



Anaphylactic Shock and Cardiac Arrest Secondary to Aprepitant

Rosas D* and Raez LE

Department of Thoracic Oncology Program, Memorial Cancer Institute/Memorial, Health Care System, Florida International University (FIU), Miami, Florida, USA

Abstract

Antiemetic medications are commonly prescribed, especially in the Oncologic population. Every group of antiemetics have their specific mechanism of action and side effect profile. There is little evidence that NK-1 agonists can produce an anaphylactic shock. We report a case of a 57-year-old female diagnosed with advanced stage lung adenocarcinoma who received aprepitant as a premedication for chemotherapy that caused anaphylactic shock and cardiac arrest. The literature we found on anaphylaxis due to aprepitant, were mainly case reports and case series. We encourage more research on this topic to come to the best treatment approach for these patients for a better outcome.

Keywords: Aprepitant; Neurokinin-1 receptor antagonist; Anti-emetic; Adverse drug reaction; Infusion reaction

Introduction

The patient is of a 57-year-old female with past medical history of arthritis and former smoker for 30 years without any other medical history that was diagnosed with stage IV adenocarcinoma of the lung with adrenal gland, left internal iliac and pararectal lymph node metastases. Next generation sequencing was negative for actionable mutations, PDL 1 status 50%, Micro Satellite Instability (MSI-H) not detected. She was started on chemoimmunotherapy regime with IMPOWER 150: carboplatin+paclitaxel+bevacizumab+atezolizumab and zoledronic acid for bone metastasis. Concomitantly, the patient was taking at home the following medications: mirtazapine, omeprazole, ondansetron, albuterol. During the first chemotherapy cycle the patient had a minor rash after the infusion of aprepitant and the beginning of paclitaxel that was managed with steroids and diphenhydramine and restarting the paclitaxel at slower rate. During the second cycle after the administration of aprepitant and the first minutes of the paclitaxel infusion the patient became hypotensive, developed a rash and had a alter mental status. The rapid response team was called and when she was being transported to the hospital, she developed cardiac arrest and she needed to be resuscitated and intubated for the next 48 hours. Finally, she recovered well, was extubated and she was able to be treated with pembrolizumab immunotherapy achieving disease stabilization for her lung cancer that lasted several months.

Case Report

We present here the case of anaphylactic reaction after aprepitant infusion during the second cycle after having a minor anaphylactoid reaction during the first cycle. Chemotherapy leads to nausea and vomiting (N/V), and this significantly affects patient's daily functioning, ability to eat and overall quality of life [1]. Patients with uncontrolled require more health care resources, show a greater health care costs, require a chemotherapy dose reduction or cycle delay that can ultimately affect their outcome [2,3]. N/V incidence is multiple factor dependent such as anxiety, female sex, and young age but the most important factor is the chemotherapy's ability to cause emesis, also known as emetogenicity [4-7]. Guidelines stratify chemotherapy agents as having a high moderate or low risk of inducing N/V. Without premedication, high risk chemotherapy induces vomiting in 90% of patients who receive it, and moderate risk in 30% to 90% of patients [8]. The time course of N/V has a relapsing characteristic, where patients experience N/V within 1 or 2 hours after starting the medications. Lasting around 24 hours, later ceasing and reemerging at 48-72 hours [7].

Discussion

N/V are mediated by a feedback system between the gastrointestinal track and the Central Nervous System (CNS). That is why a combination of antiemetic regimes are directed against different targets on this pathway. One of these pathways involves substance P on the NK1 receptors in the gastrointestinal tract and CNS, so targeting the NK1 receptor with NK1 antagonist is one of the common treatments used [9]. The most common antiemetic regimes used are a combination of antagonist to 5-Hydroxytryptamine Type 3 (5HT3) receptor and to neurokinin 1 receptor, being these 2 medications combined with dexamethasone. Some regimes include a fourth medication, olanzapine, which is recommended by ASCO and NCCN guidelines [10-13]. Aprepitant and its prodrug, fosaprepitant, are NK1 antagonists in IV presentation. This presentation contains the nonionic surfactant polysorbate 80 to solubilize the fosaprepitant. Polysorbate 80 is a biologically active compound present in a few IV formulations, including docetaxel [14-16]. Hypersensitivity systemic reactions and infusion-site adverse events during and after administration of these agents may be partly due to the presence of polysorbate 80 in their preparation [17]. Fosaprepitant is a medication used with dexamethasone and 5-HT3 antagonist for N/V related to chemotherapy. It is of critical importance to encourage the monitoring of patients for hypersensitivity reactions that are not infusion site pain or thrombophlebitis and that they be followed in the initial and subsequent doses [17].

Rolapitant, another NK1 antagonist, has the longest half-life of all NK1 antagonists but was removed from the market due to hypersensitivity reactions and anaphylaxis. Also, multiple NK1 RAs have potential drug-drug interactions. There have been two reports with rolapitant causing severe infusion reactions [18]. We don't know the exact mechanism of anaphylaxis seen in the patient with fosaprepitant, raising the question: does the antagonism of NK receptor lead to anaphylaxis by other mechanisms other than increasing

*Corresponding author: Rosas D, Department of Thoracic Oncology Program, Memorial Cancer Institute/Memorial, Health Care System, Florida International University (FIU), Miami, Florida, USA, Tel: +3364730701; E-mail: rosas.daniel@icloud.com

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substance P? There are some novel medications being studied for preventing and treating N/V due to chemotherapy. One of the novel agents is HTX-019. This agent has demonstrated a safety profile during a 30-minute infusion and a 2-minute injection in healthy volunteers. This study showed a tolerable safety profile in patients with cancer in a follow up prospective study and represents an alternative method for N/V prevention. Cases of anaphylaxis after aprepitant infusion, have not been reported in the literature thus it is important to show this relationship between a commonly used medication and a possible fatal outcome. Although anaphylaxis due to aprepitant is a rare entity, this type of pathology should be assessed by a multidisciplinary team for a better outcome. This case report shows the importance to have a broad differential diagnosis when it comes to anaphylactic reactions. Recognition of this kind of presentation is critical to institutions for the appropriate diagnosis and evaluation for future pre chemotherapy protocols and medication adjustments.

Conclusion

Anaphylaxis due to aprepitant is a very rare entity and we present the first case reported with aprepitant. We theorize that patients benefit from early recognition and treatment of this kind of adverse reaction, but because of the low prevalence of this adverse effect, studies regarding a standardized treatment approach for this scenario are needed. Are there NK-1 antagonists an option, or is only supportive treatment an option? We hope that with reports like this raise awareness about the need to investigate and report the real prevalence of this uncommon complication.

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