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Case Report

Adverse drug reaction to piperacillin-tazobactam mimicking Kounis syndrome in a pregnant lady diagnosed with pyelonephritis: a case report

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ABSTRACT

Piperacillin-tazobactam is commonly used to treat severe infections during pregnancy, but it can also lead to life-threatening hypersensitivity reactions like Kounis syndrome (KS). A 25-year-old primigravida (G1P0) at 20 weeks' gestation presented with intractable vomiting, fever, and abdominal pain. She was admitted to the ICU with a diagnosis of pyelonephritis with septic shock, evidenced by hypotension (70/40 mmHg), tachycardia (114 bpm), leukocytosis (20,300/mm^3), and elevated C-reactive protein (338.9 mg/l). She was initiated on IV fluids, noradrenaline, and empirical antibiotics, including piperacillin-tazobactam. Shortly after the first dose of piperacillin-tazobactam, the patient developed an acute, severe reaction characterized by hypertension (180/100 mmHg), tachycardia (130 bpm), hypoxia (89% SpO_2), angioedema, wheezing, and chest pain with widespread ST-T abnormalities on ECG, suggesting a possible KS. The drug was immediately discontinued, and the patient was stabilized. A positive re-exposure on the following day with a single challenge dose confirmed the severe hypersensitivity and established causality. The drug was permanently withdrawn, and the patient was successfully managed with meropenem. This case suggests a life-threatening piperacillin–tazobactam hypersensitivity in pregnancy, with clinical features overlapping septic deterioration and possible KS.

Keywords: Beta-lactam, Hypersensitivity, Naranjo, Hartwig

INTRODUCTION

Urinary tract infections (UTIs) are the most common bacterial infections to occur during pregnancy and are classified as either involving the lower urinary tract (cystitis) or the upper urinary tract (pyelonephritis). Physiological and hormonal changes during pregnancy can lead to a higher frequency of asymptomatic bacteriuria (ASB), which could progress to pyelonephritis and is associated with significant maternal and fetal morbidity that affects 1-2% of pregnant women.[1]

Standard management involves inpatient care with aggressive fluid resuscitation and empiric broad-spectrum intravenous antibiotics that achieve adequate renal tissue penetration. Piperacillin–tazobactam is often chosen for its extended-spectrum activity, including coverage of *Pseudomonas aeruginosa* and many extended-spectrum β-lactamase–producing organisms. Although generally considered safe in pregnancy, rare but serious hypersensitivity reactions-ranging from anaphylaxis to anaphylactoid shock-have been documented, highlighting the necessity for close monitoring during the administration.[2]

KS is a type of severe anaphylaxis which is not rare but infrequently diagnosed. Also known as allergic angina or coronary hypersensitivity disorder; which is usually

induced by antibiotics, insect bite, food etc. and presents with chest pain, allergic signs such as urticaria, angioedema, breathlessness, hypotension, tachycardia, tremors and decreased saturation.[3]

CASE REPORT

A 25-year-old primigravida woman (G1P0L0A0) at 20 weeks of gestation (5 months) presented with a 3-4-day history of multiple complaints. The patient reported multiple episodes of vomiting, which were non-blood stained, contained food particles, and were non-projectile and non-bilious. These episodes were not relieved by medication. She also had a low-grade, intermittent fever without chills, diffuse cramp-like abdominal pain of insidious onset that was progressive and not responding to medication, and intermittent cough with scant, mucoid, non-foul-smelling, non-blood-stained expectoration.

She had no prior history of diabetes, hypertension, cardiovascular or cerebrovascular disease, tuberculosis, or substance use. She had regular 30-day menstrual cycles with 3-4 days of bleeding and no history of abortions.[3]

She was admitted in OBGYN general ward, on admission (Day 0), her pulse rate was 114 bpm and blood pressure was initially unrecordable, later stabilizing to 70/40 mmHg after receiving three units of normal saline. Her SpO_2 was 98% on room air, and random blood glucose was 140 mg/dl. Arterial blood gas analysis showed a pH of 7.359, pCO_2 32.3 mmHg, and HCO_3 18.5 mmol/l. Laboratory investigations revealed a hemoglobin level of 7.8 g/dl, white blood cell counts of 20,300/mm^3, platelet count of 253,000/mm^3 and CRP 338.9 mg/l. Coagulation profile showed PT/INR of 15.0 seconds/1.11. Thyroid-stimulating hormone was 0.03 µIU/ml which was low, Renal and liver function tests were within normal limits.

