Case Report

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BILATERAL LOWER LIMB CELLULITIS ACCOMPANIED BY ACUTE FLARE PSORIASIS:A CASE REPORT

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Abstract

Mr. K, an 82-year-old Chinese man, was admitted due to worsening bilateral lower limb swelling over the past week and an exacerbation of psoriatic lesions over the past three weeks. After noticing swelling on May 15, he visited a clinic for his Methotrexate regimen for psoriasis. On May 16, he sought help at the Emergency Department at HUKM but was discharged without medication. His condition worsened, and on May 18, he became febrile and returned to the HUKM Emergency Department. Upon examination he was diagnosed with bilateral lower limb cellulitis with acute flare psoriasis as the primary diagnosis.

Keywords: Cellulitis, Psoriasis flare, Methotrexate, Lower limb swelling, Fever.

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Introduction

Background

Cellulitis typically manifests as an indistinct, warm, reddened area accompanied by swelling and tenderness upon palpation. This condition arises from an acute bacterial infection, leading to inflammation of the deep dermis and adjacent subcutaneous tissue. Notably, cellulitis does not exhibit the formation of an abscess or the presence of purulent discharge. The characteristics of edema, warmth, tenderness and palpitation are resulted from cytokine and neutrophil response from bacteria breaching the epidermis. This then prompted the cytokines and neutrophils to be recruited to the affected area leading to the epidermal response and this response was associated due to production of antimicrobial peptides and keratinocytes proliferation which then appeared upon examination findings in cellulitis. Group A Streptococci produces pyrogenic exotoxin (A, B, C and F) and superantigen that can be more invasive and are the most common cause of cellulitis. Without prompt treatment, this infection could lead to systemic infection and cause bacteremia. Hence, the clinician should get culture and sensitivity test done and by identifying the causative pathogen, it can prevent the cellulitis moves to subcutaneous soft tissue can causes endocarditis and osteomyelitis which then require extensive antibiotic treatment and longer hospital stay and, in some cases, may require surgery. Cellulitis often has few mimickers such as erysipelas, which is considered another form of cellulitis. It is a superficial infection affecting the upper dermis and presented with bright red erythema with mildly erythematous and most commonly caused by exotoxins released from group A strep such as Streptococcus pyogenes. Additionally chronic venous stasis dermatitis which appears on the lower extremities and presented with peripheral edema, edema with scaling and hyperpigmentation whereas necrotizing fasciitis is an infection that leads to the necrosis of the subcutaneous tissue and patient tends to be presented on the emergency department with fever, edema, pain upon examination and crepitus.

Whereas, psoriasis is a long-lasting skin condition caused by a buildup of keratinocytes and epidermal differentiation. This results in the production of red, scaly plaques on the skin. The development of psoriasis is influenced by an intricate interaction of genetic, immunological, and environmental variables. The condition is genetically linked to numerous genes, including the HLA-Cw6 allele found in the major histocompatibility complex (MHC) class I area on

chromosome 6. Additional genes implicated in this context are IL12B, IL23R, and TNFAIP3, which are important in immune modulation and the maintenance of epidermal barrier function. T cells, namely the Th1 and Th17 subsets, contribute to the immune response by generating pro-inflammatory cytokines. Th17 cells generate Interleukin-17 (IL-17), a crucial cytokine that promotes the growth of keratinocytes and inflammation. On the other hand, Th1 cells release interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α)[17]. The illness is characterized by a fast increase in the division of keratinocyte cells, which shortens the normal cell cycle from around 28 days to 3-5 days. This results in the thickening of the outermost layer of the skin (epidermis) and a disruption in the process of cell differentiation. This disruption is obvious by the presence of cell nuclei in the outermost layer of the skin (stratum corneum), a condition known as parakeratosis, and a change in the function of the skin barrier.

