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2. Crocker HR. Paget's disease affecting the scrotum and penis. *Trans Pathol Soc Lon* 1888; 40: 187-91.
3. Darier J, Couillaud P. Sur un case de maladie de Paget de la région perineo-anal et scrotale. *Annales de dermatologie et syphiligraphie* 1893; 4: 33.
4. Eliezra YD, Silvers DN, Horan DB. Role of preoperative topical 5-fluorouracil in preparation for Mohs micrographic surgery of extramammary Paget's disease. *J Am Acad Dermatol* 1987; 17: 497-505.
5. Chandra JJ. Extramammary Paget's disease: Prognosis and relationship to internal malignancy. *J Am Acad Dermatol* 1985; 13: 1009-14.
6. Daugaard G. Unknown primary tumours. *Cancer Treatment Reviews* 1994; 20: 119-47.

Paclitaxel-induced severe hypersensitivity reaction occurring as a late toxicity

Severe hypersensitivity reactions (HSRs) have been observed after the administration of paclitaxel (Taxol[®]), and attributed to the drug's pharmaceutical vehicle, 50% Cremophor EL [1]. The prophylactic use of steroids and histamine antagonists has reduced the incidence of HSRs to about 2%. All HSRs described to date have occurred during either the first or second courses of paclitaxel administration [1, 2].

We treated a 67-year-old male with advanced non-small-cell lung cancer with a combination of cisplatin (80 mg/m²) and paclitaxel (175 mg/m², 3-hour infusion) once every 3 weeks according to a study protocol (EORTC 08925). He was not known to have chronic obstructive pulmonary disease. Premedication consisted of dexamethasone 20 mg orally 12 and 6 hours prior to paclitaxel infusion, and clemastinefumarate 2 mg i.v. and famotidine 40 mg i.v. 30 minutes prior to paclitaxel infusion.

Six days after his first infusion with paclitaxel he developed a supraventricular tachycardia. A cardiac ultrasound showed no abnormalities. Sotalol 80 mg two times daily was started. Cisplatin was discontinued after two cycles due to a reversible rise in serum creatinine. From the second cycle on our patient had a transient rise in blood pressure during paclitaxel infusion and his blood pressure was periodically elevated between infusions. At the start of the sixth cycle his blood pressure was 140/90 mm Hg, and four hours after the start of infusion of paclitaxel he developed an acute life-threatening dyspnoea. No pruritis or urticaria were observed. Physical examination showed a blood pressure of 200/120 mm Hg, a pulse rate of 76/minute and a normal central venous pressure. He was breathing 36 to 50 times per minute. Cardiac auscultation was normal. Over both lungs a prolonged wheezing and rhonchi were heard, but no crepitations. There was no peripheral edema. The electrocardiogram was normal. An arterial bloodgas showed a pH 7.35, pCO₂ 39.5 mm Hg, pO₂ 47.2 mm Hg and bicarbonate 21.9 mmol/l. A chest X-ray showed marked bilateral pulmonary

edema. He was treated with adrenaline 0.5 mg i.m. twice, dexamethasone 20 mg i.v., clemastinefumarate 2 mg i.v., aminophylline 240 mg as loading dose and 720 mg/24 hours as maintenance dose i.v., furosemide 80 mg i.v., oxygen 5 l/min and salbutamol combined with ipratropiumbromide inhalation. After 40 minutes his condition improved, and eventually, he recovered completely.

We conclude that our patient had a life-threatening HSR with severe bronchospasm, hypertension and pulmonary edema during his sixth cycle of paclitaxel. Only a single case of paclitaxel-related pulmonary edema has been reported [3]. The supraventricular tachycardia, which occurred after the first cycle, may also have been caused by paclitaxel [4]. There is evidence that β -blockers increase the sensitivity to allergens by competitive inhibition at the β -adrenergic receptor site. This may result in a decrease in intracellular levels of cyclic AMP which lowers the threshold of mediator release by mast cells and basophils [5]. Thus, the sotalol may have potentiated the HSR in our patient.

In the absence of an elevated central venous pressure and peripheral edema, it is not likely that congestive heart failure was the underlying cause of the pulmonary edema we observed. The absence of angioedema and urticaria do not indicate an increased vascular permeability. The blood pressure measured during this event suggests vasoconstriction. Thus, the lung edema seems to have resulted from a selective reaction of the pulmonary vascular bed to the permeability-enhancing activity of paclitaxel and/or its pharmaceutical vehicle.

Due to the late occurrence of HSR in our patient, routine observation for several hours after each infusion of all patients treated with paclitaxel may be warranted.

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References

1. Weiss RB, Donehower RC, Wiernik PH et al. Hypersensitivity reactions from taxol. *J Clin Oncol* 1990; 8: 1263-8.
2. Peereboom DM, Donehower RC, Eisenhauer EA et al. Successful retreatment with Taxol after major hypersensitivity reactions. *J Clin Oncol* 1993; 11: 885-90.
3. Thigpen T, Blessing J, Ball H et al. Phase II trial of Taxol as second-line therapy for ovarian carcinoma: A Gynaecologic Oncology Group Study. *Proc Am Soc Clin Oncol* 1990; 9: 156 (Abstract).
4. Arbruck SG, Strauss H, Rowinsky E et al. A reassessment of cardiac toxicity associated with Taxol. *Monogr Natl Cancer Inst* 1993; 15: 117-30.
5. Jacobs RL, Rake GW, Fournier DC et al. Potentiated anaphylaxis in patients with drug-induced beta-adrenergic blockade. *J Allergy Clin Immunol* 1981; 68: 125-7.