Ultrasound KUB revealed a wedge-shaped hypointensity in the right kidney extending to the cortex, p/o pyelonephritis and gall bladder polyp; while the left kidney appeared normal. Echocardiography showed an ejection fraction of 60%. She was clinically diagnosed to be a case of pyelonephritis with septic shock, for which she was shifted to medicine ICU (Day 1) and was managed as follows:

Initial management included Ringer's lactate at 50 ml/hour, noradrenaline infusion (16 µg in 50 ml at 2 ml/hour), and antibiotic therapy with piperacillin-tazobactam 4.5 g IV and azithromycin 500 mg orally. Symptomatic management included syrup citralka (disodium hydrogen), ondansetron 4 mg IV for nausea, IV and oral paracetamol for fever and pain, and dextromethorphan for cough.

Shortly after administering piperacillin-tazobactam, the patient developed acute hypersensitivity reactions including chills, tachycardia (130 bpm), palpitations, tremors, a rise in blood pressure to 180/100 mmHg, breathlessness, SpO_2 drop to 89%, retrosternal burning, angioedema (swollen lips), chest pain, nausea, vomiting, and bilateral wheezing. Also, there were widespread ST-T abnormality along with tachycardia in the ECG. After this, the antibiotic was immediately discontinued and she was managed with IV pheniramine (2 ml), IV hydrocortisone hemisuccinate (100 mg), nebulized budesonide, IV furosemide, and oral nicardipine (20 mg). Her condition stabilized with a blood pressure of 140/90 mmHg, pulse of 90 bpm, and SpO_2 of 95%.

Upon re-exposure with a single dose of piperacillin–tazobactam (4.5 g) on the next day (day 2) under strict supervision, the patient experienced identical symptoms, confirming the causality of the reaction. The drug was permanently withdrawn and the event was reported to the institutional AMC as life-threatening. Patient was treated symptomatically and subsequently managed with meropenem 1 g IV thrice daily.

Subsequently (day 3), the patient showed signs of clinical improvement. Her CRP had reduced to 68.3 mg/l, serum creatinine was 0.6 mg/dL, blood pressure was 120/80 mmHg, pulse 82 bpm, and SpO_2 98%. Ultrasound confirmed fetal viability, and patient continued to recover.

The adverse drug reaction (ADR) was classified as severe hypersensitive reaction to piperacillin–tazobactam. It was life-threatening, necessitating ICU care. The positive re-exposure confirmed the reaction's causality (as per Naranjo and Hartwig's scale). ADR report was submitted to the local adverse drug reaction monitoring centre (AMC) under the national pharmacovigilance program.

Table 1: Naranjo adverse drug reaction probability scale.[4]

S. no.	Question	Yes	No	Do not know	Score
1	Are there previous conclusive reports on this reaction?	+1	0	0	1
2	Did the adverse event appear after the suspected drug was administered?	+2	-1	0	2
3	Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	1
4	Did the adverse event reappear when the drug was re-administered?	+2	-1	0	2
5	Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	2
6	Did the reaction reappear when a placebo was given?	-1	+1	0	0

Continued.

S. no.	Question	Yes	No	Do not know	Score
7	Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
8	Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10	Was the adverse event confirmed by any objective evidence?	+1	0	0	1

Table 2: Total score (ADR).

Scores	Probability
≥9	Definite ADR
5-8	Probable ADR
1-4	Possible ADR
0	Doubtful ADR

Table 3: Hartwig's severity scale assessment.[5]

Level	Description
1	An ADR occurred but required no change in treatment with the suspected drug.
2	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. No antidote or other treatment requirement was required. No increase in length of stay (LOS)
3	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. And/ or An Antidote or other treatment was required. No increase in length of stay (LOS)
4	Any level 3 ADR which increases length of stay by at least 1 day. Or The ADR was the reason for the admission
5	Any level 4 ADR which requires intensive medical care
6	The adverse reaction caused permanent harm to the patient
7	The adverse reaction either directly or indirectly led to the death of the patient

Note: [Mild=level 1 and 2, moderate=level 3 and 4, severe=5, 6 and 7]. Report: The suspected ADR was found to be __**5**__ on Hartwig's severity scale assessment and falls in severe category.

Figure 1: Anonymized photograph of the patient in the ICU showing angioedema.

