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Case Report

Gentamicin graded challenge as an alternative therapy for cellulitis pedis in a patient with history of multiple drug allergies

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ABSTRACT

Cellulitis pedis is a complication of diabetic neuropathy affecting the foot and most commonly caused by *Staphylococcus aureus* and *Streptococcus pyogenes*. A 55-year-old female patient presented with swelling and redness of the left foot that had persisted for one week. She had a history of type 2 diabetes mellitus and multiple drug allergies, including levofloxacin and cefadroxil. These comorbidities posed challenges in selecting an appropriate and safe antibiotic choice. Intravenous gentamicin was chosen as an alternative therapy in this case. A dose of 80 mg was administered using a graded challenge method to minimize the risk of severe hypersensitivity reaction.

Keywords: Cellulitis pedis, Multiple drug allergy, Gentamicin, Graded challenge

INTRODUCTION

Cellulitis is a bacterial infection involving the dermis and epidermis that may extend to subcutaneous fat and lymphatic tissues.[1] A study reports that cellulitis pedis represents the highest incidence among cellulitis types, reaching 199 cases per 100,000 population per year. Cellulitis pedis categorized as a diabetic neuropathy complication caused by *Staphylococcus aureus* and *Streptococcus pyogenes*.[2] These bacteria may penetrate the skin barrier through minor wounds, resulting in infection marked by swelling, pain, localized erythema with indistinct borders, and warmth on the affected skin.[3] Inadequately treated cellulitis may progress to lymphangitis, elephantiasis, recurrent infections, subcutaneous abscesses, gangrene, or even fatal complications.[2]

Treatment choice for cellulitis is distinguished by the presence or absence of purulence, severity, and microbiological cause. Antibiotics are the primary treatment for cellulitis aside from symptomatic treatment and surgery when required.[3] The first-line antibiotic choice for cellulitis fall under the β-lactam group, which includes penicillin, cephalosporin, carbapenem, and monobactam. These antibiotic groups frequently associated with allergic reactions.[4] When a patient has a history of allergy to one or more β-lactam, selecting a safe alternative becomes more challenging. The consideration are the possibility of cross-reactivity, drug availability, and the risk and benefit for the patient.[5] The appropriate selection and administration method can reduce the risk of severe hypersensitivity. Graded challenge method may be considered in both therapeutic purpose and eliminate the possibility of hypersensitivity reaction.[6]

CASE REPORT

A 55-year-old woman was referred to Wangaya Hospital with swelling and redness on the left foot since a week ago. Initially, she experienced itching and noticed a small red spot, which progressed to swelling and worsening erythema. The erythema extending form dorsal pedis to the cruris and causing severe pain. She previously treated by levofloxacin and lead to an allergic reaction.

The patient had known allergies to cefadroxil and levofloxacin. Past medical history included type 2 diabetes mellitus treated with Glargine 26 units daily and Aspart 10 units three times daily. She denied chest pain, dyspnea,

asthma, hypertension, and history of chronic kidney disease. She had undergone ORIF (Open reduction and internal fixation) in 2019 and 2021.

Similar complaints on the patient's family was denied. She denied smoking, alcohol consumption, or specific diets.

Physical examination

The patient was conscious, compos mentis, blood pressure 141/70 mmHg, pulse 80/min, respiratory rate 20/min, temperature 36.0°C, body weight 80 kg, height 170 cm, BMI 27.6 (overweight), and VAS score: 8/10. Clinical manifestation on pedis sinistra shows diffuse erythematous macular lesion with indistinct borders forming a geographic pattern extending across the dorsal pedis to the cruris. A central solitary ulcer measuring 1×2×1 cm with irregular edges and a dark crust was noted. Warmth, tenderness, and non-pitting oedema were present. Dorsalis pedis pulse palpable and strong, distal pulses present bilaterally. Capillary refill was normal.

Laboratory evaluation

Laboratory examinations during hospitalization are summarized on the Table 1.

Diagnosis

The patient was diagnosed with cellulitis pedis sinistra class 2, type 2 diabetes mellitus (insulin dependent), acute-on-chronic kidney disease, stage 2 hypertension, and multiple drug allergy.

Management

The patient underwent surgical debridement and received the following inpatient treatment (Table 2).

Table 1: Laboratory results.

