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Case Report

Impact of Chemotherapy and Hormone Therapy on Lipid Metabolism in Breast Cancer Patients: A Case Report and Literature Review

Jarnige Khadija[1,3*], Kfal Youssef[1,3], El Boukhrissi Fatima[1,2], Aissaoui Mohammed[1], Slaoui Amal[1], Mahmoud Mustapha[1-4], Benbella Imane[1,3]

[1]Biochemistry Unit, Central Medical Analysis Laboratory, Hassan II University Hospital Center, Fez, Morocco
[2]Biochemistry Department, Moulay Ismail Military Hospital, Meknes, Morocco
[3]Faculty of Medicine, Pharmacy, and Dental Medicine, Sidi Mohamed Ben Abdellah University, Fez, Morocco
[4]Head of the Biochemistry Department, Central Medical Analysis Laboratory, Hassan II University Hospital Center, Fez, Morocco

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***Corresponding Author:** Jarnige Khadija
Biochemistry Unit, Central Medical Analysis Laboratory, Hassan II University Hospital Center, Fez, Morocco

Abstract

Breast cancer has become the leading cause of cancer-related death among women, partly due to therapeutic resistance and treatment-related complications. Chemotherapy and hormone therapy play a crucial role in managing breast cancer patients, providing essential treatment for both disease control and overall survival. However, as new therapeutic approaches are introduced and life expectancy continues to increase, the use of these treatments has been associated with persistent adverse effects, including dyslipidemia. This article presents the case of a breast cancer patient treated with chemotherapy and tamoxifen-based hormone therapy who developed severe mixed dyslipidemia. It also reviews lipid metabolism alterations observed in breast cancer patients, emphasizing the importance of monitoring lipid levels in these patients, particularly those undergoing hormone therapy or chemotherapy, to prevent cardiovascular complications.

Keywords: Mixed Dyslipidaemia, Breast Cancer, Chemotherapy, Tamoxifen.

INTRODUCTION

Breast cancer is the most common cancer among women, leading to the highest number of cancer-related deaths in this population. According to the World Health Organization (WHO), in 2020, 2.3 million women were diagnosed with breast cancer, and the disease was responsible for 685,000 deaths worldwide [1]. Despite the many treatment options available for breast cancer, such as surgery, radiotherapy, traditional chemotherapy, and hormone therapy, the effectiveness of these treatments is often compromised by therapeutic resistance. This resistance is partly due to the heterogeneity and complexity of breast cancer, which poses a major challenge for patients suffering from this disease [2].

In recent years, research has shown that treatment resistance is closely linked to metabolism, particularly lipid metabolism. Indeed, breast cancer cells exhibit metabolic alterations distinct from those of normal cells, including significant changes in glycolysis, amino acid, and lipid metabolism [2, 3]. Moreover, it has been observed that therapies targeting cancer cause metabolic dysregulation, disrupting lipid metabolism both locally and systemically. This complex interaction between lipid metabolism, tumor development, and anticancer treatments may contribute to an increased risk of cardiovascular morbidity and mortality in this population. Chemotherapeutic agents, in fact, impact lipid metabolism through various mechanisms [4].

The aim of this work is to report a case of mixed hyperlipidemia in a patient undergoing chemotherapy and hormone therapy for breast cancer, as well as to briefly review the various mechanisms impacting lipid metabolism.

CASE REPORT

Our patient is a 43-year-old woman who has been monitored for breast cancer since August 2021. The patient underwent Patey surgery in October 2021, followed by chemotherapy in November 2021 and

radiotherapy in April 2022. Since May 2022, she has been on tamoxifen 20 mg per day, in addition to a weekly injection of triptorelin. The patient had no history of hypertension, liver disease, or other endocrinopathies, particularly no hypothyroidism. She is not taking neuroleptics, antidepressants, beta-blockers, thiazide diuretics, antiretrovirals, or androgens.Her family history is significant for type 2 diabetes on the paternal side (including her father, grandfather, and paternal aunt) and dyslipidemia among her siblings.

The patient presented with significant hypertriglyceridemia at 13 g/l and hypercholesterolemia at 2.99 g/l in her lipid profile post-surgery and before adjuvant therapy. No treatment was initiated for these conditions. Subsequently, the patient was placed on tamoxifen and developed significant mixed dyslipidemia during her routine follow-up biological assessment (Table I). This prompted her hospitalization in the endocrinology department for management. Upon admission, the clinical examination revealed a patient in good general condition, with a normal heart rate, normal blood pressure, and a body mass index (BMI) of 24.4 kg/m². The presence of a corneal arcus (gerontoxon) was also noted. The rest of the physical examination was unremarkable. An etiological workup was conducted, which did not reveal any significant abnormalities (Table II).

The diagnosis of mixed dyslipidemia secondary to breast cancer treatment (chemotherapy, tamoxifen, and triptorelin) was made after an imputability study using the BEGAUD method [5]. Both medications were implicated with the same imputability score of I3B4: plausible. However, tamoxifen blood levels could not be measured.

The management of the patient during her hospitalization involved the administration of fenofibrate at 160 mg/day as symptomatic treatment. She also received a dietary consultation aimed at establishing a healthy lifestyle, with an emphasis on eliminating simple sugars and providing therapeutic education. The hormonal treatment with tamoxifen and triptorelin was discontinued in consultation with her oncologist. The patient's condition improved, as indicated by the improvement in dyslipidemia (Figure 1).