Case Presentation

Mr. K, an 82-year-old Chinese man, was admitted to the Medical Ward from the Emergency Department due to bilateral lower limb swelling that had been gradually worsening over the past week. He has also experienced an exacerbation of psoriatic lesions over the past three weeks. On May 15, he noticed swelling in his lower limbs and visited a private clinic for his Methotrexate regimen, prescribed for his psoriasis. Despite a history of inconsistent Methotrexate use without prior adverse reactions, the swelling developed before starting his current regimen. On May 16, he sought help at the Emergency Department due to increased swelling but was discharged without medication. The following day, he developed swelling and redness, and on May 18, he became febrile and returned to the Emergency Department. Upon arrival, his glucose level was 10.5

mmol/L, and his temperature was 37°C. He was administered IV Unasyn 1.5g, IV Tramadol 50mg, and tablet Paracetamol 1000mg. Further examination revealed multiple small guttate psoriasiform lesions on his lower back, with scaly lesions surrounding dry skin, as well as similar lesions in the inguinal region and on the anterior knee and thigh, along with fungal nail lesions.

Investigation

Table 1 shows the investigation data on vital signs and laboratory parametes. Upon arrival, the patient had a Glasgow Coma Scale score of 15/15, indicating full consciousness. His blood pressure was 113/60 mmHg, heart rate was 94 beats per minute, body temperature was 37.9°C, oxygen saturation (SpO2) was 97%, and blood glucose level (Dxt) was 10.5 mmol/L. Laboratory tests showed a total white blood cell count of 11.3 and a C-reactive protein value of
9.62. The high C- reactive protein value may correspond to inflammation due to presence of bacterial infection. Upon admission, both the creatinine and urea levels were elevated. However, through proper intervention involving the administration of sufficient fluids and frequent monitoring of the progress of acute kidney injury, both the creatinine and urea levels showed a declining trend. The baseline reading for creatinine should ideally be between 64 and 104 mmol/L, while for urea it should be between 3.2 and 7.4 mmol/L. During hospital admission, platelets, white blood cell counts, and hemoglobin levels were crucial parameters. Platelet counts were low upon admission, but dropped even lower after gastrointestinal bleeding. Blood and platelets transfusions were provided, and platelet counts gradually rose. White blood cell counts were elevated during the first two days, indicating infection. IV Unasyn was given to treat cellulitis, and counts dropped to baseline range. Hemoglobin levels were less than 8, but maintained above 8 after blood transfusion.

Differential Diagnosis

Possible alternative diagnosis for cellulitis including deep vein thrombosis (DVT), venous stasis dermatitis, and contact dermatitis. Deep vein thrombosis (DVT) may manifest as swelling, discomfort, and redness in one leg. This can be

confused with cellulitis, although DVT does not exhibit the usual indications of a superficial skin infection seen in cellulitis. Venous stasis dermatitis, which is prevalent among individuals with chronic venous insufficiency, refers to the persistent inflammation of the skin. It is characterized by symptoms such as redness, scaling, and occasionally the formation of ulcers, mainly in the vicinity of the ankles. Contact dermatitis, resulting from an allergic response or contact to an irritant, manifests as a specific area of redness, itching, and occasionally the formation of blisters, which may be mistaken for the symptoms of cellulitis. Additional evidence that confirms the diagnosis of cellulitis, rather than another potential diagnosis, includes the existence of specific indicators of a skin infection in a particular area, such as increased warmth, sensitivity, and redness with indistinct boundaries. Cellulitis, in contrast to deep vein thrombosis (DVT), usually manifests with fever and systemic indications of infection. Furthermore, cellulitis typically exhibits fast advancement and may be accompanied by regional lymphadenopathy, which sets it apart from venous stasis dermatitis, a condition that is usually more long-lasting and less intensely painful. Contact dermatitis is characterized by redness and itching, and is commonly caused by contact to a known allergen or irritant. It typically shows more distinct, patterned lesions, sometimes with vesicles or bullae, rather than the diffuse redness and swelling observed in cellulitis. Increased levels of inflammatory markers, such as a high C-reactive protein (CRP) and white blood cell count, provide additional evidence for diagnosing cellulitis rather than these other illnesses.

