Observed Treatment Adjustments and Complications in an Ovarian Cancer Patient with Inborn Error of Immunity

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Introduction

Inborn error of immunity (IEI), a category characterized by inherited disorders of the immune system, have been shown to confer an increased risk for developing cancers, most commonly lymphoid and lymphomas (Mortaz et. al, p.2,). Increased risk of gastric cancers was also reported (Kralickova et. al). Concomitant malignancies are often the cause of death in individuals with IEI (Mortaz et. al, p.1). The standard treatment of patients with immunoglobulin deficiency is intravenous or subcutaneous immunoglobulin (IVIG or scIG) therapy (Ameratunga et. al, p.203). There is sparse literature on the management of IEIs in the setting of ovarian cancer. While the knowledge on different cancers in IEI population increases, no treatment adjustment guidelines are available for physicians. Lack of literature discourages physicians to offer treatments to the patients due to the risks of health damage and negative outcomes. Some patients may be disadvantaged by a less aggressive cancer treatment chosen for fear of infection. Here we present a patient with IEI and 3c ovarian cancer with additional medical conditions, including asthma, hypertension, mixed connective tissue diseases, autoimmune thyroiditis, and Celiac disease and who was treated with a dose-adjusted combination of paclitaxel/carboplatin/avastin chemo and IVIG.

Case Presentation

Here we present the case of a 60-year-old female with inborn error of immunity (IEI), specific antibody deficiency (SAD), immune dysregulation (AI), who was diagnosed with a stage III high grade serous ovarian carcinoma. Additional medical history includes asthma, hypertension, mixed connective tissue diseases, autoimmune thyroiditis, and Celiac disease.

Following her diagnosis with ovarian cancer, the patient underwent robot assisted laparoscopic total hysterectomy, bilateral salpingo-oophorectomy, resection of rectosigmoid, and omentectomy. Prior to cancer diagnosis, her IEI treatment entailed intravenous immunoglobulin (IVIG) (40 mg) every 2 weeks. After undergoing primary debulking surgery and prior to starting chemo, IVIG was adjusted to 80 mg every 3 weeks (1.3 g/kg/3 weeks, wt 60 kg), administered 1 week prior to each cycle of chemo, to retain immunocompetence. The patient was prescribed 6 cycles in total. Chemo dosage was lowered to reduce the risk of IEI related complications. The treatment included Carboplatin (area under the curve (AUC) 4 instead of standard 5), Paclitaxel (Taxol 150 mg/m2 instead of standard 175 mg/m2) and Avastin (15 mg/kg). Additionally, the patient received colony-stimulating factor Neulasta (pegfilgastrim) through 6 cycles to prevent febrile neutropenia. For the first cycle of chemotherapy, Avastin was not included because of incompletely healed vaginal cuff after the surgery.

After the first round of chemo, the patient developed complications, including *Mycobacterium avium-intracellulare* (MAI) infection, hyperbilirubinemia, elevated LFTs, and exacerbated post-surgery urinary retention. A subsequent liver checkup revealed no liver damage, specifically, no hepatomegaly. The increase in LFT and hyperbilirubinemia was attributed to increased IVIG dose in conjunction with chemotherapy. MAI infection was treated with Vancomycin. Post-cycle-1 adjustment included reduction of the IVIG dose to 60 mg every 3 weeks, administered 1 week prior to each cycle. Chemotherapy treatment was not changed.

During cycles 2 and 3, the patient developed a urinary tract infection (UTI) due to the *Klebsiella pneumoniae*, treated with Rocephin and 7-days course of Ciprofloxin. This complication caused a delay of cycle 4 of her chemotherapy. Throughout cycles 4-6, UTI was prevented with prophylactic Bactrim and Azithromycin. She also received Myrbetriq for symptoms of urinary incontinence. The patient experienced general chemo side effects including fatigue, peripheral neuropathy, headache (relieved with Duexis), shortness of breath, palpitation with anxiety, and abdominal pain with bowel movement. The patient experienced cyclic gastro-intestinal discomforts, specifically 3-4 days of constipation followed by 1-2 days of diarrhea, after which the cycle repeated.

The patient managed to complete all 6 cycles and follow up CT scan revealed no evidence of cancer. As maintenance therapy, the patient will continue taking Avastin (15) for a one-year period.