Laboratory tests	Date			Preferences	
Complete blood count	**8th October 2025**	**9h October 2025**	**10th October 2025**		
Leukocyte count	8.76			4.0-10.0	10^3/ul
Erythrocyte count	4.03 (L)			4.20-5.40	10^6/ul
Hemoglobin	10.9 (L)			12.0-16.0	g/dl
Hematocrit	33.5 (L)			37.0-47.0	%
MCV	83.1			81.0-96.0	fl
MCH	27.0			27.0-36.0	pg
MCHC	32.5			31.0-37.0	g/l
Thrombocyte count	225			150-400	10^3/ul
Blood chemistry					
SGPT	85 (H)			0-42	U/l
SGOT	47 (H)			0-37	U/l
Random blood glucose (at 6 am)	97	120	88	80-200	mg/dl
Random blood glucose (at 8 pm)	124	91	156	80-200	mg/dl
Fasting blood glucose		120	88	80-200	mg/dl
Urea	81 (HH)		35	10-50	mg/dl
Creatinine	1.8 (H)		1.0	0.3-1.2	mg/dl

Table 2: Treatment during hospitalization.

Drug name	Instruction	Routes
Gentamycin 80 mg	@12 jam	IV
Ranitidine 50 mg	@12 jam	IV
Glargine 26 unit	@24 jam	SC
Aspart 10 Unit	@8 jam	SC
Amlodipin 10 mg	@24 jam	PO
Ramipril 5 mg	@24 jam	PO

DISCUSSION

A 55-year-old female patient was diagnosed with cellulitis pedis sinistra. The patient was referred from a previous hospital with complaints of pain, swelling, and redness in her left leg, with a history of type 2 diabetes mellitus and multiple drug allergies. The patient had been treated in another hospital with levofloxacin but developed an allergic reaction. Physical examination revealed diffuse erythematous macular lesion with indistinct borders forming a geographic pattern extending across the dorsal pedis to the cruris. A central solitary ulcer measuring

1×2×1 cm with irregular edges and a dark crust was noted. Warmth, tenderness, and non-pitting oedema were present. This lesion is characteristic of cellulitis patients. The patient met the criteria for class 2 cellulitis, with comorbid type 2 diabetes mellitus and multiple drug allergies as complicating factor. In accordance with class 2 cellulitis, and she scheduled for surgical debridement the patient was advised to be hospitalized for observation during therapy and recovery.[7]

The patient had well-controlled preoperative blood glucose. Insulin therapy was continued at the previous dose of Glargine 26 units once daily and Aspart 10 units three times daily. Insulin therapy is the standard treatment for patients with type 2 diabetes mellitus who have severe kidney or liver dysfunction, patients with oral antidiabetic intolerance, and patients with diabetes who have severe infections or undergo surgery and receive parenteral nutrition.[2] This is consistent with the laboratory results on September 8, 2025, which showed a decrease in renal function with a GFR of 44.60 mL/min, classified as category G3a.[8]

Furthermore, the patient requires antibiotic therapy as the primary treatment for cellulitis. The case is complicated because the history of hypersensitivity to cefadroxil (cephalosporin class) and levofloxacin (quinolone class). The first line antibiotic for grade 2 cellulitis would be oral antibiotics such as flucloxacillin or cephalexin. However, both of these antibiotics are contraindicated in this patient. Flucloxacillin (penicillin class) and cephalexin (cephalosporin class) belong to the β-lactam group of antibiotics.[9] The administration of these antibiotics should be avoided in this patient because of the risk of β-lactam cross-reaction.[4,10] β-lactam cross-reaction is the possibility of an allergic reaction to one type of β-lactam antibiotic after the patient has previously experienced an allergic reaction to another type of β-lactam.

Cefadroxil and cephalexin are cephalosporin antibiotics, which have the same core structure, namely a β-lactam ring fused with a dihydrotiazin ring.

Cefadroxil and flucloxacillin shared similar β-lactam ring. This can certainly pose a risk of hypersensitivity reactions that possibly worsen the patient's condition.[4]

The second-line antibiotic options are clindamycin or vancomycin. Both antibiotics are relatively safe for this patient because they do not carry a risk of β-lactam cross-reactivity. However, since these antibiotics are not available, it is necessary to choose an alternative that is appropriate in terms of both antimicrobial coverage and availability.

For this patient, the antibiotic of choice is gentamicin. Gentamicin is an aminoglycoside antibiotic effective against aerobic Gram-negative bacteria, which are common causative pathogens in cellulitis. Additionally, gentamicin does not share the ring structure of cefadroxil or levofloxacin, and therefore does not pose a risk of cross-reactivity with these medications.

Gentamicin was administered intravenously using the graded challenge method. A graded challenge is a stepwise approach to administering a medication in incrementally increasing doses under close clinical monitoring to ensure that no severe allergic reactions occur.[6] This procedure is typically performed in medical facilities equipped to manage anaphylaxis. Although hypersensitivity reactions to gentamicin are considered rare, the graded challenge method remains a reasonable precaution, especially when the medication is essential and no safer or equally effective alternatives are available.[6,10,13]

In this patient, intravenous gentamicin 80 mg every 12 hours for three days was administered. During the first administration, the graded challenge procedure was followed, and the patient was observed closely. The sequential steps of gentamicin graded challenge are depicted in Figure 2.