Table 01: Vital Signs and Laboratory Parameters

Parameters / Date	18/5	19/5	20/5	21/5	22/5	23/5	24/5	25/5
Creatinine (64 – 104 mmol/L)	133.6	-	150.7	160.9	137	126.7	122.1	122.6
Urea (3.2 – 7.4 mmol/L)	6.3	-	19.3	22.2	20.8	15.9	11.4	8.3
ALT (0 – 55 U/L)	84	-	53	-	35	33	-	44
AST (5 -34 U/L)	89	-	32	-	29	26	-	29
CRP (< 0.5)	9.62	-	11.20	-	-	-	-	-
Platelet (150 – 410 x 10^9/L)	182	-	190	115	77	36	36	68
Lactate (0.5 – 2.2 mmol/l)	-	-	-	-	2.7	-	-	-
RBC (3.5 – 4.5 x 10^12/L)	3.5	2.1	2.1	2.4	2.3	2.2	3.0	2.9
HgB (13.0 – 17.0 g/dl)	7.3	-	7.5	7.3	6.8	6.6	8.8	8.7
White Blood Cell (4 – 10 x10^9/L)	11.3	-	10.5	4.3	5.5	4.0	-	-
PRT (11.6 – 14.0)	-	-	-	16.1	16.1	-	-	15.5
Glucose (mmol/L)	10.5	-	8.5	10.7	8.6	10.3	5.4	10.0
Blood Pressure	113/60	-	116/66	147/96	98/52	105/67	119/61	138/76
Temperature	37.9	-	37.0	36.8	36.5	37.0	37.3	36.0
Oxygen Saturation (%)	97%	-	95	98	100	100	98	98

Parameters / Date	26/5	27/5	2G/5	30/5	31/5	02/6	04/6
CR (64 – 104 mmol/L)	115.5	111.6	-	-	-	-	-
Urea (3.2 – 7.4 mmol/L)	5.7	4.8	-	-	-	-	-
ALT (0 – 55 U/L)	41	33	-	-	-	-	-
AST (5 -34 U/L)	25	55	-	-	-	-	-
CRP (< 0.5)	-	-	-	-	-	-	-
Platelet (150 – 410 x 10^G/L)	43	55	65	120	180	306	451
RBC (3.5 – 4.5)	3.0	3.2	3.1	2.6	3.0	3.1	3.2
HgB (13.0 – 17.0 g/dl)	8.6	6.2	6.0	8.6	8.6	6.0	6.5
White Blood Cell (4 – 10 x10^G/L)	2.5	2.3	2.1	1.8	1.8	2.4	4.0
PRT (11.6 – 14.0)	-	-	-	-	-	15.5	-
Glucose (mmol/L)	8.0	5.4	6.8	7.3	6.0	10.5	-
Blood Pressure (mm/Hg)	135/77	137/72	127/81	118/82	130/77	113/60	125/81
Temperature (^{0}C)	37.1	37.0	37.2	36.6	36.8	36.6	36.5
Oxygen Saturation (%)	68	68	68	68	68	66	100

Treatment

For the treatment of cellulitis, the patient was administered intravenous injection of antibiotic Ampicillin/Sulbactam 1.5gm TDS for 10 days and mild opioid analgesic Tramadol 50mg as well oral antipyretic Paracetamol 1000 mg. Whereas for the treatment of his acute flare psoriasis, the patient was prescribed topical therapy of aqueous cream applied QID, Xamiol (calcipotriol 50ug + betamethasone 0.5mg) gel 30g applied 3x a week, pine tar 1%, coal tar solution 1%, salicylic acid 2% liquid 250ml (Sebitar) applied 3x a week and salicylic acid 3%+betamethasone 0.05% oint

(diprosalic) 15g applied OD. Eventually this patient was admitted longer due to unresolved acute kidney injury secondary to hypovolemic shock due to upper gastrointestinal bleeding precipitated by duodenal ulcer. For that the patient had received multiple intervention and for the management of hypovolemic shock due to gastrointestinal bleeding, patient had received, IV Esomeprazole 80mg STAT followed by IVI Esomperazole 8mg/hr for 72 hours, then 1 Pints of 0.9% NS over 1 hour then 3 Pint of NSD5% over 24 hours followed by 2 pint packed cell (slow transfusion over 4 hours) and lastly inotropic agent IVI adrenaline (0.5 - 0.3 - 0.2 mcg/kg) was administered to increase patient's cardiac output as patient had went into hypovolemic shock with blood pressure of 73/45 mmHg. Finally for the management of acute kidney failure, patient was given IV Actrapid 6U PRN with 3 Pint of NSD5% over 24 hours for management of hyperkalemia and few pints of 0.9% Normal Saline to ensure sufficient hydration

