Case Report

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# Tigecycline-induced pancreatitis in a patient with recurrent malignancy: a case report and literature review

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**Introduction and importance:** Drug-induced pancreatitis is an important health issue that makes a minority of causes of acute pancreatitis. Tigecycline-induced pancreatitis is a rare condition with poorly understood mechanism and has a small incident compared to other causes of pancreatitis

**Case presentation:** The authors present a case of a 39-year-old female patient with acute pancreatitis. Tigecycline was the suspected culprit by exclusion. The patient was managed by keeping her nill per os, rehydration, pain management and discontinuation of the drug. The patient improved gradually.

**Clinical discussion:** Tigecycline-induced acute pancreatitis is a rare but known complication that is mostly seen in patients with chronic renal insufficiency combined with high dose of administration. Onset is usually within 14 days of initiation. Discontinuation of the drug is the most effective intervention in addition to supportive management.

**Conclusion:** Acute pancreatitis should be suspected in any patient presenting with vomiting, abdominal pain and acidosis while on tigecycline. Monitoring of amylase and lipase can be beneficial especially in those with chronic renal insufficiency or those receiving a high dose.

**Keywords:** pancreatitis, renal insufficiency, sepsis, side effect, tigecycline

## Introduction

Drug-induced pancreatitis comprises less than 0.1–2% of all cases of acute pancreatitis[1], while prevalence can't be easily determined as most of the cases are published as case reports. Usually, if there is no other identifiable cause, the case is considered to be drug-induced pancreatitis if the patient is taking any of the 525 medications enlisted in WHO database, that have the side effect of possible pancreatitis[2]. Most of drug-induced pancreatitis cases are usually mild to moderate in severity, management should consist of discontinuation of offending agent as well as supportive management[1].

Tigecycline is structurally related to minocycline. Although tetracycline-induced pancreatitis has been raised as an issue recently, tigecycline-induced pancreatitis is still considered a rare incident. However, it is advised for any patient being treated with tigecycline to be monitored for abdominal pain, vomiting, diarrhoea and symptoms of acute pancreatitis[3]. Herein, we report the case of a 39-year-old female patient with tigecycline-induced pancreatitis. This case was written according to the SCARE (Surgical case report) criteria 2023[4].

### HIGHLIGHTS

- Tigecycline is structurally related to minocycline.
- Drug-induced pancreatitis is a diagnosis of exclusion.
- The onset of tigecycline-induced pancreatitis is usually within 14 days of administration.
- It's more seen in patients with chronic renal insufficiency and high dose of administration.
- Discontinuation of the drug is key to treatment.

## Case presentation

A 39-year-old female patient from Palestine, and a known case of high-grade squamous cell carcinoma of the urinary bladder, was admitted repeatedly to the hospital due to recurrent urinary tract infection. The patient was diagnosed four months ago with high-grade squamous cell carcinoma, she underwent radical cystectomy with positive margins, resulting in the creation of a permanent urostomy. She was commenced on concurrent chemoradiation with carboplatin, and finished the last session 2 months prior to presentation. Her treatment course was complicated by urinary tract infection, treated empirically with piperacillin-tazobactam, switched to ertapenem as urine culture showed growth of extended-spectrum β-lactamase (ESBL) *Klebsiella pneumoniae*, for a total of 5 days. She had a history of

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**Table 1**

**Laboratory tests at the onset of acute pancreatitis**

| Parameter | Result | Normal value |
|---|---|---|
| Haemoglobin | 10.2 ↓ | 12–15 g/dl |
| White blood cell count1 | 14.2↑ | 3.6–10.6 × 109/µl |
| Platelets | 127↓ | 150–450 × 103/µl |
| Sodium | 139 | 136–145 mmol/l |
| Potassium | 3.28 | 3.5–5.3 mmol/l |
| Calcium | 8.5 | 8.6–10.3 mmol/l |
| Creatinine | 3.06↑ | 0.5–0.9 mg/dl |
| Blood urea nitrogen | 52.9↑ | 6–20 mg/dl |
| Alanine amino transferase | 16.3 | 0–35 U/l |
| Aspartate amino transferase | 26.2 | 8–40 U/l |
| Total bilirubin | 0.66 | 0–1.2 µmol/l |
| Direct bilirubin | 0.46 | 0–0.3 µmol/l |
| Lipase | 1724↑ | 31–186 IU/l |
| Amylase | 686↑ | 27–131 IU/l |
| Triglyceride | 192↑ | 0–150 mg/dl |
| Mumps virus antibodies, IgM | 4.6 | < 20 AU/ml |
| Mumps virus antibodies, IgG | 27.4↑ | < 20 AU/ml |

