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CASE REPORT

Acute Inflammatory Edema: A Frequently Overlooked Case of Pseudocellulitis

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Abstract: Pseudocellulitis is a non-necrotizing inflammation of the dermis and hypodermis with a non-infectious etiology. One of the variants of pseudocellulitis is acute inflammatory edema (AIE), characterized by bilateral, erythematous, and edematous plaques, often found in critically ill patients. AIE is a rarely reported and frequently overlooked case of pseudocellulitis. Therefore, it needs to be differentiated from classic cellulitis, which has different management and prognosis. This case report aimed to present a case of AIE in a critically ill patient. A 71-year-old woman was admitted to intensive care with reddish swelling on four extremities. She was suffering from sepsis caused by pneumonia, congestive heart failure, tubulointerstitial disease, and hypoalbuminemia. A physical examination showed bilateral erythematous and edematous plaques that palpably felt warm. ALT-70 score was 4, indicating not likely true cellulitis. The patient was diagnosed with AIE and treated with a compression bandage, diuretics, and medications for underlying diseases. The lesions improved significantly on the second day of evaluation; unfortunately, respiratory failure caused the patient's death. Critically ill patients may have AIE misdiagnosed as cellulitis. Therefore, clinicians need to be well-versed in pseudocellulitis, especially AIE, to improve patient outcomes.

Keywords: acute inflammatory edema, cellulitis, critical illness, pseudocellulitis

Introduction

Acute inflammatory edema (AIE), also known as "erythema of edema" or "inflammatory edema of the intensive care unit", is a rare variant of pseudocellulitis that commonly occurs in patients with critical conditions. Marchionne et al were the first to report AIE in the United States (US) in 2019.[1] Following that, Chirasuthat et al in Thailand and Shalabi et al in the US reported AIE cases in 2021, with McGaugh et al in the US reporting the most recently in 2022.[2–4] Pseudocellulitis is a non-necrotizing inflammation affecting the dermis and hypodermis, with an etiology that is not related to infection.[5] It is frequently misdiagnosed as cellulitis, which can directly affect the patient and the healthcare system.[6] Misdiagnosis leads to inappropriate antibiotic use, extended lengths of time, and expensive medical costs.[1,7] As a result, it is critical for clinicians to understand pseudocellulitis, including AIE, and be able to distinguish it from cellulitis.[7,8] The clinical manifestations of AIE are bilateral, erythematous, and edematous plaques, which may be accompanied by pain and fever.[1–4] The pathogenesis of this disease is still unknown,[2] although it is considered to be caused by impaired lymph flow, which leads to fluid accumulation, microtears in the connective tissue, and a subsequent inflammatory response.[1–4] Herein, we describe a case of AIE in a critically ill patient with multiple comorbidities.

Case Illustration

A 71-year-old woman was hospitalized for complaints of cough, shortness of breath, and fever. The hospitalization was prolonged due to complications including sepsis, hypertensive heart disease (HHD), tubulointerstitial disease, and hypoalbuminemia, which required intensive care. On day 7 of hospitalization, the dermatology department was consulted for evaluation of suspected cellulitis on the upper and lower extremities. At the time of consultation, the patient was

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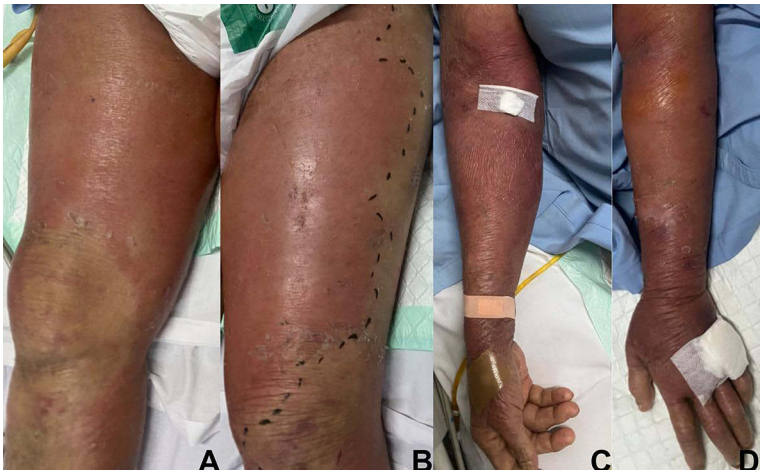

Figure 1 The patient presenting with ill-defined, blanchable, erythematous, edematous, warm plaques on (**A**) right and (**B**) left lower extremities and (**C**) right and (**D**) left upper extremities.

