Pemetrexed anaphylaxis – An unusual suspect
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**Background:** Pemetrexed is a folate antimetabolite, approved for treatment of mesothelioma and non-squamous non-small cell lung cancer. It’s usually used in combination with platinum salts, gemcitabine or docetaxel. Pemetrexed presents a good safety profile, with myelosuppression being the most common dose-limiting toxicity. However, hypersensitivity reactions to pemetrexed have been described.

**Case Report:** We report the case of a 52 year old woman, with stage IV metastatic adenocarcinoma of the lung, on palliative chemotherapy (QT) with pemetrexed plus carboplatin; for nausea control she was also receiving fosaprepitant immediately before QT. On her first treatment with these drugs, 3 minutes after starting pemetrexed perfusion, the patient developed dyspnea, cyanosis of the extremities, generalized pruritic exanthema and hypersudoresis. QT was immediately stopped and the patient was treated with hydrocortisone and clemastine. However, her status rapidly progressed to anaphylactic shock, with loss of consciousness, sphincters control, bradypnea, bradycardia, non-measurable blood pressure) and tachycardia. She received IV adrenaline and aggressive fluid resuscitation, with rapid improvement and was discharged 24h later, fully recovered. Serum tryptase during the episode was elevated at 67.5ug/L (normal range: <11.4ug/L).

The patient was referred to our drug allergy unit for study. Skin prick tests performed 6 months later were positive to pemetrexed 25mg/ml (7mm; histamine 10mg/ml=5mm) and negative to carboplatin 10mg/ml and fosaprepitant 1mg/ml; intradermal tests were also positive to pemetrexed (1/1000) and negative to carboplatin (1/1000-1/10) and fosaprepitant (1/1000-1/10). As the oncologist decided for an alternative treatment, a desensitization protocol to the culprit drug, pemetrexed, was not considered.

**Conclusion/Discussion:** Reports of hypersensitivity reactions to pemetrexed are very rare. This drug is almost exclusively used in combination with other chemotherapeutic agents, like platinum salts, which might underestimate pemetrexed as a cause of immediate hypersensitivity reactions.

To our knowledge, this is the third report of documented anaphylaxis to pemetrexed, and the first to support the diagnosis of an IgE dependent mechanism through skin tests.