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Case report

Severe hypertriglyceridemia during treatment with intraperitoneal cisplatin and paclitaxel for advanced stage fallopian tube carcinoma

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ABSTRACT

This case report describes a patient who developed severe hypertriglyceridemia (1871 mg/dL) and hyperlipidemia (LDL 132 mg/dL) during intraperitoneal (IP) administration of cisplatin and paclitaxel as adjuvant treatment for stage IIIC fallopian tube carcinoma. After an evaluation with her primary care physician, she was treated with gemfibrozil and rosuvastatin for the duration of her treatment. There was complete resolution of hypertriglyceridemia after completion of chemotherapy. This adverse event is rare and has not been reported in the literature with this chemotherapeutic regimen. A pre-chemotherapy evaluation for dyslipidemia may be beneficial in the detection and monitoring of this condition.

1. Introduction

Cisplatin and paclitaxel are common chemotherapeutic agents used to treat gynecologic malignancies as well as other solid tumors. Intraperitoneal administration of cisplatin and paclitaxel has an increased toxicity profile when compared to intravenous therapy. Grade 3 and 4 events such as leukopenia, thrombocytopenia, fever, infection, fatigue, metabolic derangements, pain, catheter complications as well as gastrointestinal, renal, genitourinary and neurologic events are also more common with IP treatment (Armstrong, 2006; Walker, 2006). Dyslipidemia is not currently a known or well-established side effect of these chemotherapeutic agents administered intravenously or intrapertioneally. However, consequences of hypertriglyceridemia can be significant, including an increased risk of cardiovascular disease and acute pancreatitis (Yuan et al., 2007).

2. Case description

Here we report the case of a 44-year-old referred to our office for evaluation of pelvic and abdominal masses discovered on imaging after she presented to her primary gynecologist with a complaint of pelvic pain. Past medical history was significant for hypertension and hyperlipidemia, not treated with medications. Routine lipid panel performed one year prior to presentation was significant for cholesterol: 236 mg/dL, triglycerides: 377 mg/dL, HDL: 55 mg/dL, LDL: 105 mg/dL. Her mother was diagnosed with premenopausal breast cancer, there was no family cancer history otherwise. Physical examination was significant for a palpable, nontender, fixed adnexal mass. Abdominal and pelvic ultrasound showed a 4 cm solid right adnexal mass and multiple solid abdominal masses. CA-125 was 218 U/mL. She underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, pelvic and para-aortic lymph node dissection, resection of sigmoid and rectal masses, and placement of an IP port. It was an R0, optimal tumor debulking. Final pathology was consistent with a stage IIIC fallopian tube poorly differentiated serous carcinoma. Genetic evaluation returned positive for BRCA1 mutation. Treatment was initiated with intravenous and intraperitoneal cisplatin and paclitaxel. Adverse events associated with cytotoxic treatment were grade 1–2 nausea and vomiting and grade 1 abdominal pain.

After her 4th cycle of chemotherapy she presented to her primary care physician for routine health maintenance. A non-fasting lipid panel was performed with results significant for triglycerides of 769 mg/dL, LDL of 287 mg/dL, HDL of 67 mg/dL. Treatment with statin medication was recommended. She desired conservative management with diet and re-testing of her lipid panel after appropriate fasting. Her lipid panel was repeated 10 days later and was significant for increasing triglycerides to 1871 mg/dL and mixed hyperlipidemia (cholesterol: 450 mg/dL; LDL 132 mg/dL; HDL 48 mg/dL). At that time the HbA1C returned at 6.9% and she endorsed symptoms of polydipsia, polyuria, and polyphagia and was diagnosed with diabetes mellitus. The patient was

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started on gemfibrozil 600 mg twice daily, rosuvastatin 20 mg daily, and metformin 500 mg twice daily.

After completion of six cycles of IV/IP chemotherapy, a repeat lipid panel revealed resolving hypertriglyceridemia of 153 mg/dL from 1871 mg/dL. The remainder of her lipid profile also demonstrated improvement (cholesterol 153 mg/dL; LDL: 66 mg/dL, HDL: 56 mg/dL). Repeat HbA1C was 5.9% and gemfibrozil and metformin were discontinued. Approximately two months after discontinuing these medications, her triglycerides returned to the pre-chemotherapy baseline level (306 mg/dL). She was last seen 22 months after completing treatment and is still without evidence of disease.