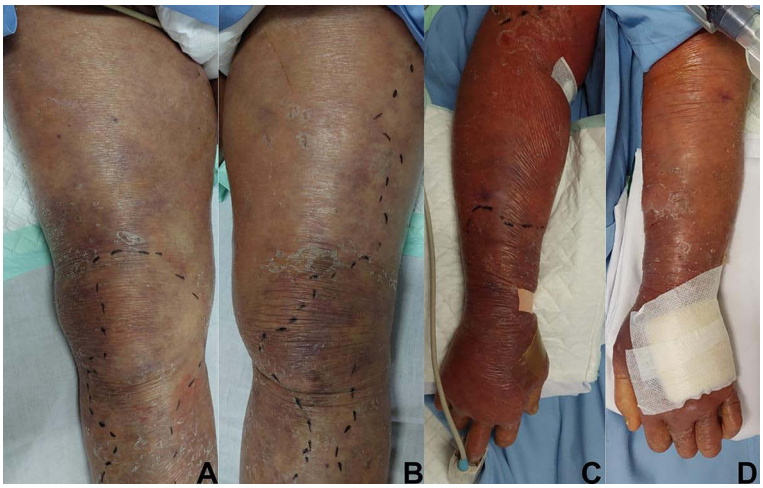

Figure 2 Reduction in redness and swelling seen the following morning on (**A**) right and (**B**) left lower extremities and (**C**) right and (**D**) left upper extremities.

receiving multiple antimicrobials (levofloxacin and ceftriaxone) for several possible sources of infection, including presumed cellulitis on the upper and lower extremities. History could not be obtained from the patient due to her altered sensorium. The family did not know the details of the patient's skin complaints. However, the attending physician confirmed that the skin lesions appeared suddenly. There was no apparent trigger for the skin lesions to occur.

On physical examination, the patient was intubated, mechanically ventilated, and frail looking. Her body temperature was 37.1°C, blood pressure was 181/68 mmHg, and her heart rate was 141 beats per minute. The patient had a body mass index (BMI) of 28.1 kg/m^2. Dermatological examination revealed ill-defined, warm, blanchable, erythematous, and edematous plaques on the bilateral upper and lower extremities (Figure 1A–D). Laboratory investigations revealed hemoglobin of 11.6 g/dL (Normal 12.3–15.3 g/dL), leukocytosis of 26,930/µL (Normal 4400–12,300/µL), hypoalbuminemia of 1.93 g/L (Normal 3.5–5.2 g/dL), and elevated C-reactive protein of 14.94 mg/dL (Normal <0.3 mg/dL). ALT-70 score which risk prediction for cellulitis in this patient was 4 points, indicated as indeterminate for cellulitis.

The patient received a wet dressing with a 0.9% sodium chloride solution two times a day, combined with compression by elastic bandages, in addition to already being administered diuretics from the internal medicine department. The next morning, the cutaneous lesions showed a marked response with a reduction in erythema and edema (Figure 2A–D). The patient was scheduled for a skin biopsy; however, she died the next day due to respiratory failure.

Discussion

Marchionne et al first described the condition in a case series involving 15 patients, noting that AIE most commonly affects individuals with fluid overload, organ dysfunction (cardiac, renal, or liver), low serum albumin levels, and a body mass index of 25 kg/m² or higher.[1] The pathogenesis of AIE is believed to involve the acute accumulation of fluid combined with lymphatic flow disturbances, leading to dermal edema and tissue microtears, which subsequently activate the inflammatory cascade.[1–4] Fluid accumulation in the tissue can be caused by increased intravascular hydrostatic pressure or decreased intravascular oncotic pressure. Organ dysfunction can also increase intravascular hydrostatic pressure, causing fluid to shift from the intravascular space to the interstitial space.[1,9] Physiologically, albumin maintains oncotic pressure within the vascular compartment, preventing fluid from moving to the interstitial space;[9] therefore, hypoalbuminemia led to decreased intravascular oncotic pressure.[1,4]

Lymphatics maintain volume homeostasis by returning filtrate to the circulation.[1] Disturbances in the lymphatic system can lead to protein accumulation in tissues, which draws fluid osmotically and results in edema.[4] In patients who are bedridden for extended periods, lymphatic dysfunction may arise from slowed lymph flow due to immobility.[1] Furthermore, in obese patients, increased lymph fluid production, reduced muscle contractions, and vessel collapse due to pressure from surrounding tissues can cause lymphatic vessel disturbances or obstructions.[10,11] Accumulation of protein-rich interstitial liquid on the tissue due to lymph dysfunction caused lymphedema.[12] Acute-onset dermal edema causes microtears in connective tissue and triggers the release of pro-inflammatory mediators, which then stimulate the movement of neutrophils and other inflammatory cells from the vasculature to the tissue.[1,8] In this case report, the patient experienced cardiac and renal dysfunction, which increased hydrostatic pressure, while hypoalbuminemia decreased oncotic pressure, resulting in fluid migration into the interstitial space. Furthermore, the patient's excessive body weight and immobility during hospitalization restricted lymphatic flow, resulting in acute volume overload.

