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Fatal Febrile Neutropenia in Post Chemotherapy Patient with Ovarian Dysgerminoma: A Case Report

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ABSTRACT

Introduction: Febrile Neutropenia (FN) is a serious condition characterized by fever and neutropenia, which poses a critical concern in cancer treatment, particularly for ovarian cancer patients undergoing chemotherapy. The incidence of FN is influenced by factors such as chemotherapy regimen, patient demographics, and overall health status.
Case Presentation: A 20-year-old woman with abdominal distension, pain, and weight loss was diagnosed with advanced intra-abdominal pathology. She received chemotherapy with regimen consist of Bleomycin (15 mg/day on days 1, 8, and 15), Etoposide (150 mg/day on days 1-5), and Cisplatin Sanbe (30 mg/day on days 1-5). Subsequent surgical exploration revealed extensive disease, necessitating suboptimal tumor debulking and a total abdominal hysterectomy with bilateral salpingo-oophorectomy. Postoperatively, the patient was at high risk for FN due to the intensive chemotherapy and extensive surgery. This case emphasizes the need for vigilant monitoring and prompt FN management in patients undergoing significant surgery post-chemotherapy. It highlights the complexities of managing post-surgical complications within the context of recent chemotherapy.
Discussion: FN in ovarian cancer patients complicates treatment, as chemotherapy-induced neutropenia increases infection risk. Prophylactic measures like granulocyte colony-stimulating factors (G-CSFs) and antimicrobial therapy are crucial in reducing FN incidence and severity. Early detection and prompt antibiotic treatment are essential for effective FN management.
Conclusion: This case underscores the challenges of managing ovarian cancer and the importance of proactive FN management. Prioritizing personalized care and early intervention can optimize outcomes and enhance patient quality of life.

INTRODUCTION

Febrile neutropenia (FN) is a critical and potentially life-threatening condition characterized by the simultaneous occurrence of fever and neutropenia. Neutropenia is defined by an abnormally low number of neutrophils (less than 1000 cells/microliter or in severe neutropenia is less than 500 cells/microliter), a type of white blood cell that plays a crucial role in fighting off infections (Budiana & Febiani, 2017). Fever in this context is often a sign of an underlying infection that the body is unable to combat effectively due to the lack of neutrophils. This condition is particularly common in cancer patients undergoing chemotherapy, as many chemotherapeutic agents can significantly reduce neutrophil counts, making patients highly susceptible to infections (Hu-Heimgartner et al., 2023).

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In ovarian cancer, a malignancy that frequently necessitates intensive chemotherapy regimens, the incidence of FN is a notable concern (Mansoor et al., 2023). The treatment protocols for ovarian cancer often involve high doses of cytotoxic drugs that, while effective at targeting cancer cells, also indiscriminately affect rapidly dividing cells in the bone marrow, leading to neutropenia (Mansoor et al., 2023). FN in ovarian cancer patients is particularly alarming because the aggressive nature of both the disease and its treatment can lead to severe complications and increased mortality (Yoo et al., 2020).

Epidemiologically, FN affects a substantial proportion of cancer patients. Study revealed that chemotherapy-induced neutropenia occurred in 147 patients (50.5%). Febrile neutropenia was observed in 20 patients (6.9%) across 25 cycles (1.5%) (Ali et al., 2022). Another study found that FN episodes were more prevalent in patients with solid tumors (57%) than in those with hematological malignancies, and they were more frequently linked to Gram-negative bacterial infections (56.25%). (A, 2016) Several risk factors contribute to the likelihood of developing FN, including the type and dosage of chemotherapy agents, the patient's age, overall health, nutritional status, and the presence of other medical conditions such as diabetes, cardiovascular diseases, or infections as well as advanced-stage cancer and extensive prior treatment (Xu et al., 2023).

Preventive measures are crucial in reducing the incidence and severity of FN. Prophylactic antibiotics are often used to prevent infections in neutropenic patients, while hematopoietic growth factors such as granulocyte colony-stimulating factor (G-CSF) can stimulate the production of neutrophils in the bone marrow, thereby reducing the duration and depth of neutropenia. (Griffiths et al., 2022) Rigorous infection control practices, including strict hand hygiene, use of protective environments, and immediate treatment of any signs of infection, are essential in managing patients at risk for FN (Da Silva & Casella, 2022). Additionally, dose adjustments and tailored chemotherapy schedules may be necessary to balance effective cancer treatment with the risk of severe neutropenia (Nielson et al., 2021).

