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Case Report

Bullous Cellulitis Due to Coagulase Negative Staphylococcus in Immunocompromised Patient

Septina Yosephine*, Dhelya Widasmara, Anggun Putri Yuniaswan

Department of Dermatology Venereology and Aesthetics, Faculty of Medicine, University of Brawijaya East Java, Indonesia

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CORRESPONDING AUTHOR*
Septina Yosephine
dr.josesamosir89@gmail.com
Department of Dermatology Venereology and Aesthetics, Faculty of Medicine, University of Brawijaya East Java, Indonesia

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ABSTRACT

Introduction: Bullous Cellulitis is initially characterized by erythema and rapid development of bullae. This disease is most often caused by *Beta-hemolytic streptococci* and rarely by other bacteria such as *Coagulase-Negative Staphylococcus* (CoNS) type *Staphylococcus haemolyticus*. Immunocompromised state and history of malignancy are at high risk of infection with this bacterium. Local complications such as bullae can occur in obesity.

Case Presentation: A 48-year-old woman with complaints of tensed and loose-walled blisters with a reddish base on the right thigh. The patient had a medical history of Thyroid Cancer, Acute Renal Failure, and Bulging Mass pelvic femur. On physical examination, the patient was unconscious with a ventilator. Dermatological examination of the dextra inferior extremity showed loose bullae with a positive Nikolsky sign and tensed bullae over the erythematous patches, ill-defined, irregular edges, and warm palpable. Laboratory results of leukocytosis, hypoalbumin, and CoNS bacteria from blood culture. An ALT-70 score obtained a total score of 5.

Conclusion: Cases of bullous cellulitis are quite rare; cases like this usually occur in patients with an immunocompromised predisposition and obesity. CoNS is a commensal bacteria but, in some cases, could be a pathogen causing cellulitis. Poor prognosis that ends in death could occur in patients who have various complications.

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INTRODUCTION

Cellulitis is a skin infection of the dermis and subcutaneous tissue, most commonly caused by infection with *Group A-B hemolytic Streptococci* and *Staphylococci*. *Staphylococci* are Gram-positive coccal bacteria with two classifications: *Coagulase-Positive Staphylococci* (CoPS) and *Coagulase-Negative Staphylococci* (CoNS). Risk factors for this condition include obesity, diabetes, and immunosuppression like HIV, renal disease, and malignancy. Port de-entry cellulitis can be caused by a history of intravenous line placement, lymphatic stasis, and immunocompromised conditions. Estimated incidence of 24.6 cases per 1000 person-years. Typically, the onset of cellulitis is between 40 and 60 years [1–4].

The clinical manifestations of cellulitis are erythematous areas with indistinct borders and edema, accompanied by warmth and pain on palpation. Fever and tachycardia are systemic symptoms of cellulitis. Cellulitis most commonly affects the lower extremities and is usually unilateral. A bullous cellulitis is a form of cellulitis that begins with erythema and rapidly develops into bullae. CoNS infection may be one of the aetiologies of bullous cellulitis, although cases are rare. Obese patients are predisposed to local complications such as bullae, abscesses, hemorrhagic lesions, and necrosis. Complications in the form of sepsis can lead to a poor prognosis in patients. This case report aims to describe a bullous cellulitis case caused by CoNS bacterial infection in an immunocompromised patient [1,2,5–9].

CASE PRESENTATION

A 48-year-old woman with decreased consciousness appeared with blisters with a reddish base on the patient's right thigh. Based on hetero-anamnesis with the patient's family, it initially appeared red rashes and warm palpable on the right thigh four days earlier. The next day a tense blister containing clear fluid appeared on the patient's right thigh which became increasingly widespread and spread to the surrounding area within two days. The next day, some of the tense blisters became loose and ruptured and became sores pain and got high fever. The patient suffered minor trauma before the onset of the lesion. The patient had a medical history of Thyroid Cancer, Acute Renal Failure, and Bulging Mass pelvic-femur dextra.

Investigation

Physical examination of the patient, it was found that the general condition of the obese patient appeared to be seriously ill. The patient's GCS was difficult to evaluate because the patient was on sedation medication and a ventilator. Examination of the head and neck appeared of round lump with a diameter of +/- 3 cm, rubbery consistency, immobile, skin-colored, indistinct boundaries, with a flat surface, tenderness was difficult to assess. Dermatological examination on the right lower extremity showed multiple erythematous patches, ill-defined, irregular edges, with warm palpable, blanchable diascopy. Cruris dextra region appeared multiple flaccid bullae with an erythematous base and erosion, Nikolsky sign (+). Dorso pedis dextra region appeared multiple tensed bullae (Fig.1).

