Discussion

Varying phosphate concentrations in hyperparathyroidism could perhaps be part of the explanation as to why the level of the raised blood pressure in this disease is not related to the degree of hypercalcaemia.¹ The finding of a correlation between serum phosphate and blood pressure is also in accordance with reported associations between blood pressure and idiopathic calcium stone formation,³ a condition in which low serum phosphate is common. The serum concentration of inorganic phosphate could possibly be important in the regulation of peripheral resistance,⁴ but we should like to suggest the following events as being a more likely explanation of our findings. A rise of blood pressure causes an increased excretion of ions (exaggerated natriuresis),⁵ similar to that obtained during saline diuresis. The loss of calcium stimulates the secretion of parathyroid hormone with a return of the serum calcium concentrations to normal, whereas serum phosphate will only tend to be further reset inversely to the blood pressure.

¹ Christensson, T, thesis, Stockholm, 1975.

² Hedstrand, H, *Uppsala Journal of Medical Science*, 1975, suppl 19.

³ Ljunghall, S, and Hedstrand, H, *British Medical Journal*, 1975, 4, 580.

⁴ Hilton, S M, *Circulation Research*, 1971, 28, suppl 1, 70.

⁵ Kiil, F, *Scandinavian Journal of Clinical and Laboratory Investigation*, 1975, 35, 289.

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Combination chemotherapy for thrombocytopenia with bone marrow metastases from breast cancer

Many chemotherapeutic regimens induce remission in metastatic breast cancer. All are myelotoxic and are not usually used in patients with inadequate bone marrow function. We describe successful cytotoxic treatment with vincristine, doxorubicin, and prednisolone (VDP) of four consecutive cases of thrombocytopenia with bone marrow metastases from breast cancer.

Patients and methods

Treatment was repeated every 28 days (see figure). Intravenous vincristine 1.4 mg/m² (maximum dose 2 mg) and doxorubicin 40 mg/m² (maximum dose 100 mg) were given on days 1 and 8, although some patients received a single injection initially. Oral prednisolone 20 mg daily was given on days 1-14.

Case 1—A woman aged 36 presented with metastatic breast cancer, malignant infiltration of the bone marrow, and thrombocytopenia. Oophorectomy was performed but 10 weeks later thrombocytopenia ($46 \times 10^9/l$ ($46\,000/mm^3$)) and bone marrow infiltration persisted. The platelet count steadily improved with VDP (single injection for the first course), and after eight months remained normal with complete tumour remission.

Case 2—Four years after mastectomy for breast cancer a 63-year-old woman developed thrombocytopenia. The bone marrow was infiltrated by malignant cells. She responded transiently to nandrolone and prednisolone but six weeks after stopping androgen treatment the platelet count was $42 \times 10^9/l$ ($42\,000/mm^3$). It returned to normal within one month of starting VDP and remained normal eight months later with complete tumour remission.

Case 3—Two years after mastectomy for breast cancer a 55-year-old woman developed metastases with malignant infiltration of the bone marrow. She failed to respond to nandrolone and dexamethazone and three weeks after stopping androgen treatment the platelet count was $48 \times 10^9/l$ ($48\,000/mm^3$). She responded well to VDP (single injection for the first two courses) and remained in complete remission with a normal blood count and bone marrow for 12 months. She developed septicaemia after the first course of VDP which required antibiotics.

Platelet and white cell counts in four patients on combination chemotherapy for metastatic breast cancer.

Case 4—A 35-year-old woman presented with metastatic breast cancer, malignant infiltration of the bone marrow, and thrombocytopenia. She underwent oophorectomy, but two weeks later the platelet count had fallen to $22 \times 10^9/l$ ($22\,000/mm^3$) and the white cell count to $1.2 \times 10^9/l$ ($1200/mm^3$). She was treated with VDP (single injection for the first two courses) and three months later her platelet count was $196 \times 10^9/l$ ($196\,000/mm^3$) and the white cell count was $7.5 \times 10^9/l$ ($7500/mm^3$). After the first course of chemotherapy she developed septicaemia, which was treated with antibiotics.

Comment

Thrombocytopenia and bone marrow metastases from breast cancer have been successfully treated with a combination of high-dose prednisone, ovariectomy, adrenalectomy, and 5-fluorouracil.¹ All our patients treated with VDP developed neutropenia, with septicaemia in two cases. All required blood transfusion, but not platelets or granulocytes. There were no other complications.

Transient thrombocytosis after treatment with *Vinca* alkaloids has been reported in animals and man.² This is unlikely to have caused the prolonged increase in platelets in our patients. Tumour cells are probably more sensitive to chemotherapy than platelet precursors, which may be suppressed by the tumour in the marrow. Thus patients with bone marrow metastases should be given the most effective antitumour treatment available. We gave combined chemotherapy with VDP because we have found it effective against metastatic breast cancer.³ The results suggest that it may be effective in bone marrow depression with malignant bone marrow infiltration. This does not apply to non-metastatic marrow aplasia.

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¹ Sugarbaker, P H, *et al*, *Archives of Surgery*, 1973, 107, 523.

² Robertson, J H, and McCarthy, G M, *Lancet*, 1969, 2, 353.

³ Dady, P J, *et al*, unpublished communication.

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