1. Wasserstrom WR, Glass P, Posner JB. Diagnosis and treatment of leptomeningeal metastasis from solid tumors: Experience with 90 patients. *Cancer* 1982, **49**, 759–772.
2. Einhorn L, Burgess M, Vallejos G *et al.* Prognostic correlations and responses in treatment in advanced melanoma. *Cancer Res* 1974, **34**, 1995–2004.
3. Dorval T, Palangie T, Jouve M *et al.* Clinical phase II trial of recombinant DNA Interferon (Interferon alfa-2b) in patients with metastatic malignant melanoma. *Cancer* 1986, **58**, 215–218.
4. Horoszewicz JS, Freeman Al, Aungst WC, Mirand EA. Intrathecal and intravenous administration of purified human fibroblast interferon (HFIF)-phase I studies. *Proc Am Assoc Cancer Res Soc Clin Oncol* 1980, **21**, 152 (abstract).
5. Misset JL, Mathe G, Horoszewicz JS. Intrathecal interferon in meningeal leukemia. *N Engl J Med* 1981, **304**, 1544.

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Cerebrovascular Accident Associated with Chemotherapy for Oesophageal Carcinoma

Daniel Gandia, Marc Spielmann, Jean Kac, Dominique Elias, Théodore Girinsky, Thierry Guillot and Philippe Rougier

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.

Correspondence to D. Gandia.
D. Gandia, M. Spielmann, J. Kac, T. Guillot and P. Rougier are at the Department of Medical Oncology; O. Elias is at the Department of Surgery; and T. Girinsky is at the Department of Radiotherapy, Institut Gustave-Roussy, Rue Camille Desmoulins, 94805 Villejuif Cedex, France.
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1. Graus F, Rogers LR, Posner JB. Cerebrovascular complications in patients with cancer. *Medicine* 1985, **64**, 16–35.
2. Luzzatto G, Schafer A. The prethrombotic state in cancer. *Seminars in Oncology* 1990, **17**, 147–159.
3. Doll DC, Ringenberg Q, Yarbro JW. Vascular toxicity associated with antineoplastic agents. *J Clin Oncol* 1986, **4**, 1405–1417.
4. Kukla LJ, McGuire WP, Lad T, *et al.* Acute vascular episodes associated with therapy for carcinoma of the upper aerodigestive tract with bleomycin, vincristine and cisplatin. *Cancer Treat Rep* 1982, **66**, 369–370.
5. Licciardello J, Moake J, Rudy C, *et al.* Elevated plasma Von Willebrand factor levels and arterial occlusive complications associated with cisplatin based chemotherapy. *Oncology* 1985, **42**, 296–300.
6. Canobbio L, Fassio T, Ardizzoni A, *et al.* Hypercoagulable state induced by cytostatic drugs in stage II breast cancer patients. *Cancer* 1986, **58**, 1032–1036.
7. Rogers II J., Murgo A, Fontana J, *et al.* Chemotherapy for breast cancer decreases plasma protein C and protein S. *J Clin Oncol* 1988, **6**, 276–281.
8. Clouse LH, Comp PC. The regulation of hemostasis: the protein C system. *N Engl J Med* 1986, **314**, 1298–1304.