Laboratory tests showed a decrease in free T4, an increase in cortisol, fully compensated metabolic acidosis, anemia, leukocytosis, thrombocytopenia, eosinopenia, neutrophilia, lymphocytopenia, monocytopenia, hypoalbumin, transaminitis, azotemia. Chest x-ray showed cardiomegaly with aortic sclerosis. Anteroposterior/lateral x-ray of the right femur showed metastatic bone disease. FNAB pathology anatomy of femur proximal dextra and thyroid gland showed metastasis of thyroid follicular carcinoma and thyroid follicular carcinoma. The results of the (wound) swab culture examination found *Staphylococcus haemolyticus* and the blood culture examination found *Staphylococcus coagulase negative* (Fig.2 and Fig.3). ALT-70 scoring for diagnosis was obtained with a total score of 5, and the conclusion was that cellulitis is likely. Based on heteroanamnesis, physical examination, and supporting examinations, this patient was diagnosed with Bullous Celulitis. Several days later, the patient died due to cardiac arrest due to complications from sepsis.

Differential Diagnosis

The differential diagnosis of cellulitis includes static dermatitis, irritant contact dermatitis, allergic contact dermatitis, eczematous dermatitis, lymphoedema, dermatophytosis, cutaneous lymphoma, deep vein thrombosis, static ulcers, and gout [1,3,10,11].

Treatment

The patient was also treated in collaboration with an internist and anesthesiologist by administering drip Norepinephrine 0.05 - 2 mcg/minute and intravenous Ampicillin-Sulbactam 4 x 1,5 Gram, aspiration of the bullae by maintaining the top of the bullae, normal saline compresses accompanied by topical administration of gentamicin ointment two times a day in the erosion area.

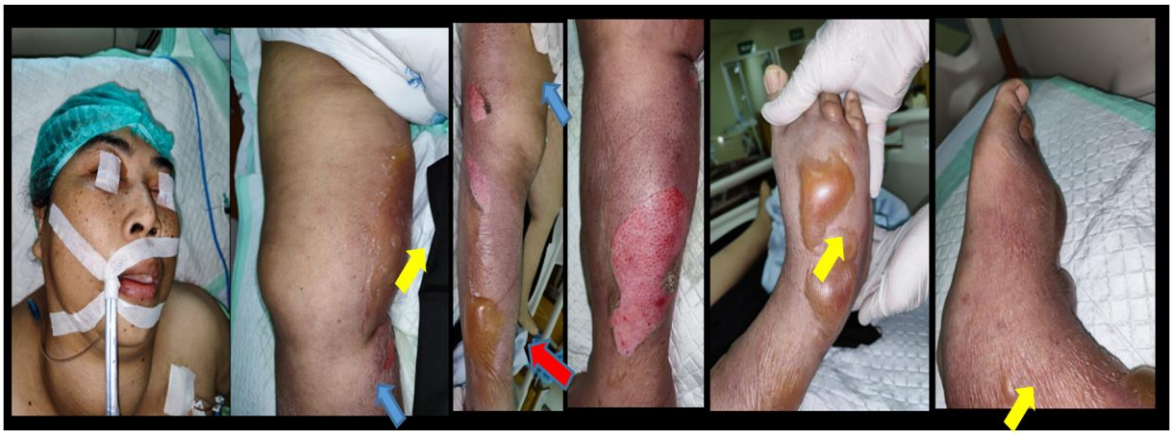

Fig.1 Dermatological Examination Multiple Erythematous Patches, Ill-defined, Irregular Edges, with Warm Palpable, Blanchable Diascopy (), Multiple Flaccid Bullae with an Erythematous Base and Erosion, Nikolsky Sign (+) () Multiple Tensed Bullae ().

