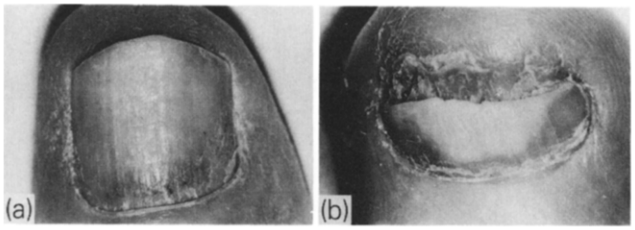

Fig. 1. Onycholysis affecting fingernails (left) and toenails (right) during mitozantrone therapy of advanced breast cancer.

combination with doxorubicin [2]. We report 2 cases seen in 297 patients (279 breast cancer, 18 ovarian cancer) treated with single-agent mitozantrone.

Case 1

A 59-year-old man with extensive local recurrence of adenocarcinoma of the breast had previously been treated with tamoxifen, megestrol acetate and aminoglutethimide as well as local radiotherapy to the supraclavicular area. Mitozantrone was started at a dose of 32 mg (14 mg/m^2) and was well tolerated without alopecia. After four cycles he developed nail tenderness and nail bed erythema, rapidly leading to thickening and lifting of the thumbnails and all toenails (Fig. 1). Fungal culture was negative but a superimposed bacterial infection improved with oral amoxycillin/clavulanic acid. The nail changes persisted during a further three cycles of mitozantrone, slowly returning to normal only after treatment was changed to cyclophosphamide, methotrexate, 5-fluorouracil and prednisone (because of progressive disease).

Case 2

A woman aged 59 with ovarian carcinoma; six cycles of carboplatin led to partial response following surgery, but relapse 5 months later. Mitozantrone was started at an initial dose of 21 mg (12 mg/m^2) with moderate nausea and vomiting but no alopecia. Other regular medications were spironolactone, diclofenac, triazolam and metoclopramide. Thickening, tenderness and lifting developed in several fingernails after three cycles while similar changes developed in the nails of both great toes during the fourth and final cycle. There was improvement of nailbed haemorrhage and exudate in the fingernails with topical clotrimazole cream and oral amoxycillin/clavulinic acid, but the nails only returned to normal 3 months after treatment was changed from mitozantrone to megestrol acetate.

Both patients developed onycholysis affecting multiple nails shortly after starting mitozantrone and then slowly improved on its cessation, strongly suggesting this to be the aetiological agent. A similar pattern has been described in 2 other cases receiving single agent mitozantrone [1]. Onycholysis as an isolated dermatological toxicity of chemotherapeutic agents is uncommon, and appears to be confined to anthracyclines [3] and their synthetic derivatives.

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Malignant Melanoma: Treatment of Metastatic Meningitis with Intrathecal Interferon alpha-2b

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THE MENINGES are frequently involved during the dissemination of malignant melanoma. The most frequent primary tumours in meningeal carcinomas are breast and lung cancer; malignant melanoma ranks third or fourth with a relative risk higher than that of any other solid tumour [1]. Meningeal carcinomatosis in malignant melanoma is always associated with a rapidly fatal course of the disease. Conventional approaches to this complication do not affect the prognosis. The use of intrathecal chemotherapy with methotrexate and/or cytarabine is ineffective and systemic chemotherapy provides very poor results [2].

Interferons have demonstrated a therapeutic role in treating disseminated malignant melanoma with a reported response rate of about 20% in phase II trials [3] and can be safely administered intrathecally [4]. Moreover, as interferons have shown anticancer activity in meningeal leukaemia [5], we treated a young patient with intrathecal interferon.