This case report presents a tragic instance of fatal febrile neutropenia in a post-chemotherapy patient with ovarian cancer, highlighting the severe impact this condition can have. It underscores the complexity and potential dangers associated with chemotherapy, which, despite being a cornerstone of cancer treatment, is far from straightforward to administer. The report illustrates the critical need for vigilant monitoring and prompt intervention in managing the risks associated with FN. Healthcare providers must be acutely aware of the symptoms and ready to implement preventive and therapeutic strategies to mitigate these risks. This case serves as a poignant reminder that chemotherapy, while lifesaving, requires a delicate balance and careful consideration of the potential for severe, life-threatening side effects such as febrile neutropenia.

CASE PRESENTATION

A 20-year-old woman presented with abdominal distension for the past two months, accompanied by increasing pain that worsened with activity. She noted a palpable abdominal mass for three months, significant weight loss of 4 kg over two weeks, and infrequent bowel movements every five days, while urination was normal. On examination, the vital sign was in a good state that is BP: 109/70 mmHg, HR: 80x/min, Respiratory Rate: 20x/min, Temperature: 37,6^{0}C. From physical examination, the thorax was symmetrical with normal vesicular breath sounds and no abnormal sounds. The abdomen was distended up to the xiphoid process with a palpable, immobile mass located two fingers below the umbilicus, positive shifting dullness and fluid wave, and no tenderness. Gynecological examination revealed a calm external appearance,

but speculum and vaginal examinations were not performed. Rectovaginal examination indicated strong rectal tone, a non-collapsed rectal ampulla, and palpable, immobile masses in both adnexa without intraluminal masses.

Ultrasound showed an anteflexed uterus with a 4.1 cm endometrial lining and a homogeneous myometrium (Figure 1). The right ovary had a multilocular cystic mass measuring 10.6 x 10.1 x 8.8 cm, and the left ovary had a unilocular cystic mass measuring 8.4 x 7.1 x 6.6 cm, with massive ascites present. The patient's laboratory results reveal a hemoglobin level of 12.2 g/dL, which is within the normal range, indicating adequate oxygen-carrying capacity of the blood. Hematocrit is 38%, reflecting the proportion of red blood cells in the blood, and is within the expected range. The white blood cell count is 4.8 x 10^9/L, indicating a normal immune response. The eosinophil count is 11.05%, which is elevated and may suggest an allergic reaction or parasitic infection. Platelet count stands at 949 x 10^9/L, which is significantly elevated and may indicate a reactive process or a myeloproliferative disorder. The alpha-fetoprotein (AFP) level is 1.85 ng/mL, within the normal range, but the CA 125 level is elevated at 642.2 U/mL, which may be suggestive of a gynecological malignancy, particularly ovarian cancer. Beta-human chorionic gonadotropin (Beta-HCG) is less than 2.00 mIU/mL, and lactate dehydrogenase (LDH) is 448 U/L, which could be elevated due to tissue damage or a hemolytic process. The fasting glucose (GDS) is 96 mg/dL, indicating normal blood sugar levels, and serum albumin is 3.88 g/dL, reflecting normal protein levels in the blood. Liver enzymes, SGOT and SGPT, are at 15 U/L and 5 U/L respectively, both within normal ranges, indicating normal liver function. The patient's albumin level is repeated at 3.88 g/dL, confirming consistent protein levels in the blood. These results need to be interpreted in the clinical context to determine their significance.

The Risk of Malignancy Index (RMI) was 1926 and the IOTA score was 95%, both indicating a high risk of malignancy. A chest X-ray showed an obscured left costophrenic angle due to pleural effusion. Pulmonology recommended preoperative thoracocentesis and assessed moderate surgical tolerance. Preoperative diagnosis included suspected malignant ovarian cystic neoplasm, massive ascites, and pleural effusion.

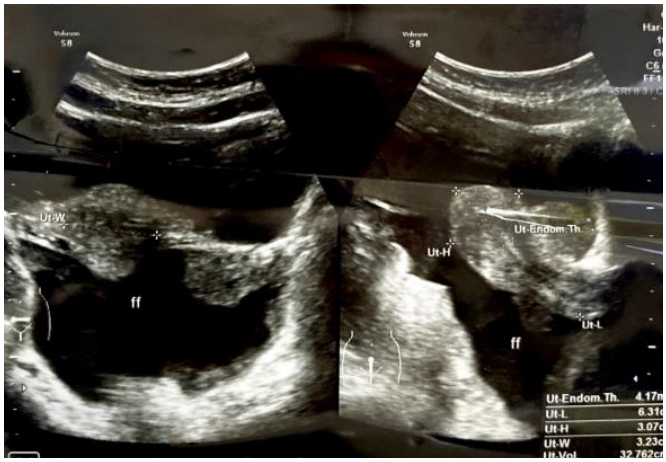

Figure 1. Ultrasound showed an anteflexed uterus.