3. Discussion

There is a paucity of literature on cisplatin/paclitaxel induced hypertriglyceridemia and the significance of this lab abnormality in patients undergoing chemotherapy has yet to be elucidated. It is possible that other factors may have caused the severe hypertriglyceridemia experienced by this patient on cisplatin/paclitaxel therapy, given she had reported a prior history of hyperlipidemia, however it is unlikely. Her fasting lipid values did demonstrate a mild derangement in triglycerides (377 mg/dL), but this was substantially lower than what was reported while on chemotherapy (1871 mg/dL). Additionally, she was not taking medications for hypertriglyceridemia prior to the start of chemotherapy, since it was non-severe. She also did not have significant changes to her diet while on intraperitoneal chemotherapy. In fact, she had poor oral intake, therefore it is unlikely that an unhealthy diet contributed to the significantly elevated triglyceride level. The lipid panel abnormalities resolved after completion of her chemotherapy. Moreover, two months after discontinuing gemfibrozil, the triglyceride level was 306 mg/dL, which was similar to her pre-chemotherapy fasting level. The patient did not undergo any specific dietary interventions towards the end of therapy. Also, she was not given a referral to a nutritionist. She was recommended to engage in physical activity, however she reports she did not. Further, she did not have significant weight loss during treatment (pre-chemotherapy: 73 kg, post-chemotherapy: 72 kg). Therefore, it is unlikely that dietary or lifestyle modifications normalized her lipid panel or enabled her to discontinue gemfibrozil. The Naranjo algorithm (Naranjo, 1981), a questionnaire designed to determine the likelihood of whether an adverse drug reaction is actually due to the drug rather than the result of other factors, scored this case 5 points, which suggests that hypertriglyceridemia was a probable adverse reaction to the chemotherapeutic agents.

There have been three reported cases of transient dyslipidemia in cancer patients treated with paclitaxel and cisplatin, however diagnoses included squamous cell carcinoma of the lung, squamous cell carcinoma of the esophagus, and synovial carcinoma of the left lower extremity (Wang et al., 2017). To our knowledge, this phenomenon has not been reported in a patient undergoing treatment for a gynecologic cancer and with an intraperitoneal port. These three patients experienced an increase in their triglyceride levels immediately after chemotherapy administration. It was hypothesized that a potential cause of this transient hypertriglyceridemia was due to hepatic dysfunction, as all three patients had transient elevations in the liver enzymes after each administration of chemotherapy similar to that of the triglyceride values (Wang et al., 2017). During the course of treatment, our patient's transaminases were within normal limits. Thus, it is unclear if hepatic dysfunction could be attributed to our patient's hypertriglyceridemia. Hypertriglyceridemia has also been described in patients undergoing treatment with the chemotherapeutic agent capecitabine (Leung et al., 2018; Han and Huang, 2015), in patients receiving treatment for acute lymphoblastic leukemia with PEG-aspariginase (Galindo, 2016) and in patients on tamoxifen for breast cancer (Colls and George, 1998).

The transient effects of chemotherapy on kidney and liver function are well known and patients receiving cisplatin and paclitaxel routinely have kidney and liver function evaluations. It is not currently the standard of care to test for dyslipidemia. Given our case and the other reports of hypertriglyceridemia in patients treated with various chemotherapeutic agents with different mechanisms of action, it is important for oncologists to consider hypertriglyceridemia when treating patients with cisplatin, paclitaxel and other chemotherapeutic agents. It may be important for oncologists to screen patients for dyslipidemia prior to administration of chemotherapeutic agents due to this risk of lipid abnormalities, which may be especially significant in patients with associated conditions such as heart disease, diabetes mellitus, and obesity (Yuan et al., 2007). Additionally, acute pancreatitis is another significant condition that can result from elevated triglycerides; as many as 5% of patients with triglycerides > 1000 mg/dL will develop this potentially life-threatening condition (Scherer, 2014). Oncologists should be prudent in monitoring for signs and symptoms of pancreatitis in these patients, especially in those with known dyslipidemia or associated conditions. Finally, as seen in our patient, medical management of hypertriglyceridemia is an effective option for patients while continuing treatment with cisplatin/paclitaxel.

In summary, hypertriglyceridemia is a possible adverse reaction from intravenous and intraperitoneal administration of cisplatin and paclitaxel. This case suggests possible exacerbation of mild baseline hypertriglyceridemia by these chemotherapy agents. Gynecologic oncologists and other physicians should be vigilant about this condition and consider pre-chemotherapy testing, as there are ways to mitigate these lab abnormalities.

Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

CRediT authorship contribution statement

Megan Lander: Data curation, Writing - original draft. **Yasmin Abedin:** Writing - original draft, Writing - review & editing. **Sofia Gabrilovich:** Writing - review & editing. **Jenna Z. Marcus:** Data curation, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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