ACG CASE REPORTS JOURNAL

CASE REPORT | PANCREAS

Acute Pancreatitis Caused by Tamoxifen-Induced Severe Hypertriglyceridemia After 4 Years of Tamoxifen Use

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ABSTRACT

We report a case of a 55-year-old woman with hypertension and diabetes mellitus, who took tamoxifen for the past 4 years. She presented with acute pancreatitis caused by markedly elevated serum triglycerides (3,883 mg/dL). Tamoxifen is known to cause a mild increase in serum triglycerides, but it rarely increases to such high levels to cause acute pancreatitis. The patient recovered well, and tamoxifen was switched to letrozole. It is crucial to monitor serum lipids up to 4 years and beyond for patients on tamoxifen, particularly in patients with known dyslipidemia or diabetes mellitus.

INTRODUCTION

Acute pancreatitis is a serious disease of the digestive system and is associated with significant morbidity and mortality.[1,2] The most common causes of acute pancreatitis are alcohol consumption and gallstones. Other causes include hypertriglyceridemia, hypercalcemia, trauma, drugs, and endoscopic retrograde cholangiopancreatography.[3,4] Tamoxifen is an antiestrogen drug used in the treatment of breast cancer. One of its known side effects is an increase in serum triglycerides. We report an unusual case of tamoxifen causing severely elevated triglycerides which led to an episode of acute pancreatitis.

CASE REPORT

A 55-year-old woman with a background history of hypertension controlled on amlodipine 5 mg daily and invasive ductal carcinoma of the left breast diagnosed in 2013, underwent neoadjuvant chemotherapy with paclitaxel, gemcitabine, and trastuzumab followed by a mastectomy. Postoperatively, she was started on tamoxifen 20 mg daily since April 2014 and had been taking it for 4 years. There was no local recurrence to date. She presented to the emergency department in March 2018 with acute epigastric pain with radiation to the back. She had no history of alcohol consumption and did not take any other drugs recently. She had no history of gallstones and no family history of pancreatitis. She did not have a history of dyslipidemia before starting tamoxifen, and her fasting triglyceride level was 122 mg/dL in 2013. One year after starting tamoxifen, she had a lipid profile checked in 2015, which showed a fasting triglyceride level of 214 mg/dL. She was given lifestyle modification advice and was not started on any new drugs. No further lipid profile was performed between 2015 and her current presentation in 2018.

On examination, she was alert and nontoxic. There was no jaundice, her breath sounds were clear, and her abdomen was not guarded but with epigastric tenderness on palpation. There was no xanthelasma. Her temperature was 38.3 °C, blood pressure 124/75 mm Hg, pulse rate 92 per minute, respiratory rate 16 per minute, and SpO_2 97% on room air.

ACG Case Rep J 2019;6:1–3. doi:10.14309/crj.0000000000000025. Published online: February 25, 2019

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Laboratory tests revealed serum lipase 479 U/L, amylase 221 U/L, and C-reactive protein 87.8 mg/L. Serum total bilirubin was 0.3 mg/dL, serum alkaline phosphatase 64 U/L, aspartate transaminase 25 U/L, and alanine transaminase 34 U/L. Hemoglobin was 13.1 g/dL and white blood cell 9.6 $\times$ $10^3/\mu L$). A diagnosis of mild acute pancreatitis was made based on the absence of organ failure and absence of local complications. An ultrasound of the abdomen showed no gallstone and no dilated intrahepatic and extrahepatic bile ducts. There was also no pancreatic necrosis or peripancreatic collection seen. A fasting lipid panel was obtained that showed a triglyceride level of 3,883 mg/dL. The other components of the lipid panel were normal. Tamoxifen was stopped, and the patient was given intravenous fluids and tramadol. To treat hypertriglyceridemia, she was given intravenous insulin infusion, oral fenofibrate 300 mg daily, nicotinic acid 500 mg daily, and atorvastatin 40 mg daily. Her triglyceride levels rapidly decreased to 428 mg/dL on day 2 of the admission. Her pain had improved, and she started oral diet on day 2. During this admission, she was also diagnosed to have type 2 diabetes mellitus with a fasting glucose of 270 mg/dL and HbA1c of 7.6%. She was started on metformin 500 mg twice daily and glipizide 2.5 mg once daily. On day 4 of the admission, her epigastric pain had resolved completely, and she was discharged from the hospital. At her next oncology consult, tamoxifen was stopped permanently, and she was prescribed letrozole 2.5 mg once daily. Two months later, her fasting triglyceride level decreased to 74 mg/dL, and she had no further abdominal symptoms.

DISCUSSION

Tamoxifen is a selective estrogen receptor modulator used as adjuvant therapy for breast cancer. It is well known that one of the side effects of tamoxifen is an increase in serum triglycerides. A study by Liu et al found that in patients with a history of hyperlipidemia, mean serum triglycerides increased from 194.79 $\pm$ 71.85 mg/dL to 268.79 $\pm$ 163.81 mg/dL after 15 months of tamoxifen.[5] Tamoxifen increases very low-density lipoproteins secretion from the liver and decreases very low-density lipoproteins catabolism because of a decrease of lipoprotein lipase and hepatic lipase activities.[6] One theory of the pathogenesis of hypertriglyceridemia-induced pancreatitis proposed that excess amounts of triglyceride-rich lipoproteins are hydrolyzed by pancreatic lipase, resulting in high concentrations of free fatty acids released into the vascular bed of the pancreas. These free fatty acids then aggregate to form micellar structures with detergent properties that damage the vascular endothelium and acinar cells producing ischemia.[7] The risk of pancreatitis increases by 4% for every 100 mg/dL increase in triglyceride concentration.[8]