Discussion

1. Cellulitis

Cellulitis therapy aims to resolve infections, alleviate symptoms, and prevent complications. Treatment depends on the presence of purulent and non- purulent factors, with extremity cellulitis having the highest prevalence. Treatment targets beta- hemolytic streptococci and S. aureus, unless a red flag condition requires immediate hospital admission or surgical intervention. Red flag conditions include severe sepsis, rapidly progressive infection, and pain. These conditions have high morbidity and mortality rates. he National Antibiotic Guideline 2019 recommends that antibiotics for moderate to severe cellulitis should be chosen based on illness severity. For moderate cases, often caused by Staphylococcus aureus and Streptococcus pyogenes, the preferred treatment is intravenous Cloxacillin at 1-2 grams every 6 hours, or Cefazolin at 1-2 grams every 8 hours. Severe cases involving the same bacteria should be treated with intravenous Ampicillin/Sulbactam at 3 grams every 6-8 hours, with Clindamycin 600 milligrams IV every 6 hours as needed. Antibiotic de-escalation should occur once culture and sensitivity results are available. According to the National Institute for Health and Care Excellence Clinical Knowledge Summary guidelines, patients with cellulitis who are systemically unwell or have comorbidities such as diabetes, obesity, peripheral vascular disease, or chronic venous insufficiency should be referred for hospitalization or IV antibiotics per local guidelines. While the therapy duration aligns with recommendations, the prescribed dose must adhere to the National Antibiotic Guideline.[18] As per Micromedex Drug Dosing, for skin and subcutaneous tissue infections, IV/IM Ampicillin/Sulbactam should be dosed between 1.5 to 3 grams every 6 hours, adjusted for illness severity. Patients with renal failure require dose adjustments based on creatinine clearance, per the July 2022 guidelines from the Antimicrobial Stewardship Team at Hospital Melaka, recommending adjustment when creatinine clearance is below 15 ml/min. Due to incomplete information, specifically the absence of the patient's body weight, creatinine clearance could not be determined. Before admission, the patient's baseline creatinine was 103-123 mmol/L with an Estimated Glomerular Filtration Rate of 51 ml/min/1.73 m^2. For pain and inflammation relief, the patient received IV Tramadol 50 mg and oral Paracetamol 1000 mg. Tramadol is preferred for chronic kidney disease patients due to its lack of nephrotoxic effects, unlike NSAIDs.

2. Acute Flare Psoriasis

The Malaysia Clinical Guideline of Management of Psoriasis Vulgaris 2013 strives to achieve complete eradication of skin lesions. However, it realizes that this may not be feasible for the majority of patients. Therefore, it recommends setting modest treatment objectives for making modifications to therapy. Ensuring patient adherence is of utmost importance, since therapies that are initiated early and taken once daily result in greater compliance. Emollients, although often utilized, have poor empirical support for their efficacy. However, when taken with betamethasone dipropionate, they can potentially decrease the need for steroid usage. Coal tar has variable effectiveness, as several studies demonstrate notable enhancement in severity ratings, and is typically well-tolerated. Topical corticosteroids are efficacious and well-tolerated when used for a short duration, and potent formulations do not result in significant side effects. The use of corticosteroids with hydrocolloid dressings or UVB therapy can improve the elimination of the condition. Calcipotriol, the sole topical vitamin D analogue accessible in Malaysia, demonstrates efficacy and synergistic effects when used in conjunction with powerful corticosteroids, surpassing the outcomes of either medication used alone.

3. Hypovolemic Shock Due to Upper Gastrointestinal Bleeding

Crystalloid solutions like lactated Ringer's solution and 0.9% sodium chloride are commonly used for resuscitation due to their tonicity. Isotonic fluids, like 0.9% sodium chloride and Lactated Ringer, are preferred due to their ability to increase intravascular volume without affecting cellular fluid changes. Isotonic solutions are affordable electrolyte solutions with tiny compounds that can quickly diffuse and distribute throughout the extracellular compartment. They primarily restore interstitial volume, requiring more crystalloids to effectively replenish blood vessel volume. Blood products should not be used to increase blood volume, but for cases where blood loss exceeds 30% of total blood volume, to ensure oxygen supply and normal coagulation. Packed red blood cells, fresh frozen plasma, and platelets are the most commonly available resuscitation fluids. Red blood cell transfusion in hemorrhagic shock should be based on the patient's physiological condition, blood loss quantity, and bleeding likelihood. Maintaining hemoglobin levels between 7 and 9 g/dL doesn't significantly impact mortality, so there's no need to give a transfusion based