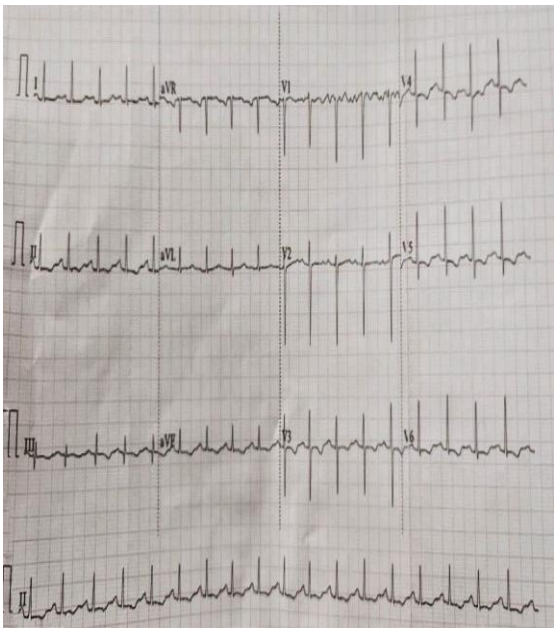

Figure 2: ECG showing sinus tachycardia with diffuse ST–T abnormalities..

DISCUSSION

The most significant factor predisposing women to cystitis and pyelonephritis in pregnancy may be ASB and is reportedly most common during the second half of pregnancy, as a result of physiological changes from the gravid uterus.[6,7] Organisms causing UTI in pregnancy most common being *E. coli*; others include *K. pneumonia, Proteus, Staphylococcus, Streptococcus, and Enterococcus species.*[8]

Empiric antibiotic therapy may be started if symptoms of UTI are present, including urinary frequency, dysuria, and hematuria. Current guidelines for acute pyelonephritis in pregnancy (e.g., ACOG 2023, IDSA/ EAU 2010 update) recommend a minimum of 14 days of antibiotic therapy, with initial parenteral treatment until clinical improvement, followed by oral therapy guided by culture sensitivities.[9-11] First-line antimicrobial management includes broad spectrum β-lactams with consideration of addition of aminoglycosides, including ampicillin plus gentamicin, or single-dose cephalosporins, such as ceftriaxone or cefepime and piperacillin-tazobactam may also be considered based on local resistance patterns or ESBL-producing organisms are suspected[12] and individual patient factors.[8,9]

Piperacillin-tazobactam (PPZ-TZB) was first approved for use in 1981. It is a broad-spectrum betalactam antibiotic consisting of 2 components: the semi-synthetic ureidopenicillin piperacillin (PPZ) and the beta-lactamase inhibitor tazobactam (TZB).[13] Immediate, IgE mediated hypersensitivity reactions (IHRs) to PPZ-TZB have been reported since 1984.[14] Similarly, small cohorts of patients with nonimmediate hypersensitivity reactions (NIHRs) non-IgE have been described since 1993, including fixed drug eruption, generalized fixed drug eruption, drug rash with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), DRESS/AGEP overlap, and Stevens-Johnson syndrome/toxic epidermal necrolysis.[15]

KS is the concurrence of an acute coronary event with conditions associated with IgE mediated massive mast–cell degranulation, usually during anaphylactic or anaphylactoid reaction.[16] KS seems to be promoted by inflammatory mediators, as histamine, chemokines and leukotrienes released by cardiac mast cells. Antibiotics are the commonest cause of drug induced KS and Betalactams are the most frequently culprit molecule. Apart from antibiotics the second most common cause for KS is insect bite.[17]

A study done by Calogiuri et al reported a case of KS which was induced by intravenous administration of piperacillin/tazobactam, where patient developed diffuse erythematous rash on his trunk, neck, face and arms bilaterally with intense itching. Patient showed malaise, shortness of breath and he quickly became hypotensive and tachycardic (approximately 140 bpm). Blood pressure collapsed to 70/40 mm Hg and he was hypoxic with 78/79% oxygen saturation.[18]

In our case, the abrupt onset of tachycardia, hypoxia, wheezing, chest pain, hypertension (which may be due to Noradrenaline) and gastrointestinal symptoms shortly after the first dose of piperacillin–tazobactam pointed toward a severe hypersensitivity reaction rather than progression of septic shock. Differentiation between worsening sepsis and antibiotic-induced hypersensitivity is challenging; however, the temporal relationship and prompt recurrence upon re-exposure satisfy criteria for causality (e.g., Naranjo adverse drug reaction probability scale).