During surgery, under epidural general anesthesia, a median incision was made, revealing 10,000 cc of ascitic fluid (Figure 2). Exploration showed adhesions among the peritoneum, omentum, uterus, and ovarian tumors, which were lysed. The right ovary had a cystic mass with solid and necrotic components (12 x 10 x 8 cm), and the left ovary had a cystic mass (6 x 5 x 5 cm) with multiple abdominal wall nodules. Suboptimal tumor debulking was performed, followed by

total abdominal hysterectomy with bilateral salpingo-oophorectomy (Figure 3), bladder flap creation, ureter identification, and vaginal stump suturing. Nodules on the peritoneum were excised, and an omentectomy was performed. Hemostasis was confirmed, an intra-abdominal drain was placed, and the abdomen was closed in layers. Estimated blood loss was 1000 cc, with a urine output of 600 cc.

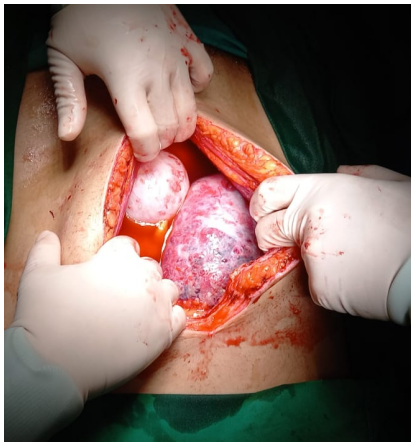

Figure 2. Intraabdominal exploration showed adhesions among the peritoneum, omentum, uterus, and the ovarian tumor with excess ascitic fluid.

Figure 3. Left and right ovarian tumors after debulking process.

The postoperative diagnosis for this patient was post-laparotomy suboptimal tumor debulking, adhesiolysis, and omentectomy due to suspected stage 3C ovarian dysgerminoma. Pathological anatomy results confirmed dysgerminoma. The patient began chemotherapy on September 2nd, 2022, with a regimen that included Bleomycin at a dose of 15 mg/day on days 1, 8, and 15; Etoposide at 150 mg/day on days 1 to 5; and Cisplatin Sanbe at 30 mg/day on days 1 to 5. Over the course of several follow-ups, the patient's response to treatment was closely monitored. Initially, the patient demonstrated a favorable response to the chemotherapy, with a reduction in tumor markers and symptomatic relief. However, subsequent follow-ups revealed fluctuations in laboratory values, and the patient's clinical condition required ongoing assessment to manage side effects and adjust the treatment plan as necessary. Further details on long-term outcomes would depend on the specific clinical data observed during these follow-up visits.

DISCUSSION

This case report details the presentation, diagnosis, and treatment of a 20-year-old female diagnosed with suspected stage 3C ovarian cancer. The patient initially presented with significant abdominal distension, increasing pain with activity, weight loss of 4 kg over two weeks, and infrequent bowel movements, all concerning for advanced intra-abdominal pathology. A thorough clinical examination revealed an immobile abdominal mass with positive shifting dullness and fluid wave tests, indicative of massive ascites.

Ovarian cancer, particularly in advanced stages, presents significant treatment challenges due to its poor prognosis and late diagnosis. Surgical intervention is often necessary for diagnosis, staging, and debulking of the tumor.(Vergote et al., 2020) In this case, the patient underwent a laparotomy, revealing extensive disease with adhesions among the peritoneum, omentum, uterus, and ovarian masses. The decision for suboptimal tumor debulking, followed by total abdominal hysterectomy with bilateral salpingo-oophorectomy, was made based on the intraoperative findings.

Postoperatively, the patient was at high risk for complications, including febrile neutropenia. Febrile neutropenia (FN) is a significant complication in the treatment of ovarian cancer, particularly in patients undergoing chemotherapy. FN is defined by the presence of fever, often above 38.3°C (101°F) or a sustained temperature of 38°C (100.4°F) for more than an hour, in combination with a neutrophil count below 500 cells/mm^3 or expected to fall below this threshold within 48 hours. Neutrophils, a type of white blood cell, are critical for fighting infections, and their reduction (neutropenia) severely compromises the immune system. The primary cause of FN in cancer patients is the myelosuppressive effects of chemotherapy (Crawford et al., 2024). Chemotherapeutic agents target rapidly dividing cells, a characteristic of cancer cells, but they also affect normal cells in the bone marrow responsible for producing blood cells, including neutrophils. The resultant neutropenia leaves patients highly susceptible to infections, as the body's first line of defense against pathogens is significantly weakened. Even a minor infection can quickly become severe, leading to potentially fatal sepsis (Nur Utomo et al., n.d.).

