

# Tamoxifen-induced hypertriglyceridemia causing acute pancreatitis

Hemant Kumar Singh, Mahendranath S. Prasad, Arun K. Kandasamy, Kadambari Dharanipragada

Department of Surgery, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

Received: 18-02-2015

Revised: 05-07-2015

Accepted: 02-08-2015

## ABSTRACT

Tamoxifen has both antagonistic and agonistic tissue-specific actions. It can have a paradoxical estrogenic effect on lipid metabolism resulting in elevated triglyceride and chylomicron levels. This can cause life-threatening complications like acute pancreatitis. To our knowledge, very few cases of tamoxifen-induced pancreatitis have been reported in the literature. We report a case of severe hypertriglyceridemia and acute pancreatitis following tamoxifen use. A 50-year-old diabetic lady was on tamoxifen (20mg/day) hormonal therapy for breast cancer. Within 3 months of starting therapy, she developed hypertriglyceridemia and acute pancreatitis. Laboratory values include: Serum amylase 778 IU/L, total cholesterol 785 mg/dL, triglycerides 4568 mg/dL and high-density lipoproteins (HDL) 12 mg/dL. Tamoxifen was substituted with letrozole and atorvastatin started. There was a prompt reversal of the adverse effects. Effects on lipid profile must be considered while initiating tamoxifen in predisposed individuals as the consequences are life threatening.

**Key words:** Breast, carcinoma, hypertriglyceridemia, pancreatitis, tamoxifen

## INTRODUCTION

Tamoxifen, a selective estrogen receptor modulator (SERM) is widely used in hormonal therapy for estrogen receptor-positive breast cancer. This drug has tissue-specific agonistic and antagonistic properties. The side effects of tamoxifen usage include nausea, vomiting, hot flushes, skin rashes, alopecia and rarely thromboembolism.<sup>[1]</sup> However, there are very few reports of acute pancreatitis due to tamoxifen-induced hypertriglyceridemia in the literature.

## CASE REPORT

A 50-year-old diabetic woman presented with stage III, estrogen receptor-positive adenocarcinoma of the breast. She was on metformin (500 mg twice daily) and her blood sugars and serum lipid levels were within the normal limits. She received three cycles of Adriamycin-based neo-adjuvant chemotherapy followed by modified radical mastectomy. This was followed by three cycles of chemotherapy (with cyclophosphamide, Adriamycin and 5-fluorouracil) and radiotherapy. Tamoxifen was started as hormonal therapy (20 mg once daily).

Three months later she presented with spontaneous onset of severe abdominal pain and vomiting of 5 days duration. On

Access this article online	
Quick Response Code:	Website: <a href="http://www.jpharmacol.com">www.jpharmacol.com</a>
	DOI: 10.4103/0976-500X.179365

### Address for correspondence:

Hemant Kumar Singh, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry - 605 006, India.  
E-mail: [hemant7771@gmail.com](mailto:hemant7771@gmail.com)

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

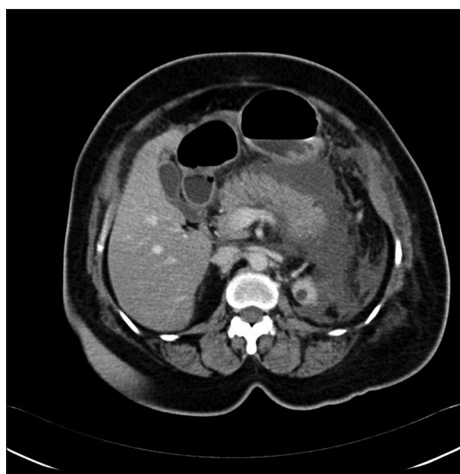
**For reprints contact:** [reprints@medknow.com](mailto:reprints@medknow.com)

**How to cite this article:** Singh HK, Prasad MS, Kandasamy AK, Dharanipragada K. Tamoxifen-induced hypertriglyceridemia causing acute pancreatitis. *J Pharmacol Pharmacother* 2016;7:38-40.

examination, her pulse rate was 115/minute, blood pressure 150/90 mmHg, respiratory rate 25/minute and temperature 100.2°F. There was marked tenderness and guarding in the epigastric region and a hepatomegaly (2 cm below the right costal margin). She had multiple papules over both the upper limbs and back. A biopsy of these papules revealed that they were xanthomas.

Pertinent laboratory values are as follows: Serum amylase 778 IU/L, total cholesterol 785 mg/dL, triglycerides 4568 mg/dL, high-density lipoproteins (HDL) 12 mg/dL, alanine aminotransferase 35 IU/L, alkaline phosphatase 200 IU/L, total bilirubin 0.8 mg/dL, fasting blood sugar (FBS) 166 mg/dL, post-lunch blood sugar (PLBS) 285 mg/dL, hemoglobin 11.6 g/dL, total leukocyte count 16,500/mm<sup>3</sup> with 85% neutrophils and C-reactive protein 15 g/dL. Ultrasonography of the abdomen showed a bulky pancreas and multiple peri-pancreatic and spleno-renal fluid collections. The gall bladder and biliary tract were normal. Liver measured 18 cm and showed fatty changes. Contrast-enhanced computed tomography showed diffuse enlargement of the pancreas with heterogeneous enhancement. There were peripancreatic and left paracolic space collections communicating with pelvic and retroperitoneal spaces suggestive of acute pancreatitis [Figure 1]. There was also associated ascites and minimal left side pleural effusion. No evidence of pancreatic parenchymal/ductal calcification or ductal dilatation was noted.