To our knowledge, there have been 10 case reports in the literature on tamoxifen causing severe hypertriglyceridemia leading to acute pancreatitis.[9–18] In most of the cases, the patients had a history of either dyslipidemia (n = 5) or diabetes mellitus (n = 3). Interestingly, in 9 of the 10 cases, the episode of acute pancreatitis occurred within 12 months from starting tamoxifen. Our patient developed acute pancreatitis 4 years after the commencement of tamoxifen. This suggests that it may be prudent for patients on tamoxifen to have regular monitoring of their fasting serum lipids. The period of monitoring should continue even after the initial 12 months of therapy because our case demonstrated that the complication can be delayed up to 4 years after starting the drug. An alternative adjuvant drug to use instead of tamoxifen is letrozole: an aromatase inhibitor, which has been shown to have no significant effects on serum lipid concentrations and risk of pancreatitis.[19]

DISCLOSURES

Author contributions: TT Tey wrote the manuscript, reviewed the literature, and is the article guarantor. AC Maung reviewed the literature. KW Lim edited the manuscript. JC Hsiang supervised and edited the manuscript.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received June 10, 2018; Accepted December 20, 2018

REFERENCES

1. Peery AE, Dellon ES, Lund J, et al. Burden of gastrointestinal diseases in the United States: 2012 update. *Gastroenterology*. 2012;143:1179–87.
2. Wall I, Badalov N, Baradarian R, et al. Decreased morbidity and mortality in patients with acute pancreatitis related to aggressive intravenous hydration. *Pancreas*. 2011;40:547–50.
3. Frossard JL, Steer ML, Pastor CM. Acute pancreatitis. *Lancet*. 2008; 371(9607):143–52.
4. Badalov N, Baradarian R, Iswara K, Li J, Steinberg W, Tenner S. Drug-induced acute pancreatitis: An evidence-based review. *Clin Gastroenterol Hepatol*. 2007;5:648–4.
5. Liu CL, Yang TL. Sequential changes in serum triglyceride levels during adjuvant tamoxifen therapy in breast cancer patients and the effect of dose reduction. *Breast Cancer Res Treat*. 2003;79:11–6.
6. Hozumi Y, Kawano M, Saito T, Miyata M. Effect of tamoxifen on serum lipid metabolism. *J Clin Endocrinol Metab*. 1998;83:1633–5.
7. Ewald N, Hardt PD, Kloer HU. Severe hypertriglyceridemia and pancreatitis: Presentation and management. *Curr Opin Lipidol*. 2009;20: 497–504.
8. Murphy MJ, Sheng X, MacDonald TM, Wei L. Hypertriglyceridemia and acute pancreatitis. *JAMA Intern Med*. 2013;173(2):162–4.
9. Noguchi M, Taniya T, Tajiri K, et al. Fatal hyperlipaemia in a case of metastatic breast cancer treated by tamoxifen. *Br J Surg*. 1987;74: 586–7.
10. Colls BM, George PM. Severe hypertriglyceridaemia and hypercholesterolaemia associated with tamoxifen use. *Clin Oncol (R Coll Radiol)*. 1998;10:270–1.
11. Elisaf MS, Nakou K, Liamis G, Pavlidis NA. Tamoxifen-induced severe hypertriglyceridemia and pancreatitis. *Ann Oncol*. 2000;11(8):1067–9.
12. Artac M, Sari R, Altunbas H, Karayalcin U. Asymptomatic acute pancreatitis due to tamoxifen-induced severe hypertriglyceridemia in a patient with diabetes mellitus and breast cancer. *J Chemother*. 2002;14:309–11.
13. Lin HH, Hsu CH, Chao YC. Tamoxifen-induced severe acute pancreatitis: A case report. *Dig Dis Sci*. 2004;49(6):997–9.
14. Alagozlu H, Cindoruk M, Unal S. Tamoxifen-induced severe hypertriglyceridaemia and acute pancreatitis. *Clin Drug Investig*. 2006;26: 297–302.

15. Sakhri J, Ben Salem C, Harbi H, Fathallah N, Ltaief R. Severe acute pancreatitis due to tamoxifen-induced hypertriglyceridemia with positive rechallenge. *JOP*. 2010;11(4):382–4.
16. Kim YA, Lee S, Jung JW, et al. Severe acute pancreatitis due to tamoxifen-induced hypertriglyceridemia with diabetes mellitus. *Chin J Cancer Res*. 2014;26(3):341–4.
17. Czyzykowski R, Połowinczak-Przybyłek J, Janiak A, Herman J, Potemski P. Tamoxifen-induced acute pancreatitis: A case report. *Prz Menopauzalny*. 2014;13(1):70–2.
18. Kataria PSC, Kendre PP, Patel AA, Bohra MZ, Tahiliani N. Tamoxifen induced pancreatitis: An unusual complication of commonly used drug. *J Clin Diagn Res*. 2017;11(8):XD05–6.
19. Wasan KM, Goss PE, Pritchard PH, et al. The influence of letrozole on serum lipid concentrations in postmenopausal women with primary breast cancer who have completed 5 years of adjuvant tamoxifen. *Ann Oncol*. 2005; 16(5):707–15.