Table I: Evolution of the Patient's Lipid Parameters

	Postoperative Assessment Pre-chemotherapy 25/10/2021	**Post-chemotherapy and Hormone Therapy Assessment 15/08/2022**	**Progression after Admission and Initiation of Treatment 24/08/2022**
Triglycerides	13 g/l	56 g/l	14 g/l
Total Cholesterol	2,99 g/l	13 g/l	7 g/l
HDL Cholesterol	0,25 g/l	0,25 g/l	0,37 g/l
LDL Cholesterol	1,97 g/l	4 g/l	3,84 g/l

Table II: Results of the Various Parameters from the Etiological Workup.

Parameter	**Result**
TSH	1.8 UI/ml
Fasting Glucose	0,7 g/l
HbA1C	5.4%
Urea	0.07 g/l
Creatinine	06 mg/l
AST (GOT)	11 UI/L
ALT (GPT)	5 UI/L

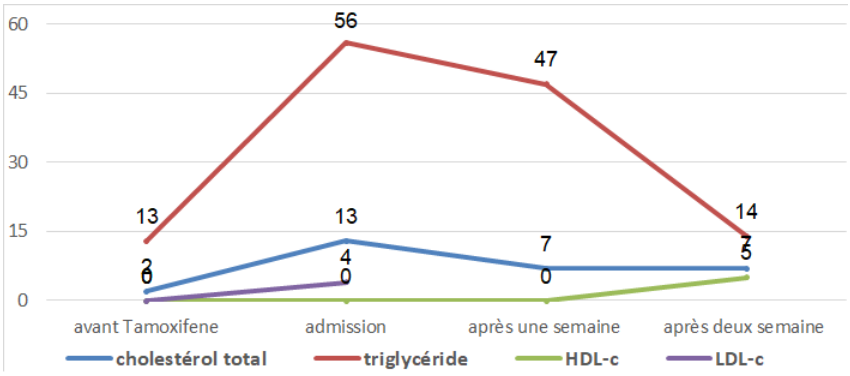

Figure 1: Evolution of Lipid Parameters During Hospitalization

DISCUSSION

Cholesterol, as a precursor of steroid hormones, plays a critical role in cellular signaling, thereby influencing breast cancer progression [3-6]. This influence extends to the lipid metabolism of tumor cells, which can be reprogrammed to meet increased energy demands and support rapid tumor growth [7]. By increasing lipid synthesis or mobilizing stored lipids, cancer cells adapt their metabolism to survive and proliferate [8]. Additionally, these metabolic alterations are not limited to mere tumor growth; they can also contribute to resistance to anticancer treatments by modulating signaling pathways that make cancer cells less responsive to medications [9].

Adjuvant chemotherapy is well-established to improve disease-free survival and overall survival in patients with breast cancer [10]. However, the side effects of chemotherapy, particularly in terms of cardiac toxicity, remain concerning [10]. In our patient, the cardiac assessment at admission revealed hypertrophic cardiomyopathy with impaired diastolic relaxation and an ejection fraction of 59% on transthoracic echocardiography (TTE). Subsequent updates could not be obtained as the patient is followed in another city. Several studies have shown that chemotherapy leads to significant changes in blood lipid and lipoprotein levels, thereby increasing the risk of dyslipidemia, a well-documented risk factor for cardiovascular disease [11].

Research shows that chemotherapy can contribute to the development of cardiovascular diseases by inducing dyslipidemia [10]. For example, after chemotherapy, levels of total cholesterol (TC), triglycerides (TG), and LDL-cholesterol (LDL-C) significantly increase, while HDL-cholesterol (HDL-C) levels decrease. These changes are consistent with the findings of several previous studies that have observed similar alterations in lipid profiles following chemotherapy [12-14].

The underlying mechanism of chemotherapy-induced dyslipidemia may be related to endothelial dysfunction and changes in cytokines, as well as increased lipid peroxidation due to systemic oxidative stress. This stress affects liver function and alters lipid metabolism by disrupting plasma adiponectin levels, leading to changes in serum lipid levels [15].

Additionally, some endocrine therapies, such as Tamoxifen, are also associated with cases of significant hypertriglyceridemia. Tamoxifen appears to stimulate the synthesis and secretion of very low-density lipoproteins (VLDL), thereby increasing triglyceride levels [16]. This hypertriglyceridemia is often observed in dyslipidemic patients or those with a family history of dyslipidemia. The literature reports that these lipid abnormalities can appear a few months, or even years, after the initiation of treatment [4-18].

In our case, the patient experienced a significant worsening of hypertriglyceridemia three months after starting Tamoxifen treatment, corroborating the findings of previous studies. In response to this situation, the treatment of hypertriglyceridemia involves lifestyle and dietary measures, the use of lipid-lowering medications, and in some cases, discontinuation of Tamoxifen in consultation with the treating physician [19]. For our patient, Tamoxifen discontinuation was recommended after consulting with the oncologist.

CONCLUSION

The complex interactions between lipid metabolism and breast cancer are increasingly recognized, highlighting the dual influence of lipids, which play a role both in tumor development and in complications associated with anticancer treatments. Current data emphasize the crucial importance of monitoring lipid levels in patients undergoing chemotherapy or hormone therapy, due to the increased risk of dyslipidemia and associated cardiovascular complications. While targeting lipid metabolism as a therapeutic approach remains in the exploratory phase, emerging strategies offer promising prospects for improving the prognosis of patients with breast cancer.

Conflict of Interest Statement: The authors declare that they have no conflicts of interest.

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