

CASE REPORT

Cross-reactivity between paclitaxel and hazelnut: a case report

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A 73-year-old Caucasian woman with metastatic bladder cancer developed hives, itching, difficulty in breathing, and general ill-feeling during the first 10 min of her first infusion of paclitaxel. Paclitaxel was discontinued and the symptoms resolved after intravenous diphenhydramine and hydrocortisone treatment. Upon discussion with the patient, she described the sensation as similar to her reaction to hazelnuts. The patient's only other allergy was to azithromycin, which presented as hives. A PubMed literature search revealed that paclitaxel is found in the components of the hazelnut tree and its nuts.

While a nut-protein allergy cannot be ruled out, a cross-reaction between paclitaxel and hazelnuts is a possibility. Patients who describe an allergy to hazelnuts must be carefully observed while being treated with paclitaxel. The hazelnut allergy may not be a nut-protein allergy at all, but rather an allergy to the components of paclitaxel that reside in the hazelnut itself. *J Oncol Pharm Practice* (2007) 13: 53–55.

Key words: allergies; hazelnut; nut proteins; paclitaxel

Sir – Paclitaxel plays an integral part in the treatment of ovarian cancer, breast cancer, lung cancer, bladder cancer, and AIDS-related Kaposi's Sarcoma.^{9,10} Physiochemically, the drug is a viscous solution requiring cremophor to enhance dissolution. It is difficult to procure from the pacific yew tree, and the supply has been limited since its discovery, coupled with increasing applications in chemotherapy. The availability and cost of the drug remain an important issue, and synthesis of the drug has proven to be difficult.^{5,6} Thus, the availability from hazelnut trees

and products has a significant impact on the use of this agent.^{6,7} The rate of hypersensitivity to paclitaxel is greater than 10% of patients who receive the drug, and presents as a nonimmunologically mediated release of histamine and other vasoactive substances. It is almost always seen within the first hour of an infusion and approximately 75% of the allergic symptoms will occur within the first 10 min of the infusion. This incidence is reduced by premedication.^{5,9} We describe a patient who developed an immediate hypersensitivity reaction upon her initial administration of paclitaxel, and whose allergic symptoms were identical to the ones she experienced with her hazelnut allergy.

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A 73-year-old Caucasian female with a history of metastatic bladder cancer was started on carplatin AUC = 5 on day 1, gemcitabine 800 mg/m² on day 1

and day 8, and paclitaxel 175 mg/m² on day 1. The dose of paclitaxel was scheduled to run over 3 h. She was pretreated with intravenous diphenhydramine 50 mg, ranitidine 50 mg, dexamethasone 20 mg, and oral granisetron 1 mg. Within 10 min of the start of the paclitaxel infusion, the patient reported a generalized ache with ensuing rash on her face and neck, with difficulty in breathing. The paclitaxel infusion was immediately discontinued and the patient received intravenous diphenhydramine 50 mg and hydrocortisone 100 mg per institutional hypersensitivity protocol. The patient's symptoms resolved, and it was decided not to rechallenge the patient with paclitaxel because of the possible association of the above described reaction with paclitaxel and her history of hazelnut allergy.

DISCUSSION

Paclitaxel is derived from the bark of the pacific yew tree.^{1-3,6} The process of procuring paclitaxel from the yew tree is difficult, the yield is small, and the cost ranges between \$10,000 and \$12,000 per course of paclitaxel.^{1,2} The discovery of paclitaxel in the hazelnut tree was accidentally reached by a professor of horticulture from the University of Portland, Oregon attempting to find the cause of a fungal attack on hazelnuts known as the Eastern Filbert Blight.^{1-3,5} Paclitaxel in the hazelnut tree can be found in the bark, leaves, shells, fungus, and even the nuts.^{1,3,5} This discovery led to the synthesis of paclitaxel from hazelnut trees. The latter is more common than the pacific yew thus increasing the drug's availability and reducing costs. The allergic reaction in this patient occurred immediately after about 3 mL of the first dose of paclitaxel was infused. The fact that the reaction resolved on discontinuation of the drug and administration of diphenhydramine and hydrocortisone suggest that the reaction was a probable drug-induced reaction according to the Naranjo Probability Scale.⁸ The exact lot number and expiration date of the paclitaxel used for this particular patient was untrackable as records were not available from the distributor of the product, Bedford Laboratories.

At therapeutic doses, the most frequently reported adverse reactions are allergic (primarily nonimmunologically mediated release of histamine and other vasoactive substances almost always seen in the first

hour of the infusion), cardiovascular (bradycardia), dermatologic (alopecia, erythema, tenderness, discomfort), hematologic (myelosuppression, leukopenia, neutropenia, thrombocytopenia), hepatic (mild increase in liver enzymes), and neurotoxicity (neuropathy).^{9,10} Paclitaxel is contraindicated in patients sensitive to paclitaxel, cremophor, or any component of the formulation.^{9,10} However, the prescribing information for paclitaxel does not include hazelnut sensitivity as a contraindication for the administration of paclitaxel. An extensive PubMed search of the literature (May 1986 to October 2006) showed no reports of cross-reactivity between hazelnuts and paclitaxel. This may be the first case report of a patient with a history of hazelnut allergy to have a similar reaction to paclitaxel. This finding suggests a correlation between hazelnut allergy and paclitaxel sensitivity.

SUMMARY

Cross-reactivity between hazelnuts and paclitaxel is a possibility given the recent discovery of paclitaxel in the shell, barks, and leaves of the hazelnut tree. A complete allergy history, including food allergies, should be assessed prior to administering paclitaxel. Care should be taken in patients contemplating paclitaxel chemotherapy who report a hazelnut allergy.

REFERENCES

- 1 Susman ED. Hazelnut trees found to produce taxol®. *Oncology Times* 2000; 22: 88-90.
- 2 Fauber J. Researchers link hazelnut to anti-cancer drug. *Milwaukee J Sentinel* 2000: G-4.
- 3 Boone RB, Hoffman A, *et al.* How taxol® was found in hazelnut trees. *Journal of the Australian Nut Industry Council* 2000; 14: 36.
- 4 Hoffman A, Khan J, Worapong G, *et al.* Bioprospectives for Taxol® in angiosperm plant extracts-using high performance liquid chromatography-thermospray mass spectrometry to detect the anti cancer agent and its related metabolites in filbert trees. *Spectroscopy* 1988; 13: 22-32.
- 5 Barofsky D. Mass spectrometric analyses in agriculture and natural product research. *Brazilian Journal of Physics* 1999; 29: 432-9.

- 6 Guo BH, Kai GY, *et al.* Taxol[®] synthesis. *African Journal of Biotechnology* 2006; 5: 15-20.
- 7 Gelmon K. The taxoids: paclitaxel and docetaxel. (Drug profile). *Lancet* 1994; 344: 1266-67.
- 8 Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, *et al.* A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981; 30: 239-45.
- 9 Product information. Taxol[®] (paclitaxel). Bristol-Myers Squibb, 2003.
- 10 Solimando D. *Drug information handbook for oncology*, 5th Ed, Lexi-comp, 2005: 638-46.
- 11 Stopher W. Paclitaxel (Taxol[®]) found in hazelnut trees. *Herbalgram, Journal of the American Botanical Council* 2000; 49: 21.

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