

# International Journal of Case Reports & Short Reviews

Case Report

# Anaphylactic Shock and Cardiac Arrest Secondary to Aprepitant - 🗟

## Daniel Rosas<sup>1\*</sup> and Luis E Raez<sup>2</sup>

<sup>1</sup>Thoracic Oncology Program, Memorial Cancer Institute/Memorial, Health Care System, Miami, FL, USA

<sup>2</sup>Health Care System, Florida International University (FIU), Miami, Florida USA

\*Address for Correspondence: Daniel Rosas, Thoracic Oncology Program, Memorial Cancer Institute/Memorial, Health Care System, Miami, FL, USA,Tel: +133-647-307-01; ORCiD: https:// orcid.org/0000-0001-8909-5760; E-mail: rosas.daniel@icloud.com; dani090894@hotmail.com

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#### **KEYWORDS**

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

#### **INTRODUCTION**

Antiemetic medications are commonly prescribed, especially in the oncologic population. Every group of antiemetic has its 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 current literature of anaphylactic due to aprepitant are mainly casing reports and case series, thus we encourage more research on this area to come to the best diagnostic and treatment approach for this kind of patients for a better overall outcome.

#### **CASE PRESENTATION**

The patient is of a 57-year-old female with past medical history of arthritis and a 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 perirectal 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 chemo immunotherapy 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 a slower rate and completing the administration with no more. 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 an altered 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.

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-Induced Nausea and Vomiting (CINV) significantly affect patient's daily functioning, ability to eat and overall quality of life [1]. Patients with uncontrolled CINV require more health care resources, show greater health care costs, require a chemotherapy dose reduction or cycle delay that can ultimately affect their outcome [2,3].

CINV incidence depends on several factors, including female sex, anxiety and young age but the most important factor is the chemotherapy regimen's ability to cause emesis, also known as emetogenicity [4-7].

Antiemetic guidelines classify chemotherapeutic agents as having high, moderate, low, or minimal risk of inducing CINV. Without effective prophylaxis, Highly Emetogenic Chemotherapy (HEC)

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induces vomiting in 90% of patients who receive it, and Moderately Emetogenic Chemotherapy (MEC) induces vomiting in 30%-90% of patients [8]. CINV has a relapsing time course. Patients usually experience intense CINV within 1-2 hours of initiating chemotherapy, lasting for about 24 hours (acute phase) and symptoms usually seise but reemerge at 48-72 hours (delayed phase) [7].

CINV is mediated by a complex feedback system in the gastrointestinal and central nervous system, and that is why a combination of antiemetic regimens are indicated to target multiple pathways. One pathway involves substance P on NK-1 receptors in the gut and central nervous system. Chemotherapy induces substance P release in these regions during CINV, so antagonizing the NK-1 receptor prevents emesis [9].

The standard three-drug regimen consists of a combination of a 5-Hydroxytryptamine Type 3 (5HT3)-Receptor Antagonist (RA), a Neurokinin 1 (NK-1) RA, and dexamethasone, with olanzapine added for four-drug regimens, which are recommended by ASCO and NCCN [10-12]. Adding an NK-1 RA to 5HT3 RA and dexamethasone significantly improves CINV control vs the two-drug regimen [13].

Aprepitant and it is Intravenous (IV) prodrug, Fosaprepitant, are commonly used, NK-1 receptor antagonists. The IV presentation contains the nonionic surfactant polysorbate 80 to solubilize the Fosaprepitant. Polysorbate 80 is a biologically active compound present in a number of IV formulations, including docetaxel [14,15].

Hypersensitivity Systemic Reactions (HSRs) and Infusion-Site Adverse Events (ISAEs) during and after administration of these agents may be partly due to the presence of polysorbate 80 in their preparation [16]. Fosaprepitant is an essential antiemetic that is used in combination with dexamethasone and a 5-HT3 receptor antagonist for the use of CINV. It is important that monitoring of hypersensitivity reactions outside of local infusion site pain, erythema, or thrombophlebitis be followed not only for the initial dose but for any subsequent doses [16].

Another NK-1 receptor antagonist, rolapitant, has the longest half-life of NK-1 RAs, and should not be administered more frequently than every 2 weeks. In general, NK-1 RAs are well tolerated however, rolapitant was removed from the market because of hypersensitivity and anaphylaxis. Also, multiple NK-1 RAs have potential drug-drug interactions. There have been two reports with rolapitant causing severe infusion reactions [17]. The FDA issued a Health Care Provider Letter stating that anaphylaxis, anaphylactic shock, and other serious hypersensitivity reactions have been reported in the post-marketing setting in January 2018 [18]. We don't know the exact mechanism of anaphylaxis seen in the patient with Fosaprepitant, raising the question: does the antagonism of the NK-1 receptor lead to anaphylaxis by other mechanisms other than increasing substance P?

HTX-019 is a novel injectable emulsion formulation of the neurokinin 1 Receptor Antagonist (RA) aprepitant, approved for preventing acute and delayed Chemotherapy-Induced Nausea and Vomiting (CINV). HTX-019 has demonstrated a tolerable safety profile when administered during a 30-min Intravenous (IV) infusion and 2-min IV injection in healthy volunteers. This prospective study showed the safety of HTX-019 administered via 30-min IV infusion and 2-min injection (IV push) in patients with cancer. The short injection of HTX-019 had a tolerable safety profile in patients with cancer and represents an alternative method for CINV prevention [19].

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Cases of anaphylaxis due to aprepitant have not been reported so far in the literature and it is important to make the medical field aware of this type of cases because there could be a significant number of patients with anaphylaxis due to aprepitant that could be assessed and possibly offer a better treatment strategy. Although anaphylaxis due to aprepitant is a rare entity, this type of pathology should be assessed by a multidisciplinary team for better outcomes.

This case illustrates 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 Fosaprepitant. Patients benefit from early recognition and treatment, but because of its low prevalence, there aren't studies regarding a standardized treatment approach for this scenario. 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.

#### **INFORMED CONSENT**

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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