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5-Fluorouracil-induced Raynaud's Phenomenon

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THERE ARE increasing numbers of reports describing acute vascular toxicity following the administration of cytotoxic chemotherapy. 5-Fluorouracil (5-FU) is a widely used cytotoxic agent. Although relatively unknown, 5-FU-induced coronary artery vasospasm is well described in the literature [1–3]. Nevertheless, perhaps surprisingly, reports of digital ischaemia and associated Raynaud's phenomenon have been described very rarely in relation to 5-FU, and usually in the context of it being used in combination with other drugs [4, 5]. We report a case of a man who developed significant digital ischaemia and Raynaud's phenomenon after receiving 5-FU/leucovorin (LV) based chemotherapy.

A 58-year-old caucasian man underwent antero-posterior resection for a Dukes' B rectal carcinoma in March 1991. He was a non-smoker and the only other history of note at presentation was mild hypertension for which he was prescribed atenolol (50 mg/day) a year earlier by his General Practitioner. In May 1995, he presented with hepatomegaly. Multiple liver metastases were confirmed on computerised tomography (CT) scanning and he was administered 5-FU based chemotherapy. The treatment comprised LV 200 mg/m^2 intravenous infusion (i.v.) over 2 h, then 5-FU 400 mg/m^2 i.v. over 5 min, followed by 400 mg/m^2 i.v. over 22 h on day 1, all repeated on day 2, of a 2 week cycle. Following six cycles, he achieved an objective radiological response, but by cycle 7 he developed severe Raynaud's phenomenon with digital ischaemia. The symptoms worsened with each subsequent cycle and the treatment was discontinued after the 9th cycle. At the same time atenolol was stopped. Examination revealed a digital infarct on the tip of the middle finger of the left hand; nailfold microscopy showed abnormal capillaries. Thermography confirmed severely reduced flow in that finger. An electrocardiogram and echocardiography performed at the time were reported as normal. Antinuclear antibody (ANA) was 1:80 speckled, but other serology was negative. The erythrocyte sedimentation rate (ESR) was raised at 57 mm/1st hour. On subsequent follow-up, the digital infarct had healed completely and he remained asymptomatic. Twelve months later, ANA at 1:80 persisted with a speckled pattern. The patient died from further disease progression in February 1997. The mechanism leading to acute ischaemia in this case is uncertain, although direct vascular toxicity, alteration of platelet activity or the induction of a hypercoagulable state following the administration of 5-FU are possible explanations [6–8]. 5-FU, either alone or in combination with other antineoplastic agents, has been associated with acute vascular events, in particular coronary artery spasm [1–3, 9]. Our patient, who was relatively young, had no signs suggestive of diffuse atherosclerosis and no significant cardiac history; he had been taking a selective β-blocker for 6 years prior to developing Raynaud's phenomenon. Despite the association between β-blockers and the development of Raynaud's, we feel that there was a clear temporal relationship from the time of administration of 5-FU and the onset of symptoms. Stopping the 5-FU provided adequate relief of symptoms. Increased awareness of this 5-FU-related side-effect should help minimise exposure to the drug in susceptible individuals.

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