For this case we had all the blood markers done, but we did not have the resources to do the IgE test and the angiography to confirm the case for KS. Since the chest pain persisted even after stopping the drug till next day and with ECG changes; the chances of KS are high.

CONCLUSION

This case suggests a life-threatening piperacillin-tazobactam hypersensitivity in pregnancy, with clinical features overlapping septic deterioration and possible KS. Highlighting the importance of monitoring pregnant patient's haemodynamics and respiratory function while administering broad spectrum β lactams, recognising hypersensitivity signs, and discontinuing the offending agent immediately. Moreover, it highlights the importance of pharmacovigilance reporting with detailed ADR submission to the local AMC which will contribute to enhanced drug safety data, particularly in vulnerable populations such as pregnant women.

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REFERENCES

1. McGready R, Wuthiekanun V, Ashley EA, Tan SO, Pimanpanarak M, Viladpai-Nguen SJ, et al. Diagnostic and treatment difficulties of pyelonephritis in pregnancy in resource-limited settings. Am J Trop Med Hyg. 2010;83(6):1322-9.
2. Zhang H, Yang L. Adverse reactions of piperacillin: A literature review of case reports. Open Med. 2024;19(1):20240931.
3. Kounis NG. Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and therapeutic management. Clin Chem Lab Med. 2016;54(10):1545-59.

4. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30(2):239-45.
5. Petrova G, Stoimenova A, Dimitrova M, Kamusheva M, Petrova D, Georgiev O. Assessment of the expectancy, seriousness and severity of adverse drug reactions reported for chronic obstructive pulmonary disease therapy. SAGE Open Med. 2017;5:205031211769040.
6. Farkash E, Weintraub AY, Sergienko R, Wiznitzer A, Zlotnik A, Sheiner E. Acute antepartum pyelonephritis in pregnancy: a critical analysis of risk factors and outcomes. Eur J Obstet Gynecol Reprod Biol. 2012;162(1):24-7.
7. Smaill FM, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. Cochrane Database Syst Rev. 2019;2019(11):CD000490.
8. Wing DA, Fassett MJ, Getahun D. Acute pyelonephritis in pregnancy: an 18-year retrospective analysis. Am J Obstet Gynecol. 2014;210(3):219.e1-6.
9. Urinary Tract Infections in Pregnant Individuals. Obstet Gynecol. 2023;142(2):435-45.
10. Sheffield JS, Cunningham FG. Urinary tract infection in women. Obstet Gynecol. 2005;106(5 Pt 1):1085-92.
11. Molina-Muñoz JS, Cuadrado-Angulo J, Grillo-Ardila CF, Angel-Müller E, Cortés JA, Leal-Castro AL, et al. Consensus for the treatment of upper urinary tract infections during pregnancy. Rev Colomb Obstet Ginecol. 2023;74(1):37-52.
12. Corrales M, Corrales-Acosta E, Corrales-Riveros JG. Which Antibiotic for Urinary Tract Infections in Pregnancy? A Literature Review of International Guidelines. J Clin Med. 2022;11(23):7226.
13. Joint Formulary Committee, British National Formulary. Piperacillin with tazobactam J Drug j BNF content published by NICE. London: Pharmaceutical Press; 2020. Available at: https://bnf.nice.org.uk/drug/piperacillin-withtazobactam.html. Accessed on 12 October 2025.
14. Romano A, Di Fonso M, Viola M, Adesi FB, Venuti A. Selective hypersensitivity to piperacillin. Allergy. 2000;55(8):787.
15. Casimir-Brown RS, Kennard L, Kayode OS, Siew LQC, Makris M, Tsilochristou O, et al. Piperacillin-Tazobactam Hypersensitivity: A Large, Multicenter Analysis. J Allergy Clin Immunol Pract. 2021;9(5):2001-9.
16. Kounis NG. Kounis syndrome (allergic angina and allergic myocardial infarction): a natural paradigm? Int J Cardiol. 2006;110(1):7-14.
17. Ridella M, Bagdure S, Nugent K, Cevik C. Kounis syndrome following beta-lactam antibiotic use: review of literature. Inflamm Allergy Drug Targets. 2009;8(1):11-6.
18. Calogiuri GF, Nettis E, Di Leo E, Vacca A, Ferrannini A, Kounis NG. Kounis Syndrome induced by intravenous administration of piperacillin/tazobactam: a case report. Int J Cardiol. 2012;155(3):e42-4.

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