hypertension and chronic renal failure but had no history of cholecystitis or pancreatitis.

On presentation, the patient was febrile, her oral temperature was 38°C in a state of lethargy, but no hypotension or tachycardia. Her abdomen showed epigastric tenderness, with turbid, foul-smelling urine. Her lower limbs showed no oedema.

The patient's basic metabolic panel showed a creatinine of 1.9 mg/dl which is her baseline creatinine, her C-reactive protein was 228, with no leukocytosis. She was started empirically on piperacillin-tazobactam, adjusted based on creatinine clearance.

Urine culture grew *Klebsiella pneumonia*-ESBL, her antibiotic regimen was downgraded to ciprofloxacin after three days of empiric piperacillin-tazobactam. During admission, her creatinine continued to rise, computed tomography (CT) showed right-sided hydroureteronephrosis, so she underwent a right nephrostomy placement and continued on the same regimen.

On day 3 of ciprofloxacin, the patient had an episode of chills without fever, a new septic workup was obtained and she continued on the same antibiotic regimen. Blood culture revealed carbapenem-resistant *Klebsiella pneumoniae*-carbapenem-resistant enterobacteriaceae (CRE), drug sensitivity testing showed that the microorganism was sensitive to gentamicin, with intermediate sensitivity to colistin. Urine culture revealed two microorganisms; *Klebisella pneumoniae*-CRE and *Escherichia coli*-ESBL. The newly obtained anal swabs revealed colonization with *Klebsiella pneumonia*-CRE.

The patient regimen was switched to a triple regimen of colistin, gentamicin and a high dose of tigecycline, with dose adjustment based on her renal function. The patient finished a total of 13 days of the above regimen, with two sterile blood and urine cultures obtained since commencing the new regimen. During this period, the patient had intermittent intestinal obstruction, managed with nasogastric tube and nothing by mouth (NPO) until she had a bowel motion, these episodes were remitting and relapsing.

On day 13, she had an episode of altered level of consciousness with hypotension, she was transferred urgently to the intensive care unit. New laboratory tests are shown in Table 1. After stabilization, a new abdominal CT was obtained, showing pelvic free fluid and signs of pancreatic inflammation as shown in Figure 1. Amylase and lipase levels were high, 686 and 1700 mg/dl, respectively. The patient was managed as a case of acute pancreatitis by keeping her NPO, inserting a nasogastric tube, managing her pain and intravenous hydration.

Gallbladder stone, alcoholism, hypercalcemia and mumps were excluded as the culprit. It was concluded that the only medication that could have been the cause of her pancreatitis was tigecycline, all of the above-mentioned medications were discontinued, and the patient was started on ciprofloxacin 500 mg twice daily per os, as the patient's case was critical and she was covered prophylactically for necrotizing pancreatitis. The patient's condition improved, ciprofloxacin was stopped after seven days following clinical improvement and two negative sets of blood culture. The patient was transferred to the ward afterward, subsequent assessment showed widespread recurrence of her malignant disease, she was discharged to home for best palliative care and died afterward. A summary of events can be found in Table 2.