After completing the graded challenge, no signs of allergic reaction were detected, and the patient's vital signs remained stable, indicating that the patient did not exhibit hypersensitivity to gentamicin. Subsequent doses were therefore administered directly without repeating the graded challenge.

Gentamicin carries a risk of nephrotoxicity. In patients with impaired renal function, strict monitoring of kidney function during therapy is essential.[11] In this patient, kidney function tests were performed before and after gentamicin therapy. After three days of treatment, the patient showed significant clinical improvement, the cellulitis resolved, and the patient's comorbid conditions were well controlled.

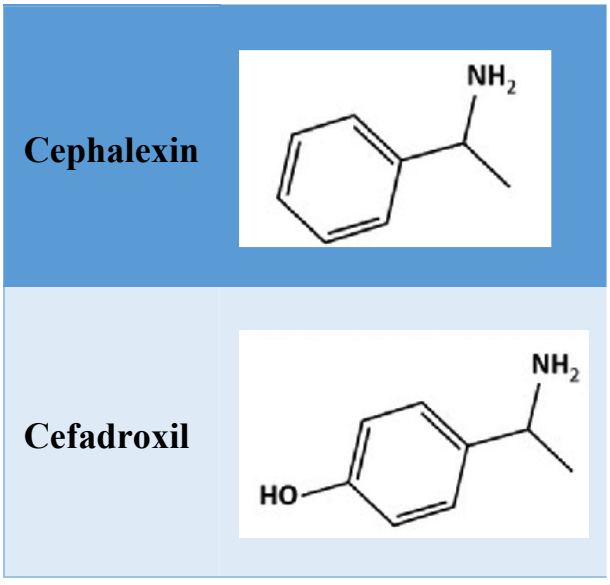

Figure 1: Dihydrotiazin structure of cefadroxil and cephalexin.[4]

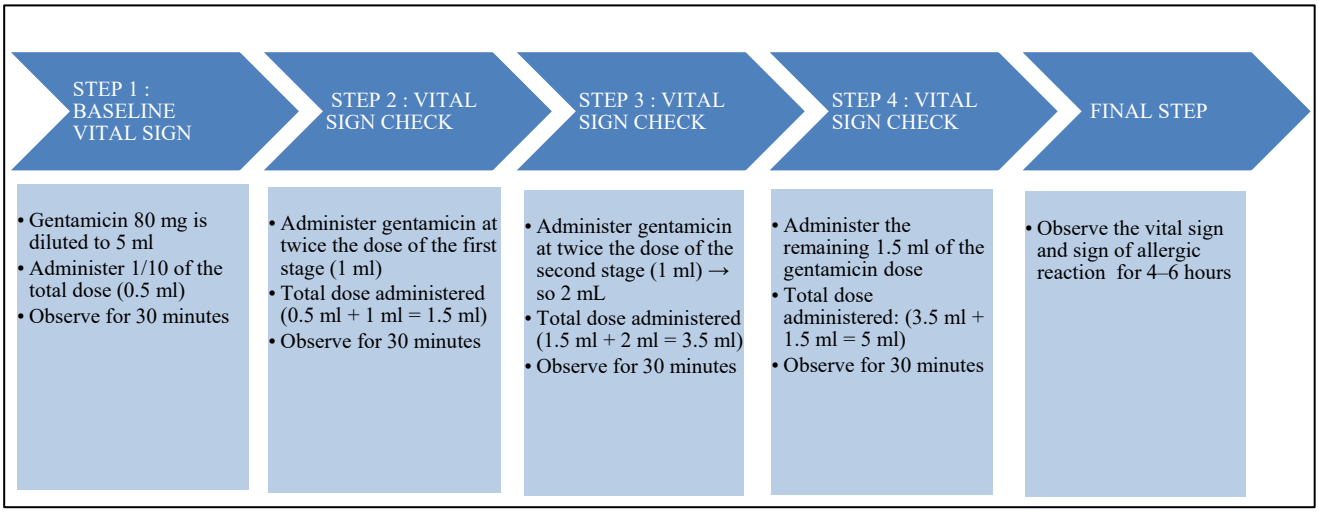

Figure 2: Steps of gentamicin graded challenge.

CONCLUSION

Cellulitis pedis is a diabetic neuropathy complication most commonly caused by *Staphylococcus aureus* and *Streptococcus pyogenes*. Antibiotic therapy is the primary treatment. In cellulitis patient who have multiple drug allergies to first-line antibiotic, comprehensive consideration and selection of appropriate alternative antibiotics are essential. When safe and effective options are limited, a graded challenge may be considered to minimize the risk of severe hypersensitivity reactions.

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