the context of DIC, hypercoagulable states consistently present a range of cutaneous manifestations. In a study of 36 DIC patients, skin findings were the initial indicators in 47% of the cases [**5**]. However, this was not observed in our patient. In our case, cutaneous manifestations arose days after blood cultures showed strep bacteremia, followed by laboratory indicators of DIC like elevated d-dimer and fibrinogen.

Pneumococcal necrotizing fasciitis's most notable feature is its predilection for lower extremity infections, a feature evident in our patient [**7**]. Its early symptoms, which include tenderness, swelling, erythema, and pain in the affected area, can be misleading. The non-specific symptoms of necrotizing fasciitis can easily be mistaken for milder soft tissue infections like cellulitis and erysipelas, complicating early diagnosis. A hallmark of necrotizing fasciitis is the intense pain experienced at the onset, which is disproportionately severe compared to the physical finding [**8**]. Because necrotizing fasciitis is a highly aggressive infection, the likelihood of sepsis is much greater than average [**9**]. It's worth noting that necrotizing fasciitis caused by Streptococcus pneumonia is not just uncommon; it's exceptionally rare [**6**].

Bacterial systemic infection (BSI) and septic shock are primary reasons for intensive care unit admissions and mortality in cases of Stevens-Johnson syndrome (SJS) and Toxic epidermal necrolysis (TEN) [**11**]. SJS and TEN are dermatological emergencies marked by extensive epidermal necrolysis and shedding. The distinction between them lies in the extent of skin involvement: SJS impacts less than 10% of the skin and almost invariably affects mucosal membranes, such as the mouth or eyes [**10**]. In contrast, TEN, a more severe variant of SJS, involves over 30% of the skin's surface area. In this case, the initial generalized petechial rash progressed, leading to the formation of bullous lesions on the lower limbs. However, this affected less than 10% of the body's surface. Given the limited skin involvement and the absence of other defining features, TEN was ruled out as a potential diagnosis.

Conclusion:

In this case report, we delineate the progression and emergence of cutaneous manifestations in a septic patient. Disseminated Intravascular Coagulation (DIC), commonly associated with bacterial sepsis, manifests through a variety of skin symptoms. The symptoms of necrotizing fasciitis, while distinct, can often be mistaken for less severe infections. Given the escalated sepsis risk linked with this condition, this similarity accentuates the urgency of a timely and precise diagnosis. The primary distinguishing factor between Stevens-Johnson syndrome and Toxic epidermal necrolysis is the degree of skin involvement. Furthermore, the case underscores the potential for Streptococcus Pneumonia bacteremia to lead to skin necrosis as a consequence of DIC. Such an association is crucial to consider when evaluating septic patients presenting with skin symptoms.

FIGURE 1

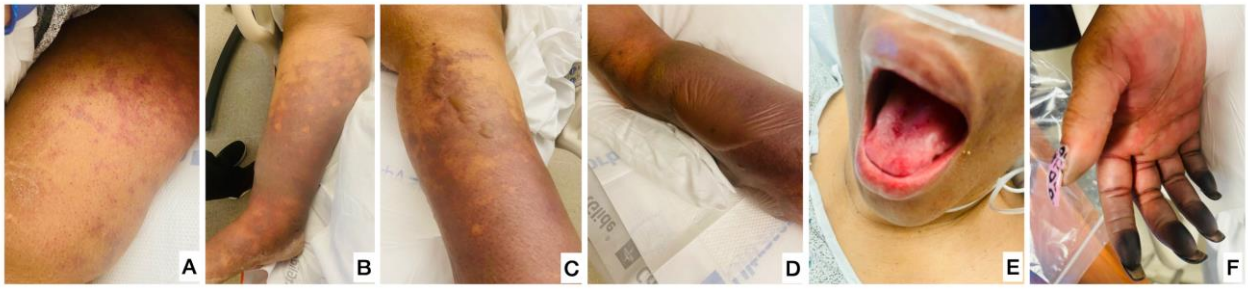
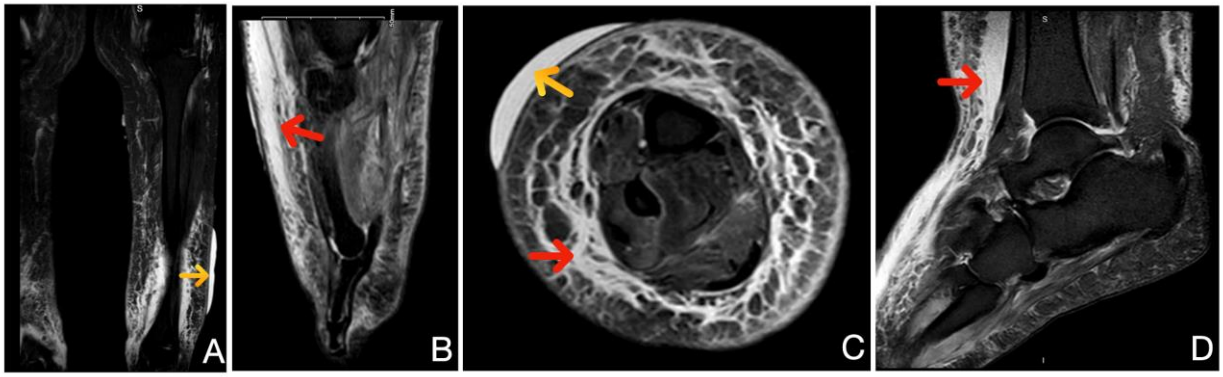


Figure1 A-D, shows the progression of generalized petechia rash to coalescing petechial rash with further progression to blisters formation. 1E shows oral lesions. 1F shows necrotic finger tips with hyperemic palms.

FIGURE 2



MRI STIR sagittal and axial showing extensive fat stranding/edema (red arrows) throughout the lower extremity with associated blister formation (yellow arrows)

Table1

WBC	22.3		
Hgb	15.3		
MVC	87.6		
PLT	27		
BAND	43%		
SED RATE	32mm/hr		
CRP	13.5mg/dL		
HAPOGLOBIN	296mg/dL		
FERRITON	721ng/mL		
PT	26.2secs		
INR	2.3		
PTT	58.3secs		
FIBRINOGEN	170		
D-DIMER	128.00ug/mL		
SODIUM	139mmol/L		
POTASSIUM	3.9mmol/L		
CHLORIDE	113mmol/L		
CO2	15mmol/L		
BUN	34mg/dL		
CREATININE	3.32mg/dL		
eGFR	16mL/min/1.73m2		
LACTIC ACID	7.5mmol/L		
PROCALCITONIN	>200.00NG/ML		

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