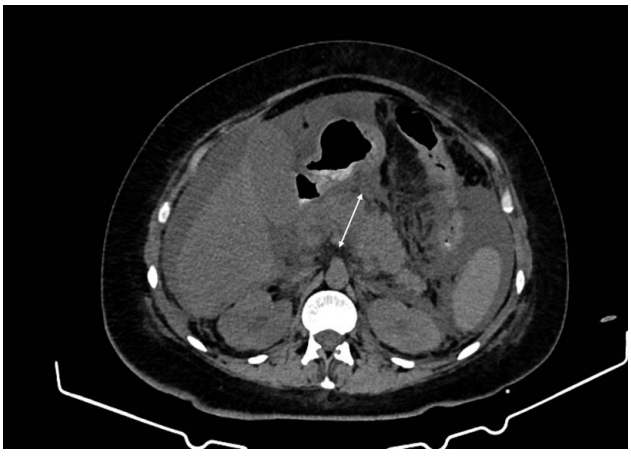

**Figure 1.** Abdominal computed tomography scan shows an enlarged pancreas (white arrow) with free fluid. These acute findings combined with elevation of amylase and lipase are suggestive of acute pancreatitis.

## Discussion

Acute pancreatitis is commonly caused by gallbladder stones, alcohol, hypercalcemia, hypertriglyceridemia, viral infection and certain drugs[5]. The diagnosis of drug-induced pancreatitis is difficult to establish. Diagnosis is usually based on the following criteria: acute pancreatitis occurred during drug administration, symptoms disappear after drug withdrawal, reappear after re-challenge, and all other common causes are excluded. Due to ethical considerations, re-challenge is usually not performed[6].

Tigecycline is a drug and a group in itself, similar to minocycline. It has broad-spectrum activity against Gram-positive bacteria, Gram-negative bacteria, anaerobes, methicillin-resistant *Staphylococcus aureus*, penicillin-resistant *Streptococcus pneumoniae*, vancomycin-resistant *Enterococcus*, and resistant *Acinetobacter baumannii*. Its clinical use ranges from complicated soft tissue infections, complicated intra-abdominal infections, and community-acquired pneumonia[7].

**Table 2**

**A summary of events**

| Event | Clinical data | Date |
|---|---|---|
| Date of admission | The patient was admitted as a case of UTI and acute on-top-of chronic kidney injury | 8/12/2023 |
| Start of antibiotics | The patient was started on piperacillin-tazobactam | 8/12/2023 |
| Urine culture results | Urine culture grew *Klebsiella pneumoniae* ESBL, antibiotics switched to ciprofloxacin | 10/12/2023 |
| Onset of symptoms (sepsis) | Fever and chills recurred, she was switched to colistin | 13/12/2023 |
| Starting tigecycline | Tigecycline was added | 14/12/2023 |
| Blood culture withdrawn | New cultures obtained | 13/12/2023 |
| Result of blood culture | Result of culture showed *Klebisella pneumoniae*-CRE and *Escherichia coli*-ESBL | 17/12/2023 |
| Onset of symptoms (pancreatits) | The patient developed an altered level of consciousness with abdominal pain and vomiting | 27/12/2023 |
| Antibiotics stopped | After reviewing the patient chart, tigecycline was suspected to be the culprit, a diagnosis by exclusion, so it was stopped | 28/12/2024 |

CRE, carbapenem-resistant enterobacteriacae; ESBL, extended-spectrum β-lactamase; UTI, urinary tract infection.

Wang and colleagues suggested that tigecycline-induced pancreatitis usually presents within two weeks of starting treatment[8]. In our case, the onset of pancreatitis was on the 13th day of starting tigecycline. Re-challenge was not performed, but the patient improved within 7 days after discontinuation of the offending agent and following the treatment protocol of pancreatitis.

The mechanism by which tigecycline causes acute pancreatitis is still unclear[9]. Steinberg claimed that the accumulation of an unidentified toxin caused tetracycline-induced pancreatitis[10]. Elmore and Rogger hypothesized that the interaction of tigecycline with 30S ribosomal units, blocking protein synthesis caused the accumulation of triglycerides in the pancreas[11]. Gilson *et al*. suggested that a single dose of 100 mg of tigecycline produced a high tissue: fluid concentration in bile, which he claimed was the mechanism by which tigecycline caused pancreatitis[12,13]. Due to having a CRE bloodstream and urinary tract infection, the patient was started on a high dose of tigecycline, consisting of 200 mg loading dose followed by 100 mg twice daily according to Smith H[14]. This might be one of the triggering factors that cause drug-induced pancreatitis.