This definition leading the high risk of patient to get FN because of her condition from laboratory finding that shows increasing white blood cells count. Given the high risk of FN in this patient, especially due to her diagnosis of stage 3C ovarian dysgerminoma and the aggressive chemotherapy planned, implementing preventive measures is crucial. Preventive strategies include antibiotic prophylaxis to reduce the risk of bacterial infections during periods of neutropenia. Granulocyte Colony-Stimulating Factors (G-CSFs), such as filgrastim or pegfilgrastim, should be administered to stimulate the production of neutrophils and reduce the duration of neutropenia. Additionally, the patient should undergo regular monitoring of blood counts and be vigilant for signs of infection to initiate early intervention if FN develops. Close monitoring and preventive care are essential to mitigate the risks associated with FN and to ensure prompt and effective treatment should it occur.The management of FN is critical, as it can significantly impact patient morbidity and mortality (Joudeh et al., 2023).

In patients with ovarian cancer, FN can complicate the course of treatment by necessitating dose reductions or delays in chemotherapy, which can adversely impact the overall efficacy of cancer treatment. This emphasize the need for effective management strategies to mitigate the risks associated with FN. The occurrence of febrile neutropenia among ovarian cancer patients fluctuates depending on the chemotherapy regimen administered.(Leon Rapoport et al., 2023) Research indicates that specific treatments, particularly those combining platinum-based

therapies with taxanes, can lead to febrile neutropenia rates ranging from 15-25% in individuals with advanced ovarian cancer.(Leon Rapoport et al., 2023) This underlines the significance of carefully selecting treatment regimens and actively managing the risk of neutropenia to enhance patient outcomes in ovarian cancer care, mirroring the considerations in early-stage breast cancer (Leon Rapoport et al., 2023).

Recent literature underscores the importance of proactive management strategies to prevent and treat FN in patients undergoing chemotherapy. A study by Crawford et al. (2021) highlights the role of G-CSFs in reducing FN incidence and improving patient outcomes. G-CSFs stimulate the bone marrow to produce more white blood cells, thereby reducing the duration and severity of neutropenia (Laali et al., 2020).

Klastersky et al. (2016) discuss the use of antimicrobial prophylaxis and early intervention strategies for managing FN. These strategies include the administration of broad-spectrum antibiotics at the first sign of fever, before the onset of neutropenia, to preemptively address potential infections. This approach is essential for patients with a high risk of FN, such as those with advanced ovarian cancer undergoing aggressive chemotherapy (Klastersky et al., 2016).

In this case, postoperative management should include close monitoring for signs of infection and neutropenia. Prophylactic administration of G-CSFs, as well as broad-spectrum antibiotics, may be warranted to reduce the risk of severe infections. The implementation of such prophylactic measures has been supported by various studies. Alyamani et al. (2022) demonstrated that primary prophylaxis with G-CSFs in high-risk patients significantly reduced the incidence of FN and associated healthcare costs (Alyamani et al., 2022). Furthermore, a study by Suzuki et al. (2022) reinforced the efficacy of prophylactic antibiotics and G-CSFs in reducing the occurrence and severity of FN in cancer patients undergoing chemotherapy (Suzuki et al., 2022).

The patient's postoperative course would require a multidisciplinary approach, integrating oncologists, hematologists, and infectious disease specialists to optimize outcomes. The management of FN involves prompt identification of fever, immediate initiation of broad-spectrum antibiotics, and supportive care to manage symptoms and complications. Early and aggressive treatment of FN can significantly improve survival rates and quality of life for patients with ovarian cancer.

CONCLUSION

In conclusion, this article highlights the challenges faced in managing advanced ovarian cancer, especially regarding FN following chemotherapy. FN, marked by fever and low white blood cell count, poses serious risks to patients. It requires quick identification and treatment. The discussion emphasizes the need for early detection, prompt action, and teamwork among healthcare providers in addressing FN effectively. Chemotherapy, while crucial in cancer treatment, isn't without risks. Each patient's treatment plan must balance its benefits and potential side effects, like FN. This case reminds us that managing ovarian cancer goes beyond just surgery or chemotherapy. It requires a holistic approach that considers the patient's overall well-being. By prioritizing personalized care and proactive measures, we aim to improve outcomes and enhance the lives of ovarian cancer patients.

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