The diagnosis of AIE is based on the clinical symptoms.[1] AIE is characterized by bilateral, erythematous, edematous plaques.[1,3] Typically, the lesions present in dependent areas such as the upper legs, abdomen, and waist.[1–4] Skin biopsy and culture from the lesions can help confirm the diagnosis of AIE. Histopathological findings of AIE show irregular acanthosis in the epidermal layer, extensive ballooning of keratinocytes, and keratinocyte necrosis.[2] Edema is observed in the papillary dermis, with lymphocytic, neutrophilic, and histiocytic infiltration in the perivascular and interstitial areas.[1–4] Laboratory tests in AIE patients may reveal leukocytosis, likely due to the patient's critical condition.[1] Although the patient in this case did not underwent a skin biopsy, the clinical characteristics were consistent with AIE, presenting as bilateral, erythematous, edematous plaques on both upper and lower extremities. The patient's leukocytosis could be attributed to her critical condition or sepsis related to pneumonia.

The condition of AIE is clinically differentiated from cellulitis, which is usually unilateral, by its bilateral distribution that spares areas of pressure.[6,11,13] Clinically, cellulitis presents acutely with spreading, ill-defined erythema and edema and is often warm and painful.[13] Cellulitis has been predominantly reported to occur in the lower extremities.[14] It is often accompanied by fever, lymphadenopathy, lymphangitis, and leukocytosis.[13] The ALT-70 score is frequently used to help diagnose cellulitis.[13] This score is based on clinical manifestations of asymmetry (3 points), leukocytosis ≥10,000/μL (1 point), tachycardia (1 point), and age over 70 (2 points).[6] Patients with scores of 0–2 have a very low likelihood of classic cellulitis and require re-evaluation. Patients with scores of 3–4 are in the indeterminate group and require consultation with a dermatologist. Patients with scores ≥5 are likely to have classic cellulitis and may be treated empirically with antibiotics.[15,16] If antibiotics do not respond, the possibility of pseudocellulitis should be considered.[11] In this case report, a 71-year-old patient presented with the involvement of all four extremities, with leukocytosis and tachycardia, resulting in an ALT-70 score of 4, which was included in the indeterminate group. However, due to ineffective antibiotic treatment, the diagnosis of pseudocellulitis was made rather than cellulitis.

Managing AIE focuses on supportive care aimed at optimizing volume status. Key therapeutic strategies include fluid restriction, diuresis, frequent repositioning, and increased mobility.[1,3] In addition, conservative treatment of lymphedema includes the use of compression garments.[12] Specific treatment for underlying conditions causing AIE, such as hemodialysis for kidney failure[2,4] or transcatheter aortic valve implantation for heart failure,[3] is part of AIE management.

Antibiotics are not recommended in AIE[2] and should be discontinued if misdiagnosed as cellulitis.[3] The significant improvement following compression and correction of fluid status supported our diagnosis of AIE in this case.

Conclusion

AIE exhibits clinical features similar to typical cellulitis. However, when erythematous and edematous plaques appear bilaterally in critically ill patients, AIE should be considered as a diagnosis instead of classic cellulitis. Clinicians need to be well-versed in pseudocellulitis, especially AIE, to improve patient outcomes.

Abbreviations

AIE, acute inflammatory edema; BMI, body mass index; HHD, hypertensive heart disease; US, United States.

Ethic Approval and Consent to Participate

Ethical review and approval were required to publish the case details in accordance with the local legislation and institutional requirements. This study ethics approval was obtained from the Research Ethics Committee of Dr. Hasan Sadikin General Hospital Bandung with the registry number DP.04.03/D.XIV.6.5/428/2024.

Consent for Publication

As the patient was unable to provide informed consent due to decreased consciousness from the onset of observation, and the progression of sepsis led to further deterioration, written consent was obtained from the patient's biological child. Approval has been obtained from Dr. Hasan Sadikin General Hospital to publish the case details.

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Disclosure

The authors report no conflicts of interest in this work.

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