A Not So “Paclital” Case

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Introduction Paclitaxel, a member of the taxane family of chemotherapies, is one of the first-line treatments for breast cancer. Is widely used and frequently responsible of hypersensitivity reaction representing potent global health problem in cancer therapy. Herein we illustrate a case consecutive delayed and severe IgE-mediated anaphylaxis to Paclitaxel triggered by cremophor EL.

Observation A 75-year-old woman treated with paclitaxel, carboplatin, and pembrolizumab for breast cancer developed a maculopapular rash after the second chemotherapy session. A check point inhibitor immune skin reaction was suspected. She was then treated by paclitaxel alone and experienced severe grade III anaphylaxis requiring intensive care. Hypersensitivity to paclitaxel or its excipient Cremophor EL (CrEL) was suspected, Skin prick tests for macrogols, polysorbate 80 (PS80), taxanes with and without CrEL (paclitaxel, docetaxel and Abraxane) were negative, but urticarial plaques appeared right after intra-dermal test at 10^{-2} dilutions of taxane with CrEL resolved within hours suggesting CrEL sensitization. Twenty-four hours reading of Intradermal testing was positive for CrEL. Basophil activation test was also positive. These findings confirm our case as IgE-mediated anaphylaxis and delayed hypersensitivity to paclitaxel involving CrEL.

Discussion We report a complex case of both immediate and delayed hypersensitivity reactions to paclitaxel, a drug often limited by its high incidence of reactions (44% mild, 10% severe) (1). These reactions can be immediate or delayed, with some patients experiencing immediate reactions upon re-exposure, as seen in our patient. The excipient Cremophor EL, rather than paclitaxel itself, is often responsible for these reactions. Allergologists played a crucial role in ruling out other causes, ensuring the appropriate management of the patient’s reaction, and avoiding delays in the cancer treatment. A rapid histological analysis could have expedited decision-making and therapeutic adjustments by differentiating it from the lichenoid drug reactions often seen with anti-PD1 therapies. Management depends on reaction severity, with desensitization or alternative treatments like Abraxane (free of Cremophor EL and polysorbate 80) being considered for at-risk patients. The sequence of delayed then immediate hypersensitivity is not well understood but immune stimulation induced by ICI could play a role in developing multiple ways of sensitization.

Conclusion This case highlights the complexity of hypersensitivity reactions to paclitaxel, including both delayed and immediate responses. It underscores the importance of prompt diagnosis and management. Given the risk of immediate reactions in patients with delayed hypersensitivity, alternatives like Abraxane or desensitization protocols should be considered to ensure patient safety. Additionally, it emphasizes the underestimated risks of PEG sensitization and cross-sensitization to PEGylated drugs and related derivatives. Allergologal assays could be useful in these cases with immediate and late readings.

References

1. D’Errico S, Baldari B, Arcangeli M et al. Mast cells activation and high blood tryptase levels due to paclitaxel administration. Is Cremophor EL the culprit? Medicine (Baltimore). 2020 Oct 23;99(43):e22814.