Hypertriglyceridemia secondary to tamoxifen usage was suspected as the cause of acute pancreatitis and the patient was treated with prompt withdrawal of the drug, intravenous fluids and analgesics for 5 days. Simultaneously atorvastatin (10 mg once daily) was started to control the lipid levels. She showed a dramatic improvement with the resolution of her symptoms and return of lipid levels to normal by the end of



**Figure 1:** Contrast-enhanced computed tomography showing diffuse enlargement of the pancreas with heterogeneous enhancement and peripancreatic fluid collections

1 month. No re-challenge test with tamoxifen was tried to prove the causal relationship. The patient was started on letrozole (2.5 mg once daily) and was under strict follow up.

## DISCUSSION

Acute pancreatitis is a life-threatening condition. Heavy alcohol intake and gall stones are the most important causes. Drug-induced pancreatitis accounts for less than 2–3% of the cases.<sup>[2,3]</sup>

Tamoxifen has both antagonistic and agonistic tissue-specific actions. It can have a paradoxical estrogenic effect on lipid metabolism resulting in elevated triglyceride and chylomicron levels.<sup>[4]</sup> Increased blood levels of triglycerides causes lodging in pancreatic capillaries, resulting in ischemia and necrosis. The resultant release of pancreatic lipases causes release of free fatty acids from triglycerides followed by an inflammatory response.<sup>[5]</sup>

To our knowledge, very few cases of tamoxifen-induced pancreatitis have been reported in the literature.<sup>[6-11]</sup> The dosage of tamoxifen used in these reports was 20 mg/day in all but one case. In most cases, there was an antecedent history of dyslipidaemia which was lacking in the present case. However, it must be borne in mind that type 2 diabetes and dyslipidaemia may have a common genetic predisposition.<sup>[12]</sup> The levels of triglycerides that precipitated acute pancreatitis ranged from 900 to 7000 mg/dL. The delay in the onset of symptoms in most of these reports was more than 6 months after initiation of therapy with tamoxifen. However, the present patient presented within 3 months of initiation of therapy. The severity of pancreatitis also varied in these reports. Majority had mild pancreatitis while one patient had necrotizing pancreatitis. The outcome was favorable in most of these reports as was with the present case.

An extensive overview on drug-induced pancreatitis by Trivedi *et al.* was based on medication re-challenge to confirm association.<sup>[13]</sup> However, in our patient no re-challenge was tried due to the fear of precipitating severe form of pancreatitis. A causal relationship with tamoxifen use could be established by the fact that there was no hypertriglyceridemia prior to the initiation of tamoxifen and withdrawal of the drug showed a prompt reversal.

Some clinicians recommend a reduced dose of tamoxifen (10 mg a day) to lower the risk of hypertriglyceridemia.<sup>[14]</sup> In a recent study, letrozole showed no significant adverse effects on serum lipid levels in women without hyperlipidaemia at baseline.<sup>[15]</sup> The present patient tolerated letrozole well with no adverse reactions.

Clinicians should be aware of this life-threatening complication associated with tamoxifen. Screening for dyslipidaemia prior to the initiation of tamoxifen is strongly advisable. A great deal of caution must be exercised and regular monitoring of lipid levels performed in predisposed individuals. At the first instance of suspicion, the drug should be discontinued and preferably no re-challenge tried due to risk of inducing acute severe pancreatitis.

#### Financial support and sponsorship

Nil.

#### Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Zurrada S, Veronesi U. Milestones in breast cancer treatment. *Breast J* 2015;21:3-12.
2. Kaurich T. Drug-induced acute pancreatitis. *Proc (Bayl Univ Med Cent)* 2008;21:77-81.
3. Deshpande PR, Khera K, Thunga G, Hande M, Gouda ST, Nagappa AN. Atorvastatin-induced acute pancreatitis. *J Pharmacol Pharmacother* 2011;2:40-2.
4. Shapiro CL, Recht A. Side effects of adjuvant treatment of breast cancer. *N Engl J Med* 2001;344:1997-2008.
5. Ewald N, Hardt PD, Kloer HU. Severe hypertriglyceridemia and pancreatitis: Presentation and management. *Curr Opin Lipidol* 2009;20:497-504.
6. Noguchi M, Taniya T, Tajiri K, Miwa K, Miyazaki I, Koshino H, *et al.* Fatal hyperlipaemia in a case of metastatic breast cancer treated by tamoxifen. *Br J Surg* 1987;74:586-7.
7. Colls BM, George PM. Severe hypertriglyceridaemia and hypercholesterolemia associated with tamoxifen use. *Clin Oncol (R Coll Radiol)* 1998;10:270-1.
8. Elisaf MS, Nakou K, Liamis G, Pavlidis NA. Tamoxifen-induced severe hypertriglyceridemia and pancreatitis. *Ann Oncol* 2000;11:1067-9.
9. 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.
10. Sakhri J, Ben Salem C, Harbi H, Fathallah N, Ltaief R. Severe acute pancreatitis due to tamoxifen-induced hypertriglyceridemia with positive rechallenge. *JOP* 2010;11:382-4.
11. Kim YA, Lee S, Jung JW, Kwon YJ, Lee GB, Shin DG, *et al.* Severe acute pancreatitis due to tamoxifen-induced hypertriglyceridemia with diabetes mellitus. *Chin J Cancer Res* 2014;26:341-4.
12. Qi Q, Liang L, Doria A, Hu F, Qi L. Genetic predisposition to dyslipidemia and type 2 diabetes risk in two prospective cohorts. *Diabetes* 2012;61:745-52.
13. Trivedi CD, Pitchumoni CS. Drug-induced pancreatitis: An update. *J Clin Gastroenterol* 2005;39:709-16.
14. 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.
15. Wasan KM, Goss PE, Pritchard PH, Shepherd L, Palmer MJ, Liu S, *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 (NCIC CTG MA.17L). *Ann Oncol* 2005;16:707-15.