The patient, 23 years old, presented with metastatic malignant melanoma confined to skin and lymph nodes and received recombinant DNA interferon (IFNα_{2b}) at a dose of 10^6 international units (U) subcutaneously three times a week. After 1 month of treatment during which there was no change in tumour size the patient complained of headache, nausea, vomiting and photophobia. A lumbar puncture was performed and cerebrospinal fluid (CSF) analysis confirmed metastatic meningitis with presence of tumour cells, raised CSF albumin and decreased CSF glucose. A computed tomography scan of the brain did not show evidence of brain metastasis. The patient received an intrathecal injection of interferon three times a week at an increasing dose from 3–10 $\times$ 10^6 U per injection, according to clinical and laboratory tolerance. Systemic administration of interferon was stopped. Assessment consisted of clinical examination, blood count, blood chemistry and CSF analysis. Functional symptoms slowly abated and disappeared within 2 weeks of therapy; CSF examination showed a dramatic decrease in tumour cell count and cytological and chemical normalisation after the eighth injection. General safety of therapy was excellent as no side effects were observed.

When CSF normalisation was acquired and because of a persistent extrameningeal metastatic disease, interferon was administered both intrathecally once a week and subcutaneously three times a week. The side effects were moderate and did not require any modification of therapy; meningeal cytological remission was checked weekly and persisted. The patient died 3 months later from malignant pericarditis. Interferon warrants further study as a treatment for meningeal carcinomatosis in melanoma.

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Cerebrovascular Accident Associated with Chemotherapy for Oesophageal Carcinoma

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A 59-YEAR-OLD man with advanced squamous oesophageal carcinoma (stage IV AJCC) was admitted for chemotherapy. He smoked cigarettes, consumed alcohol and had no previous history of cardiovascular disease. Following three cycles of epirubicin (total cumulative dose 255 mg/m^2), there was no tumour response. He was treated subsequently with 5-fluorouracil (5-FU) 1 g/m^2 as a 24-h intravenous infusion on days 1–5, cisplatin 100 mg/m^2 intravenously on day 1 over 3 h, and bleomycin 12 mg intravenous push on day 1 plus 10 mg/m^2 as a 24-h infusion on days 1–5. During the 5th day of therapy, he presented with an acute confusional state, motor aphasia and visual disturbances. Lumbar puncture was normal. Computed tomography (CT) of the brain 48 h after the onset of symptoms showed no abnormality. A second CT and nuclear magnetic resonance scan 6 days later showed a left occipital posterior infarctation. The neurological signs lasted for more than a week, following which he gradually recovered his normal neurological status, but had persistent visual problems and difficulty in reading. Cisplatin-based chemotherapy was interrupted and he was treated with palliative radiotherapy. Three months after the neurological disturbance, he died of a massive upper gastrointestinal haemorrhage.

Cerebrovascular complications in cancer patients may be due to vasculitis associated with malignancy, tumour embolisation, non-bacterial thrombotic endocarditis, consumptive coagulopathy or complications related to the antineoplasic therapy [1–3]. Kukla *et al.* [4] described 6 patients with squamous cell carcinoma of the upper aerodigestive tract who developed cerebrovascular episodes associated with cisplatin, bleomycin and vincristine. 5 died as a result of the cerebrovascular accident.

Others [5] have reported acute arterial occlusive complications (2 cerebrovascular accidents, 1 haemolytic-uraemic syndrome) after cisplatin and bleomcyin or cisplatin and vindesine for squamous-cell carcinoma of the lung and head and neck. Our patient received 5-FU instead of vincristine and cisplatin and bleomycin were differently scheduled and administered compared with Kukla *et al*'s report.

Although the time relation between the administration of chemotherapy and the vascular episode suggests a causal association, the precise aetiology of our patient's cerebrovascular accident cannot be determined. If the complication was related to chemotherapy a variety of possible mechanisms may have been implicated, including perturbation of the clotting system [6], decreases in plasma protein C and S [7, 8], platelet activation, drug-induced vascular endothelial cell damage and alteration of prostacyclin-thromboxane homoeostasis. The previous three cycles of chemotherapy may have played a role, perhaps by inducing a hypercoagulable state.

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