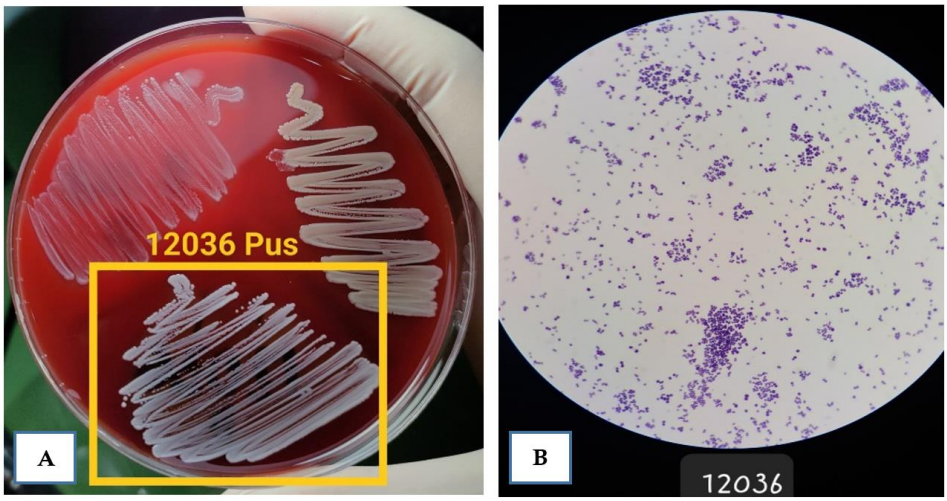

Fig.2. Microbiological Examination of (Wound) Swab Culture showed *Staphylococcus haemolyticus*. A. Macroscopic Feature; B. 100x Magnification Microscopic Feature

DISCUSSION

Cellulitis is a skin infection of the dermis and subcutaneous tissue, most commonly caused by bacterial infection. The most common bacteria causing cellulitis are Group A-B hemolytic *Streptococcus* (*Streptococcus pyogenes*) and *Staphylococcus* (most commonly S. aureus), but it can also be caused by *Streptococcus* species (Groups B, C, G) and CoNS, *Haemophilus influenzae type B*, *Pseudomonas spp*. Examination of this patient's (wound) swab and blood cultures revealed colonies of CoNS, which was the source of infection in this patient. Bullous Cellulitis is initially characterized by erythema and rapid development of bullae, which may become hemorrhagic and cause skin necrosis [1–3,12,13,15,24].

The clinical manifestations are characterized by erythematous patches with ill-defined edema and warm, painful sensation to palpation. These symptoms may be accompanied by fever and tachycardia. Cellulitis most commonly affects the lower extremities but can also affect the upper extremities, trunk and head, and neck. In the majority of cases, the lesions are unilateral. Patients with congestive heart failure, neutropenia, and hypoalbuminemia may have an increased risk of local complications, systemic complications (multi-organ failure), and even death. Complications of cellulitis include lymphadenopathy, superficial thrombophlebitis, bacterial sepsis, endocarditis, post-infectious glomerulonephritis, toxin-mediated systemic syndrome, and osteomyelitis. This patient developed systemic complications and septic shock and died [1–3,15,16].

Risk factors for this disease are obesity, connective tissue disease, elderly population, diabetes, and immunocompromised conditions such as HIV, kidney and liver disease, and malignancy. Port de entry can be caused by a history of intravenous line placement, surgical sites, bite wounds, lymphatic stasis, and immunocompromised conditions. Several variants of cellulitis are erysipelas, purulent cellulitis, periorbital cellulitis, orbital cellulitis, and bilateral cellulitis. In this case report, there are risk factors of obesity and immunocompromising conditions caused by a history of Thyroid Cancer, Acute Renal Failure, and Bulging Mass pelvic-femur dextra, which increase the occurrence of local complications, namely bullous cellulitis [1,5,7,15,17,18,25].

Laboratory tests that may be found in this condition include leukocytosis, elevated erythrocyte sediment and C-reactive protein, procalcitonin, microbiological culture (blood culture, pustules or abscesses), histopathology, ultrasonography, or MRI. The scoring that can be used to diagnose cellulitis is ALT-70, which consists of asymmetry (unilateral) (3 points), leukocytosis (1 point), and tachycardia (1 point), occurring at age >70 years (2 points). ALT-70 scoring classification, where a total score of 0-2 indicates pseudocellulitis, 3-4 indicates that the patient should be referred to a dermatologist, and a score of 5-7 is a positive predictor of cellulitis. The differential diagnosis of cellulitis includes static dermatitis, irritant contact dermatitis, allergic contact dermatitis, eczematous dermatitis, lymphoedema, dermatophytosis, cutaneous lymphoma, deep vein thrombosis, static ulcers, and gout. The prognosis for cellulitis is good if treated well, although recurrence may occur in 10% of cases, usually in high-risk patients. This patient's laboratory results showed leukocytosis and negative staphylococcal coagulase on blood culture. ALT-70 scored a total score