on low hemoglobin levels without signs of inadequate oxygen delivery. Norepinephrine is a strong alpha-1 and beta -1 agonist with slight beta -2 agonist activity demonstrated to have vasodilatory shock and cardiogenic shock and most commonly employed in the treatment of sepsis and refractory hypotension. It increases mean arterial pressure via vasoconstriction and therefore increases cardiac output and systemic vascular resistance to increase organ perfusion and normalize the blood pressure. Dose can be initiated at 2-10 mcg/min and titrated to MAP with a maximum dose of 0.5 mcg/kg/min or 30 mcg/min. As to the guidelines from the American Academy of Family Physicians on Upper Gastrointestinal Bleeding in Adults (2020), proton pump inhibitors (PPIs) are highly recommended as the primary therapy for both preventing and managing gastrointestinal bleeding. Patients with a high risk, especially those with high-risk endoscopic lesions, should be given extensive PPI medication, namely esomeprazole (Nexium) at a dosage of 80 mg per day, within the first 72 hours after endoscopy. This is because the likelihood of bleeding happening again is greatest during this time frame. Following the initial period of intense therapy, individuals at high risk continue taking PPIs twice a day for a maximum of 14 days, while low-risk patients can switch to a once-daily dosage. The patient was prescribed Nexium 40 mg twice daily for a duration of 2 weeks, and then switched to a once-day dosage for the subsequent 10 weeks, in accordance with the instructions provided in the guidelines. The Clinical Practice Guideline for the Management of Non- Variceal Upper Gastrointestinal Bleeding also suggests using comparable dosage procedures with medications such as Omeprazole or Pantoprazole to ensure that they are consistent with the patient's treatment plan.

4. Acute Kidney Injury

There is no universally accepted pharmacological protocol for treating acute renal failure, as management varies based on individual patient characteristics. Fluid therapy is crucial to maintain hydration and prevent septic shock in cases where volume depletion or hemorrhagic shock exacerbates preexisting renal failure. Diuretics may be used for managing edema resulting from acute renal damage. In this case, acute renal failure due to gastrointestinal bleeding impaired kidney perfusion, treated with 0.9% normal saline to restore fluid volume in the blood vessels, akin to managing hypovolemic shock as per the 2012 Acute Kidney Injury guidelines from the American Family Physicians Journal. The goal is to maintain osmolarity balance by using a solution with a similar concentration to body fluids. Targeting a mean arterial pressure above 65 mm Hg is advisable as acute renal injury often causes electrolyte imbalances, such as hyperkalemia from reduced potassium excretion. Treatment for hyperkalemia involves IV short-acting insulin and dextrose 50% to shift potassium into cells and therefore lowering its plasma levels. In severe cases, slow infusion of 10% calcium gluconate may be initiated in stabilizing cardiac membranes to prevent arrhythmias, though it wasn't necessary here as the patient's potassium levels stayed below 5.5 mEq/L.

Outcomes and Follow-Up

The patient was discharged from the hospital after a stay of over two weeks. Prior to discharge, significant improvement was noted in the patient's kidney function, as indicated by markedly reduced urea and creatinine levels, reflecting a positive recovery trajectory. The cellulitis infection also resolved, with normalized white blood cell counts and C-reactive protein markers. Effective interventions, including blood and platelet transfusions, successfully restored the patient's hemoglobin and platelet levels following gastrointestinal bleeding. A follow-up scope is scheduled for six weeks post-discharge to monitor ongoing recovery.

Conclusion

This patient was given appropriate regime nevertheless some pharmaceutical care issues were spotted during the hospital admission and therefore pharmacist involvement can be made to mitigate some drug related problem.

Conflict of Interest

Author does not have any conflict of interest.

Author Contributions

Author Contributed Equally.

Abbreviations

None

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