JOURNAL OF COMMUNITY HOSPITAL INTERNAL MEDICINE PERSPECTIVES
2021, VOL. 11, NO. 1, 143–144
https://doi.org/10.1080/20009666.2020.1845929

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CASE REPORT

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A case of meropenem-induced liver injury and jaundice

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ABSTRACT

This report describes what we believe is the first reported case of clinically significant cholestasis and acute liver injury within three days of meropenem therapy. An 83-year-old Hispanic female was admitted for sepsis of unknown origin and was started on intravenous meropenem. Three days following initiation of the antibiotic, the patient developed mixed hepatocellular and cholestatic liver injury with jaundice and pruritus. Possible causes of cholestasis were excluded after extensive investigations. A drug-induced liver injury was suspected and meropenem was discontinued. Following discontinuation of meropenem, the patient demonstrated symptomatic and laboratory improvements, and her liver enzymes and bilirubin levels were normalized.

ARTICLE HISTORY
Received 1 September 2020
Accepted 30 October 2020

KEYWORDS
Drug-induced liver injury; antibiotic-induced liver injury; antibiotic-induced jaundice; meropenem-induced cholestatic jaundice

1. Introduction

Meropenem is a broad-spectrum antibiotic that has excellent activity against many gram-negative, gram-positive and anaerobic organisms. It is commonly used in the hospital setting for complicated infections. Mild, transient, asymptomatic aminotransferase elevations have been reported with meropenem use, but it rarely results in clinically apparent, symptomatic cholestasis [1–3].

2. Case report

An 83-year-old female with a medical history of hypertension and type II diabetes mellitus presented to the emergency department with a two-day history of dark color stools. Patient had no prior history of gastrointestinal (GI) bleed; she denied fever, abdominal pain, jaundice or weight loss. Her home medications include metformin and lisinopril. Patient was afebrile; initial vital signs were significant for sinus tachycardia and blood pressure was 150/72 mmHg. Physical examination revealed dark color stool on rectal exam. The rest of the physical examination was unremarkable. Initial laboratory studies were significant for a white blood cell count of 15.2 mm^3, lactic acid 3.8 mmol/L, hemoglobin 7.3 g/dL and hematocrit 31%. Liver enzymes and bilirubin level were within normal limits. Urinalysis, chest radiograph and influenza viral testing were negative. Computed tomography (CT) scan of abdomen without contrast was unremarkable. The patient was admitted for acute anemia and sepsis of unknown origin. While a septic workup was undertaken, the patient received two units of packed red blood cell transfusion, intravenous (IV) fluid resuscitation and was started on broad spectrum antibiotic with IV meropenem 500 milligrams every eight hours. Post-transfusion hemoglobin was 9.4 g/dL and remained stable. No further episode of dark stool was reported. Fecal occult blood testing was negative. Blood cultures showed no growth after two days of incubation.

Three days following hospital admission, routine laboratory study showed a markedly elevated liver function test (LFT) with aspartate aminotransferase (AST) 230 U/L and alanine transaminase (ALT) 753 U/L, total bilirubin 8.3 mg/dL, direct bilirubin 6.7 mg/dL and serum alkaline phosphatase (ALP) 167 U/L. On physical examination, patient was noted to have mild jaundice. She denied any GI symptoms. Right upper quadrant ultrasound showed normal gallbladder and biliary ducts, no evidence of gallstones or biliary dilation. On the following day, repeat laboratory study showed worsening LFT with AST 370 U/L and ALT 1191 U/L, total bilirubin 12 mg/dl, direct bilirubin 10.89 mg/dl and serum ALP 192 U/L. Lactate dehydrogenase and serum inflammatory markers erythrocyte sedimentation rate (ESR) and c-reactive protein (CRP) were within normal limits. Patient denied GI symptoms but reported to have generalized pruritus. On physical examination, vital signs were stable; conjunctival icterus and worsening jaundice were noted. Viral

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hepatitis serology, autoimmune markers including antinuclear antibodies, anti-smooth muscle antibodies and anti-mitochondrial antibodies were unremarkable. Further investigation with abdominal CT scan, magnetic resonance imaging (MRI) of abdomen and magnetic resonance cholangiopancreatography (MRCP) were unrevealing; there was no evidence of gallstones or choledocholithiasis, no intra- or extrabiliary ductal dilatation. Given recent dark colored stools, patient also underwent upper endoscopy and colonoscopy which revealed mild gastritis and a few small colonic polyps, respectively; no source of anemia was identified during the procedures. However, patient's liver enzymes and bilirubin levels continued to rise with worsening jaundice and pruritus. A drug-induced liver injury (DILI) was suspected, her medication list was reviewed and meropenem was discontinued. Two days following discontinuation of meropenem, the patient demonstrated symptomatic improvements. Her liver enzymes, bilirubin and ALP levels improved steadily and returned to normal by Day 5 following meropenem discontinuation. Patient was discharged home and was instructed to follow up with gastroenterologist as outpatient.

3. Discussion

Meropenem is a beta-lactam antibiotic that belongs to the carbapenem class; it acts by binding to the penicillin-binding proteins and interferes with the structural integrity of bacterial cell wall. Meropenem has a broad spectrum of activity against many gram-negative and gram-positive organisms; it is administered intravenously with the recommended dosage of 0.5–1 gram every 8 hours. Meropenem is mainly cleared by renal excretion and is a generally well-tolerated antibiotic with most common adverse GI effects being nausea, vomiting and diarrhea [3]. Meropenem was reported to cause mild, asymptomatic, transient serum aminotransferase elevation when it is being used daily for more than 14 days and it rarely requires dose adjustments or discontinuation [4]. To our knowledge, clinically apparent, symptomatic cholestasis and liver injury within three days of meropenem therapy, as the patient in our case, has not been reported in the literature [1,3,4].

DILI is a diagnosis of exclusion. It is diagnosed when other potential causes of liver injury such as viral hepatitis, autoimmune disease, immunologic conditions, biliary obstruction and malignancy have been excluded and laboratory abnormality correlates with drug exposure and subsides after cessation of medication [2,5]. Beta-lactam antibiotics such as amoxicillin-clavulanate are well-recognized causes of cholestasis [6]; however, meropenem-induced jaundice and liver injury are very rarely reported. Review of literature shows there is one instance of meropenem induced vanishing bile duct syndrome after three weeks of therapy [1] and one reported case of DILI with asymptomatic liver enzyme elevation after meropenem use [4]. The patient in our case developed mixed hepatocellular and cholestatic liver injury with jaundice and pruritus within a few days of meropenem therapy; cessation of the antibiotic lead to laboratory and symptomatic improvements; after ruling out other potential causes, we believe this is a DILI caused by meropenem.

Early recognition of drug-induced jaundice and liver injury is important; it should be part of the differential diagnoses when managing a patient with unexplained jaundice and abnormal LFTs. Clinicians should be aware of such side effect of meropenem since it is a widespread used antibiotic in the hospital setting.

Authors' contributions

S. Cheung performed chart review, literature review, and is the author of the manuscript and article guarantor.
J. Bulovic, A. Pillai, T. Manoj and K. Neeraj performed literature review and editing of the manuscript.

Disclosure statement

The authors report no conflict of interest.

Informed consent

Informed patient consent was obtained for this case report.

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