

GEMCITABINE-INDUCED DROP IN PLATELET COUNTS: A CASE REPORT

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ABSTRACT

Chemotherapy with anticancer drugs is known to be beneficial, but like a double-edged sword, it has its own demerits in the form of adverse effects. Cancer chemotherapy-induced thrombocytopenia is troublesome, and platinum-based regimens, namely carboplatin and cisplatin, are known to cause it very commonly. Gemcitabine, in combination with platinum compounds, is known to cause severe thrombocytopenia. Hence, we report a case of thrombocytopenia induced by gemcitabine when used as a single agent in the treatment of ovarian cancer.

Keywords: Gemcitabine hydrochloride, Thrombocytopenia, Naranjo's scale, Solid organ tumors.

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INTRODUCTION

Gemcitabine is used in the treatment of several solid tumors. Despite its very high antitumor activity, the adverse effects due to chemotherapy with gemcitabine always play a spoil sport. It is used in the treatment of various cancers such as ovarian, breast, and pancreatic malignancies and it acts by inhibiting the growth of cancer cells which is proven in many clinical trials as well as by *in vivo* and *in vitro* tumor models [1]. It causes various adverse effects ranging from nausea, vomiting, hair loss, diarrhea, myelosuppression, weakness, anemia, and so on. Hence, we report a case of gemcitabine-induced thrombocytopenia in a 52-year-old female diagnosed of ovarian malignancy.

CASE REPORT

A 52-year-old female patient diagnosed of metastatic ovarian carcinoma underwent cytoreduction surgery and was started on gemcitabine-based chemotherapy post-surgery. Informed consent was obtained from the patient. As on September 07, 2015, the patient had received three cycles of chemotherapy, and 1 week after the third cycle on September 14, 2015, the patient developed severe fall in platelet counts. The patient also had elevated blood urea nitrogen (46 mg/dl). Before the start of the third cycle, platelet counts were normal. Other system examination was normal, and there was no other abnormality. All the other causes of thrombocytopenia including infections, other concomitant medications causing fall in platelet counts were ruled out, and gemcitabine was suspected to be the causative agent. No specific treatment was given, and the patient recovered back with normal platelets on September 9, 2015 (Table 1), before the start of the next chemotherapy cycle.

DISCUSSION

Gemcitabine hydrochloride with a molecular formula of $C_9H_{11}F_2N_3O_4 \cdot HCl$ is a 2'-deoxy-2',2'-difluorocytidine monohydrochloride. It is a white powder with a PKa of 3.6, soluble in water and methanol, but insoluble in alcohol [1]. It was initially investigated as an antiviral agent but soon claimed its place as an effective antitumor agent. Now, in medical field, gemcitabine is used in the treatment of bladder cancers, non-small cell lung cancer, and metastatic pancreatic cancer as a single agent. It is also used in combination chemotherapy with other anti-cancer agents in the treatment of ovarian cancer and breast cancer. Gemcitabine, a cytidine analog, is a prodrug and it requires phosphorylation to generate active metabolites. The active metabolite of gemcitabine which is gemcitabine triphosphate gets incorporated into deoxyribonucleic acid (DNA) and acts by stopping the DNA chain elongation by inhibiting

DNA polymerase enzyme. Recent evidence also reports that it acts by poisoning topoisomerase I and results in breakage of DNA strand [2].

As cancer therapy is always known to cause side effects, gemcitabine is not indifferent. It causes various side effects including nausea, vomiting, hair loss, myelosuppression, skin rashes, and even lung toxicity. Thrombocytopenia is a very common side effect of cancer therapy and usually cancer regimens associated with thrombocytopenia include anthracycline-based regimens and taxane-based regimens including cisplatin and carboplatin. In one adverse drug assessment study in India, it was noted that thrombocytopenia occurs in 6.6% in males and 11.2% in females receiving anticancer treatment [3]. In other study, thrombocytopenia occurred in 82% of those receiving only carboplatin, and in 58%, 64%, and 59% of those receiving combination therapies with carboplatin, gemcitabine, or paclitaxel, respectively [4]. In one systemic review, it was found that gemcitabine as a single agent causes 7.8% and 3.4% of Grade 3 and Grade 4 thrombocytopenia, respectively [5]. The most common mechanism associated with gemcitabine-induced thrombocytopenia is direct myelosuppression and thrombotic microangiopathy which is often referred to as hemolytic uremic syndrome. However, usually, chemotherapy-induced thrombocytopenia has various confounding factors which include the solid organ tumor itself contributing to thrombocytopenia, immune-mediated thrombocytopenia, infection-associated, concomitant administration of drugs such as heparin, vancomycin, valganciclovir, post-blood transfusion-associated drop in platelet counts, and chemotherapy-associated thrombotic microangiopathy [5].

In our case, all the other causes of thrombocytopenia were ruled out, and gemcitabine was found to be the causative agent. More to it, platelet counts reached a nadir after 7 days of last chemotherapy cycle and returned to normal levels after 14 days [5]. Hence, it also supports gemcitabine to be suspected as the causative factor. Hence, to establish causative relationship between adverse effect and drug (Table 2), causality assessment was done using Naranjo's scale [6] and a probable causal relationship was ascribed. Severity assessment was done using Hartwig's scale [7] and adverse effect was found to be of mild severity. Adverse drug reaction was found to be not preventable using Thornton's preventability scale [8].

CONCLUSION

Since gemcitabine is a single-agent chemotherapy used in the treatment of many solid organ tumor, monitoring of thrombocytopenia

Table 1: Platelet counts before and after third cycle

Date	Platelet counts/mm ³
September 04, 2015	1.8 lakhs
September 14, 2015	1.1 lakhs
September 19, 2015	4.1 lakhs

Table 2: Adverse drug assessment

Scaling	Assessment
Naranjo's	Probable
Hartwig's	Mild severity
Thornton's	Not preventable

associated with it is very important as it may be one of the presenting features of hemolytic uremic syndrome. Hence, further prospective studies are warranted to find the incidence of thrombocytopenia in solid organ cancer patients' treatment with gemcitabine-based regimens.

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