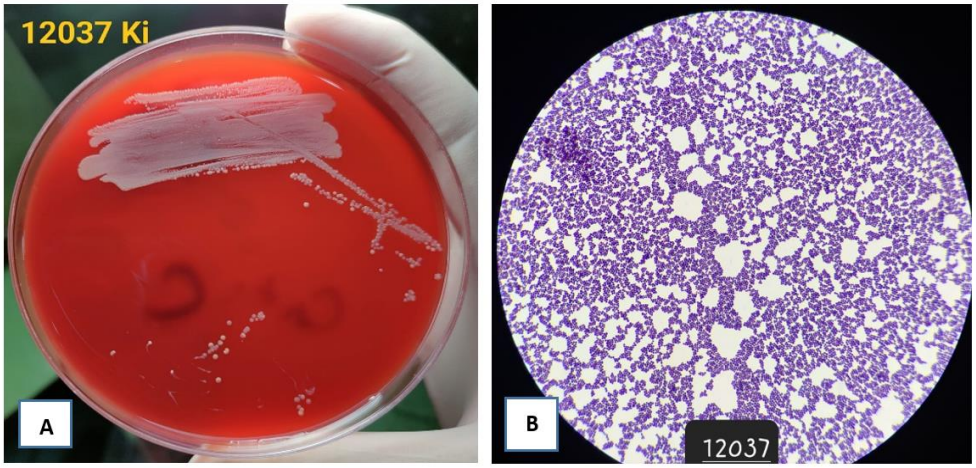

Fig.3. Microbiological Examination of Blood Culture showed *Staphylococcus coagulase negative*. A. Macroscopic Feature, and B. 100x Magnification Microscopic Feature

of 5, which is a positive predictor of cellulitis [1,3,11,13,15,20].

First-line antibiotic therapy is penicillin/cephalosporin (cephalexin and dicloxacillin); for MRSA, clindamycin/macrolides, tetracycline, trimethoprim-sulfamethoxazole can be given for 5 to 10 days. Giving analgesics can help reduce the inflammation that occurs with cellulitis. This patient was given a penicillin antibiotic, namely ampicillin-sulbactam 4x1.5 Grams, for ten days, but on the second day of administration, the patient died of septic shock [1,5,8,11,19–21].

Staphylococci are Gram-positive coccus bacteria with a diameter of 0.5 -1µm and are usually grape-shaped. These bacteria are non-motile, non-sporeforming, aerobic, and facultative anaerobic. This bacteria is symbiotic in the human body and can be found in the skin, mucous membranes, mouth, intestines, genitourinary tract, and upper respiratory tract. Certain conditions can cause these bacteria to become pathogenic. *Staphylococcus* is classified into (CoPS) and (CoNS). CoPS includes *S. aureus, S.intermedius, S.pseudointermedius, and S. schleiferi subsp. coagulants, S.hyicus*, while those included in CoNS are *S. saprophyticus, S.epidermidis, and S. haemolyticus*. Previously, CoNS bacteria were known to be commensal bacteria. They were non-pathogenic, but these bacteria have been revitalized as pathogenic bacteria, which are often found to cause infections in immunocompromised patients, such as patients with a history of malignancy and organ transplantations. The pathogenicity of CoNS bacteria is produced by slime (sugar matrix, with sessile cells and biofilm formation).

Biofilms are known to reduce the ability of antibiotics and the ability of the immune system. S. hemolyticus is capable of producing phenol-soluble modulism (PSMs) consisting of short amphipathic, α-helical peptides which are strong cytolytic against neutrophils and several other cell types. Apart from that, the biofilm in S.hemoliticus is ica-independent, which consists of polysaccharide independent adhesion (PIA), and also secreted fibronectin-binding protein (FnBP), which plays a role in the attachment of bacteria to the extracellular matrix. *S.hemoliticus* also secreted enterotoxins and hemolysins which act as superantigens to produce cytotoxins. *S.haemoliticus* is capable of causing bacteremia, meningitis, eye infections, skin infections, peritonitis, urinary tract infections, and male genital dysfunction. *S.hemoliticus* is also a pathogen that causes nosocomial infections in hospitals [11,13,15,22,23].

Bullous Cellulitis is a form of cellulitis that begins with erythema and rapidly develops into bullae, which may become hemorrhagic and cause skin necrosis. The most common cause of bullous cellulitis is infection with *Streptococcus* (*Streptococcus pyogenes*) and *Staphylococcus*, especially CoPS (*S. aureus*), but it can also be caused by CoNS such as *S. hemolyticus*, although cases are very rare. Immunocompromised patients are more likely to have polymicrobial infections. In obese patients, if skin damage occurs, it will be more difficult to repair the skin structure to its original state. This patient is immunocompromised and obese, which causes bullous cellulitis. However, the patient died due to complications from associated malignancies [2,9,11,18].

CONCLUSION

Cases of bullous cellulitis are quite rare, such cases usually occur in patients with a predisposition to be

immunocompromised and obese, the cause by CoNS bacteria type of Staphylococcus hemolyticus is very rarely found as a cause of cellulitis infection. The prognosis for cellulitis is good if appropriate empirical therapy is given according to the bacterial culture found. However, this patient ended up dying due to complications from the patient's medical history of Thyroid Cancer, Acute Renal Failure, and Bulging Mass pelvic-femur dextra.

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CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

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