Possible tigecycline related acute pancreatitis in an adult with cystic fibrosis

Kistik fibrozis tanılı erişkinde muhtemel tigesiklin ilişkili akut pankreatit

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The aim of this case report is to increase the awareness of pancreatitis due to tigecycline, especially in patients with high risk. A 19-year-old male patient with cystic fibrosis was commenced an antibiotic regimen containing tigecycline with the diagnosis of acute bronchitis. On the 12th day of the treatment, severe epigastric abdominal pain and nausea appeared, and pancreatic enzyme levels increased 10 times more than normal. After eliminating other causes of pancreatitis, tigecycline treatment was discontinued, and the patient's clinical condition improved and laboratory findings returned to normal gradually. Clinicians should be careful when using tigecycline, especially in patients with high risk of developing pancreatitis, such as cystic fibrosis.

Key words: *Tigecycline, acute pancreatitis, cystic fibrosis*

Bu vaka sunumunun amacı, özellikle yüksek riskli hastalarda tigesikline bağlı pankreatit farkındalığının artırılmasıdır. 19 yaşında bilinen kistik fibrozis tanılı erkek hastaya akut bronşit nedeniyle tigesiklin içeren antibiyotik tedavisi başlandı. Tedavinin 12. gününde hastada şiddetli epigastrik karın ağrısı ve bulantı şikayetleri ortaya çıktı ve pankreatik enzim düzeylerinde normalin 10 katına kadar artış görüldü. Diğer akut pankreatit nedenleri ekarte edildikten sonra tigesiklin tedavisi kesildi. Takiplerinde hastanın klinik semptom ve bulguları giderek geriledi ve laboratuvar değerleri normale döndü. Klinisyenler özellikle kistik fibrozis gibi pankreatit gelişim riski yüksek olan hastalarda tigesiklin kullanırken dikkatli olmalıdırlar.

Anahtar kelimeler: *Tigesiklin, akut pankreatit, kistik fibrozis*

INTRODUCTION

Tigecycline is a broad-spectrum glycylcycline class antibiotic and is effective against gram-positive, gram-negative, anaerobic and multidrug-resistant bacteria (1). It has been approved by the Food and Drug Administration (FDA) for the treatment of community-acquired bacterial pneumonia, complicated skin and skin structure infections, and complicated intraabdominal infections. The most common side effects are nausea, vomiting and diarrhea (2). A subsequent retrospective cohort analysis and a review of Phase 3 and 4 comparative tigecycline studies have also been performed, with mixed conclusions (3). There are several publications which show that the drug causes pancreatitis, and recently there are increasing concerns about its pancreatoxic effect 4,5). We present a report of acute pancreatitis induced by tigecycline in an adult patient with cystic fibrosis.

CASE REPORT

Nineteen-year-old male diagnosed with cystic fibrosis applied to the emergency department with complaints of fever, cough, shortness of breath and sputum production that started 1 week ago.

There was no frequent hospitalization history until 2 years ago. When he applied to the hospital 2 years ago with similar complaints, the growth of mycobacterium abscessus proliferation was observed in the bronchoalveolar lavage culture and therefore received antimycobacterial therapy for 6 months. The patient also had a history of cholecystectomy 2 years ago due to cholelithiasis, but never had pancreatitis. He had no growth retardation, did not describe steatorrhea, and he used 600 mg of 25.000 U Creon 3 times a day. He did not use alcohol and cigarettes.

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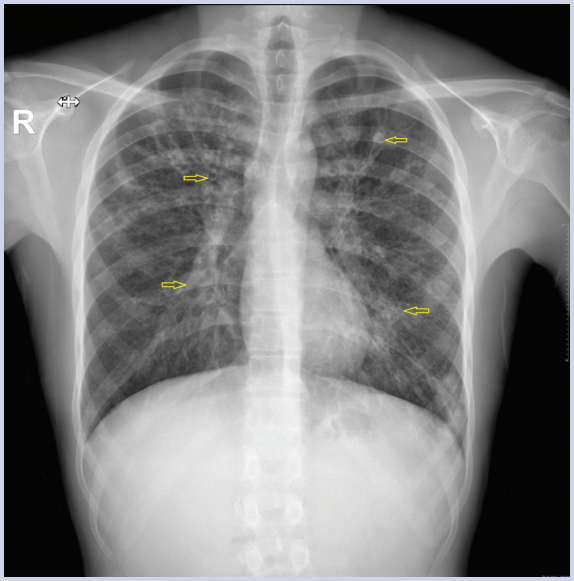


Figure 1. Chest radiograph - Increased bronchial opacity and bronchiectasis.