Genetic evaluation of chromosomal and somatic mutations showed no targetable mutations. The results would make the patient eligible for Nirapirib (PARP inhibitor), however, it was not added to her to prevent exacerbation of the immunodeficiency.

Importance of Case

Our literature review revealed the sparsity of this unique patient population presenting with a combination of IEI and ovarian cancer. Lack of available data challenges designing appropriate adjustments for treating ovarian cancers and managing IEI. The cases registered (as of 2021):

USIDNET (United States Immunodeficiency Network):
5 cases within 2011-2020 | No treatment information
National Cancer Institute (NIH):
1 case (unknown time frame) | No treatment information

Table 1. Treatment Chronology and Summary of Complications and Adjustments

Timeline and intervention	IVIG therapy	Chemotherapy	Complication(s)	Adjustment(s)
Debulking surgery **Date: 4/22/2020**	40 mg of IVIG every 2 weeks			
Chemo Cycle 1 **Date: 6/14/2020**	80 mg of IVIG every 3 weeks (1.3 g/kg/3 weeks, wt 60 kg), administered 1 week prior to chemo cycle 1.	Carboplatin (area under the curve (AUC) 4), Paclitaxel (Taxol 150 mg/m2), Neulasta (dose) Holding Avastin due to incompletely healed vaginal cuff	• MAI infection, • Elevated LFT and hyperbilirubinemia (thought to be secondary to IVIG in conjunction to chemotherapy) • Urinary retention	• Reduced IVIG from 80 mg to 60 mg. • Cycle 2 postponed for a week. • No chemotherapy adjustment
Chemo Cycle 2 **Date: 8/4/2020**	60 mg of IVIG (1g/kg/4 weeks, wt 50 kg), 1 week prior to c2	Carboplatin (area under the curve (AUC) 4, Paclitaxel (Taxol 150 mg/m2) and Avastin (15 mg/kg)	UTI infection, Klebsiella pneumoniae	No adjustments
Chemo Cycle 3 **Date: 8/25/2020**	60 mg of IVIG (1g/kg/4 weeks, wt 50 kg), 1 week prior to c3	Carboplatin (area under the curve (AUC) 4, Paclitaxel (Taxol 150 mg/m2) and Avastin (15 mg/kg)	UTI infection, Klebsiella pneumoniae	• Rocephin • 7-days course of Ciprofloxin
Chemo Cycle 4 **Date: 9/29/2020 (delayed due to UTI)**	60 mg of IVIG (1g/kg/4 weeks, wt 50 kg), 1 week prior to c4	Carboplatin (area under the curve (AUC) 4, Paclitaxel (Taxol 150 mg/m2) and Avastin (15 mg/kg)	Urinary incontinence	• Prophylactic Bactrim and Azithromycin. • Myrbetriq for urinary incontinence
Chemo Cycle 5 **Date: 10/20/2020**	60 mg of IVIG (1g/kg/4 weeks, wt 50 kg), 1 week prior to c5	Carboplatin (area under the curve (AUC) 4, Paclitaxel (Taxol 150 mg/m2) and Avastin (15 mg/kg)	General side effects including fatigue, neuropathy of hands and feet, headache (relieved with Duexis), shortness of breath upon exertion, palpitation with anxiety, abdominal pain with bowel movement, bone pain, and cyclic GI discomfort.	• Prophylactic as in cycle 4 • Duexis (for neuropathy relief) • Hydromorphone (for bone pain relief)
Chemo Cycle 6 **Date: 11/10/2020**	60 mg of IVIG (1g/kg/4 weeks, wt 50 kg), 1 week prior to c6	Carboplatin (area under the curve (AUC) 4, Paclitaxel (Taxol 150 mg/m2) and Avastin (15 mg/kg)	Same as cycle 5	Same as cycle 5
Post-treatment	60 mg of IVIG (1g/kg/4 weeks, wt 50 kg) every 3 weeks (as of March 26th)	Avastin (15 mg/kg) for 1 year	Vulnerability to lung infections	

Conclusions

In this case report, a patient with inborn error of immunity presented with ovarian cancer underwent a modified treatment course. The positive treatment outcome may suggest that patients with combination of diseases may require a multidisciplinary team approach.

Larger studies are needed on how to adjust therapy to decrease risk of infection but still treat cancer aggressively for optimal long-term outcomes.

References:

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