Tigecycline is excreted renally, thus, a history of renal insufficiency seems to contribute to the development of tigecycline-induced pancreatitis[15]. Our patient had chronic renal failure, which progressively worsened during admission, acute kidney injury on top of chronic kidney injury occurred.

A case report of a bacteremia case, the patient had a positive culture for *Pseudomonas aerogenosa*, *Enterococcus faecalis* and *Staphylococcus hominis*, the patient was treated for two weeks with tigecycline in addition to other antibiotics. She developed vomiting, fever and loss of appetite. Upon discontinuation of tigecycline the patient's symptoms improved[9].

## Conclusion

Tigecycline-induced pancreatitis is a rare and not well-understood complication. Abdominal pain, vomiting, and an unexplained increase in amylase and lipase should raise suspicion of acute pancreatitis. Regular monitoring of white blood cells and amylase is recommended especially when a high dose of Tigecycline is administered or when the patient has renal impairment.

## Ethical approval

Not applicable.

## Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.


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## Author contribution

A.S. conceived the idea. H.A. and D.S. collected the data. H.A. and D.S. wrote the original draft of the manuscript. All authors reviewed and approved the manuscript.

## Conflicts of interest disclosure

The authors declare that they have no conflict of interest.

## Research registration unique identifying number (UIN)

Not applicable.

## Guarantor

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## Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Provenance and peer review

Not commissioned, externally peer-reviewed.

## References


[1] Jones MR, Hall OM, Kaye AM, *et al*. Drug-induced acute pancreatitis: a review. Ochsner J 2015;15:45–51.

[2] Nitsche CJ, Jamieson N, Lerch MM, *et al*. Drug induced pancreatitis. Best Pract Res Clin Gastroenterol 2010;24:143–55.

[3] Hung WY, Kogelman L, Volpe G, *et al*. Tigecycline-induced acute pancreatitis: case report and literature review. Int J Antimicrob Agents 2009; 34:486–9.

[4] Sohrabi C, Mathew G, Maria N, *et al*. The SCARE 2023 guideline: updating consensus Surgical CAse REport (SCARE) guidelines. Int J Surg 2023;109:1136–40.

[5] Ren D, Lv M, Ye D, *et al*. Bedside ultrasound in tigecycline-associated acute pancreatitis: a case description. Quant Imaging Med Surg 2023;13: 8793–8.

[6] Marot JC, Jonckheere S, Munyentwali H, *et al*. Tigecycline-induced acute pancreatitis: about two cases and review of the literature. Acta Clin Belg 2012;67:229–32.

[7] Wang PF, Zou H, Zhu JH, *et al*. Acute pancreatitis caused by tigecycline: a case report and literature review. Medicine 2021;100: e28245.

[8] Maringanti BS, Ganipisetti VM, Jun SS, *et al*. Tigecycline Tango: a case of antibiotic-induced pancreatitis. Cureus 2023;15:e44538.

[9] Pan J, Ye C, Zhou L-Z, *et al*. The spectrum of tigecycline-induced pancreatitis in clinical characteristics, diagnosis, and management. Int J Gen Med 2023;16(null):2971–9.

[10] Steinberg WM. Acute drug and toxin induced pancreatitis. Hosp Pract 1985;20:95–102.

[11] Elmore MF, Rogge JD. Tetracycline-induced pancreatitis. Gastroenterology 1981;81:1134–6.

[12] Mitchell RM, Byrne MF, Baillie J. Pancreatitis. Lancet (London, England) 2003;361:1447–55.

[13] Gilson M, Moachon L, Jeanne L, *et al*. Acute pancreatitis related to tigecycline: case report and review of the literature. Scand J Infect Dis 2008;40:681–3.

[14] Smith HZ, Hollingshead CM, Kendall B. Carbapenem-Resistant Enterobacterales. [Updated 2024 Feb 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551704/

[15] Yu M, Wu S, Qi B, *et al*. Rational use of tigecycline and tigecycline blood concentration monitoring in patients with severe infection. Biomed Rep 2023;19:51.