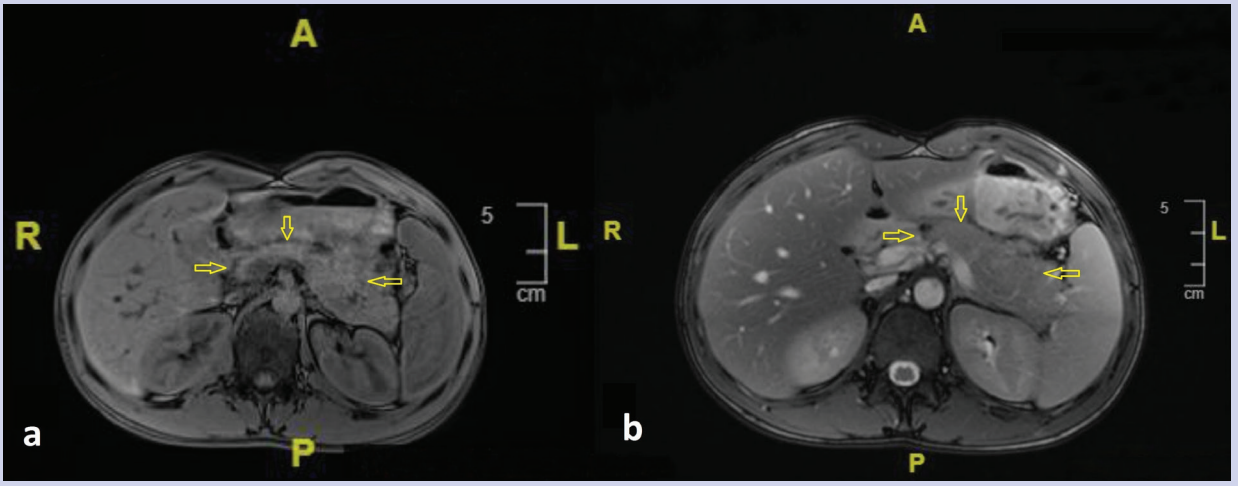
On physical examination, bilateral rough rales in the lungs and coarse breathing sounds were detected. The patient was evaluated as bronchiectasis with bacterial infection (infective exacerbation) and amikacin, imipenem, clarithromycin and tigecycline treatment was started (Figure 1. Tigecycline was administered intravenously, with a dose of 50 mg every 12 hours.

On the 12th day of antibiotic regimen, the patient developed complaints of dull and steady epigastric abdominal pain radiating to the back. The patient also had concomitant nausea. On palpation, sensitivity was detected in the epigastric region. In laboratory tests, serum amylase was 636 U/L (normal range: 28-100), pancreatic amylase was 451 U/L (normal range: 8-53), and lipase was 1152 U/L (normal range: <67) (Table 1). The patient had no hypercalcemia and hypertriglyceridemia. In the magnetic resonance imaging (MRI) of the upper abdomen and magnetic resonance cholangiopancreatography (MRCP), there were no pathological findings other than a mild fullness in the pancreas (Figure 2). Abdominal ultrasonography (US) and computed tomography (CT) examinations were also normal (Figure 3). At the 2-day follow-up, the patient's abdominal pain was deteriorated and serum amylase and lipase levels increased up to 1139 U/L and 1961 U/L respectively. The patient was diagnosed as

Tablo 1. Results of biochemical blood tests.

