A Possible Case of Filgrastim-Induced Death

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ABSTRACT

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This is a case report focusing on a 50 year old woman's death possibly due to Filgrastim. Filgrastim is considered to be a drug of choice in neutropenic cases. But in this case, Filgrastim has developed several severe Adverse Drug Reactions resulting into the death of patient. Naranjo's Causality Assessment Algorithm was used to assess the cause of death & the algorithm indicated Filgrastim as a possible cause of death.

Keywords: Filgrastim, Filgrastim-Induced Death, Drug-Induced Neutropenia & Granulocyte-Colony Stimulating Factor

INTRODUCTION

Commercially available Granulocyte-Colony Stimulating Factor (G-CSF) preparations have significantly improved the quality of life (QoL) of patients with neutropenia internationally.[1] This report summarizes the development of sore throat, breathlessness (dyspnoea), tachycardia & wheezing sound in chest associated with the use of Filgrastim which finally lead to patient's death.

CASE REPORT

A 50 year old woman was admitted in one of a private hospital in Maharashtra, with following chief complaints;

- Diffused scaly lesions over the exterior surface of right forearm,
- Similar kind of lesions over the sun-exposed areas of face & lips &
- Black colored discoloration of skin.

On local examination, the skin of patient was observed to be dry over the lesions with presence of extensive scaling & patient was unable to open her mouth freely due to presence of sub-mucosal fibrosis (due to betel nuts chewing habit) over buccal region. On the basis of this data, a preliminary/ provisional diagnosis was done as exposure dermatitis & drug hypersensitivity. The past medical & medication history of patient was asthma since 18 years & unknown anti-asthmatic medications. Patient was not having any past medical history of cancer. Clinical laboratory tests (hematological tests) were carried out, which revealed that there was a gradual decrease in the neutrophil count (21.2%) & total count (500cells/mm^3) & increase in the Erythrocyte Sedimentation Rate (98mm/hr). A final diagnosis was then done as Drug-induced neutropenia on the basis of these clinical laboratory values. Identification of drug/s which induced neutropenia was not done. A 300 mcg prefilled syringe of Filgrastim was administered subcutaneously once daily, for 4 days to treat drug-induced neutropenia. Other drugs like ceftriaxone, amikacin, liquid paraffin lotion, and chlorhexidine mouthwash were also given to treat lesions & sub-mucosal fibrosis respectively.

On very next day (day 2) of the treatment, patient started complaining of having sore throat, throat pain & fever. On day 3, she developed breathlessness (dyspnoea), tachycardia & drowsiness along with continuing sore throat & throat pain. On examining lungs, wheezing sounds from the chest were heard. On day 4, patient's daughter reported patient's restlessness which on observation was found to be severe seizure attacks with froth coming out of her mouth followed by cardiac arrest. On examination, she was found to be unconscious, her pulse was not palpating, pupils were not dilated & not reacting to light, no heartbeats & no breathing sounds were heard. Cardio-Pulmonary Resuscitation (CPR) was tried on the patient by starting chest compressions with ambu-bag (at the rate of 30:2 breaths) to save her life. CPR was given for around 20-25 minutes (6 times). Along with

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CPR, Intravenous (IV) bolus injections of atropine – 1mg/ml (10 ampoules) & adrenaline – 1mg/ml (2 ampoules) were also given. In spite of all the above resuscitation methods according to Advanced Cardiac/Cardiovascular Life Support (ACLS) protocols,[2, 3] the patient couldn't survive & was been medically declared as dead.

DISCUSSION

In this case, drug-induced neutropenia was diagnosed & treated on the basis of clinical laboratory investigations other than Absolute Neutrophil Count (ANC) which is a main key for diagnosing neutropenia.[4] Furthermore the patient was treated with Filgrastim without identifying the drug/s that caused neutropenia. Filgrastim is considered to be a drug of choice in neutropenic cases.[1, 5] But in this case, development of sore throat, breathlessness (dyspnoea), tachycardia & wheezing sound in chest may be triggered due to Filgrastim, as because sore throat is observed as an Adverse Drug Reaction (ADR) or an undesirable effect in some of the randomized clinical trials conducted on Filgrastim & the other effects (dyspnoea, tachycardia & wheeze) are given under the "WARNING" column of Filgrastim as serious allergic reactions.[6-8] Secondly, as the patient had a past medical history of asthma, more care was to be taken in prescribing Filgrastim to the patient because of the possibility of these systemic allergic-like reactions. In one of a randomized, open-labelled, multicenter study, patients with severe allergic history (seasonal/recurrent asthma) were excluded (kept in exclusion criteria) from their study due to these reasons.[9] Taking all these information under consideration, a causality assessment of death was done by using Naranjo's Causality Assessment Algorithm[10] & the algorithm indicated Filgrastim as a possible cause of death with Naranjo score = 3.

CONCLUSION

This case report accentuates the importance of collecting complete data of patient's history such as; past medical history, past medication history, current clinical laboratory tests, etc. before initiating any treatment. Also monitoring, reporting & management of ADRs are necessary in order to avoid such types of severe events.

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