CASE REPORT | OLGU SUNUMU

Tamoxifen-induced severe acute pancreatitis after a short-term therapy: a case report

Kısa süreli tamoksifen tedavisine bağlı ciddi akut pankreatit: Olgu sunumu

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Short-term therapy of tamoxifen-induced severe hypertriglyceridemia and acute pancreatitis in a patient with breast cancer is described in this article. Interestingly, no pre-existing history of dyslipidemia was noted in comparison to the relevant literature review. Tamoxifen is the most widely used anti-estrogen in adjuvant endocrine treatment of primary breast cancer. However, due to its estrogen-like activity in lipid metabolism, a small increase in serum triglycerides is also commonly found in long-term users. This finding is usually insignificant and without clinical manifestations.

Key words: Pancreatitis; tamoxifen; triglycerides.

Bu makalede kısa süreli tamoksifen kullanımına bağlı ciddi hipertrigliseridemi ve akut pankreatitli meme kanserli bir hasta sunuldu. İlginçtirki, bu konuda daha önceki literatürlerden farklı olarak hastada dislipidemi hikayesi yoktu. Tamoksifen meme kanserli hastaların adjuvan endokrin tedavisinde en yaygın kullanılan ajandır. Her nekadar lipid metabolizması üzerinde östrojene benzer etkisiyle serum trigliserid düzeylerinde hafif artışlar yapsa da, bu bulgu genellikle önemsizdir.

Anahtar sözcükler: Akut pankreatit; tamoksifen; hipertrigliseridemi.

Tamoxifen is the most widely used anti-estrogens in adjuvant endocrine treatment of primary breast cancer, as well the leading hormonal therapy in receptor positive metastatic breast cancer, mainly in premenopausal patients. Studies in pre- and post-menopausal women documented well that tamoxifen has favourable effects on lipid and lipoprotein profile by decreasing total and low-density lipoprotein (LDL) cholesterol levels. However, due to its estrogens-like activity in lipid metabolism, a small increase in serum triglycerides is also commonly found in long-term users. This finding is usually insignificant and without clinical manifestations. Although, marked hypertriglyceridemia due to tamoxifen is a rare complication, it may lead to acute pancreatitis, sometimes being severe and mortal.

We describe a patient who developed tamoxifen-induced severe hypertriglyceridemia and pancreatitis, following a short-term therapy.

CASE REPORT

A-41-year-old premenopausal woman had a modified radical mastectomy for breast cancer in February 2009, followed by 4 courses of adjuvant chemotherapy with AC (adriamycine, cyclophosphamide). Following the end of chemotherapy, tamoxifen was started at a dose of 20 mg/day orally. Three months later, the patient was admit-

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ted to our department with severe abdominal pain, epigastric discomfort, nausea and vomiting. Serum amylase and lipase levels were markedly elevated (amylase 693 IU/L and lipase 120 IU/L). Triglyceride level was found to be very high at 7929 mg/dl (normal values 30-150 mg/dl). The patient's serum was grossly lipemic. Other lipid profile showed low LDL (47 mg/dl, normal values 50-100 mg/dl) and low high-density lipoprotein (HDL) (35 mg/dl, normal values 40-90 mg/dl). Other blood chemistry results were within normal levels, including glucose. Complete blood count revealed mild leukocytosis at 13.6/dl, but otherwise normal limits and differentiation. Whole abdominal computed tomography (CT) scan showed peripancreatic inflammation, edema of the pancreas and fluid accumulation in the adjacent pancreas. There were no gallstones, nor dilatation of the common bile duct. A diagnosis of acute pancreatitis was made.

The patient was treated with oral restriction, fluid and electrolyte repletion, pain relief, and oral fenofibrate 200 mg twice and rosuvastatin 20 mg daily. Tamoxifen was stopped. Two days later she was free of abdominal pain. By the 7th. day amylase and lipase levels were back to normal, and triglyceride level was below 400 mg/dl. Past medical history did not reveal alcohol consumption, gallstones, diabetes; any prescribed medication and history of previous hypertriglyceridemia. Complete lipid profile study which was done 5 months ago proved normal triglyceride levels. The patient was discharged on the 10th day of hospitalization.

DISCUSSION

Acute pancreatitis is a condition that leads to necrosis of pancreatic tissue and ultimately to a multiple organ dysfunction syndrome (MODS). Most cases are related to gallstones or heavy alcohol intake, abdominal trauma, drugs, vasculitis, viral infection, peritoneal dialysis, cardiopulmonary bypass, and endoscopic retrograde cholangiopancreatography (ERCP).[1]

Approximately 2-5% of cases of pancreatitis are drug related. Among these drugs are azothioprine, mercaptopurine, asparaginase, tetracyclines, estrogens, sulphonamides, thiazides, furosemide, and glucocorticoids.[2] Tamoxifen is a non-steroidal estrogen antagonist that has been used in the adjuvant therapy of breast cancer as well as in hormone receptor positive metastatic breast cancer. The side effects of tamoxifen are generally mild and tolerable, including the effects on lipid metabolism. Tamoxifen lowers low density lipoproteins (LDL cholesterol), and increases triglyceride and high density lipoprotein cholesterol levels (HDL cholesterol). Tamoxifen, like estrogens, stimulates the synthesis of very low density lipoproteins (VLDL), which is the main circulating carrier of triglycerides.[3] Tamoxifen decreases VLDL catabolism however, as a result of decreasing lipoprotein and hepatic lipase activities.[4] Having said that the drug can induce only modest elevations in serum triglycerides in normolipidemic patients. Large increases in lipid levels can occur in patients with pre-existing dyslipidemia.

Our patient developed severe hypertriglyceridemia after tamoxifen administration, resulting in acute pancreatitis. In the literature, there are few cases of severe hypertriglyceridemia (triglycerides >1000 mg/dl) due to tamoxifen. The majority of these patients had a family history of dyslipidemia, diabetes mellitus or impaired glucose tolerance, although recently marked hypertriglyceridemia has been reported in normolipidemic patients.[5]

Our patient developed severe hypertriglyceridemia only three months after the administration of tamoxifen, resulting in acute pancreatitis. Tamoxifen may need a rather prolonged therapy to increase triglyceride concentration, since short-term studies have failed to observe dramatic changes in serum triglyceride levels.[6] Of the previously reported 12 tamoxifen-induced hypertriglyceridemia cases in the literature, 9 had a history of pre-existing dyslipidemia, 3 of them with also family history of hypertriglyceridemia and only 3 without a history of dyslipidemia.[1] However those 3 patients without history, had diabetes mellitus and impaired glucose tolerance. Interestingly only four cases of severe hypertriglyceridemia-induced pancreatitis have been reported in the literature.[7,8] One of these patients had fulminant acute pancreatitis and died of MODS.

In most reported cases, the increased serum triglycerides returned to to pre-treatment values after stopping tamoxifen. However, gemfibrozil or fibrate treatment is necessary in patients with very high triglyceride concentrations as it was here.

In our case, there is no history of pre-existing dyslipidemia, heavy alcohol consumption, gallstones, diabetes mellitus or family history of hypertriglyceridemia. Tamoxifen therapy is rather short-term (only 3 months) in comparison to the previously reported cases in the literature. We conclude that tamoxifen should be used with caution in patients with pre-existing hypertriglyceridemia and diabetes mellitus, as well as in normolipidemic patients. Since dangerous lipid abnormalities may occur in months as well as years during therapy, it is advised to monitor fasting lipids in patients on tamoxifen, especially in patients with endogenous dyslipidemia (familial hypertriglyceridemia).

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