Laboratory Tests	Results	Normal Range
Na (mEq/L)	139	136-146
K (mEq/L)	4.79	3.5-5.1
Cl (mEq/L)	107	101-109
BUN (mg/dl)	16.5	6-20
Creatinine (mg/dl)	0.75	0.67-1.17
GFR (ml/min/1,73m^2)	>60	>60
Uric acid (mg/dl)	5.8	3.5-7.2
ALT (U/L)	13	<50
AST (U/L)	20	<50
ALP (U/L)	144	30-120
GGT (U/L)	22	<55
Bilirubin, total (mg/dl)	1.00	0.3-1.2
Bilirubin, direct (mg/dl)	0.27	0-0.2
Amylase (U/L)	636	28-100
Pancreatic amylase (U/L)	451	8-53
Lipase (U/L)	1152	<67
Calcium, total (mg/dl)	8.57	8.8-10.6
CRP (mg/dl)	1.64	0-0.8

Na: Sodium; K: Potassium; Cl: Chloride; BUN: Blood urea nitrogen; GFR: Glomerular filtration rate; ALT: Alanine aminotransferase; AST: Asprtate aminotransferase; ALP: Alkaline phosphatase; GGT: Gamma-glutamyl transferase; CRP: C-reactive protein.



Figür 2. Upper abdominal MRI (A-T1 and B-T2) - Typical radiological findings of acute or chronic pancreatitis have not been observed. The pancreas has a slightly plump appearance.

MRI: Magnetic resonance imaging.

acute pancreatitis and tigecycline treatment was discontinued considering its relation to the current condition. Afterward, the patient's symptoms improved and pancreatic enzyme levels decreased gradually in the follow-up.

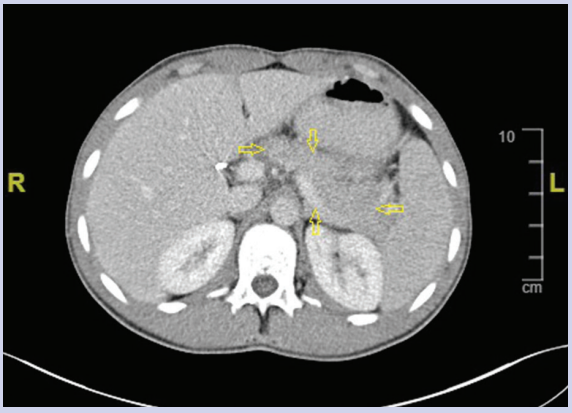


Figure 3. CT of the abdomen - patient with cholecystectomy, dilatation was not observed in the intra and extrahepatic biliary tract, the pancreas was normal.

CT: Computed tomography.

DISCUSSION

Cystic fibrosis is one of the most common autosomal recessive disease in the white population, characterized by a mutation in the CFTR gene (6). The disease can affect the pancreas in three different ways: exocrine pancreatic insufficiency, pancreatitis and diabetes mellitus (7). Approximately 85% of patients develop pancreatic insufficiency before 1 year of age. The remaining 15% will have enough pancreatic residues to provide digestive function, but the risk of developing pancreatic insufficiency continues over time (8). The severity of pancreatic involvement of patients is correlated with the type of CFTR mutation. Thus, class I, II, III and VI mutations are characterized by early pancreatic insufficiency and class IV and V are mild mutations and are characterized by pancreatic sufficiency (9). In published studies, the risk of developing pancreatitis was found to be much higher in patients with mild type mutation (6).

Although the mechanism of pancreatitis is still unknown, several cases of tigecycline-induced pancreatitis have been reported in the literature. Only one of the previously presented cases had cystic fibrosis (2). Although the risk of pancreatitis is reported to be below 1% in phase 3 and 4 clinical trials, an increasing number of case reports raise concerns about the pancreatoxic effect of the drug (3). In our patient, it was decided to discontinue tigecycline treatment considering the recently published cases. The fact that our patient received combined antibiotic therapy may be the limitation of the study. Even if the disease regressed after stopping tigecycline, the pancreatoxic effect of the drug may have increased in combined use. Further studies are needed to confirm the drug`s relationship with pancreatitis.

In conclusion, our recommendation is to be careful in the use of tigecycline, especially in patients with high risk of pancreatitis.

Conflicts of Interest: *The authors declare that they have no conflict of interest.*

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